Semarang Gastroentero-Hepatology Update 2020

Gastrointestinal and Liver Disease : From Precision Medicine to Clinical Practice

Editor:
Hirlan
Hery Djagat Purnomo
Agung Prasetyo
Didik Indiarso

Semarang, 21 - 23 Agustus 2020

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WORKSHOP

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Kata Pengantar

Assalamu'alaikum warahmatullahi wabarakatuh.

Segala Puji dan syukur kami haturkan kepada Allah Subhanahu wa ta'alaa yang telah melimpahkan rahmat dan hidayah-Nya kepada kita semua sehingga buku naskah Semarang Gastroenterohepatology Update 2020 dapat selesai pada waktunya.

Dalam buku naskah ini akan dibahas perkembangan terbaru dalam topik hepatologi, gastroenterologi dan endoskopi untuk dapat sebagai sumber referensi dalam pelayanan penyakit dibidang tersebut pada semua tingkatan pelayanan; primer, sekunder maupun tersier sehingga diharapkan dapat memberikan bekal klinisi untuk meningkatkan mutu pelayanan kepada pasien dan masyarakat.

Seperti yang kita semua ketahui, ilmu kedokteran tidak pernah berhenti berkembang, demikian juga bagi seorang dokter, profesinya adalah suatu perjalanan mencari ilmu sepanjang hidup. Dalam SGU 2020 ini, kami hadirkan para pembicara dan moderator sebagai narasumber yang sudah dikenal baik di tingkat nasional dan bahkan internasional yang merupakan pakar di bidang gastroenterohepatologi.

Kami menyadari mungkin akan ditemukan kekurangan dalam buku ini, dan kepada para penulis yang telah meluangkan waktunya untuk menulis sampai pada hari-hari terakhir serta semua pihak yang telah membantu dalam proses pembuatan buku ini, kami ucapkan terima kasih tiada terhingga.

Akhir kata, Semoga buku ini bermanfaat bagi sejawat dalam peningkatan keilmuan dan profesionalisme para sejawat dalam praktek klinis menghadapi problem medis di bidang gastroenterohepatologi sehari- hari, karena pada akhirnya semua upaya kita ini adalah demi pasien yang telah mempercayakan jiwa dan raganya pada kita. Selamat membaca

Wassalamu'alaikum warahmatullahi wabarakatuh.

Semarang, 21 Agustus 2020

Editor

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Sambutan Ketua Panitia

Assalamu'alaikum warahmatullahi wabarakatuh.

Segala puji dan syukur kepada Allah Subhanahu wata'alaa yang telah melimpahkan rahmat dan hidayah-Nya kepada kita semua. Atas nama seluruh panitia Semarang Gastroentero-Hepatology Update 2020, kami mengucapkan selamat datang kepada seluruh pembicara, moderator, peserta simposium dan workshop.

Perkembangan Ilmu Gastroenterohepatologi dan endoskopi semakin meningkat seiring dengan kemajuan penelitian dan teknologi diagnostik dan terapi. Disisi lain juga terjadi peningkatan tuntutan dari konsumen (internal maupun eksternal) akan pelayanan kesehatan yang lebih bermutu, komprehensif dan terjangkau oleh masyarakat dan pemerintah.

Kami menyelenggarakan SGU 2020 ini dengan harapan penerapan ilmu terbaru di bidang Gastroenterohepatologi dan endoskopi, dan juga kaitannya dengan cabang Ilmu Penyakit Dalam lain maupun terkait dengan bidang ilmu lain seperti radiologi, dapat lebih bermanfaat dalam menuju pelayanan kedokteran yang bermutu pada praktik klinik.

Pada kesempatan ini kami mengucapkan terima kasih sebesar-besarnya kepada Panitia, Penulis, dan Tim Editor atas kerja kerasnya dalam penyelenggaraan acara Semarang Gastroentero-Hepatology Update 2020.

Kami berharap semoga sejawat dapat mengambil manfaat yang sebanyak-banyaknya pada penyelenggaraan SGU 2020 tahun ini dan buku yang telah kami terbitkan.

Wassalamu'alaikum warahmatullahi wabarakatuh.

Semarang, 21 Agustus 2020

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Workshop

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Chromoendoscopy & Image-Enhanced Endoscopy (IEE)

Christopher Khor

Chromoendoscopy refers to the topical application of a stain or dye to improve characterisation or diagnosis during endoscopy. Image-Enhanced Endoscopy (IEE) is defined as the use of tools to improve imaging characterisation or diagnosis in endoscopy, so Chromoendoscopy may be considered to be the dye-based form of IEE. In the past 15 years or so the endoscope system manufacturers have incorporated proprietary forms of electronic image enhancement into their high-definition systems, and these are known as Equipment-based IEE.

This talk will describe the forms of IEE that are in wide clinical practice today, beginning with Chromoendoscopy (ie. Dye-based IEE), and then moving to Equipment-based IEE. The principles of Chromoendoscopy will be described and illustrated, followed by the same for Equipment-based IEE. The various sites in the GI tract where these techniques may be applied and the clinical utility of these techniques will be illustrated with still images and video cases.

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Abstract

Colonoscopy Polypectomy: From Evidence to Practise

Hery Djagat Purnomo

Colorectal cancer (CRC) is a leading cause of cancer-related morbidity and mortality. Most of CRC develop from polyps (adenoma,serrated adenoma) and colonoscopy is effective at reducing the risk through the removal of adenomatous polyps. Polypectomy is a fundamental skill for all endoscopists who perform colonoscopy. Effective colonoscopic polypectomy reduces the incidence of colorectal cancer (CRC) and prevents mortality due to CRC. There is significant variability in the effectiveness of polypectomy between endoscopists. There is significant variation between endoscopists for detection rates of precursor lesions such as conventional adenomas and sessile serrated adenomas (SSA).

The key points of polypectomy are assessment, decision making before resection, preparing for polypectomy during the procedure, choosing the snare or diathermia, polyp specific polypectomy technique, management anticoagulant or antiplatelet therapy and survailance after polypectomy. There are several specific polypectomy technique such as diminutive polyps (<5 mm), small polyps (5-9mm), non pedunculated (10-19 mm), large nonpedunculated polyps (> 20 mm).

Techniques for endoscopic polyp resection include cold or hot biopsy forceps and cold or hot snare, and significant variation exists in clinical practice. Cold snare polypectomy is rapidly replacing hot snare and biopsy forceps as the preferred technique for the removal of colorectal polyps up to 10 mm. Cold snare polypectomy reduces the risks of delayed bleeding and perforation associated with electrocautery and is more effective than cold biopsy forceps resection for diminutive polyps . However, over 10 % of sessile polyps may be incompletely resected by snares, which may result in residual polyp regrowth and ultimately progression to CRC.

Different polypectomy tools and techniques have evolved and it is important that endoscopists are familiar with these so they can select the most appropriate technique for each polyp. The objective of this workshop is to present the principles, theory and technique of polypectomy.

Endoscopic Hemostasis in Acute Non-variceal Upper GI Bleeding

M. Begawan Bestari

Abstract

Endoscopy therapy for non-variceal upper gastrointestinal bleeding (NVUGIB) has developed in recent decades. Monotherapy with dilute epinephrine injection alone is assumed as a suboptimal intervention, thus second therapy modality is required. Definitive hemostasis ability after monotherapy with thermo-coagulation or hemo-clipping is comparable with dual therapy, each modality is effective in achieving hemostasis. Hemospray powder and ankaferd blood stopper are the promising new hemostatic compound, although those requires a comparative study between those with other modalities. These modalities can be taken into consideration as temporary therapy whether conventional therapy failed or unavailable. Stronger hemoclip with better torque control and wider range is now available. An over-the-scope clip is used in closure of GI defects and tissue approximation and may prove beneficial in refractory bleeding. Experimental treatments include an endoscopic suturing system developed to over-sew bleeding lesions, and the use of endoscopic ultrasonography (EUS) guided puncture of bleeding sub-serosal arteries.

Keywords: endoscopic, therapeutic, upper, gastrointestinal, bleeding, non-variceal

Abstrak

Terapi endoskopik untuk perdarahan gastrointestinal bagian atas non-variseal terus berkembang dalam beberapa dekade terakhir. Metode injeksi dengan epinefrin yang telah dilarutkan dianggap sebagai suatu tindakan yang kurang adekuat, dan terapi standar saat ini harus mencakup modalitas kedua jika injeksi epinefrin digunakan. Kemampuan hemostasis definitif sesudah mono-terapi dengan termo-koagulasi atau hemo-clipping sebanding baik dengan terapi kombinasi. Penggunaan powder adsorptif (*Hemospray*) dan penghenti perdarahan ankaferd merupakan suatu tindakan yang menjanjikan meskipun memerlukan penelitian komparatif antara *hemospray* atau ankaferd dengan modalitas lainnya. Sehingga dapat dipertimbangakan sebagai terapi sementara apabila terapi konvesional sebelumnya gagal atau tidak tersedia. Hemo-clip yang lebih kuat dengan kontrol turk (torque) yang lebih baik dan rentang (span) yang lebih lebar sekarang telah tersedia. *Over-the-scope clips* menjepit sejumlah besar jaringan dan dapat terbukti bermanfaat pada perdarahan yang refrakter. Tindakan eksperimental mencakup *endoscopic stitch device* (peralatan penjahitan memakai endoskop) untuk *over-sew* lesi perdarahan dan menargetkan terapi untuk arteri yang mengalami perdarahan sub-serosa ketika dipandu dengan echo-endoscopy.

Kata kunci: terapi, endoskopi, perdarahan, gastrointestinal, non-variseal

Pendahuluan

Perdarahan akut gastrointestinal (GI) bagian atas merupakan salah satu keadaan darurat medis yang paling umum. Kondisi ini terkait dengan angka kematian dan kebutuhan intervensi hemostasis yang lebih tinggi dibandingkan perdarahan saluran cerna bagian bawah Insidensi perdarahan saluran cerna atas lebih tinggi (67-103 per 100000/tahun) dibandingkan perdarahan saluran cerna bawah. Penyebab tersering perdarahan saluran cerna bagian atas non-variseal adalah ulkus peptikum (20-50%). Tinjauan ini bertujuan untuk menggambarkan intervensi endoskopik terkini pada perdarahan akut GI bagian atas dengan penyebab non-variseal dan untuk memaparkan bukti ilmiah terkini mengenai perkembangan tindakan endoskopik.

Modalitas Tindakan Endoskopik pada Perdarahan Non-Variseal

a. Injeksi epinefrin

Telah hampir empat dekade berlalu sejak laporan pertama mengenai terapi injeksi untuk ulkus peptikum yang mengalami perdarahan dipublikasikan oleh Soehendra tahun 1977. Tindakan hemostatik endoskopik terus berkembang. Dewasa ini mono-terapi injeksi dengan epinefrin yang dilarutkan merupakan suatu tindakan suboptimal. Terapi injeksi bekerja terutama berdasarkan tamponade volume pada arteri. Terapi ini tidak menginduksi trombosis pembuluh darah. Soehendra mengusulkan konsep asli terapi kombinasi pra-injeksi dengan epinefrin yang telah dilarutkan yang diikuti oleh tindakan yang ditargetkan terhadap arteri. Calvet dkk menyampaikan temuan dari 16 penelitian yang dirandom yang membandingkan injeksi epinefrin saja dengan injeksi epinefrin yang diikuti dengan tindakan tambahan untuk pembuluh darah. Meta-analisis terdiri dari 1673 pasien. Dengan menambahkan modalitas kedua terlihat penurunan perdarahan lebih jauh dari 18,4% menjadi 10,6% (Peto odds ratio [OR], 0,53%; 95% CI, 0,40-0,69; bedah darurat dari 11,3% menjadi 7,6% (OR, 0,64; 95% CI, 0,46-0,90), dan yang penting kematian dari 5,1% menjadi 2,6% (OR, 0,51; 95% CI, 0,31-0,84). Dalam analisis lain gabungan yang terdiri dari 2472 pasien, Marmo dkk membandingkan mono-terapi dengan terapi dual dan menemukan bahwa terapi kombinasi endoskopik menurunkan risiko perdarahan kambuhan (OR. 0,59; 95% CI, 0,44-0,88;

p<0,001), risiko bedah darurat (OR, 0,66; 95% CI, 0,49-0,89; p=0,03), dan memperlihatkan kecenderungan ke arah penurunan risiko kematian (OR, 0,68; 95% CI, 0,46-1,02; p=0,06). Dalam analisis subkelompok, terapi kombinasi secara signifikan terlihat lebih unggul dibandingkan dengan terapi injeksi saja untuk semua hasil akhir, tetapi gagal memperlihatkan bahwa kombinasi tindakan lebih baik daripada terapi mekanik saja atau terapi termal saja. Dua tinjauan ini menyatakan bahwa injeksi dengan epinefrin yang telah dilarutkan hanya boleh digunakan untuk menghentikan atau memperlambat perdarahan dengan tujuan memperjelas penglihatan arteri tersebut. Hemo-clipping atau termo-koagulasi pada arteri harus dilakukan sesudahnya. Jika arteri (atau pemucatan/discoloration yang protuberant) dapat terlihat tanpa injeksi, hemo-clipping atau termo-koagulasi dapat dilakukan tanpa injeksi epinefrin terlebih dahulu.

b. Hemoclips atau termo-koagulasi

Keunggulan antara metode endoskopi hemoclip dan termo-koagulasi kurang lebih dari beberapa studi serupa. Seringkali seorang ahli endoskopi beralih dari satu pilihan ke pilihan lain jika hemostasis tidak berhasil pada keadaan pertama. Sung dkk tahun 2007 melaporkan uji-klinik yang dirandom dan memakai kontrol yang membandingkan termokoagulasi dengan hemoclip dengan atau tanpa injeksi. Tingkat hemostasis definitif sesudah termo-koagulasi atau klip hampir identik (81,5% vs. 81,2%; risiko relatif, 1,00; 95% CI, 0,77-1,31). Berdasarkan Cochrane database pada tahun 2014 oleh Vergara, metode kombinasi injeksi epinephrine dan hemoclip menurunkan perdarahan berulang dan perdarahan persisten (RR 0.31, 95% CI 0.18 to 0.54) serta kebutuhan bedah cito (RR 0.20, 95% CI 0.06 to 0.62) bila dibandingkan dengan injeksi epinephrine tunggal. Kombinasi injeksi epinephire dan termo-koagulasi juga menunjukan bukti yang serupa di studi tersebut (Menurunkan perdarahan berulang (RR 0.49, 95% CI 0.30 to 0.78) dan kebutuhan intervensi bedah (RR 0.20, 95% CI 0.06 to 0.62)). Tiap modalitas efektif dalam mengamankan hemostasis. Pada perdarahan arterial, adalah hal yang umum untuk memulai dengan menggunakan hemoklip. Aplikasi hemoklip akan ideal jika terdapat “kepala” pembuluh darah

atau “protuberan” pembuluh darah yang jelas. Aplikasi hemoklip sulit dilakukan pada dinding posterior bulbus duodenum, dan kurvatur minor lambung. Aplikasi tangensial untuk hemoklip atau aplikasinya memakai *scope* pada posisi retrofleksi sering gagal. Jepitan hemoklip tidak dapat mencengkeram kedalam dasar ulkus yang keras dan fibrotik. Pada keadaan ini, kami lebih suka menggunakan termo-koagulasi kontak dan secara spesifik menggunakan heater probe berukuran 3,2 mm. Pada kondisi tertentu, perlu digunakan *side viewing duodenoscope* untuk posisi yang lebih baik dalam melakukan tindakan. Penggunaan alat termal relative lebih mudah jika dibandingkan dengan penggunaan hemoklip. Kompresi mekanik pada arteri merupakan komponen kritis dari tindakan *heater probe*. Arteri dikompresi secara kuat untuk menghentikan aliran darah yang diikuti dengan memegang dinding arteri menggunakan energi termal (konsep termo-koagulasi ko-aptif).

Endoskopi terapeutik baru

a. *Powder hemospray*

Powder hemospray (Haemospray, TC-325; Cook Medical Inc., Winston-Salem, NC, USA) adalah serbuk yang sangat adsorptif yang dibuat dari campuran mineral. Ketika kontak dengan darah, serbuk menjadi bersifat kohesif dan membentuk sumbatan mekanik yang stabil yang menutup tempat perdarahan. Hal ini telah disetujui oleh *the Food and Drug Administration of USA* untuk penggunaan traumatik eksternal. Sung dkk (tahun 2011) melaporkan penggunaannya yang pertama untuk GI pada 20 pasien penderita perdarahan ulkus peptikum Forrest I. Selama endoskopi, serbuk disemprotkan dengan kuat pakai tenaga keatas tempat perdarahan dengan menggunakan kateter penghantar yang dihubungkan dengan suatu kanister karbon-dioksida. Semburan singkat serbuk tersebut diaplikasikan sampai perdarahan berhenti. Tempat perdarahan diamati selama 5 menit. Hemostasis tercapai pada 19 dari 20 pasien. Satu pasien penderita ulkus angular besar mengalami perdarahan refrakter dan akhirnya menjalani angiografi viseral yang memperlihatkan pseudo-aneurisma pada arteri gastrik pada arteri gastrik kiri.

Aneurisma tersebut kemudian dikoil. Tidak ada perdarahan berulang signifikan pada 19 pasien yang diberi tindakan. Tidak ada efek sistemik dari Hemospray teramati ketika serbuk tidak diabsorpsi. Serbuk ini merupakan suatu senyawa hemostatik baru yang menjanjikan. Serbuk ini menarik bagi para ahli endoskopi karena cara penggunaannya yang sederhana. Lebih banyak data, terutama data-data komparatif, diperlukan untuk menentukan manfaat sebenarnya dari powder ini diantara modalitas-modalitas pengobatan lainnya yang tersedia.

Dalam konsensus internasional oleh Barkun dkk di tahun 2020, hemospray digunakan sebagai terapi sementara apabila terapi endoskopi konvensional gagal atau tidak tersedia. Hemospray hanya beraksi lokal di lesi perdarahan, berkerja selama 24 jam atau kurang, dan tidak menginduksi perbaikan jaringan.

b. Penghenti perdarahan Ankaferd *(Ankaferd blood stopper/*ABS*)*

ABS merupakan suatu agen hemostatik yang unik, merupakan derivat dari campuran herbal tradisional yang telah digunakan secara topikal selama berabad-abad di Turki untuk menghentikan pendarahan yang resisten terhadap tindakan hemostatik konvensional.

Mekanisme pasti dari setiap komponen belum sepenuhnya dipahami. Sebagai tambahan sifat hemostatiknya, ABS mungkin memiliki manfaat terapeutik lain seperti anti infeksi, dan sifat penyembuhan luka yang memungkinkan pemulihan dan mempertahankan hemostasis jaringan.

Dari penelitian yang dilakukan Gungor, menunjukkan bahwa penerapan ABS dengan penyemprotan topikal secara efektif menghentikan perdarahan non-varises GI bagian atas, terutama pada pasien muda tanpa koagulopati. ABS dapat digunakan sebagai bagian dari pengobatan kombinasi untuk kasus-kasus dengan kemungkinan tinggi perdarahan ulang tanpa koagulopati, pada lesi Dieulafoy atau perdarahan arteri.

c. Klip baru

Hachisu dkk pertama kali melaporkan penggunaan hemoklip pada tahun 1989. Beberapa klip telah tersedia dipasaran yang mencakup *the Quick clips* oleh Olympus (Tokyo, Jepang), *Resolution clip* (Boston Scientific Co., Natick, MA, USA), *the three pronged triclip* dan baru-baru ini *Instinct clip* yang besar (Cook Medical Inc., Winston-Salem, NC, USA). Klip terbesar lebarnya membuka sampai 18 mm. Klip yang ideal harus cukup kuat untuk mencengkeram kedalam jaringan dengan kuat untuk aproksimasi, mampu membuka dan menutup sebelum selesai tugasnya dan mempunyai kontrol tork yang baik untuk orientasi dan pemposisiannya yang optimal. Penggunaan hemoklip pada *side-viewing endoscope* sering menjadi masalah. Terdapat beberapa penelitian komparatif mengenai tipe klip yang berbeda. Dalam suatu penelitian yang dirandom pada 100 pasien, triklip dibandingkan dengan hemoklip dalam mengamankan hemostasis ulkus. Hemostasis awal lebih tinggi dengan penggunaan hemoklip (94% vs. 76%). Jepitan pada *the three pronged design* sering tidak cukup kuat pada ulkus fibrotik. Uji-klinik menegaskan bahwa salah satu elemen kunci untuk keberhasilan hemostasis adalah kekuatan jepitan.

Klip *Over-the-scope* (Ovesco Endoscopy, Tubingen, Jerman) sudah dipasarkan untuk digunakan pada penutupan defek GI dan aproksimasi jaringan. Suatu nitinol klip dihubungkan sebelumnya pada suatu tudung (cap) yang kemudian ditempelkan ke ujung endoskop. Jaringan ditarik kedalam tudung dengan cara penghisapan, atau dengan menggunakan pegangan pencengkeram-kembar yang dirancang khusus untuk aproksimasi (mendekatkan) jaringan atau mengaitkan. Desain ini mencengkeram sejumlah besar jaringan dan lebih aman dibandingkan dengan klip lain dalam eksperimental. Sistem ini sedang digunakan pada perdarahan GI yang kompleks. Satu klip tunggal sudah mencukupi untuk sebagian besar keadaan dan karena itu prosedurnya lebih singkat jika dibandingkan dengan aplikasi hemoklip yang multipel.

d. Penjahitan memakai endoskop

Penjahitan endoskopi menggunakan suatu benang jahit yang diaplikasikan selama pembedahan. Masih diperdebatkan mengenai bentuk yang aman dalam hemostasis. Suatu sistem penjahitan endoskopik *Eagle Claw* (Olympus) dikembangkan dan diuji pertama kali pada suatu model Erlangen dan kemudian suatu hewan coba hidup dengan ulkus yang mengalami perdarahan dari suatu arteri berukuran > 2 mm, alat ini efektif untuk menghentikan perdarahan tersebut. Versi terdahulunya memerlukan simpul ekstra-korporeal yang ditalikan dan didorong ketempatnya dengan memakai *knotting cap*. Berdasarkan pada konsep yang sama, sistem penjahitan endoskopik *Overstitch* (Appollo Endosurgery Inc., Austin, TX, USA) sudah dipasarkan untuk digunakan pada aproksimasi jaringan endoskopik. Sistem ini mempunyai satu jarum lengkung dengan ujung yang dapat dilepaskan yang membawa benang jahit 2.0 atau 3.0. Jarum lengkung ini didorong melalui mukosa. Ujungnya kemudian dilepaskan dan jarum keluar melalui mukosa. Benang jahit “diikat” kebawah dengan menggunakan suatu *cinching device*. Dengan banyaknya tembusan jarum, sistem ini mampu melakukan banyak perulangan kegiatan dan menginterupsi jahitan hanya dengan insersi tunggal suatu endoskop.

Kesimpulan

Modalitas endoskopik terkini memiliki kemampuan hemostasis yang dapat bertahan lama pada mayoritas kasus. Dengan kemajuan yang terus berlanjut pada endoskopi terapeutik, terdapat kemungkinan bahwa angka perdarahan berlanjut atau kambuhan akan terus menurun yang pada akhirnya akan menurunkan angka kematian pasien akibat kondisi ini.

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Simposium

Semarang Gastroentero-Hepatology Update 2020

Mistakes in Management of Decompensated Liver Cirrhosis

Irsan Hasan

Pendahuluan

Sirosis hepatis merupakan salah satu masalah kesehatan utama di dunia. Studi yang dilakukan oleh *Global Burden of Disease* (GBD) menunjukkan angka kematian akibat sirosis sebanyak 1.320.000 pada wanita dan 883.000 pada laki-laki di seluruh dunia. Sekitar 2.4% penyebab kematian di seluruh dunia pada tahun 2017 adalah sirosis. Tercatat pula bahwa terdapat setidaknya 10.600.000 kasus sirosis dekompensata di seluruh dunia pada tahun 2017[1]. Perjalanan penyakit sirosis sendiri memiliki karakteristik progresi dari fase kompensata ke fase dekompensata, hingga karsinoma hepatoselular atau kematian. Komplikasi-komplikasi yang dapat ditemukan pada fase dekompensata adalah pendarahan variseal, asites, ensefalopati, dan ikterus.

Secara patofisiologi, ketika terjadi transisi dari sirosis asimtomatik ke sirosis dekompensata, itu menandakan disfungsi multi-organ mulai terjadi. Gastropati hipertensi porta yang terjadi menyebabkan terbentuknya kolateral disertai peningkatan aliran darah splanknik. Akibatnya, terjadi ketidakseimbangan hemodinamik dan sindrom sirkulatori hiperdinamik yang disebabkan oleh vasodilatasi arteri perifer. Hal-hal tersebut menyebabkan penurunan volume cairan tubuh yang efektif, sehingga terjadi penurunan perfusi organ, terutama ginjal. Selain itu, terdapat pula aktivasi sistem renin-angiotensin-aldosteron (RAAS), aktivasi sistem saraf simpatik, dan sekresi arginin-vasopresin yang menyebabkan peningkatan retensi air dan natrium. Manifestasi lain terkait kelainan hemodinamika adalah sindrom hepatopulmoner, disfungsi sirkulatori yang menyebabkan mudah terjadi syok, serta kardiomiopati sirotik[2]. Oleh karena itu diperlukan strategi yang tepat agar pasien sirosis dekompensata memiliki kualitas hidup yang baik dan kesintasan Panjang. Sayangnya pada prakteknya terjadi berbagai kesalahan sehingga penganan pasien tidak optimal. Berikut ini akan dibahas beberapa kesalahan yang banyak terjadi terkait penatalaksanaan pasien sirosis dekompensata.

PPI Jangka Panjang Sebagai Terapi Gastropati Hipertensi Porta

Penggunaan *proton pump inhibitor* (PPI) yang berlebihan pada pasien sirosis saat ini tengah menjadi sorotan. Secara umum, indikasi penggunaan PPI adalah untuk tatalaksana ulkus peptikum, penyakit refluks gastroesofageal (GERD), pendarahan saluran cerna atas non-varises, dan profilaksis untuk pengguna obat anti-inflamasi non-steroid (OAINS). Sebuah studi retrospektif yang dilakukan Chavez-Tapla, et al pada 243 pasien sirosis menunjukkan bahwa PPI diresepkan pada 112 pasien (46.1%), namun hanya 30 (12.3%) pasien yang benar-benar memiliki indikasi pemberian PPI[3].

European Association for the the Study of the Liver (EASL) juga tidak merekomendasikan penggunaan PPI pada pasien sirosis bila tidak ada indikasi karena dapat meningkatkan risiko terjadinya peritonitis bakterial spontan[2]. Mekanisme peritonitis bakterial spontan akibat PPI saat ini masih belum jelas, namun hipotesis yang diusung adalah karena terjadinya peningkatkan translokasi bakteri patogen. Efek PPI yang dapat meningkatkan pH lambung, serta motilitas lambung dapat memicu terjadinya pertumbuhan berlebih bakteri di usus halus dan disbiosis. Selain itu, PPI juga dianggap dapat mempengaruhi sistem imunitas melalui penurunan fungsi neutrofil dan monosit. Peningkatan translokasi bakteri patogen juga dapat memicu terjadinya ensefalopati hepatikum[4].

Pemberian PPI pada gastropati hipertensi porta juga dinilai tidak bermanfaat untuk menurunkan angka kejadian pendarahan saluran cerna. Studi yang dilakukan oleh Garcia, et al. pada 72 pasien dengan gastropati hipertensi porta menunjukkan tidak adanya hubungan yang signifikan secara antara penggunaan PPI dan rendahnya insidensi pendarahan saluran cerna atas (OR 0.83, 95% CI 0.5-1.3, *p-value* 0.51). Analisis yang dilakukan pada pasien dengan pendarahan variseal menunjukkan 18.7% pasien sedang menggunakan PPI saat terjadi pendarahan, dan 14% pasien tidak sedang menggunakan PPI[5].

Salah satu terapi farmakologis terbaru yang saat ini sedang diusung untuk mengatasi pendarahan variseal pada gastropati hipertensi porta adalah rebamipide. Mekanisme utama rebamipide adalah perlindungan terhadap radikal bebas, sehingga dapat meredakan stres oksidatif dan menurunkan proses nitrasi residu tirosin dari

jalur ERK. Hal-hal tersebut berkontribusi terhadap proses penyembuhan mukosa yang lebih baik pada gastropati hipertensi porta[6]. Selain memiliki efek antioksidan, rebamipide juga dapat menstimulasi ekspresi gen reseptor prostaglandin E4 yang meningkatkan sekresi mukus[7]. Studi yang dilakukan oleh Kinjo, et al. menunjukkan peran rebamipide dalam menurunkan proses nitrasi pada jalur ERK pada tikus dengan hipertensi porta. Pada kondisi hipertensi porta, mukosa gaster mengalami peningkatan stres oksidatif yang berakibat pada meningkatnya senyawa nitric oksida (NO), sehingga terjadi pula peningkatan nitrasi residu tirosin oleh peroksinitrit, sehingga proses penyembuhan mukosa gaster menjadi lambat[8].

Pemberian Infus Albumin Berdasarkan Indikasi Hipoalbuminemia

Secara molekular, albumin merupakan protein globular berukuran kecil dan bermuatan negatif yang disintesis oleh sel-sel hati (kurang lebih 10-15 gram per hari, namun dapat meningkat hingga 3-4 kali lipat saat kebutuhan meningkat). Albumin merupakan protein yang paling banyak ditemukan pada komponen ekstraselular tubuh, sehingga memiliki peran penting dalam regulasi distribusi cairan tubuh. Albumin juga memiliki beberapa fungsi non-onkotik, seperti aktivitas antioksidan. Pada pasien dengan sirosis hati, albumin mengalami gangguan post-transkripsi (sisteinilasi dan/ atau trunkasi bagian N-terminal dan glikosilasi) yang meningkat seiring dengan meningkatnya keparahan penyakit. Ekspansi volume plasma, dilusi protein-protein ekstraselular, dan peningkatan pelepasan moleku-molekul melalui pembuluh darah kapiler ke ekstravaskular juga menjadi penyebab rendahnya kadar albumin. Oleh karena itu, pada pasien sirosis, tidak hanya terjadi penurunan jumlah, namun juga penurunan fungsi albumin[9].

Terdapat tiga indikasi dasar pemberian albumin pada pasien dengan sirosis dekompensata. Pertama, untuk pencegahan disfungsi sirkulatori pasca parasentesis (PPCD). Berdasarkan konsensus dari EASL dan *American Academy of Family Physician* (AAFP), parasentesis terapeutik saat ini direkomendasikan sebagai terapi lini pertama pada asites refrakter atau asites derajat tiga[2,10]. Komplikasi dari parasentesis dalam volume besar yang sering ditemukan adalah PPCD. PPCD didefinisikan sebagai peningkatan aktivitas basal renin plasma sebanyak lebih dari 50% dalam kurun waktu 4-6 hari setelah parasentesis. Parasentesis dalam volume

besar menyebabkan penurunan tajam dari tekanan intra-abdominal, sehingga meningkatkan aliran balik vena ke jantung dan curah jantung. Namun, karena terjadi penurunan berlebih dari resistensi perifer vaskular, maka terjadi pula penurunan volume efektif cairan tubuh. Hal ini dapat menyebabkan terjadinya penurunan tekanan darah arteri, gangguan fungsi ginjal, hiponatremia hipervolemik, dan ensefalopati hepatikum[9]. Oleh karena itu, EASL merekomendasikan ekspansi volume plasma melalui pemberian albumin (8 gram per liter dari cairan asites yang dipungsi) segera setelah parasentesis lebih dari 5 liter cairan asites[2]. Sebuah meta-analisis yang disusun oleh Bernardi, et al. menunjukkan penurunan risiko PPCD sebanyak 93% pada pemberian albumin dibandingkan dengan kelompok yang tidak mendapatkan terapi (*pooled* OR 0.07, CI 0.02-0.22). Dibandingkan dengan kelompok yang mendapatkan terapi lain, pemberian albumin juga menurunkan risiko PPCD sebanyak 61%. Tingkat mortalitas pasien dengan pemberian albumin juga lebih rendah (74 kematian [14.4%] dari 513 pasien kontrol dan 50 kematian [12.1%] dari 414 pasien kontrol) dengan selisih *odds* sebanyak 36% (*p-value* 0.038)[11].

Indikasi kedua adalah mencegah perburukan fungsi ginjal pada pasien dengan peritonitis bakterial spontan. Definisi peritonitis bakterial spontan oleh EASL adalah hitung jenis neutrofil di atas 250 sel/mm^3 pada cairan asites. Peningkatan risiko terjadinya peritonitis bakterial spontan adalah karena pada sirosis terjadi peningkatan translokasi bakteri dari usus, serta disfungsi sistem imun. Rekomendasi pemberian albumin pada kondisi ini adalah sebanyak 1.5 gram/kgBB pada hari pertama, dilanjutkan 1 gram/kgBB pada hari ketiga[2]. Berdasarkan studi-studi sebelumnya, manfaat pemberian terapi albumin pada peritonitis bakterial spontan terutama ditemukan pada pasien dengan gangguan fungsi hati berat (bilirubin total > 4 mg/dL, gangguan fungsi ginjal [kreatinin serum > 1 mg/dL])[9].

Pemberian albumin juga direkomendasikan untuk pasien-pasien dengan sindrom hepatorenal. Seperti yang telah disebutkan di atas, terdapat dua mekanisme yang terjadi pada pasien sirosis: vasodilatasi pembuluh darah splanchnic dan kardiomiopati sirotik. Sistem Renin-Angiotensin-Aldosteron, sistem saraf simpatik, dan arginin-vasopresin sebagai mekanisme kompensasi, menyebabkan terjadinya vasokonstriksi intrarenal, hipoperfusi ginjal, dan, pada akhirnya, gagal ginjal. Terdapat dua tipe sindrom hepatorenal: tipe 1 yang berupa penurunan fungsi ginjal dalam waktu singkat

(peningkatan kreatinin serum sebanyak dua kali lipat dari batas bawah dan > 2.5 mg/dL dalam kurun waktu dua minggu) dan tipe 2 yang berupa penurunan fungsi ginjal secara lambat dan bertahap (kreatinin serum > 1.5 mg/dL). Pendekatan terapeutik terhadap sindrom hepatorenal yang ada saat ini untuk peningkatan perfusi ginjal adalah dengan pemberian albumin disertai vasokonstriktor; seperti terlipressin[9].

Analog Nukleosida Tidak Bermanfaat dalam Tatalaksana Sirosis Dekompensata

Hingga saat ini, terdapat dua golongan obat Hepatitis B yang dapat diterima secara luas, yaitu golongan interferon dan golongan *nucleoside analogue*[12]. ada beberapa obat dari golongan *nucleoside analogue* yang saat ini banyak digunakan yaitu, tenofovir, entecavir, lamivudin, adefovir, dan telbivudin[12]. Terdapat beberapa konsensus internasional untuk terapi Hepatitis B, seperti pada Tabel 1.

Tabel 1. Rekomendasi terapi NA berdasarkan pedoman internasional [12,13,14,15]

PPHI 2017	EASL 2017	AASLD 2018	APASL 2015
Lini pertama · Tenofovir 300 mg per hari (A1) · Entecavir 0,5 mg per hari (A1) Lini kedua · Lamivudin 100 mg per hari (A2) · Adefovir 10 mg per hari (A2) · Telbivudin 600 mg per hari (A2)	Obat yang dianjurkan: · Entecavir (ETV) · Tenofovir disoproksil fumarat (TDF) · Tenofovir alafenamid fumarate (TAF) Monoterapi tidak dianjurkan: · Lamivudin (LAM) · Adefovir (ADV) · Telbivudin (LdT)	Obat yang dianjurkan: · TAF 25 mg sekali sehari · Entecavir 0,5 mg sekali sehari · TDF 300 mg sekali sehari	Pasien yang belum mendapatkan terapi (treatment naïve) dapat diberikan: · TDF 300 mg sekali sehari (A1) · ETV 0.5 mg sekali sehari (A1) · ADV 10 mg sekali sehari (A2) · LdT 600 mg sekali sehari (A2) · LAM 100 mg sekali sehari (A2) TDF atau ETV sebaiknya digunakan sebagai terapi lini pertama (A1)

Pengaruh Tenofovir pada Pasien Sirosis Dekompensata

Tenofovir adalah obat golongan *nucleoside analogue* yang memiliki tingkat efikasi yang baik untuk hepadanavirus dan retrovirus. Pada awalnya, tenofovir digunakan sebagai modalitas terapi untuk HIV. Akan tetapi pada penelitian penelitian terhadap tenofovir, obat ini menunjukan efektifitas yang sangat baik dalam pengobatan Hepatitis B[12].

Ada beberapa studi yang meneliti tentang keamanan dan efektifitas tenofovir pada pasien sirosis. Salah satu studi yang dilakukan oleh Lee et al. menemukan bahwa pada grup intervensi yang mendapatkan tenofovir, menunjukan adanya perbaikan pada rerata skor Child-Pugh dan MELD score setelah pemberian tenofovir selama 12 bulan ($p<0.001$) seperti terlihat pada Gambar I[16].

Lee et al. juga menemukan bahwa terjadi penurunan eGFR pasien pada grup intervensi setelah pemberian tenofovir selama 12 bulan. Akan tetapi perbedaan penurunan antara grup intervensi dan grup kontrol tidak bermakna secara statistik (7% vs 2,5%,$P<1.000$)[16]. Pada studi lainnya, Tsai et al. menemukan bahwa pada pasien dengan pengobatan tenofovir, angka mortalitasnya lebih rendah jika dibandingkan dengan pasien pada kelompok kontrol (43% vs 85%, $P=0.03$)[17].

Pengaruh Entecavir pada Pasien Sirosis Dekompensata

Entecavir merupakan obat dengan analog 2-*deoxyguanosine*. Mekanisme kerja obat ini melalui 3 jalur yaitu[12]:

1. Menghambat *priming* DNA polymerase virus
2. Menghambat *reverse transcription* dari rantai negatif DNA
3. Menghambat sintesis rantai positif DNA

Obat ini biasanya digunakan pada pasien yang mempunyai resistensi pada pengobatan lamivudin[12].

Beberapa studi banyak meneliti tentang efikasi dari entecavir dan keamanannya pada pasien sirosis hati. Contohnya pada studi yang dilakukan oleh Gai et al. pada

tahun 2017 menemukan bahwa pada pasien pasien yang diobati dengan entecavir menunjukan adanya penurunan pada skor Child-Turcotte-Pugh secara signifikan pada minggu ke 24, 48 dan 96. Studi dari Gai et al. juga menunjukan bahwa semakin lama pengobatan entecavir pada subjek penelitian, semakin banyak pasien yang menunjukan adanya penormalan nilai ALT[18].

Pada studi lain, yang dilakukan oleh Cholongitas et al., menunjukan bahwa pada pasien yang mendapatkan entecavir tidak menunjukan adanya perubahan yang signifikan pada eGFR pada bulan ke 6 dan ke 12 pengobatan[19]. *Review* yang dilakukan oleh Tsai et al. juga menemukan bahwa pengobatan entecavir pada pasien dengan sirosis dekompensata menurunkan angka mortalitas.

Akan tetapi, sebuah studi yang dilakukan oleh Lange et al. menemukan bahwa penggunaan NA pada pasien mempunyai efek samping yang sangat berbahaya yaitu asidosis laktat. Meskipun kejadian asidosis laktat sangat jarang terjadi, akan tetapi hal ini patut diperhatikan oleh para klinisi saat merawat pasien sirosis dengan NA. hal ini diperkuat oleh studi yang dilakukan oleh Lange et al. Pada studi tersebut Lange et al. menemukan bahwa pasien dengan skor MELD lebih dari 20 beresiko untuk mendapatkan asidosis laktat saat pengobatan entecavir[20].

Efek Lamivudin Pada Sirosis Dekompensata

Lamivudin merupakan obat golongan NA pertama yang dipakai dalam pengobatan Hepatitis B. Obat ini bekerja dengan cara berkompetisi dengan dCTP untuk berikatan dengan DNA virus sehingga akan menterminasi pemanjangan DNA virus[12].

Secara umum penggunaan lamivudin dapat ditoleransi dengan baik dan cukup aman. Pada studi awal lamivudin, peneliti menemukan bahwa pasien dengan pengobatan lamivudin menunjukan adanya peningkatan serum albumin yang signifikan, penurunan pada serum bilirubin dan penurunan pada skor Child-Turcotte-Pugh[21].

Akan tetapi, pada *review* yang dilakukan oleh Tsai et al. pada tahun 2015 menemukan bahwa tidak ada perbedaan pada angka mortalitas pada pasien yang mendapatkan terapi lamivudin dan kontrol. Pada satu studi yang di review oleh Tsai et al. menemukan bahwa intervensi dini sangat berperan untuk menurunkan angka mortalitas pada pasien yang mendapatkan lamivudin[17].

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Precision Medicine in Gastro Intestinal and Liver Diseases

Sultana MH Faradz

Genomics is an area within genetics that concerns the sequencing and analysis of an organism's genome. Genomics has become especially important during the last decade as we have entered the "genomic era." The dramatic improvement of sequencing technologies and the massive reduction in the cost of sequencing, progress the growing role of genomics in healthcare, for patient diagnoses, treatment and disease prevention including predictive genetic testing. Genomics is the leading driver of an early identification strategy, once individual profiles (e.g. polymorphisms) are available.

Precision medicine is to target treatments to individual needs by integrating genetic, biomarker, phenotypic, and psychosocial characteristics that distinguish one patient from others with similar clinical presentations. The prospect of applying precision medicine broadly is supported by large scale biological databases, powerful methods for characterizing patients (e.g. proteomics, metabolomics, genomics) and computational tools for analyzing large sets of data. In cancer precision medicine is a strategy designed to treat individual patients with the most suitable therapy at the most appropriate time based on the patient's biologic and molecular features, using the analyses of genes of the patient's cancer cells with a new tool next-generation sequencing (NGS). These genes panel analyses can detect cancer-specific gene mutations, and molecular targeted drugs can be designed to be effective for one or more specific gene mutations.

The concept of employing genetics to make major contributions to clinical practice has been progressively extended to the entire human genome. Cancer is a disease of the genome, oncology has been the obvious target of this strategy, for example targeting HER2 over expression with the monoclonal antibody, trastuzumab improved outcome in metastatic breast cancer, the tyrosine kinase inhibitor, imatinib for the treatment of patients with *BCR-ABL* fusion gene in chronic myeloid leukemia. The

introduction of gene panels using NGS, it has become possible to identify a variety of mutations and genetic biomarkers in Gastro Intestinal (GI) cancer. These progressions will make it feasible to incorporate clinical, genome-based, and phenotype-based diagnostic and therapeutic approaches and apply them to individual GI cancer patients for precision medicine. The discovery that abnormalities in the epidermal growth factor receptor (EGFR) contribute to the development and growth of CRC was the starting point for personalised treatment based on the molecular characteristics of an individual colon cancer. The availability of drugs that could block the receptor was crucial. The anti-EGFR monoclonal antibodies cetuximab is the most important example. EGFR is a transmembrane tyrosine kinase which role signals of intracellular pathways for surviving and regulating cellular proliferation, commonly appear on colorectal cancer cells. The cell differentiation, proliferation, migration, angiogenesis, and apoptosis, which become deregulated in cancer cells, are regulated by EGFR signaling pathway. Anti-EGFR therapy for advanced colorectal cancers has been shown to be effective with combination chemotherapy when KRAS is wild type, but “not when KRAS is mutant”. This again suggests that EGFR-targeted agents can be used only in appropriately selected patients.

Non alcoholic steatohepatitis (NASH) is a severe form of non alcoholic fatty liver disease (NAFLD) characterised by liver fat accumulation, inflammation and progressive fibrosis. Advances in human genetics present new opportunities to address the need for NASH therapeutics, based on improved understanding of the multifactorial pathogenesis of NASH and the interaction between genetic and environmental risk factors. These new findings have opened up the possibility of precision medicine for patients with NASH based on inherited genetic variants. In this approach, the identification of people who carry a specific genetic variant predisposing them to NASH allows targeting of the same specific gene or molecular pathway to reverse their hepatic steatosis, inflammation and fibrosis.

There were some genes already been reported that related to NAFLD such as *PNPLA3*, *TM6SF2, GCKR, MBOAT7* and *HSD17B13.* The first genetic variant found to be associated with NASH is a nonsynonymous single nucleotide polymorphism (SNP) in the gene Patatin like Phospholipase domain containing protein 3 (*PNPLA3)* known as c.444 C > G p.I148M. The C to G base substitution at nucleotide position 444 of *PNPLA3* encodes an isoleucine (I) to methionine (M) substitution at amino

acid position 148 of PNPLA3 protein (adiponutrin). The *PNPLA3* I148M (substitution Isoleucine to Methionine) variant has large effects, with approximately two fold increased chance of NAFLD and three fold increased chance of NASH and Hepato Cellular Cancer per allele (of the gene). The extensive genetic, molecular and cell biological evidence that therapies able to modulate *PNPLA3* expression levels may represent precision medicine approaches in patients with NASH. Many new drugs target specific molecular aberrations or cell-signalling pathways, but these drugs are only active in a subset of patients due to molecular differences between each disease. Consequently, a 'one-size-fits-all' approach to treatment should be changed considerably and so there has been increasing interest in a more personalized approach to treatment.

Semarang Gastroentero-Hepatology Update 2020

Reversibility of Hepatic Fibrosis and Cirrhosis: From Concept to Treatment

David Handojo Muljono

Fibrosis: a wound-healing response to injury

Chronic liver diseases (CLD) progression is characterized by a long-standing chronic parenchymal injury and persistent activation of inflammatory response which trigger sustained activation of liver fibrogenesis in an attempt to limit the consequences of chronic liver injury within the so-called “chronic wound healing reaction”. This liver fibrogenesis is paralleled persisting pathological angiogenesis, contributing to the expansion of tissue fibrosis.

Fibrosis represents a response to many causes of chronic injury to maintain organ integrity when extensive necrosis or apoptosis occurs. For the liver, the etiologies of fibrosis are related to chronic infection such as by hepatitis B virus (HBV) and hepatitis C virus (HCV), and in the last decades are associated with alcoholic and non-alcoholic fatty liver disease (NAFLD), both recently named as metabolic-associated fatty liver disease (MAFLD), and to a certain with biliary diseases. Repeated and chronic liver injury causes inflammatory damage, matrix deposition, parenchymal cell death and angiogenesis leading to progressive fibrosis. The major actors in the fibrogenetic process are the activated myofibroblasts that derive from hepatic stellate cells (HSCs) and portal fibroblasts. Other cell types within the liver parenchyma take part in the fibrogenic pathway, including sinusoidal endothelial cells, Kupffer cells, hepatocytes, and cholangiocytes.

Cirrhosis and development to hepatocellular carcinoma

Following resolution of the tissue injury, fibrosis reverses within a few weeks; therefore, it is considered a dynamic event rather than a static process. However, repeated and chronic damage is accompanied with a progressive decline in the reversibility potential, even after the elimination of the triggering cause. This could be

the result of different factors, including the acquisition of an atypical extracellular matrix (ECM) composition with advanced vascular remodeling, the extensive crosslinking of ECM components that makes fibrinolysis difficult to occur, and the loss of cellular elements able to digest the scar tissue.

As fibrosis continues to progress, cirrhosis occurs, with the replacement of functional parenchyma by scar tissue accompanied by a disruption of the architectural and vascular structure. Without effective treatments at an early stage, reversible liver fibrosis will lead to irreversible cirrhosis, leading to the development of hepatocellular carcinoma (HCC). Regression of fibrosis and early cirrhosis stages can be achieved in patients if the etiologies can be controlled or eliminated, such as patients with chronic HBV and HCV infection who are treated with recently available antivirals; and also those with alcohol-induced injury, NASH, iron and copper overload, hemochromatosis, secondary biliary cirrhosis, and autoimmune hepatitis. However, once cirrhosis is established, the chance for reversing this process is decreased.

Diagnosis of fibrosis

Diagnosis of fibrosis can be divided into two maid approaches, liver biopsy, which is an invasive procedure, and various non-invasive methods. Liver biopsy is still considered to be the gold standard to assess the grade of fibrosis in the tissue. It is, however, should be performed by a trained physician to obtain an adequate liver biopsy sample, and examined by an experienced pathologist to interpret the result. Several noninvasive test have been developed, from biomarker methods such as: 1) Aspartate aminotransferase (AST)-to-platelet ratio index (APRI), which is a simple index for estimating hepatic fibrosis based on a formula: (AST level/ULN) x 100) / platelet count (109/L); 2) FIB-4A, a simple index for estimating hepatic fibrosis based on a calculation derived from AST, ALT and platelet concentrations, and age. Formula for calculating FIB-4: FIB-4 = (age (yr) x AST (IU/L)) / (platelet count (109/L x [ALT (IU/L)1/2]).; and 3) FibroTest, which uses five serum markers, α-2-macroglobulin, γGT, apolipoprotein A1, haptoglobin, total bilirubin, together with the age and sex of the patient, to calculate a score to predict the level of fibrosis in patients with HBV or HCV infection, and has been applied in NAFLD.

Current and Future Treatment Strategies

The best therapy for liver fibrosis is the treatment of disease etiology. In situations in which treating the underlying process is not possible, controlling inflammatory activity and fibrosis progression is an important alternative strategy to rescue the liver beyond existing standard of care. This strategy includes maintaining liver integrity and function, stopping or reversing damages, and preventing further scar accumulation. A number of antifibrotic agents have been used in humans: a) Compounds with anti-inflammatory, anti-oxidant, or general effects, e.g. Glycyrrhizin, Ursodeoxycholic acid (UDCA) and Vitamin E, Interleukin-10, Propylthiouracil, Silymarin, Salvianic acid, b) Compounds with specific antifibrotic effects, e.g. colchicines, polyunsaturated phosphatidylcholines (PC). These compounds have the property in helping cell protection, increase general immunity through the activation humoral and cellular immunity cells. Other strategies under development are: degradation of extracellular matrix; regulation of apoptosis; inactivation of HSC; and Stem cell therapy.

One example of antifibrotic agent is Glycyrrhizin (GL), which is a glycosylated saponin from licorice root (*Glycyrrhiza glabra*). Several clinical studies reported that GL was efficacious in the treatment of various types of inflammation (mainly in liver), but also in lung, kidney, intestine, and spinal cord. In liver, GL can reduce steatosis and necrosis of hepatocytes significantly, prevent the inter-interstitial inflammation and liver fibrosis via suppression of TNF-5α and caspase-3, and inhibits the release of cytochrome C from mitochondria into the cytoplasm. A recent study found the cytotoxicity of glycyrrhizin and its derivative on cancer cells but not in normal cells, highlighting the potential use as a chemotherapeutic agent against hepatocellular carcinoma cells.

In conclusion, liver fibrosis should be viewed as a clinical problem in its own entity that may result in different forms of chronic liver disease with various etiological backgrounds. Controlling inflammatory activity and fibrosis progression is an important alternative strategy to rescue the liver beyond existing standard of care.

Semarang Gastroentero-Hepatology Update 2020

NAFLD Update: From New Definition of MAFLD to Potential Treatment

Hery Djagat Purnomo

Metabolic dysfunction-associated fatty liver disease (MAFLD), formerly named non-alcoholic fatty liver disease (NAFLD), affects about a quarter of the world's adult population, poses a major health and economic burden to all societies and yet has no approved pharmacotherapy.[1] The population prevalence of NAFLD in Asia is around 25%.[2] Based on the ultrasonography visitation data obtained from the radiology department, the number of patients with NAFLD in Dr. Kariadi hospital Semarang also displayed a steady annual increase.[3] The prevalence is expected to increase in accordance with increasing population of obesity, sedentary lifestyle, metabolic syndrome, and development of diabetes.[2]

The nomenclature and metabolic dysfunction associated fatty liver disease, MAFLD, has been proposed as a more appropriate term to describe the liver disease associated with known metabolic dysfunction.[1] The new definition clearly establishes this disease as a metabolic disorder as criteria now require evidence of hepatic steatosis accompanied by one of three features: that is, either overweight or obesity, T2DM, or lean or normal weight with evidence of metabolic dysregulation.[4] The two most important and significant differences between MAFLD and NAFLD are, MAFLD diagnosis does not require exclusion of patients with alcohol intake, or other chronic liver diseases and the presence of metabolic abnormality is necessary for diagnosis of MAFLD. The utility of these criteria has not thoroughly explored. In the recent study, Lin Su et al. concluded that MAFLD definition is more practical for identifying patients with fatty liver disease with a high risk of disease progression.[5]

The pathogenesis of the NAFLD is multifactorial and its understanding is still incomplete.[6] The "two hit pathogenesis" has been replaced by "multiple hit" theory, which genetic factors cooperate with metabolic and environmental factors to promote the accumulation of fat in hepatocytes and successively cause inflammation, cellular death and fibrosis.[7] New concepts of inflammation are important in MAFLD, as

treatment strategies might need anti-inflammatory approaches to target this disease successfully in the future.

There are many promising targets for NAFLD treatment. In current NAFLD drug research and development, researchers usually select protein targets from the three aspects, including metabolism, inflammation and fibrosis.6 Different classes of drugs can be identified: antidiabetic drugs, antioxidants, prebiotics, drugs acting on the bile acid system and lipid-lowering therapies. Other novel therapeutic agents are explored, especially regarding dietary component and the so called nutraceuticals and molecular targeted therapy.[7-8] In this review, we will summarize a series of aspects of the MAFLD, mainly including new criteria, pathogenic mechanisms, and therapeutic targets.

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Semarang Gastroentero-Hepatology Update 2020

Role of Surgery in HCC Management: New Insight

Erik Prabowo

The incidence of liver cancer in Indonesia in 2018 ranks as the fourth most common malignancy in all age groups combined for men and woman, and is the fourth leading cause of death of all malignancies. Surgery for hepatocellular carcinoma (HCC) still plays the important role worldwide as the potential curative therapy. Surgery includes liver resection (LR) and liver transplantation (LT). LT is the most effective procedure in the management of HCC, but unfortunately it has many challenges in developing countries include Indonesia, starting from the high cost, the large team of doctors, and most of the cases that come are not suitable for LT because of restrictive criteria (one nodule 3-5 cm or two to three nodules <3 cm without macrovascular invasion).

Hepatic resection for HCC according to NCCN guidline 2020 is indicated as potential curative treatment with following circumstances: adequate liver function, without major vascular invasion, adequate future liver remnant (FLR) at least 20% without cirrhosis or at least 30-40% with Child-Pugh A cirrhosis, and adequate inflow/outflow from vascular and biliary duct. LR is now safer, with a low rate of mortality and morbidity. Selective preoperative morphological and radiological assessment, preoperative use of portal vein embolization for increasing future remnant liver volume and the improvement of surgical techniques such as the use of intermittent clamping and glissonean pedicle approach are factors that improve the safety and tolerance of LR.

In patients with early stage of HCC who performed LR long-term survival can be achieved with 5 year survival rate more than 70% after anatomical resection that removes the tumor and its portal vein territory. These good results of LR have renewed the place of LR as a bridge treatment before LT.

Semarang Gastroentero-Hepatology Update 2020

Targeting on Innate and Adaptive Immune Response in Treatment of Chronic HBV Infection

I Dewa Nyoman Wibawa

Pendahuluan

Infeksi Virus hepatitis B (VHB) menyebabkan masalah kesehatan sangat penting teradap umat manusia. Diperkirakan VHB telah menginfeksi sepertiga dari populasi dunia dan sekitar 360 juta individu pembawa infeksi VHB menahun. Di seluruh dunia, 0,5-1,2 juta kematian setiap tahun diakibatkan infeksi VHB. Oleh karenanya, adalah sangat penting melakukan upaya pengendalian infeksi VHB secara global dan efektip. Infeksi VHB dapat diintervensi dengan memutuskan mata rantai transmisi, mengobati pasien terinfeksi menahun, dan mencegah kelompok populasi rentan dengan imuno-profilaksis.[1]

Perjalanan klinis dan kemungkinan perkembangan kearah penyakit hati menahun pada infeksi VHB sangat bervariasi dan tergantung usia saat terpapar. Pada mereka dengan akuisisi VHB saat perinatal atau selama masa bayi, perkembangan kearah penyakit hati menahun 90%. Apabila paparan berlangsung antara usia 1-5 tahun, risiko menahun turun menjadi 30%. Untuk paparan saat anak usia diatas 5 tahun dan orang dewasa, kemungkinan berkembang menjadi infeksi menahun sekitar 2%. Persistensi tinggi pada infeksi VHB perinatal dihubungkan dengan maturasi dan respon imun bawaan dan adaptip inang yang belum adekuat.[2]

Para ahli telah menetapkan definisi kesembuhan infeksi VHB sebagai tolok ukur kemajuan terapi baru. Kesembuhan steril (sterilizing cure) didefinisikan sebagai eradikasi VHB, termasuk cccDNA intrahepatik dan DNA VHB terintegrasi. Sebuah kesembuhan fungsional adalah HBsAg dan DNA VHB tidak terdeteksi dalam serum (dengan atau tanpa antibodi terhadap HBsAg), setelah penyelesaian pengobatan yang terbatas, resolusi sisa cedera hati, dan penurunan risiko kanker hati. Akhirnya, kesembuhan parsial didefinisikan sebagai HBsAg yang masih terdeteksi tetapi secara persisten DNA VHB tidak terdeteksi dalam serum setelah selesainya pengobatan.[3]

Dalam upaya menyembuhkan infeksi HBV, perlu diingat bahwa VHB tidak hanya bertahan melalui cccDNA, tetapi juga terintegrasi ke dalam genom inang. [4,5]

Kurang dari 1 % per tahun, infeksi VHB dapat disembuhkan dengan obat anti virus. Hal ini mengakibatkan dibutuhkannya terapi jangka panjang dan merupakan tantangan bagi pasien dan sistim kesehatan. Oleh karena kesembuhan diikuti dengan pemulihan imunitas antivirus, maka kombinasi antara agen antivirus kerja langsung dengan imuno-terapi tampaknya memang dibutuhkan. Upaya ekstensip sudah dikerjakan untuk mengidentifikasi determinan kegagalan respon imun terhadap VHB pada pasien dengan infeksi VHB menahun. [6]

Respon imun infeksi virus hepatitis B

Infeksi VHB adalah virus hepatotropik non-sitopatik. VHB tidak langsung dapat merusak sel hati inang. Keberhasilan tubuh mengusir VHB atau kerusakan hati yang terjadi pada individu terinfeksi diakibatkan oleh kompleks interaksi respon imun inang dan VHB. Kerusakan hati akibat invasi VHB mencakup hepatitis B akut, hepatitis B kronis, sirosis hati dan kanker hati primer. [7]

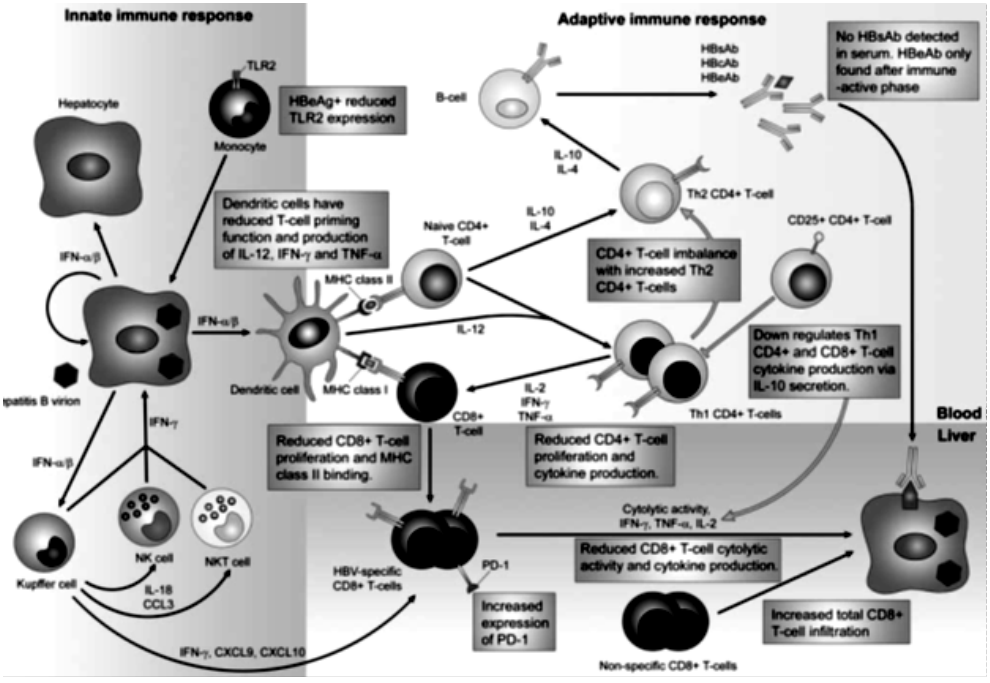
Efisiensi respon imun spesifik VHB telah terbukti selama resolusi infeksi akut, hampir 100% hepatosit terinfeksi.[8] Pasien yang sembuh Infeksi VHB akut memiliki respon kuat sel T CD4 + dan sel T CD8+ terhadap virus. Sel-sel ini menghasilkan sitokin antivirus dan memberikan ko-stimulasi ke sel B. Sel B. memproduksi anti-HBs, yang membersihkan antigen dan virus dari sirkulasi dan mencegah atau membatasi re-infeksi, bersama dengan antibodi terhadap antigen e hepatitis B (HBeAg) dan anti VHBcore antigen. Adanya dikotomi antara pasien yang berhasil sembuh dari infeksi akut dan mereka yang berkembang menjadi infeksi menahun tampaknya bergantung pada seberapa kuatnya serta fungsi respon imun inang. Sel T spesifik VHB terdeteksi secara signifikan lebih rendah pada mereka yang terinfeksi menahun dibandingkan akut. Sel T spesifik VHB dijumpai pada semua fase infeksi VHB menahun, akan tetapi oleh karena jumlahnya rendah tampaknya mengalami kesulitas untuk rekognisi hepatosit terinfeksi tanpa ekspansi *in vitro*. [9, 10,11]

Sesudah terinfeksi VHB, terjadi hepatitis awal yang mungkin dapat disertai atau tanpa gejala. Keberhasilan klirens dan resolusi VHB tergantung usia saat akuisisi

infeksi dan status imun inang serta kebanyakan infeksi pada individu dewasa imuno-kompeten dapat sembuh sendiri (self-limiting). Persistensi atau infeksi menahun kemungkinan terjadi setelah transmisi vertikal (ibu kepada anak) atau transmisi horizontal pada anak atau dewasa imuno-kompromis. Determinan imun yang bertanggung jawab terhadap keberhasilan klirens VHB belum sepenuhnya dimengerti, akan tetapi respon imun baik imunitas seluler maupun humoral keduanya berperan penting.[7]

Kontrol terhadap infeksi VHB memerlukan kerjasama antara respon imun bawaan dan respon imun adaptif, mencakup baik imunitas seluler maupun imunitas humoral. Terdapat beberapa mekanisme yang dihubungkan dengan persistensi infeksi atau infeksi VHB menahun, berkurangnya kemampuan sel Dendrit untuk memicu sel T dan memproduksi sitokin disamping juga berkurangnya ekspresi TLR2 pada monosit perifir. Sel T cenderung berubah kearah fenotip Th2 CD4+. Sisa Th1 CD4+ kapasitas proliferasinya berkurang dan produksi sitokin antivirus-nya terganggu. Berkurangnya fungsi sel T Th1 CD4+ dan menurunnya stimulasi sel Dendrit keduanya mengganggu fungsi dan jumlah sel T CD8+ spesifik VHB. Adanya anegi sel T CD8+ spesifik VHB ini mungkin meningkatkan ekspresi PD1. Kerusakan sel hepatosit masih berlangsung dan terutama dimediasi oleh infiltrasi sel T CD8+ non-spesifik VHB.[7]

Pada individu terinfeksi VHB menahun respon sel T CD4+ dan CD8+ spesifik VHB secara signifikan berkurang. Disamping itu terdapat juga disfungsi dari sel Dendrit dan juga terganggunya respon imun bawaan lainnya. Reseptor TLR 2 dijumpai berkurang pada infeksi VHB menahun terutama pada individu terinfeksi VHB dengan HBeAg positip. Jumlah sel NK (Natural Killer) meningkat pada individu fase imuno-tolerant (*Viral load* tinggi dan ALT normal) infeksi VHB dibandingkan mereka yang berada pada fase imuno-klirens (ALT abnormal), diduga mungkin keberadaan sel NK secara fungsional mungkin tidak aktip terhadap VHB. Gangguan respon sistim imun bawaan mungkin penting pada infeksi VHB menahun disamping juga penurunan efek aktivitas respon imun adaptif perlu mendapat perhatian lebih lanjut.[7]



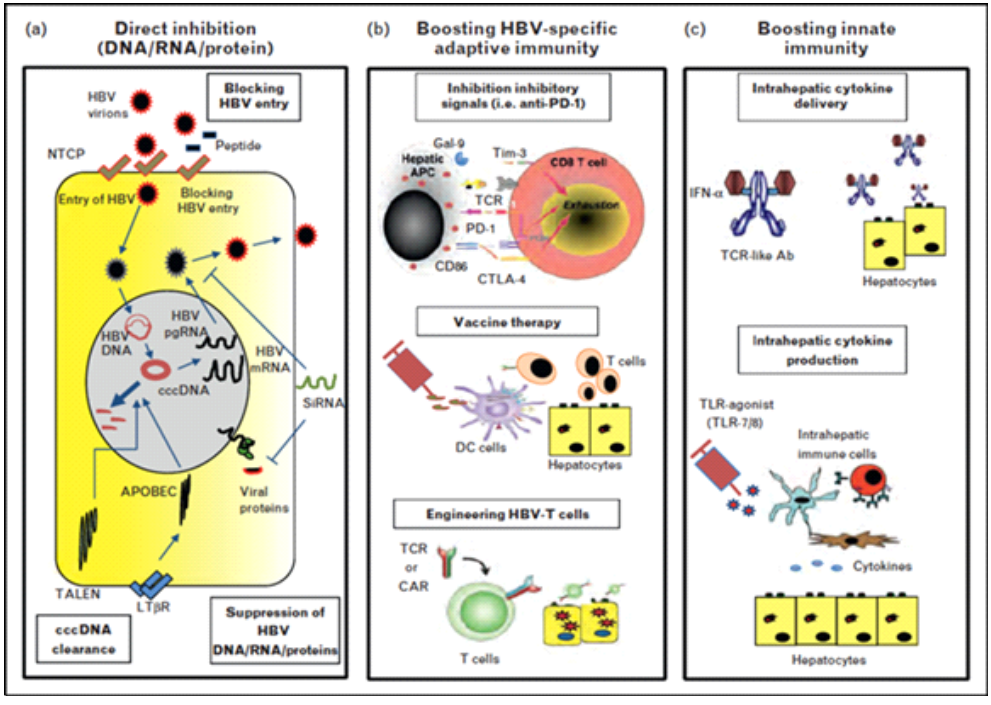
Gambar 1. Respon imun bawaan dan adaptif infeksi VHB dan efek infeksi menahun. [7]

Meskipun sel efektor imun dan respon imun tidak mencukupi pada pasien dengan infeksi VHB kronis, terdapat bukti bahwa aktivasi imunitas bisa membersihkan virus. Kontrol infeksi VHB dapat tercapai dengan aktivasi sel T CD8+ VHB spesifik intrahepatic dikombinasi dengan sel T sitotoksik perifir penghasil sitokin. Replikasi VHB dapat dikontrol dengan interferon (IFNs) dan sitokin lainnya yang di produksi oleh sel imuno-kompeten lain. Sel T dan sel Natural Killer (NK) dapat mengontrol bahkan eleminasi infeksi VHB tanpa sitolsisis.dengan mengeluarkan sitokin [6]

Disamping sel T, sel B juga diperlukan untuk kontrol infeksi VHB menahun. Pada infeksi VHB menahun, produksi antibodi oleh sel B, dengan deplesi sel B, dapat mengakibatkan terjadinya reaktivasi VHB pada 60% pasien infeksi VHB menahun, bahkan mungkin juga menimbulkan *flare* berat. [6]

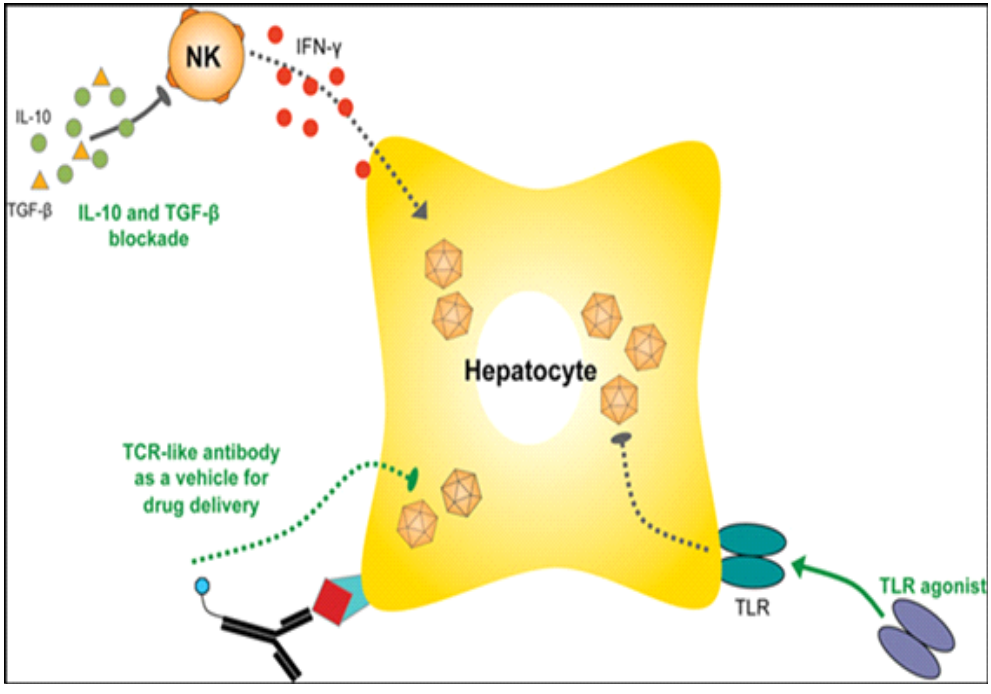
Target respon imun inat/bawaan dan adaptif pada terapi hepatitis kronik B

Imuno-terapi merupakan suatu pendekatan untuk mengatasi masalah infeksi VHB menahun. Dengan merangsang aktivasi sistim imun bawaan dan mengaktifkan respon imun adaptif secara bersamaan dapat diharapkan kombinasi dengan obat anti virus akan meningkatkan kendali infeksi VHB menahun. Kontrol imun merupakan target imunoterapi yang mampu menggeser respon imuno-toleran ke respon imuno-klirens. [6]



Gambar 2. Skema representasi dari strategi baru terapi virus hepatitis B. (a) penghambatan langsung (DNA / RNA / Protein). (b) Meningkatkan kekebalan adaptif spesifik-HBV. (c) Meningkatkan kekebalan bawaan. Ab, antibodi; APC, *antigen-presenting cell*; CAR, reseptor antigen chimeric; cccDNA, DNA melingkar kovalen tertutup; DC, sel dendritik; HBV, virus hepatitis B; IFN, interferon; LTb, limfotoksin-b; NTCP, sodium taurokolat *cotransporting* polipeptida; TALEN, *transcription activator-like effector nucleases*; TLR, toll-like receptor.[12]

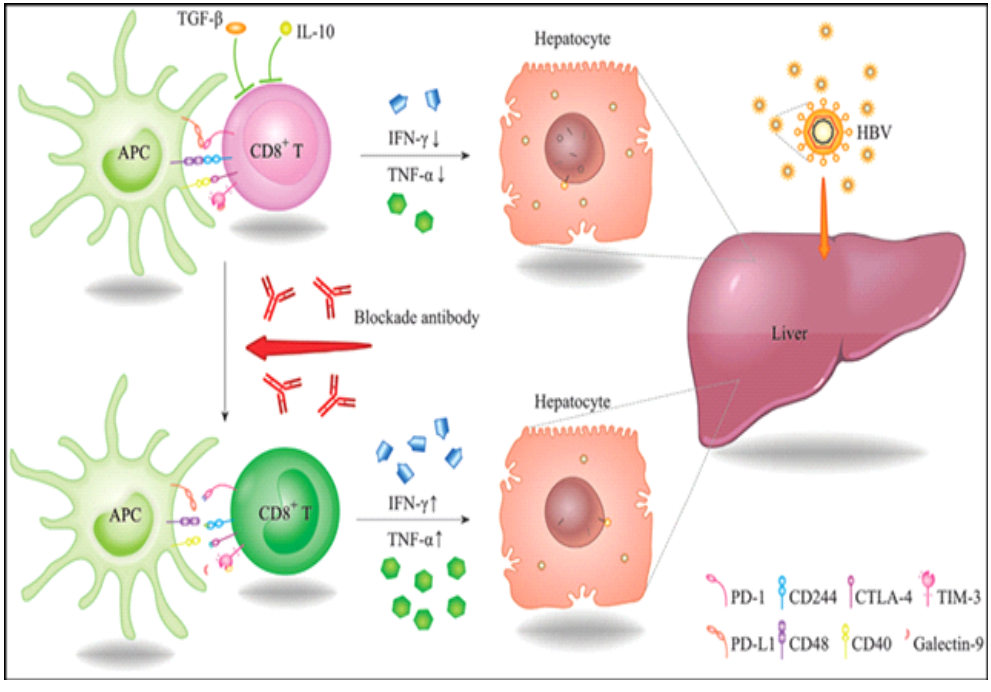
Berdasarkan konsep imunobiologi infeksi VHB terdapat beberapa cara pendekatan terapi infeksi VHB kronik seperti: (a) penghambatan langsung (DNA / RNA / Protein), (b) Meningkatkan kekebalan adaptif spesifik-VHB. (c) Meningkatkan kimunitas bawaan.(Gambar 2).[12]



Gambar 3. Kemungkinan target untuk modulasi respon imun bawaan pada infeksi VHB.[13]

Penggunaan agonis TLR untuk stimulasi respon imun bawaan pada hepatosit yang terinfeksi VHB adalah pendekatan imunoterapi sangat menjanjikan. Selanjutnya, efek dari obat antivirus seperti interferon-á mungkin ditingkatkan dengan pengiriman langsung obat ke sel yang terinfeksi VHB melalui *TCR-like antibodies* yang berfungsi sebagai pengangkut. Sebaliknya, pendekatan terapi terhadap target ini mungkin membantu untuk membatasi efek samping obat. Terlepas dari efek langsung pada hepatosit yang terinfeksi, pemulihan fungsi sel NK oleh blokade sitokin penghambat seperti IL-10 dapat digunakan untuk modulasi respon imun bawaan terhadap VHB.[13] (Gambar 3).

Kelelahan sel T, merupakan target sejumlah jalur sinyal melalui mana reseptor inhibisi/penghambat dapat mengirimkan sinyal penekan untuk menghambat respons fungsional dan proliferasi selama infeksi VHB kronis. Data yang ada mendukung bahwa reseptor penghambat termasuk PD-1, CTLA-4, TIM-3 dan CD244 semua mengambil bagian dalam mekanisme *immunoregulatory* kelelahan sel-T.Oleh karena itu, pemulihan fungsi kelelahan sel-T tampaknya efektif dengan salah memblokir reseptor penghambat atau bersamaan memblokir beberapa molekul penghambatan. Selain itu, memblokir sitokin penghambat seperti IL-10 atau TGF-β juga dianggap sebagai pendekatan yang bermanfaat untuk memodulasi fungsi sel-sel T. Setelah blokade antibodi, kemampuan sel T untuk berproliferasi dan mengeluarkan sitokin dapat dipulihkan pada pasien yang terinfeksi VHB kronis. Berdasarkan observasi ini, pendekatan immunoterapeutik layak dieksplorasi lebih baik untuk pengobatan anti-virus pasien VHB.[14] (Gambar 4).



Gambar 4. Imunoterapi pada pengobatan VHB dengan pemulihan kelelahan sel T.[14]

Ringkasan

Interaksi antara VHB dengan respon imun inang, baik bawaan dan adaptip, menentukan hasil akhir infeksi VHB. Pengobatan saat ini yang ada hanya efektif menekan replikasi virus tetapi pada kebanyakan kasus gagal untuk eleminasi VHB. Efek kombinasi antara obat anti-virus dan rekonstitusi respon imun spesifik VHB sangat dibutuhkan untuk klirens jangka panjang infeksi VHB. Interaksi spesifik antara komponen virus dan elemen sistim imun mungkin memberikan tanda penting untuk memahami mekanisme persistensi infeksi dan pemahaman mendasar “switch” dari fase imuno-toleran kearah imuno-klirens/ imun-aktip dalam upaya pengendalian infeksi VHB menahun. Salah satu pendekatan yang menjajnjikan adalah penggabungan antara obat anti-virus dengan imuno-terapi VHB.

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Real Life Cases in the Treatment of Chronic Hepatitis B using Pegylated Interferon

Hery Djagat Purnomo

Hepatitis B virus (HBV) infection is a major public health problem.1 Approximately 240 million people are chronic HBV surface antigen (HBsAg) carriers, with a large regional variation of HBsAg positive patients between low (<2%) and high (>8%) endemicity levels.3 It is estimated that about 780 000 people die each year due to consequences of hepatitis B, such as liver cirrhosis and liver cancer.1 The Asia Pacific region has the largest share of HBV infec-tion in the world, and 74% of global deaths from liver cancer occur in Asia. A nationwide study in Indonesia (Riskesdas 2013) that covered 33 provinces, showed that there has been a decline in the prevalence of HBsAg (9.4% in 2007 to 7.1% in 2013), indicating that Indonesia has moved from high to moderate endemicity of HBV infection.2

There are currently two main treatment options for CHB: treatment with a nucleoside analogue or treatment with pegylated interferon-α-2 (PEG IFN). The loss of HBsAg is regarded as the optimal treatment endpoint, termed 'functional cure', but it is only rarely achieved with our current antiviral armamentarium.3,4 Recent meta-analyses showed that in patients with HBsAg seroclearance, the risk for HCC was significantly lower compared with those patients who were persistently HBsAg positive. In addition, the achievement of HBsAg seroclearance allows for the safe discontinuation of long-term NA treatment. However, current treatment with NAs or pegIFN results in only low rates of HBsAg seroclearance.5

The rationale for a PegIFN based approach is to induce long term immunological control with a finite duration treatment.3 IFN monotherapy/combination had a small but significant increase in HBsAg loss over NA, associated with standard dose of IFN and >48 weeks of therapy, although this effect faded over time.1 Information on the efficacy of pegylated interferon (PEG-IFN) treatment of chronic hepatitis B (CHB) patients and predictors of the sustained virological response based on real-life data is limited.6 Preliminary Real cases Study at Kariadi Hospital Semarang showed that

Peg-INF therapy in management of CHB had good virological and histological response. HbeAg positive and HBV DNA < log 6 were strong predictors for virological response. A recent real-life study at Kariadi Hospital of 96 treatment naïve CHB patients showed that at the week 96, patients with baseline HBV DNA < log 6 IU/mL, ALT >2x upper normal limit, and age <35 year were more likely to achieve SVR.

More studies are warranted to confirm the predictive value of the immunologic and virological biomarkers for functional cure and treatment failure.7 This review provides an overview of the evidence supporting the use of pegIFN for chronic hepatitis B patients on daily basis.

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Telemedicine: Medical, Legal dan Ethical Perspective

Kris Pranarka

I. Pendahuluan

Kata “tele” berasal dari bahasa Yunani , yang artinya “jauh/jarak” sehingga telemedik dapat diartikan sebagai pelayanan kedokteran yang dipisahkan oleh jarak.

Secara keseluruhan layanan telemedis bearti layananyang menggunakan fasilitas komunikasi elektronik untuk memberikan pelayanan atau dukungan medis tidak bertatap muka tapi dari jarak yang terpisah. Fasilitas komunikasi yang digunakan bermacam-macam dapat berupa telepon, panggilan video, situs internet atau alat canggih lainnya.

Praktek telemedik perlu dilandasi ilmu/pengetahuan khusus sehingga tidak ada keraguan atas profesionalitasnya.

Setiap penyelenggara sistim elektronik harus dapat menyelenggarakan sistim elektronik secara andal, aman serta bertanggung jawab terhadap operasional sistem elektonik tersebut. (UU no 11 , Informasi danTransaksi Elektronik).

Perlunya keadilan sosial dalam hal pelayanan kesehatan bagi seluruh masyarakat Indonesia juga harus dilandasi kerja sama dan regulasi antara para pekerja kesehatan, dengan penyedia jasa telekomunikasi dengan pengawasan Pemerintah.

Lewat Telemedik pelayanan medik dapat diberikan dengan cara audio visual, dan dapat menghubungkan fasilitas pelayanan kesehatan meskipun secara geografis terpisah. Telemedik diperkirakan akan berkembang pesat dimasa yang akan datang sehingga harus dipersiapkan juga cara-cara regulasinya. Karena disamping manfaat ada juga potensi berbagai problema hukum. Antara lain berkenaan dengan privasi, kerahasiaan rekam medik, pemberian lisensi dan akreditasi, serta asuransi.

Pemerintah dan komunitas kesehatan perlu memperhatikan aspek medis, legal dan etika dalam penggunaan teknologi komunikasi dalam pelayanan kesehatan.

II. Medical Perspective

Praktek kedokteran telemedik diselenggarakan berdasarkan pada kesepakatan antara dokter (termasuk dokter gigi) dengan pasien dalam upaya untuk pemeliharaan kesehatan, peningkatan kesehatan, pencegahan penyakit, pengobatan penyakit dan pemulihan kesehatan.

Dokter dalam menyelenggarakan praktek kedokteran wajib mengikuti standar pelayanan kedokteran/kedokteran gigi menurut jenis dan sarana pelayanankesehatan yang kesemuanya diatur dengan Peraturan Menteri Kesehatan.

Sedangkan kewenangan dokter dalam UU Pradok pasal 35 , mengharuskan dokter telah memiliki STR sesuai dengan pendidikan dan kompetensi yang dimiliki, sehingga dapat melakukan:

a. Melakukan anamnesa

b. Pemeriksaan fisik dan status mental

c. Menentukan pemeriksaan penunjang yangdibutuhkan

d. Menegakan diagnosis

e. Penatalaksanaan / Pengobatan pasien antara lain melakukan tindakan kedokteran sesuai teknologi kedokteran

f. Menulis resep obat dan alkes

g. Menyimpan obat dalam jumlah serta jenis yang diijinkan dan meracik obat bila tidak ada apoteker misalnya di daerah terpencil

h. Menerbitkan Surat Keterangan Dokter.

Kewenangan lainnya diatur oleh peraturan Konsil Kedokteran Indonesia.

Pelayanan telemedicine antar fasilitas pelayananan kesehatan dilaksananakan antara pelayanan kesehatan satu dengan pelayanan kesehatan lain berupa konsultasi untuk menegakan diagnosis , terapi dan/atau pencegahan penyakit. Fasyankes adalah suatu tempat dan/atau alat yang digunakan untuk menyelenggarakan upaya pelayanan kesehatan baik promotif, preventif, kuratif maupun rehabilitatif yang dilakukan oleh pusat, daerah dan/atau masyarakat.

Fasyankes pemberi konsultasi adalah yang menerima permintaan dan memberikan pelayanan konsultasi telemedik.

Fasyankes peminta konsultasi adalah yang mengirim permintaan konsultasi telemedik. Sedangkan yang dimaksud dengan expertise adalah hasil analisis dan kesimpulan oleh dokter spesialis/subspesialis atau ahli lainnya terkait pembacaan image/foto dari hasil penunjang medis dan hasil pemeriksaan lain yang digunakan sebagai penegak diagnosa pasien.

Hasil pelayanan telemedik dicatat dalam catatan digital yang dipergunakan dokter sebagai dokumen rekam medik dan menjadi tanggung jawab dokter untuk menjaga kerahasiannya serta dipergunakan sesuai dengan ketentuan peraturan perundang-undangan.

Rekam Medik juga harus segera dilengkapi setelah pasien selesai menerima pelayanan kesehatan. Rekam Medik wajib dilakukan setiap dokter yang menjalankan praktik kedokteran. Dan setiap catatan rekam medik harus dituliskan nama, tempat dan waktu serta tanda tangan petugas yang memberikan pelayanan/tindakan

III. Legal Perspective

Pelayanan telemedik mempunyai dasar hukum yang resmi dan cukup kuat.

A. Surat Edaran no HK 02.01/Menkes/303/2020 tentang pelayanan kesehatan melalui pemanfaatan teknologi informasi dan komunikasi dalam rangka pencegahan penyebaran Covid-19.

   Ringkasan isinya, memberi kewenangan pada dokter untuk memberikan pelayanan telemedik.

Juga ada Surat Edaran DirJen YanKes no.YR.03/03/111/1118/2020, antara lain:

a. Mengembangkan pelayanan jarak jauh(telemedicine) atau aplikasi online lainnya.

b. Dokter, perawat dan tenaga kesehatan lain, yang berusia diatas 60 tahun dan memiliki penyakit penyerta, dianjurkan untuk bekerja di rumah dengan memanfaatkan aplikasi online.

Walaupun didukung dan dianjurkan dengan Undang-Undang, tetap ada kewajiban yang harus dipatuhi oleh dokter dalam melaksanakan telemedik, antara lain:

a. Berpegang pada standar profesi dan standar prosedur operasional serta kebutuhan medis pasien.

b. Merujuk ke dokter dengan keahlian dan kemampuan yang lebih baik, bila perlu.

c. Melakukan pertolongan daurat atas dasar perikemanusiaan.

d. Merahasiakan segala sesuatu yang diketahuinya tentang pasien, bahkan juga setelah pasien meninggal dunia.

Harus juga dipenuhi persetujuan tindakan medik pada pelayanan telemedik setelah cukup diberikan penjelasan, sekurang-kurangnya mencakup:

a. Diagnosis dan tata cara tindakan medis

b. Tujuan tindakan medis yang dilakukan

c. Alternatif tindakan lain dan risikonya

d. Risiko dan komplikasi yang mungkin terjadi

e. Prognosis terhadap tindakan yang dilakukan.

Persetujuan ini dapat diberikan secara lisan, kecuali yang dengan risiko tinggi harus secara tertulis yang ditandatangani oleh yang berhak memberikan persetujuan.

IV. Ethical Perspective

Layanan telemedik umumnya tidak berbenturan dengan masalah Etika, selama diatur secara jelas peranan dan tanggung jawab masing-masing pihak, kejelasan informasi yang diberikan pada pasien, sampai-sampai pengaturan tarif. Pada umumnya dokter yang bertatap muka tersebut tetap bertanggung jawab atas pelayanan yang sedang berlangsung dan menjadi DPJP setidaknya pada saat itu.

Kelebihan utama layanan telemedik adalah mengeliminasi batasan jarak dan geografis serta biaya yang terkait. Khususnya di daerah yang terpencil dan keterbatasan tenaga medis. Hal ini menjadi sangat relevan untuk diterapkan di Indonesia.

KODEKI pasal 14 diantaranya menyatakan agar ketika tidak mampu melakukan pengobatan, wajib merujuk ke dokter lain yang lebih kompeten, dengan persetujuan pasien/keluarganya. Dan dokter konsultan harus menghargai konsultasi ini dan tidak sebaliknya minta agar malahan menyuruh sejawat tersebut melakukan hal diluar kompetensinya, kecuali memang tidak memungkinkan antara lain kendala kondisi atau transportasi.

Salah satu contoh manfaat dari Telemedik adalah kasus-kasus Dermatologi karena sebagian diagnosisnya dapat ditegakkan dengan inspeksi.

Hendaknya jangan disalahgunakan dengan pengalihan delegasi yang tidak bertanggungjawab, ketika bermaksud mengalihkan perawatan pada konsultan karena pasien memerlukan tindakan diluar kompetensinya.

Informed consent juga perlu diperhatikan karena melibatkan pihak ketiga diluar interaksi klasik yang biasa antara dokter- pasien.

Dokter yang memberikan layanan telemedik harus berhati-hati memberikan saran medisnya sebagaimana dalam praktik tatap muka biasa.

Pada dasarnya KODEKI dengan peraturan-peraturan yang berlaku dapat menjadi pegangan untuk mengarahkan perkembangan layanan telemedik sebagai wahana penghubung antar dokter maupun dokter - pasien.

MKEK dan IDI dapat mengawal layanan telemedik ini untuk memberi manfaat secara luas tanpa mengesampingkan nilai-nilai luhur profesi kedokteran bahkan memperkuat.

Sistim telemedik yang dikembangkan dengan baik antara lain dapat mengatasi ketimpangan kebutuhan dokter atau dokter spesialis antara kota besar dengan daerah terpencil.

V. Kesimpulan

Pelayanan telemedik dikerjakan oleh dokter dengan menggunakan teknologi informasi - komunikasi untuk mendiagnosis, mengobati, dan mengevaluasi kondisi kesehatan pasien. Kegiatan itu dilakukan sesuai kompetensinya yang tertera dalam STR dengan tetap memperhatikan mutu pelayanan dan keselamatan pasien serta bertanggung jawab terhadap pelayanan kesehatan yang diberikan serta menjamin keamanan data pasien.

Kewenangan dokter dalam telemedik meliputi anamnesa, pemeriksaan fisik tertentu yang dapat dilakuka nmelalui audiovisual, anjuran pemeriksaan penunjang, penegakan diagnosis, pengobatan, penulisan resep obat/alkes dan penatalaksanaan pasien, surat rujukan atau tindakan lebih lanjut.

Hasil pelayanan telemedik dicatatkan dalam catatan digital/manual sebagai dokumen rekam medik.

Salah satu upaya mencegah penyebaran Covid 19 pada pelayanan bidang kesehatan adalah dengan melakukan pembatasan kontak dengan pasien yang dapat diwujudkan dengan sistim telemedik.

VI. Penutup

Sebagai penutup, berikut adalah rekomendasi dari Majelis Pengembangan Pelayanan Keprofesian (MPKK) IDI pada Ketua Umum IDI No. 020/PB/MOOK/06/2020.

Rekomendasi
Majelis Pengembangan Pelayanan Keprofesian (MPPK)
Tentang
Pelayanan Telemedis Di Saat Pandemi Covid-19

1. Defenisi

a. *Tele-health*adalah integrasi antara sistem telekomunikasi dengan praktek kesehatan yang lebih bersifat preventif dan promotif.

b. *Telemedis* adalah penggabungan teknologi informasi komunikasi dengan kepakaran medis untuk memberikan layanankesehatan tanpa terbatas ruang atau dilaksanakan dari jarak jauh. Telemedis lebih mengacu kepada pelayanan kuratif.

2. Ragam Telemedis seacara garis besar terbagi menjadi :

a. *Tele-expertise*, yang menghubungkan dokter dengan dokter terkait ekspertise, misal interpretasi hasil radiologi, hasil EKG, atau second opinion

b. *Tele-konsultasi*, yang menghubungkan antara dokter dengan pasien

c. *Tele-monitoring*, petugas kesehatan memonitor berbagai parameter tubuh pasien secara virtual

d. *Tele-assistance*, memberikan arahan kepada pasien, misalnya pasien proses rehabilitasi

e. *Tele-robotik*, pengendalian jarak jauh terhadap sebuah robot, digunakan dalam tele-surgency

3. Permasalahan

a. Sejak tanggal 11 Maret 2020, WHO menetapkan Covid-19 sebagai pandemi global yang kemudian pada tanggal 31 Maret 2020 Presiden RI

menetapkan Darurat Kesehatan Nasional karena Covid-19 angka morbiditas dan mortalitas di Indonesia terus meningkat sehingga banyak pasien-pasien yang takut/khawatir untuk datang berobat secara tatap muka ke fasilitas kesehatan

b. Perlu meningkatkan kewaspadaan tenaga medis dalam menjalankan praktik di fasilitas pelayanan kesehatan (fasyankes) baik FKTP maupun FKTRL

c. Telah terbit surat edaran Kementerian Kesehatan RI No. HK.02.01/ MENKES/303/2020 tentang Penyelenggaraan Pelayanan Kesehatan Melalui Pemanfaatan Teknologi Informasi dan Komunikasi Dalam Rangka Pencegahan Penyebaran Corona Virus Disease 2019 (Covid-19)

4. Dasar Hukum

a. Undang-Undang No.29 tahun 2004 tentang Praktik Kedokteran

b. Undang-Undang No.36 tahun 2009 tentang Kesehatan

c. Peraturan Pemerintah No.46 tahun 2014 tentang Sistem Informasi Kesehatan

d. Peraturan Pemerintah No.47 tahun 2016 tentang Fasilitas Kesehatan

e. Keputusan Presiden Nomor 11 tahun 2020 tentang Penetapan kedaruratan Kesehatan Masyarakat Corona Virus Disease

f. Peraturan Menteri Kesehatan No.2052 tahun 2011 tentang Izin Praktik dan Pelaksanaan Praktik Kedokteran

g. Peraturan Menteri Kesehatan No.20 tahun 2019 tentang Penyelenggaraan Pelayanan Telemedicine Antar Fasilitas Pelayanan Kesehatan

h. Peraturan Konsil Kedokteran Indonesia No.74 tahun 2020 tentang Kewenangan Klinis dan Praktik Kedokteran Melalui Telemedicine Pada Masa Pandemi Covid-19 di Indonesia

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6. Rekomendasi kepada Dokter dan Fasyankes

a. Dokter yang melakukan praktik melalui telemedis wajib memiliki Surat Tanda registrasi (STR) dan Surat Izin Praktik (SIP) di fasyankes. Hal ini sesuai dengan Peraturan Konsil Kedokteran Indonesia No. 74 tahun 2020 yang juga didasarkan pada Peraturan Menteri Kesehatan No.2051 tahun 2011.

b. Pelayanan telemedis tidak bisa langsung antara tenaga medis dengan pasien tanpa melalui fasyankes. Kategori fasyankes mengacu kepada Peraturan Pemerintah No.47 tahun 2016 tentang Fasilitas Kesehatan.

c. Aplikasi telemedis yang digunakan dapat merupakan aplikasi yang dibangun oleh fasyankes ataupun kerjasama dengan pihak ketiga dengan pertimbangan mengenai aspek keamanan, kerahasiaan dan standarisasi data.

d. Mohon berhati-hati terhadap penggunaan aplikasi telemedis yang belum dipastikan aspek keamanan serta standarisasi rekam medik elektronik maupun resep elektronik. Pertimbangan mengenai aspek hukum kepemilikan dokumen dan isi rekam medik.

e. Kasus yang dapat ditangani melalui telemedis hanya kasus lama yang kondisinya stabil dan tidak termasuk dalam kategori kasus darurat medis.

f. Pasien yang dapat menjalani pelayanan telemedis harus pasien lama yang telah terdaftar di fasyankes tersebut.

g. Kasus yang ditangani harus sesuai dengan kompetensi dokter yang memberikan pelayanan.

h. Tindakan berupa anamnesis dan pemeriksaan fisik tertentu dilakukan melalui audiovisual yang mengacu kepada panduan yang diterbitkan oleh masing-masing perhimpunan sebagai dasar menegakkan diagnosis.

i. Jika diperlukan tindakan penunjang atau tindakan lanjut, pasien disarankan mendatangi fasyankes.

j. Penulisan resep dalam bentuk resep elektronik (e-prescribtion) harus sesuai dengan standar pelaksanaan resep elektronik. Dilarang untuk memberikan resep narkotika atau psikotropika kepada pasien melalui telemedis.

k. Perlu ditetapkan besaran jasa medis bagi dokter dalam melakukan pelayanan telemedis.

7. Rekomendasi kepada Pemerintah

a. Mendorong Kementerian Kesehatan segera menerbitkan peraturan Menteri Kesehatan khusus terkait Rekam Medik Elektronik.

b. Mendorong Kementerian Kesehatan segera menerbitkab peraturan Menteri Kesehatan khusu terkait pelaksanaan Resep Elektronok (e-prescribtion) dengan melibatkan Ikatan Dokter Indonesia (IDI) dan Ikatan Apoteker Indonesia (IAI).

c. Meningkatkan status Surat Edarab Menteri Kesehatan No. HK.02.01/ MENKES/303/2020 tentang Penyelenggaraan Pelayanan Kesehatan

Melalui Pemanfaatan Teknologi Informasi dan Komunikasi Dalam Rangka Pencegahan Penyebaran Corona Virus Desease 2019 (Covid-19) menjadi Peraturan Menteri dengan perbaikan substansi peraturan.

d. Pemerintah segera menyusun peraturan terkait pembiayaan jika pelayanan telemedis dapat dilakukan untuk pasien-pasien peserta Jaminan Kesehatan Nasional (JKN).

e. Jika diperlukan percepatan, Kementerian Kesehatan dapat membentuk Kelompok Kerja Khusus yang melibatkan pemangku kebijakan lain termasuk organisasi profesi.

f. Pemerintah wajib melakukan pengawasan penggunaan aplikasi telemedis oleh dokter maupun fasyankes untuk menghindarkan kerugian yang akan dialami oleh dokter, fasyankes, dan pasien.

Semoga rekomendasi ini dapat menjadi dasar pertimbangan Pengurus Besar IDI untuk segera menerbitkan Panduan Pelaksanaan Telemedis oleh Dokter saat Pandemi Covid-19 yang juga memuat panduang-panduan masing-masing perhimpunan terhadap anggotanya.

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Management of Refractory GERD

F Soemanto Padmomartono

Introduction

Gastroesophageal Reflux Disease (GERD) is one of the most common gastrointestinal (GI) disease in clinical practice worldwide, especially in western countries. GERD affected 18-28% of North American peoples, and 20-40% of Americans have GERD symptoms. GERD may impact to the quality of life (QoL), potential complications of GERD (eg ulcer, stenosis, Barrett, oesophageal cancer), and economic burden. The National GI Survey, population-based survey (by MyGiHealth), conducted to 71.812 peoples in US found that GERD symptoms was to be common: 2 of 5 participant had GERD symptoms in the past, 1 of 3 had symptoms in the past week, and the half of PPI user have persistent symptoms. GERD is a condition related to the reflux of gastric contents into the eosophagus, that lead to troublesome symptoms (classically heartburn and regurgitation), and it's complications. Empiric Proton-pump inhibitor (PPI) therapy is cost-effective strategy for the management of GERD. The majority of GERD patients have good response with empiric PPI therapy and life-style modification. However, approximately 10-40% GERD patients fail to respond GERD symptomatically, either partially or completely to PPI therapy. Almost 70% of GERD population are NERD type, and study results found the lowest response rate to one-daily PPI therapy 4 weeks compared to EE patients (37% NERD vs 56% EE). GERD patients that inadequate response to PPI therapy, were labelled as refractory GERD (rGERD). The definition of PPI refractory GERD is still controversial. PPI Refractory GERD (rGERD) is defined as the persistence troublesome GERD symptoms and adequate objective findings of GERD (elevated acid exposure and or reflux burden persist) despite optimised (twice-daily) PPI therapy after at least 8 weeks. Refractory GERD is a major clinical challenge for gastroenterologis, and the management of rGERD is potentially difficult and costly to diagnosis and treatment.

Differential diagnosis for Refractory GERD

Expert estimated that more than 2/3 of GERD patients refractory to PPI therapy referred to gastroenterologist are do not have GERD after several diagnostic testing. There are several diseases or conditions as a differential diagnosis of rGERD, that can be divided into 3 groups:

A. Insufficient acid suppression or increased reflux: including compliance, PPI timing, CYP2C19 polymorphism, weakly acidic reflux or non-acid reflux, nocturnal breakthrough, missed diagnosis unrelated to GERD, acid pocked, and duodenogastroesophageal reflux.

1. ***Proton-pump inhibitors:*** Poor compliance with PPI timing and adherence are very important as a cause of inadequate and rGERD. Studies showed the compliance were only 57 - 68 % patients filled their PPI prescription were 80% of the time. Timing is also important issue, the studies showed that only 46% of patients used PPI at proper time, and reported 36% of physician did not give proper direction and timing to their patients. In US, a study reported that 70% of primary care physicians and 20% of gastroenterologist encouraged their patients to take PPI at bedtime, or believed that timing to be unimportant. Administration PPI before meal provides better control of intragastric pH compared to during or after meal. Expertises and Gastroenterology Consensus recommend the optimal timing of PPI therapy is 30-60 minutes before breakfast.

2. ***Cytochrome P450 2C19 (CYP2C19) polymorphism***. PPIs are metabolised by liver enzyme CYP2C19 with 3 genotype: extensive, intermediate and poor metaboliser. PPI response rate varies between genotypes, poor metaboliser have the higher response to PPI, and 66% extensive metaboliser more likely to refractory to PPI. Currently, there is insufficient evidence of genetic polymorphism testing for rGERD. An empiric PPI therapy with CYP2C19-independent (rabeprazole and esomeprazole) provides more cost-effective than performing genetic testing

3. ***Weakly acidic or nonacid reflux***. Multivariate analysis studies found reflux episodes with mixed liquid-gas composition were significantly related with symptoms regardless or pH status of the reflux. The mechanism of weakly acidic or nonacid reflux is not completely understood, may be due to combination of mechanical distention and or reflux contents. Both bile acid and pepsin may be present in this condition, and may contribute to chemical irritation of the oesophageal lining, and make oesophageal pain and hypersensitive.

4. ***Nocturnal acid breakthrough (NAB)***. NAB sometimes happened in patients on PPI therapy. One study showed the efficacy of add-on H2RA (ranitidine) at night with omeprazole 20 mg twice daily almost complete eliminating NAB. However, another study showed the similar symptoms severity scores wether or not treated with ranitidine despite the reduction of NAB. Currently, there is insufficient evidence that NAB alone is significant cause of rGERD.

5. ***Missed diagnosis unrelated to GERD***. Current testing for GERD has limitations (uncomfortable, potential false-negative results) and GERD is chronic condition that esophageal testing for 48 hours period is likely fails to capture the chronic nature of GERD.

6. ***Acid pockets (AP).*** AP is refer to postprandial collection of strong gastric acid near the gastroesophageal junction that does not mixed with food. AP may migrate into oesophagus shortly after eating, causing reflux symptoms. PPI can reduce the size of AP and increase gastric pH. It.s not known how significantly the acid pocked contribute the rGERD.

7. **Duodenogastroesophageal refluks (DGER)**. DGER is refer to the reflux of duodenal content to stomach and into the oesophagus. Bile acid may play role in rGERD through either weakly acidic or nonacid reflux. More severe forms of GERD have been shown to have both acidic and bile reflux content compared to less severe forms. There is a significant association between DGER and rGERD, with 88% of PPI-rGERD patients having evidence of DGER compared to 27% of PPI responders.

B. Functional Esophageal Disorders.

Functional Gastrointestinal Disorders (FGID) are defined as symptomatic disorders without any evidence of organic etiology. **Functional Heartburn (FH) and Reflux Hypersensitivity (RH):** FH is define (by Rome IV criteria) as episodic retrosternal pain for at least 3 months with symptoms onset > 6 months, without evidence of reflux or underlying motility disorders (normal EGD, normal pH testing and negative association between symptoms and reflux events) It's estimated that 60% of rGERD as having FH. RH is define RH is defined (by Rome IV criteria) as retrosternal symptoms including heartburn and chestpain, for at least 3 months with symptoms inset >6 months, with normal EGD and absence evidence of EoE, major oesophageal motor disorders, and evidence of triggering of symptoms by reflux events despite normal acid exposure on pH or pH-impedance monitoring (response to anti secretory therapy does not exclude the diagnosis). RH is also define as increased oesophageal sensitivity to various chemical, mechanical, electrical and temperature stimuli, which may be related to enteric nervous system sensitisation to acid via dilated intracellular spaces in oesophageal mucosa. Some rGERD patients have been shown to have increased pain sensitivity to both mechanical and electrical stimuli. Furthermore, overlap could exist reflux event between true GERD and RH. Both FH and RH are also amplified by psychological stress. Psychological co-morbidities may provide an explanation of FH. Patients with poor correlation of symptoms with reflux events display high level of anxiety. In population-based study, found that anxiety and depression also demonstrated increased GERD-related symptoms. However, the exact role of psychological co-morbidities in relation to rGERD is still controversial.

C. Alternative Diagnosis Unrelated to GERD

There several diseases or conditions unrelated to GERD, can mimic of GERD, and should be considered for a patient with PPI-refractory symptoms, including: Zollinger-Ellison syndrome, Autoimmune skin condition (eg. Lichen plants), Pill-induced eosophagitis, Infection esophagitis, Caustic eosophagitis, Radiation-induced eosophagitis, Eosinophylic eosophagitis, Eosophageal

cancer, Achalasia, Gastroparesis, H. Pylori carrier status, and Rumination syndrome. The disorders that can lead to heartburn and or regurgitation deserve special attention. Refractory GERD can be distinguished from these condition by diagnostic testing.

1. **Eosinophilic Esophagitis (EoE)**: is an important clinical consideration in rGERD patients. EoE is also have an aero-allergen or food-allergen. Diagnosis is by EGD with biopsy revealing more 15 eosinophils per high power field. AGA recommended to EGD with oesophageal biopsy for all patients with rGERD to rule out EoE.

2. **Achalasia** is a rare oesophageal dysmotility disorder characteristic by aperistalsis and hypertensive LES to relax. Patients often complain of solid and liquid dysphagia, regurgitation and sometimes heartburn. Some patient may only report heartburn symptoms refractory to PPI that is actually retained food and liquid above LES. The diagnosis can be made by EGD and can be confirmed by oesophageal manometry.

3. **Gastroparesis.** Is characteristic by a delay of gastric emptying into a small intestine leading to increased reflux. Symptoms typically include epigastric pain, early satiety, postprandial bloating, and nausea.

Approach diagnosis for Refractory GERD patients.

Refractory GERD) is a major clinical challenge for gastroenterologist. Management for rGERD is potentially difficult and costly in diagnosis, treatment and management. To diagnosis or evaluate the several etiology of rGERD (refer to Diferential Diagnosis od rGERD) is may difficult to perform in the hospital and or gastroenterology centres with limited diagnostic testing modalities. Firstly, a careful patient history and physical examination can help determine the alarm symptoms that need to perform EGD.

The initial assessment of rGERD the physician should be sought the compliance to PPI therapy and specifically, and timing in relation to meal. Patients with continued symptoms should be careful reassessed, paying specific attention to the type of ongoing symptoms, and the degree to which symptoms may have improved or

worsened. It's important to recognize that complete relief of heartburn with PPI occur at rate 11.5% per week. Thus, endoscopic healing and symptoms generally achieved in 8 weeks in the majority of patients, but in severe eosophagitis (Los Angeles stage C n D) may take longer to healing. (approximately 12 weeks).

The diagnostic modalities for rGERD are including: upper endoscopy, reflux testing, impedance pH testing, high-resolution oesophageal manometry, and gastric emptying testing. However, this complete diagnostic modalities may be available only in tertiary referral hospital or gastroenterology centre. In primary health care unit and primary hospital may need careful patient history, physical exam and use some modalities (eg. laboratory, USG, EGD-scopy), and more attention to the specific symptoms and sign related to specific diseases or conditions as a cause or may be influence to the refractory symptoms (refer to Diferential Diagnosis of rGERD). And the physician can empiric treatment patient according the specific symptoms and signs of the patients.

Management for Refractory GERD patients.

The management strategy for rGERD patients expand beyond PPI to include other pharmacologic or invasive interventions. Since mechanisms of PPI refractory GERD are varied, the choice of management strategy should be personalized to the patients needs and mechanistic dysfunction. There are several treatment modalities for rGERD patients, are include:

A. General measures.

Lifestyle and dietary modification should be reinforced. Lifestyle modification include weight loss for patients overweight, stop smoking, elevation at the head of the bed in patients with NAB. Dietary modification including avoidance of identified some food or drink that triggering symptoms, regular meal time and meal volume (low portion. low fatty food), less or stop alcohol, coffee or heavy fatty food., refraining from assuming a supine position after meals and avoidance of meals 3 hours before bedtime.

B. Medical therapy and psychotherapy for rGERD

1). PPI. Optimizing PPI therapy is still have benefit effect in patients with non-compliance and or improper timing of PPI therapy, and to the patients with normal endoscopy, pH testing or impending testing. Optimal timing for one daily PPI therapy is 30-50 minutes before breakfast. An effort to increase compliance is very important to improve PPI response therapy. The empiric PPI therapy with CYP2C19-independent PPI therapy (rabeprazole, esomperazole) is reasonable as the first step.

2). H2RA. H2RA can be use to help reduce nighttime heartburn in conjunction with double dose PPI. Although there controversy regarding H2RA help to reduce NAB, studies have shown in patients on both double PPi and nightly H2RA, nighttime reflux are improve and less sleep disturbance. Due to H2RA tolerance, the benefit or adding H2RA may wane over time.

3). **Alginate antacids.** Alginate antacids (such as Gaviscon) work by forming a mechanical barrier between gastric content and the lower oesophageal spinchter (LES) when exposed to gastric acid. Alginate antacids may be effective in controlling post-prandial heartburn and have a benefit in controlling postprandial heartburn and regurgitation. When exposed to gastric acid, alginates precipitate and form a floating raft to function as physical barrier between gastric content and the LES. The low side effect and unique mechanism of action make alginate helpful to partial PPI response.

4). GABA-agonist. ABA-agonist (such as Baclofen) have been shown to decrease thenumber of TELSR event and reduce heartburn and regurgitation symptoms in PPI refractory GERD when compared to placebo. Potential side effect of GABA agonist including CNS depression, should be considered when selecting patients to start therapy.

5). Prokinetics. Prokinetics (cisapride, metoclopramide, etc) as add-on of PPI therapy may be helpful in rGERD patients with evidence of gastroparesis

6). Neuromodulators. Tricyclic antidepressant (TCA, imipramine), selective serotonin reuptake inhibitors (SSRI, fluoxetine). For patients with functional heartburn or reflux hypersensitivity, neuromodulators with the aim to decrease the pain processing pathway of the central nervous system have benefit in rGERD with this conditions. PPI with add-on neuromodulators reduce the incidence of heartburn over the placebo or PPI alone.

7). Psychoterapy, Hypontherapy and Accupuncture. Psychoterapy and hypnotherapy may be have benefit in rGERD patients with evidence or assuming related to psychological conditions (stress, anxiety, depression, etc). If physician unable to handle of patients psychological problems, is better to consult psychologist, hypnotherapy or psychiatrics. Acupuncture has been evaluated in rGERD patients. Small randomised trials in rGERD showed that the acupuncture group (PPI plus accupuncture) had significant improvement in heartburn and regurgitation compared to PPI alone. Additional studies are needed to define the role of acupuncture in rGERD patients.

8). Potassium-Competitive Acid Blocker (P-CAB). Vonoprazan, is an effective P-CAB, exhibited rapid, strong, and continuous gastric acid suppression. Vonoprazan was significantly effective in the treatment of H.pylori infection, GERD, and LDA-induced peptic ulcers. Vonoprazan also effective for PPI-resistent reflux esophagitis and PPI-resistent symptoms. More RCT studies with adequate sample size are needed to define the role of Vonoprazan for rGERD patients.

C. Endoscopic therapy for rGERD

Endoscopic therapy for rGERD in whom do not response to medical therapy may need endoscopic therapy, such as: **transoral incisionless fundoplication (TIF), radiofrequency ablation (RFA).** In TEMPO study, for 6-months follow-up TIF was superior to high dose PPI in regurgitation, improvement in GERD-reported outcome, and oesophageal pH. But, after 5-

years follow-up, showed that 34% patients need one daily PPI as compare 100% patients at screening. It's mean that TIF may be limited to predominant regurgitations symptoms. In the long-time period follow-up after TIF, some patients with heartburn may need for PPI therapy. In RFA study (Stretta, Restech) result for rGERD, in 10-years follow-up 70% patients showed normalisation of quality of life (GERD-HRQL). However due to lack of controlled data and lack of physiologic testing, it's sill need further prospective controlled trials with physiologic testing to determine the role of RFA in rGERD.

D. Anti-reflux surgery (ARS) for rGERD

Laparascopic fundoplication (Nissens, LNF) may be useful for typical GERD symptoms responsive to PPI therapy. Predictive factors to response of ARS include at least 50% symptoms improvement with PPI therapy, compliance with anti-reflux medications, typical symptoms of GERD, and objective findings of acid reflux. Caution should be made to careful selection of rGERD patients for ARS. Success rate of this surgery range from 67% to 95%, and are highly dependent to surgeon expertise, adequate preoperative evaluation and patient selection.

Magnetic Sphinter Augmentation (MSA). Minimally invasive antireflux surgery offered the new modalities for anti reflux surgery, including MSA. In retrospective case-control series of MSA and LINK, the results showed that both techniques were improved the GERD-HRQL, and the ability to belch and feeling gas and bloat. The limitation of MSA in rGERD are lack of prospective or randomized data, and lack of power for primary outcome of the study, not just patient-reported outcome.

The physicians or gastroenterologist in referral hospital and gastroenterology centre can read and may follow the recent management algorithm of Refractory GERD (Naek, et all, Gastroenterology Hepatology, April 2020) (see appendix)

Summary

GERD is common in clinical practice and usually can be treated with lifestyle modification, dietary modification and empiric PPI therapy. Mostly patients have good response to this treatment strategy. However, in some patients have inadequate or non response to this treatment and patient are labelled as Refarctory GERD (rGERD). There are several cause, diseases or conditions as the differential diagnosis of rGERD. A careful history of symptoms, response to PPI therapy, adherence, compliance, and timing should be evaluate. Optimizing PPI therapy, and may add-on to other therapy may help to improve the persistence symptoms. When patients are still refractory, alternative causes must be considered, and some modalities diagnostic such as EGD, and other testing (reflux test,. impedance pH test, high-resolution oesophageal manometry, and gastric emptying test) may be helpful to have specific diagnosis of rGERD. Further therapy including several medical therapy, endoscopic therapy and antireflux surgery may be use to treat specifically to the specific cause of rGERD patients. It's hope that further management in accordance with the real cause of rGERD will be great benefit to the patients.

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Appendix

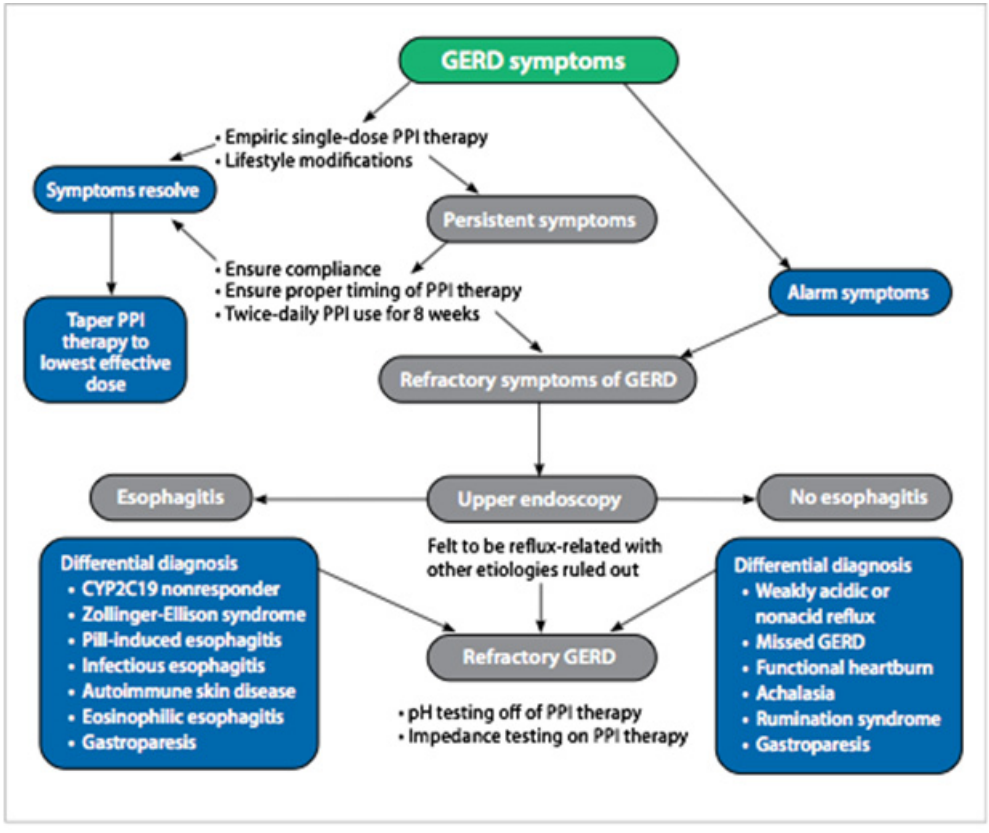

Figure. Management algorythm for refractory symptoms of GERD

Semarang Gastroentero-Hepatology Update 2020

Update in Management of IBS-C and Chronic Idiopathic Constipation

Ari Fahrial Syam

Konstipasi adalah gejala defekasi yang tidak memuaskan, yang ditandai oleh buang air besar kurang dari 3x dalam 1 minggu atau kesulitan dalam evakuasi feses akibat feses yang keras. Pada Kriteria ROME IV "Konstipasi kronik" didefinisikan sebagai adanya gejala-gejala di atas yang telah berlangsung sekurang-kurangnya 3 bulan. Kriteria diagnosis IBS Rome 4 tahun 2016, nyeri perut berulang rata-rata sedikitnya 1 hari per minggu sedikitnya dalam 3 bulan terakhir, berhubungan. Dengan 2 atau lebih kriteria berikut yang berhubungan dengan 2 atau lebih yang berubungan dengan defekasi, berhubungan dengan perubahan frekuensi buang air besar, berhubungan dengan bentuk feses. Kriteria ini terpenuhi jika terjadi selama 3 bulan terakhir dengan onset gejala minimal 6 bulan sebelum diagnosis ditegakkan.

Secara praktis jika kita merujuk bentuk feses yang kita gunakan adalah *Bristol stool chart.* Chart ini membagi bentuk feses menjadi 7 dari tipe 1 sampai tipe 7. Tipe 1 berbentuk keras dan sulit untuk dikeluarkan sedang tipe 7 bentuk cair. Sedang bentuk normal tipe 4, sedang konstipasi umumnya pada tipe 1 sampai tipe 3. Faktor risiko konstipasi yang perlu menjadi perhatian buat para klinisi adalah konstipasi lebih sering terjadi pada wanita daripada laki-laki, aktivitas fisik kurang, asupan makanan yang kurang, diet rendah serat, obat-obatan, depresi serta riwayat pelecehan seksual. Faktor risiko konstipasi yang berhubungan dengan penyakit antara lain neurologi (Parkinson's, stroke), penyakit metabolic (DM, hiperkalsemia, hipotiroid), pseudoobstruksi usus, mekanik (tumor, penyumbatan, diverticulosis). IBS saat ini dibagi menjadi 3 subtipe: yaitu IBS-C dengan dominasi konstipasi, IBS-D dengan dominasi diare dan IBS M yang merupakan campuran dari kedua gangguan buang air besar tersebut. Pasein yang tidak masuk pada tiga tipe tersebut dipertimbangkan sebagai IBS yang tidak bisa diklasifikasi (*unclassified*).

Pasien konstipasi fungsional bisa datang sebagai IBS-C atau konstipasi kronik idiopatik (*chronic idiopathic constipation*), kedua gangguan gastrointestinal fungsional

yang umumnya terjadi ini bisa berdampak pada kualitas hidup dan bisa menimbulkan beban ekonomi yang signifikan pada sistim pelayanan Kesehatan.

Penderita konstipasi perlu mendapatkan terapi komprehensif untuk mengembalikan fungsi BAB yang fisiologis. Pada pasien konstipasi kronik yang tidak menunjukkan tanda alarm dan diduga tidak ada konstipasi sekunder, terapi empirik dapat dimulai. Terapi empirik dapat diberikan dengan terapi obat dan non obat. Terapi non-farmakologis (modifikasi gaya hidup) antara lain meningkatkan konsumsi makanan berserat dan minum yang cukup, meningkatkan aktivitas fisik, mengatur kebiasaan defekasi, menghindari mengejan, membiasakan buang air besar setelah makan atau waktu yang dianggap sesuai dan cukup, menghindari obat-obatan yang dapat menyebabkan konstipasi.

Terapi farmakologis terdiri dari *Bulk laxative : psyllium, plantago ovata, methyl cellulose*, laksatif osmotik (saline laxative: magnesium hidroksida, sodium phosphate, disakarida yang tak diserap : laktulosa, *sugar alcohol*: sorbitol, mannitol, *poly ethylene glycol*/PEG), laksatif stimulan : bisacodyl (Dulcolax®), anthraquinone, castor oil, sodium picosulphate, stool softener (dioctyl sodium sulphosuccinate), rektal enema / suppositoria : phosphate enema, bisacodyl, prokinetik : tegaserod (sudah ditarik). Terapi empirik ini dievaluasi selama 2-4 minggu. Bila tidak ada perbaikan maka harus dilakukan investigasi lebih lanjut.

Selain mengatasi kontipasi yang terjadi terapi antispasmodic juga penting dalam terapi pasien konstipasi. Sudah diketahui bahwa subgroup pasien IBS akan mengalami perubahan transit gastrointestinal dan kontraktilitas usus halus abnormal yang menyebabkan terjadi gangguan pada kebiasaan buang air besar dan menimbulkan nyeri. Obat yang masuk golongan antispasmodik ini mempunyai mekanisme kerja yang bermacam-macam antara lain antikolinergik (missal butyl scopolamine, hyoscine, cinetropiumn bromide, pirenzepine), relaksan usus halus langsung (papaverine, mebeverine) dan calcium channel blocker (alverine citrate, otilonium bromide, pinaverium bromide). Obat-obatan ini berkontribusi untuk menghilangkan nyeri pada IBS.

Pendekatan Diagnosis dan Manajemen Hematokezia, dari Layanan Primer Sampai Tersier

Didik Indiarso

Pendahuluan

Hematokezia didefinisikan sebagai keluarnya darah merah segar atau maroon dari rektum. Secara klasik hematokezia diidentikan dengan perdarahan saluran cerna bagian bawah (PSCBB), yang didefinisikan sebagai perdarahan yang bersumber dari distal ligamentum Treitz. Perdarahan dari usus halus atau saekum dapat bermanifestasi sebagai melena (berak hitam seperti petis/ter), sebaliknya perdarahan saluran cerna bagian atas (PSCBA) yang masif dapat bermanifestasi sebagai hematokezia.

Tabel 1. Etiologi Hematokesia berat pada Kolon (%)

	Studi			
Lesi	A[1]	B[2]	C[3]	D[4]
Divertikulosis	**30**	**33**	N/A	**33**
Kanker kolon atau polip	18	21	28.6	5.2
Kolitis	17	17	12	N/A
Kolitis Iskemik	N/A	7	N/A	11.2
IBD	N/A	4	N/A	3.6
Kolitis non-infeksi	N/A	5	N/A	2.7
Kolitis infeksi	N/A	1	N/A	1.2
Angioektasia	7	6	N/A	5
Ulkus pospolipektomi	6	N/A	N/A	7.8
Ulkus rektum	N/A	1	N/A	8.4
Hemoroid	N/A	20	**44.7**	10.3
Anorektal lain	4	3	N/A	1.8
Kolitis Radiasi	0	0.5	N/A	2.2
Ulkus anastomosis kolon	N/A	N/A	N/A	2.1
Lain-lain	8	3	N/A	4.1
Tidak diketahui	16	0	14.7	0

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Prevalensi hematokezia mencapai lebih dari 20% populasi dewasa, dengan angka hospitalisasi 21 per 100.000. Spektrum klinis cukup luas dari perdarahan yang mengancam jiwa hingga yang ringan berhenti spontan. Spektrum klinis tersebut membutuhkan pendekatan diagnostik yang tepat agar tidak terlalu *over diagnosis* atau sebaliknya *under diagnosis*. Kasus yang ringan harapannya bisa ditangani dilayanan primer, tetapi kasus berat atau berisiko perdarahan ulang sebaiknya ditangani di layanan sekunder atau mungkin tersier.

Etiologi yang sering dari laporan di luar negeri adalah perdarahan divertikular (30-33%). Studi di Indonesia pernah dilaporkan etiologi yang sering adalah perdarahan dari hemoroid varises (52%). Etiologi dari hematokesia dapat dilihat pada tabel 1 disamping.

Pendekatan Diagnosis Hematokezia

Seperti disebut sebelumnya spektrum klinik hematokezia cukup luas, pasien dengan sasaran penting dalam pendekatan diagnosis hematokezia adalah untuk menentukan derajat keparahan penyakit dan menentukan lokasi serta etiologi perdarahan. Pada saat pasien datang harus dilakukan anamnesis terarah, pemeriksaan fisik yang terstruktur dan pemeriksaan penunjang yang tepat. Terdapat beberapa langkah yang penting agar dapat dicapai diagnosis yang akurat sehingga bisa dilakukan manajemen pengelolaan yang tepat Langkah-langkah pendekatan diagnostik hematokesia sebagai berikut :

1. Evaluasi instabilitas hemodinamik

Evaluasi awal pasien dengan hematokezia adalah evaluasi hemodinamik. Pasien yang disertai gangguan hemodinamik, maka pertimbangan pertama asal perdarahan adalah dari saluran cerna atas, mempunyai risiko mortalitas yang tinggi. Penyebab tersering adalah penyakit ulkus peptikum (PUP) disusul varises esofagus maupun gaster, fistula aortoenterik dan lesi Dielafoy.

Tabel 2. Prediktor dini keparahan dan perdarahan ulang pada saluran cerna bawah

Perdarahan:
Denyut jantung > 100 kali/mnt
Tekanan darah sistolik < 115 mmHg
Sinkop
Tidak ada nyeri tekan abdomen
Masih ada perdarahan perektal dalam 4 jam masuk RS
Aspirin
Lebih dari 2 penyakit komorbid

Anamnesis awal diarahkan untuk menggali informasi tentang adanya riwayat sinkop dan gejala presinkop. Tanda vital dievaluasi adanya takikardi, hipotensi atau hipotensi ortostatik yang terkait dengan kehilangan darah. Pada pasien dengan instabilitas hemodinamik, stabilisasi pasien lebih diutamakan daripada diagnosis pasien. Segera dilakukan resusitasi cairan intra vena secara agresif dengan sasaran normalisasi tekanan darah dan denyut jantung. Tranfusi dengan PRC diberikan untuk menjaga Hb diatas 7 g/dL atau lebih tinggi pada kondisi dengan komorbid.

Dilakukan segera stratifikasi risiko terhadap pasien dan dirawat di ruang intensif jika terdapat terdapat risiko tinggi. Prediktor awal terhadap tingkat keparahan dan risiko perdarahan ulang pada PSCBB dipaparkan pada tabel 2.

Pasien dengan risiko rendah (tidak ada faktor risiko) memiliki risiko perdarahan ulang 0%, risiko sedang (1-3 faktor risiko) 45% perdarahan ulang dan risiko tinggi (>3 faktor risiko) 77% terjadi perdarahan ulang.

Setelah pasien stabil dapat dilakukan anamnesis yang lebih mendalam untuk mencari kemungkinan etiologi. Konsumsi NSAID harus ditanyakan karena faktor risiko yang kuat untuk PUP. Riwayat penyakit hati sebelumnya, diagnosis hepatitis atau konsumsi alkohol dapat mengarahkan ke perdarahan variseal. Riwayat aneurisma aorta abdominal atau prostetik intra-aortik graft kemungkinan berhubungan dengan fistula aortoenterik. Pemeriksaan fisik penting dicari tanda stigmata hati kronik.

Pemasangan NGT dapat dikerjakan untuk diagnosis kemungkinan PSCBA dengan aspirasi isi gaster, tetapi beberapa studi tidak menunjukan superioritas dalam outcome pasien. NGT dapat juga digunakan untuk mempermudah prosedur pembersihan kolon untuk persiapan kolonoskopi. Dalam menegakan diagnosis PSCBA dapat mengunakan rasio peningkatan ureum terhadap kreatinin. Rasio ureum : kreatinin > 30 : 1 menguatkan kemungkinan sumber perdarahan dari atas. Disamping akibat PSCBA, hematokesia dengan instabilitas hemodinamik juga bisa berasal dari perdarahan divertikular yang masif. Sehingga pasien harus ditanya riwayat kolonoskopi sebelumnya.

2. Manifestasi Perdarahan

Menentukan tingkat keparahan dan lokasi perdarahan dapat diperkirakan dengan melihat durasi, frekuensi, volume dan warna darah dari hematokesia. Perdarahan dari saluran cerna atas yang bermanifestasi sebagai hematokesia yang berat, pasti berdampak instabilitas hemodinamik, dibandingkan PSCBA yang lebih ringan dengan manifestasi melena. Perdarahan dari usus halus dan kolon dapat bermanifestasi sebagai berak darah merah segar atau maron dengan volume sedang, dalam beberapa refensi mendiskripsikan sebanyak “secangkir” darah. Perdarahan dari kelainan di anorektal bermanifestasi sebagai perdarahan “outlet” yaitu bercak / garis darah segar pada feses atau darah menetes setelah defekasi. Perdarahan outlet tersebut mengindikasikan sumber perdarahan dari hemoroid interna, ekterna atau fisura ani.

Tabel 3. Diagnosis banding hematokezia berdasarkan Nyeri

Tanpa Nyeri	Disertai Nyeri
Karsinoma kolorektal	Penyakit Ulkus Peptikum
Divertikular hemoragik	Iskemia intestinal
Malformasi arteriovena (AVM)	*Inflammatory bowel disease* (IBD)
Polip kolon	Ulkus rektum soliter
Proktitis radiasi	Hemoroid eksterna
Hemoroid internal	Fisura ani

3. Nyeri abdomen atau Pelvis

Hematokesia dengan nyeri abdomen atau pelvis mempunyai diagnosis banding yang berbeda dengan tanpa nyeri, sehingga harus ditanyakan. Hematokesia yang berasal dari karsinoma kolorektal, divertikular hemoragik, malformasi arteriovena (AVM), polip kolon, proktitis radiasi dan hemoroid internal biasanya tidak terdapat nyeri. Untuk membedakan etiologinya harus berdasarkan kolonoskopi.

Proktitis radiasi sebagai kemungkinan etiologi jika ada riwayat radiasi eksternal daerah abdomen. Perdarahan post-polipektomi juga tanpa nyeri, bisa sebagai penyebab hematokesia jika terdapat riwayat polipektomi dalam 30 hari terakhir.

Hematokesia disertai nyeri abdomen, penyebab paling mungkin adalah PUP, Iskemia intestinal dan inflammatory bowel disease (IBD). PUP sering disertai nyeri epigastrik atau kwadran kanana atas yang berkaitan dengan makan. Pasien dengan iskemia kolon disertai dengan nyeri kram abdomen ringan hingga sedang yang mendahului defekasi beberapa jam sebelumnya. Nyeri pada Iskemia mesenterika akut lebih berat, lokasi periumbilikal dan nyeri tidak proposional dengan temuan fisiknya. Nyeri pada IBD bersifat nyeri kram kronik yang memberat selama eksaserbasi akut, dan disertai gejala lain seperti diare, penurunan berat badan dan komplikasi penyakit (obstruksi usus, abses perianal dan fistula). Pasien dengan Ulkus rektum soliter, hemoroid eksterna dan fisura ani mungkin tidak mengeluh nyeri abdomen tetapi terdapat nyeri saat defekasi dan riwayat konstipasi.

4. Pemeriksaan Colok Dubur (Rectal Touche/RT)

Pemeriksaan RT sangan penting dalam mengidentifikasi kelainan pada anorektal dan konfirmasi warna kotoran. Inspeksi pada RT, kita evaluasi adanya hemoroid eksternal, ukuran atau ada tidaknya inflamasi. Dilihat juga tanda-tanda perianal dari penyakit Crohn seperti skin tag, fisura ani, abses perianal atau fistula. Pasien diminta melakukan valsava

manuver, kita nilai desensus perineal, jika tidak terdapat desensus mungkin terdapat disfungsi dasar panggul yang menyebabkan konstipasi, sebagai faktor risiko hemoroid dan fisura ani.

Palpasi pada RT dimulai dengan evaluasi nyeri saat jari mulai masuk, nyeri yang hebat saat RT bisa disebabkan oleh fisura ani, hemoroid eksternal dan abses perianal. Adanya stenosis anal bisa disebabkan oleh penyakit Crohn. Pemeriksaan harus melakukan palpasi internal untuk evaluasi hemoroid internal, massa rektum dan kontraksi puborektalis saat valsava. Setelah pemeriksaan komplet, perhatikan ujung jari sarung tangan apakah terdapat darah.

5. Pertimbangan Diagnosis Banding Perdarahan Saluran cerna yang tidak jelas

Pasien dengan hematokezia jika dugaan sumber perdarahan bukan dari saluran cerna atas, maka pemeriksaan kolonoskopi menjadi pilihan modalitas pertama, kecuali jika klinisi cukup “percaya diri” yakin bahwa sumber perdarahan dari anorektal dengan pemeriksaan RT. Jika kolonoskopi tidak bisa mengungkap sumber perdarahan EGD menjadi modalitas berikutnya. Tetapi jika kedua pemeriksaan ini normal maka disebut perdarahan saluran cerna tidak jelas (*obscure*), yaitu didefinisikan sebagai perdarahan yang masih berlangsung dan tidak dapat dijelaskan meskipun sudah dilakukan kolonoskopi dan EGD. Perdarahan ini dapat terjadi pada 5% dari PSCBB. Penyebab paling umum adalah perdarahan pada usus halus, walaupun masih mungkin perdarahan tidak teridentifikasi pada endoskopi sebelumnya.

Diagnosis banding berdasarkan umur pasien. Pada pasien usia muda (< 20 tahun) penyebab paling mungkin adalah divertikel Meckel atau penyakit Crohn. Pada usia pertengahan (20-60 tahun) penyebab tersering tumor vaskular usus halus (Gastrointestinal stromal tumor (GIST) dan tumor Karsinoid), penyakit Crohn dan AVM. Varises pada usus halus juga mungkin didapatkan pada pasien dengan sirosis hati.

Kolonoskopi Sebagai Modalitas Diagnosis Dan Terapi

Sebaiknya semua pasien dengan hematokesia dilakukan kolonoskopi sebagai modalitas awal baik sebagai diagnosis maupun terapi. Tujuan kolonoskopi adalah identifikasi titik perdarahan dan melakukan hemostatik sesuai indikasi. Temuan kolonoskopi sebagai penyebab perdarahan seperti pada tabel 1 diatas. Dalam kolonoskopi, mukosa kolon harus dievaluasi dengan teliti, baik saat insersi maupun saat menarik skop. Rekomendasi dari AGA agar setiap residu kotoran dan darah harus dibersihkan dengan agresif untuk menghindari hasil negatif palsu. Direkomendasikan juga agar skop mencapai ileum terminal untuk menyingkirkan sumber perdarahan dari sebelah proksimal kolon.

Persiapan pembersihan kolon merupakan hal yang sangat penting sebelum kolonoskopi. Segera setelah pasien stabil hemodinamik mulai dilakukan pembesihan kolon yang adekuat dengan 4-6 L larutan polyethylene glycol dalam 3-4 jam sampai kotoran menjadi cair jernih. Tidak direkomendasikan kolonoskopi tanpa persiapan pembersihan kolon.

Pada pasien hematokesia dengan gambaran klinis risiko tinggi disertai tanda atau gejala perdarahan yang masih berlangsung, sebaiknya segera dilakukan persiapan pembersihan kolon setelah hemodinamik stabil dan dilakukan kolonoskopi dalam 24 jam kemudian. Rekomendasi ini didasarkan akan kebutuhan terapi hemostatik pada kasus tersebut, dimana akan meurunkan risiko perdarahan ulang, pembedahan emergensi dan panjang perawatan rumah sakit. Terapi hemostatik diindikasikan pada lesi dengan stigmata perdarahan risiko tinggi, yaitu perdarahan aktif (spurting dan oozing), lesi nampak pembuluh darah dan tertutup klot darah. Beberapa modalitas terapi hemostatik pada hematokezia dapat dilihat pada tabel 4 diatas.

Tabel 4. Modalitas hemostatik pada kolonoskopi

Jenis perdarahan	Modalitas
Perdarahan Divertikel	*Trough the scope endoscopic clipsContact thermal teraphyBand ligation*
Perdarahan Angioektasia	*Argon plasma coagulation*
Perdarahan post-polypectomi	*Mechanical clipcontact thermal teraphyw or w/o epinephrine injection*

Intervensi Non-Kolonoskopi

Intervensi non-kolonoskopi dilakukan dalam 2 kondisi yang berbeda. Kondisi pertama jika telah dilakukan modalitas kolonoskopi dan EGD dengan hasil negatif. Tujuan intervensi non kolonoskopi ini untuk evaluasi sumber perdarahan pada usus halus. Modalitas yang direkomendasikan adalah video kapsul endoskopi dan Computed tomography (CT) enterography. Kondisi yang kedua terjadi jika kolonoskopi tidak bisa dikerjakan pada kondisi hemodinamik tidak stabil sehingga preparasi kolon tidak bisa dikerjakan atau terapi hemostatik pada kolonoskopi tidak bisa menghentikan perdarahan. Tujuan untuk menghentikan perdarahan akut pada kolon. Modalitas yang direkomendasikan adalah intervensi radiologi dengan angiografi untuk embolisasi, CT angiografi dan intervensi pembedahan.

Kesimpulan

Hematokesia merupakan problem klinis yang sering didapatkan, dengan spektrum klinis yang luas dari yang mengancam jiwa hingga klinis tidak bermakna. Dibutuhkan pendekatan diagnosis yang tepat agar pasien mendapatkan perawatan sesuai tingkat layanan kesehatan. Terdapat 5 langkah pendekatan diagnosis yaitu dimulai dengan evaluasi instabilitas hemodinamik, evaluasi manifestasi perdarahan, tanyakan nyeri abdomen, lakukan pemeriksaan RT dan mempertimbakan diagnosis banding perdarahan saluran cerna yang tidak jelas. Kolonoskopi menjadi modalitas pertama dan utama pada hematokesia. Intervensi non-kolonoskopi dilakukan jika hasil kolonoskopi negatif atau hemostatik kolonoskopi tidak bisa dikerjakan atau tidak berhasil.

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Semarang Gastroentero-Hepatology Update 2020

Colorectal Cancer Screening Who, When and How to Test

Jacobus Albertus

The global burden of colorectal cancer (CRC) has been rising rapidly with population growth, changes in demographics and Westernization of lifestyle habits. It was estimated to have 18.1 million new cancer cases, and 9.6 million deaths caused by cancer in year 2018. CRC is the second commonest diagnosed cancer and the second leading cause of cancer-related mortality. According to the World Health Organization (WHO) GLOBOCAN database, there are 1,849,518 estimated new CRC cases and 880,792 CRC-related deaths in 2018. Regional estimates show that among half of the new cases, deaths and 5-year prevalent cases were found in Asia.

Colorectal cancer (CRC) screening is the process of detecting early-stage CRCs and precancerous lesions in asymptomatic people with no prior history of cancer or precancerous lesions. The U.S. Multi-Society Task Force of Colorectal Cancer (MSTF) is a panel of expert gastroenterologists representing the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy. The MSTF, like others, has long endorsed systematic offers of CRC screening to average-risk persons (persons without a high-risk family history of colorectal neoplasia) beginning at age 50 years.

A common statement made with regard to CRC screening is that “the best test is the one that gets done.” The MSTF endorses this concept because it is generally better for any person who is eligible to be screened to undergo some screening test rather than not be screened at all. On the other hand, the core concept underlying sequential testing is that offering the “best” test(s) first optimizes the sensitivity and or cost-effectiveness of screening and still leaves the opportunity to offer other tests when patients decline. Achieving the goal of increasing the uptake of CRC screening in the United States to 80% by 2018 may have a considerable public health impact by averting approximately 280,000 new cancer cases and 200,000 cancer deaths

within < 20 years. The tier 1 tests representing the cornerstone of CRC screening are colonoscopy every 10 years and annual FIT. The use of these 2 tests as the primary screening measures provides a framework for screening that is simple and accommodates almost every screening setting.

There is evidence for the presence of SARS-CoV-2 RNA in stool specimens independent of the presence of diarrhea. Endoscopy units face significant risks and challenges. Recent position statements from some endoscopy societies warned about the significant exposure to droplets from patients during maneuvers requiring close contact (less than 1 meter), e. g. resuscitation maneuvers and endoscopy, particularly if they last more than 15 minutes studies showed that stool continued to be positive for SARS-CoV-2 RNA even after respiratory samples became negative. Restriction of mobility, patients' fear of becoming infected, and the safety procedures to be followed for avoiding a possible contagion may result in a limitation to perform a colonoscopy. Among the procedures being delayed are colonoscopies, the most commonly used test to screen for and prevent colorectal cancer, nearly 23 million adults aged 50 to 75 are past due for screening, and an estimated 53.000 Americans will die from colorectal cancer this year. Delaying colorectal cancer screening for the 23 million adults who are past due will lead to delayed diagnoses and cancer deaths. While it is impossible to know how much screening will be missed because of the pandemic, a look at the number of new colorectal cancer cases projected for 2020 in the U.S., two months with little or no screening theoretically could postpone diagnosis of cancer in 24,650 patients, among those some 9,860 cancers that may be at an advanced stage already. Telemedicine also provides an opportunity to communicate with patients and provide continued patient care while reducing risk of exposure to COVID-19 to patients and health care workers.

Kualitas Kolonoscopi untuk Meningkatkan *Adenoma Detection Rate*

T Yuli Pramana

Kolonoskopi digunakan secara luas untuk mendiagnosis dan menterapi kelainan kolon. Tindakan kolonoskopi yang benar, secara umum adalah aman, akurat dan cukup ditoleransi. Visualisasi mukosa seluruh usus besar dan ileum terminalis distal biasanya dapat dikerjakan selama kolonoskopi.

Kualitas kolonoskopi dapat dinilai dari strukturnya, proses dan 'outcome'/ hasil. Struktur meliputi infrastruktur yang memadai termasuk fasilitas (tempat dan alat) dan training bagi dokter. Proses kolonoskopi dan hasil mengacu pelaksanaan kolonoskopi dan hasil berupa status kesehatan serta hasil dari struktur dan proses konoskopi (missal adanya perforasi kolon dan deteksi adenoma).

Indikator kualitas konoskopi dicermati pada tiga periode: preprosedur, intraprosedur dan postprosedur. Preprosedur dimulai dari semua kontak dengan pasien, penetapan indikasi, 'informed consent', kualitas 'urus-urus'/ 'bowel preparation', sampai dengan sedasi atau insersi skop. Intraprosedur mencakup insersi skop sampai penarikan-keluarnya skop; postprosedure mencakup pembuatan laporan dan dokumentasi serta pemulihan pasien dan 'follow up'.

Persiapan kolonoskopi / 'bowel preparation' salah satu parameter penting, menjadi indicator kualitas kolonoskopi. Persiapan kolonoskopi ini akan berpengaruh kepada indicator kualitas kolonoskopi yang lain, yakni: 'ADR : adenoma detection rate', waktu penarikan-keluar skop dan intubasi skop ke 'caecum'.

Kualitas Intraprosedur kolonoskopi, selain endoskopist akan dipengaruhi fasilitas dan peralatan juga teknik colonoskopi yang digunakan. Teknologi endoskopi ditingkatkan, antara lain adanya fasilitas NBI (Narrow-band imaging), FICE (Fujinon Intelligent color enhancement), i-SCAN colonoscopy, autofluorescence imaging, Full spectrum endoscopy, transparent cap, endocuff, G-eye ballon endoscope.

Pemakaian sedasi dan propofol meningkatkan ADR; begitu juga pemakaian teknik ‘Water Exchange’ atau ‘water immersion’.

ADR merupakan indicator penting dalam kolonoskopi skrining, adalah proporsi pasien dengan paling tidak satu adenoma kolon terdeteksi di antara semua pasien yang diperiksa kolonoskopi oleh endoskopist. Menurut Douglas K, dkk; ADR adalah prosentase pasien umur e” 50 tahun pertama kali dilakukan pemeriksaan skrining kolonoskopi dam ditemukan satu atau lebih adenoma dan diambil. ADR mempunyai peranan dalam menurunkan angka kesakitan dan kematian karena ‘colorectal cancer’ (CRC). ADR dan interval CRC terdapat hubungan yang terbalik, setiap kenaikan ADR 1% akan menurunkan interval CRC 3%. Strategi untuk meningkatkan ADR dalam intraprosedure antara lain ‘cecal intubation rate’, withdrawal time’, pemakaian obat antispasmodic, posisi pasien, retroflexi dan pemeriksaan ulang pada kolon proksimal, retroflexi rectum.

Disepakati indicator kualitas kolonoskopi yang dinilai antara lain: ‘bowel preparation’ proporsi prosedur dimana pembersihan kolon sangat bagus atau bagus > 90%; ADR > 20% (laki-laki > 25% dan wanita > 15%); ‘withdrawal time’ > 6 menit, ‘cecal intubation rate’ > 95%.

Bacaan

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Semarang Gastroentero-Hepatology Update 2020

Haruskah Semua Pasien Hepatitis B di Obati?

Poernomo Boedi Setiawan

Problem utama dalam tatalaksana infksi virus hepatitis B adalah eradikasi virus belum dapat dilakukan secara sempurna sampai dengan saat ini . Siklus hidup Hepatitis B menunjukkan adanya cccDNA dalam inti sel hati yang merupakan pusaka genetik virus dan sampai dengan saat ini obat 2 an belum mampu untuk meng - eradikasi cccDNA dengan akibat infeksi hepatittis B terus berlanjut, sehingga dapat dinyatakan penyakit Hepatitis B kronis belum dapat "disembuhkan" secara sempurna, namun dapat dikendalikan.

Tatalaksana infeksi virus hepatitis berdasar suatu pedoman ("guideline") diantaranya pedoman Asia Pasifik, Eropa, Amerika Serikat, WHO, dan Indonesia (PPHI 2017).

Beberapa pokok tatalaksana mungkin sesuai dari berbagai "guideline" tersebut adalah sbb:

1. Diagnosis hepatitis B kronis adalah adanya HBsAg yang menetap lebih dari 6 bulan

2. Pada umumnya hepatitis B kronis hanya diobati dalam keadaan aktif, ditandai dengan peningkatan ALT yang persistent atau bukti lain dan bila perlu dengan biopsi hati

3. Pemeriksaan HBV DNA dipakai sebagai "alarm of treatment", memonitor pengobatan dan menentukan keberhasilan pengobatan

4. Pemeriksaan HBeAg dan Anti HBe dipakai untuk menentukan strategi pengobatan yang membagi pasien dalam dua kelompok yaitu e positive dan e negative

5. Kadar ALT dapat dipakai untuk memonitor perjalanan klinis penyakit ,

menentukan pertanda pengobatan dimulai, memonitor hasil pengobatan, menentukan sebagian hasil pengobatan

6. Biopsi hati dilakukan pada kondisi tertentu, yaitu bila diduga pasien sangat perlu mendapat pengobatan namun pemeriksan klinis belum cukup kuat sebagai indikasi klinis pengobatan. Perlu di fahami cara lain yang non invasive untuk menentukan derajad keparahan penyakit semisal dengan tes APRI, Fib Test, atau elestografi (FibroScann)

7. Pemilihan obat antara Peg IFN dengan Analog Nukleosida (AN), memerlukan pemahaman yang baik, khususnya tentang kondisi fungsi hati, dan karakteristik obat dan juga kesepkata dengan pasien.

8. Pemakaian AN pada umumnya berjangka panjang, mengharuskan memonitor pengobatan dengan baik, termasuk menduga kemungkinan terjadinya resistensi obat. Pada sat ini PPHI (2017) menyatakan Entecavir dan Tenofovir adalah pilihan awal lini pertama untuk golongan AN.

9. Penggantian AN atau kombinasi AN memerlukan tambahan kompetensi seorang dokter.

Strategi pengobatan hepatitis B kronis ada 2 yaitu :

(1). Pengobatan dengan durasi terbatas dengan **interferon**

(2). Pengobatan dengan durasi jangka panjang dengan analog **nukleos(t)ida(AN)**

Obat lini pertama untuk terapi hepatitis B kronik adalah **pegylated interferon, entecavir, atau tenofovir**. Pada pasien non sirosis yang menginginkan terapi untuk jangka waktu tertentu, terapi yang lebih direkomendasikan adalah Peg-IFN. Pemilihan lini pertama obat analog nuklesida (entecavir dan tenofovir) karena golongan obat ini mempunyai daya anti virus yang kuat dengan angka resistensi jangka panjangpengobatan yang sangat minimal. Pada saat ini juga tersedia **Tenofovir Alafenamide** mempunyai **efek samping minimal pada gangguan fungsi ginjal.**

Dengan adanya obat lini pertama khususnya golongan AN, maka walaupun tidak semua pasien hepatitis B kronis harus diobati, **namun secara aktif** harus ditentukan adanya indikasi pengobatan yang lebih cermat .

Penentuan indikasi yang lebih baik tepat dapat ditentukan ditentukan berdasar: gambaran histologi hati yaitu terapi dapat dimulai apabila ditemukan inflamasi sedang – berat skor aktivitas Ishak >3/18 atau skor METAVIR A2–A3 atau fibrosis signifikan (ditandai dengan hasil biopsi skor fibrosis METAVIR >F2 atau Ishak >3, dan hasil *liver stiffness* berdasarkan pemeriksaan *transient elastography* >8 kPa,atau skor APRI >1,5 .

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Semarang Gastroentero-Hepatology Update 2020

Non Variceal Upper Gastrointestinal Bleeding in International Consensus: Whats's New?

Agung Prasetyo

Manajemen UGIB telah maju dengan teknik endoskopi baru, dan lanskap farmakologis telah berubah. Terapi antikoagulan atau antiplatelet, termasuk terapi kombinasi, menjadi lebih umum, secara substansial meningkatkan risiko UGIB.

Disini ditampilkan 2 guideline internasional yaitu Guideline Recommendations From the International Consensus Group 2019 dan Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018, serta dibandingkan dengan Konsensus Indonesia agar kita dapat membandingkan kemajuan yang ada dan membuat kita berintrospeksi sehingga akan membimbing untuk lebih maju.

International Consensus Group dari 11 negara yang tergabung dalam grup Internasional setuju bahwa pemutakhiran rekomendasi 2010 untuk pengelolaan perdarahan saluran cerna atas, dimana pemutakhiran ini berfokus pada resusitasi dan penilaian risiko; manajemen preendoskopi, endoskopi, dan farmakologis; dan profilaksis sekunder untuk perdarahan saluran cerna atas berulang.

Di Asia Pasifik (Asia and Australasia :Australia, China, Hong Kong, India, Japan, Korea, Malaysia, Philippines, Singapore dan Taiwan) telah terjadi kemajuan yang signifikan dalam manajemen klinis pasien di ketiga tahap tersebut. Ini termasuk skor stratifikasi risiko pra-endoskopi, transfusi darah dan trombosit, penggunaan inhibitor pompa proton; endoskopi teknik hemostasis baru (semprotan bubuk hemostatik dan klip over-the-scope); dan manajemen pasca endoskopi. Masalah yang muncul adalah meningkatnya penggunaan agen antiplatelet ganda dan antikoagulan oral langsung pada pasien dengan penyakit jantung dan serebrovaskular.

Untuk Indonesia sampai saat ini menggunakan konsensus nasional penatalaksanaan perdarahan saluran cerna atas nonvariseal yang banyak disandarkan pada International

Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding (ICON UGIB) tahun 2010 , Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding tahun 2011, yang disesuaikan dengan keadaan di Indonesia waktu tahun dibuat (2012). Sehingga dengan adanya pembaharuan dari sumber tersebut semestinya diperlukan juga pembaharuan juga pada consensus nasional penatalaksanaan perdarahan saluran cerna atas non varises Indonesia tahun 2012.

Meskipun kemajuan terapeutik yang signifikan telah dibuat, banyak dari prinsip dasar manajemen perdarahan salurancerna atas non variseal tetap tidak berubah. mengenai proton pump inhibitor (PPI) mewakili perubahan besar bagi banyak dokter. Karena banyak yang dibahas berkaitan dengan perlindungan terhadap terapi anti platelet dan anti trombotik serta perlindungan terhadap post terapi endokopi perdarahan saluran cerna atas. Dalam hal ini juga disampaikan pemberian PPI interavena dosis tinggi dan oral dosis tinggi.

Rekomendasi ambang batas transfusi hemoglobin 8 g / dL lebih tinggi dari 7 g / dL yang direkomendasikan dalam International consensus 2019 (ICON UGI) lebih tinggi dibandingkan dalam beberapa pedoman lain. Dalam hal in juga perlu diperhatiakn pula pada kondisi komorbid kardiovaskuler, karena memerlukan Hb yang lebih tinggi, tetapi cairan juga harus dibatasi.

Dalam endoskopi juga dibahas mengenai kapan tindakan endoskopi dapat dilakukan pada pada pasien denagn pedarahan saluran cerna atas non variseal yang menerima antikoagulan (antagonis vitamin K atau antikoagulan yang bekerja langsung) dan hasrus melanjutkan profilaksis tersebut.

Dalam hal ini juga dibahas mengenai waktu tindakan endoskopi pada kasus perdarahan saluran cerna atas nonvariseal dalam waktu 24 jam setelah masuk , dan pendapat bagaimana bila sarana dan situasi tidak mendukung dalam memenuhi waktu tersebut.

Kata kunci: Consensus, Nonvariceal Upper Gastrointestinal Bleeding.

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Semarang Gastroentero-Hepatology Update 2020

Non Surgical Treatment Options for Hemorrhoid

Suyatmi Awizar

Pendahuluan

Hemoroid berasal dari bahasa Yunani *haemorrhoides* yang berarti darah yang mengalir (*haem* = darah, *rhoos* = mengalir). Dalam bahasa Indonesia digunakan istilah wasir atau ambeien (dari bahasa Belanda diambil dari kata buah arbij). Pada umumnya praktisi medis maupun nonmedis beranggapan bahwa hemoroid suatu proses patologis yang menyakitkan didaerah kanalis anus.Sebenarnya hemoroid suatu struktur anatomi normal yang dapat terjadi pada setiap orang baik muda maupun tua. Struktur ini terdiri dari 3 unsur yaitu: lapisan permukaan (mukosa). Stroma (mengandung vena hemoroidalis), otot polos dan jaringan penunjang. Serta jaringan ikat dari sfingter ani interna.(1)

Dengan bertambahnya usia, jaringan ikat melemah, akibatnya hemoroid menonjol kedalam lumen kanalis anus. Vena hemoroidalis inferior dan superior mengalami dilatasi membentuk pleksus hemoroidalis atau bantalan anus, dalam lapisan submukosa rektum. Ini semakin meningkat setelah usia melewati dekade ke tiga. Sehingga semua orang dewasa merupakan kandidat bagi berkembangnya hemoroid yang simptomatis yang disebut sebagai penyakit hemoroid.(1)

Pada berbagai penelitian hemoroid dapat ditemukan pada hampir 80% orang dewasa, tetapi umumnya asimtomatis. 88% dari pasien dengan keluhan perdarahan peranum, sakit sekitar anus, prolapsus ani terdapat hemoroid. Pada pasien pasien yang asimtomatis umumnya ditemukan hemoroid derajat I–II, sedangkan hemoroid derajat III dan IV ditemukan pada 25% dari seluruh penderita. Dari yang simtomatik dan asimtomatik 25% mempunyai hemoroid yang besar.(1,2) Di USA penyakit hemoroid dialami 4,2% pasien. Hampir 2,5 juta berobat ke dokter karena keluhan hemoroid, 160.000 operasi hemoroid tiap tahun. Insidensi hemoroid laki laki sama dengan wanita. Prevalensi teringgi pada umur 45-65 tahun.(3,4)

Etiopatofisiologi

Secara patofisiologi hemoroid terjadi akibat degenerasi jaringan penunjang bantalan anus, sehingga terjadi desensi, bendungan, edema, iskemi dan inflamasi non infeksi. Beberapa faktor yang diduga turut berperan pada terjadinya hemoroid adalah: Obstruksi Vena. Mekanisme dasar terjadinya hemoroid adalah pembendungan dan hipertrofi bantalan anus interna yang disebabkan oleh: kegagalan pengososngan vena bantalan anus secara cepat saat defekasi. Bantalan anus yang terlalu mobile. Terperangkapnya bantalan anus oleh sfingter anus yang ketat.(1) Prolaps bantalan anus: Bantalan anus dipertahankan oleh *ligamentum Parks*/*ligamentum Treitz* dan lapisan muskularis submukosa. Bantalan vaskuler ini menempel secara longgar pada lapisan otot sirkuker, hingga saat defekasi terjadi rotasi kearah luar dari bantalan anus tersebut. Bila ligamen lemah karena pengaruh endokren, usia dan konstipasi terjadi gangguan eversi dan rotasi. Mengejan yang lama mendorong bantalan anus untuk prolaps.(1) Pengaruh vaskuler: Jaringan mikrosirkulasi *arteri – venous shunt* / pleksus hemoroidalis dipengaruhi oleh stimulasi hormonal dan neuro–fisiologik. Makanan yang merangsang dan pedas akan mengubah fungsi vasomotor usus dan pelvis, terjadilah perubahan aliran darah arteria hemoroidalis superior disertai spasme spingter prekapiler. Akibatnya terjadi peningkatan tekanan dan dilatasi pleksus hemoroidalis, hemoroid akan menonjol, dapat terjadi perdarahan dan proktitis[1,5]. Pembengkakan mukosa anus akan mempermudah terjadinya trauma saat mengejan waktu berak, hingga terjadi perdarahan rectal karena banyaknya *arteriovenous shunt*.[1] Prolap dari hemoroid interna akan menyebabkan pengeluaran mukous dan lembab yang menyebabkan pruritus dan merupakan predisposisi terjadinya incarserasi dan strangulasi.[2,6]

Penyebab hemoroid dapat terjadi pada : konstipasi kronis, sering duduk terlalu lama, sering mengejan berlebihan, penurunan alir balik vena, kehamilan, hipertensi portal, varises anorektal. Sedangkan faktor predisposisi hemoroid adalah: jarang posisi berdiri, faktor keturunan, status sosial ekonomi yang tinggi, diare kronik, keganasan kolon, penyakit hepar kronis, obesitas, tekanan intra anal yang tinggi waktu istirahat, jedas pada koluna vertebralis, kehilangan tekanan muskulus intra rektal, operasi rektum, episiotomi, *anal intercourse*, I B D.[2,6]

Gambaran klinis

Berdasarkan letak anatomisnya hemoroid dibagi dua: Hemoroid externa dan hemoroid interna. Hemoroid ekterna berasal dari pleksus hemoroidalais inferior, terletak dibawah linea dentata dan ditutupi oleh epitel skuamosa komplek. Hemoroid interna berasal dari pleksus hemoroidalis superior, terletak proksimal dari linea dentata.

Klasifikasi standart hemoroid didasarkan pada progresifitas hemoroid interna dari yang normal samapai ke posisi prolaps.[1,3]

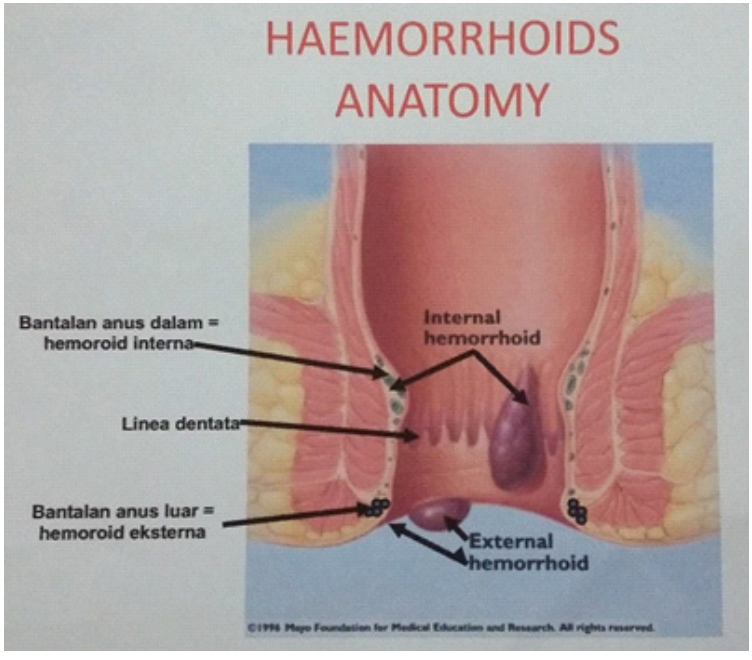
Klasifikasi hemoroid dari *Goligher* [7]

Derajat I : Hemoroid berdarah tetapi tidak prolaps

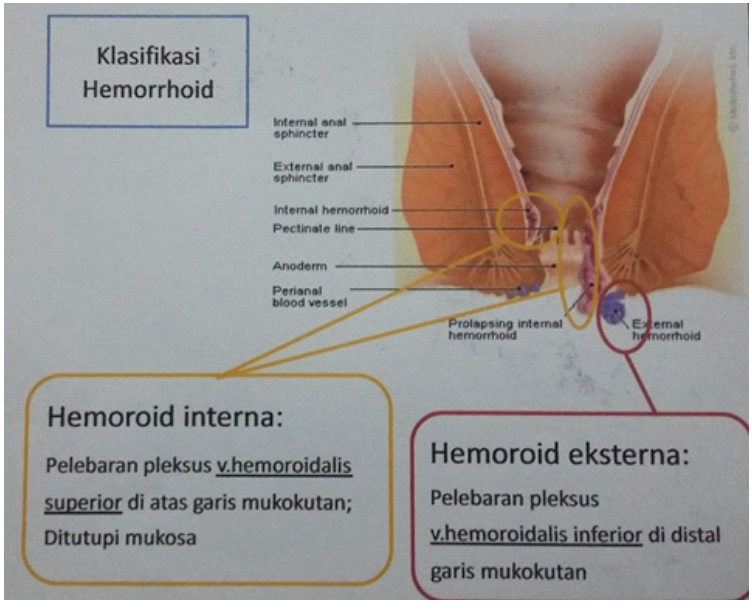
Derajat II : Hemoroid prolaps saat mengejan sampai melewai linea dentata, masuk spontan setelah selesai mengejan

Derajat III : Hemoroid prolaps melewati kanalis anus dan harus direposisi secara manual

Derajat IV : Hemoroid prolaps melewati kanalis anus dan tidak dapat direposisi secara manual, atau prolaps lagi setelah direposisi



Gambar I : Anatomi Hemoroid.



Gambar II : Klasifikasi Hemoroid

Manifestasi klinis: Sebagian besar pasien hemoroid asimtomatis, sebagian lagi diketahui pada waktu pemeriksaan retoskopi atau kolonoskopi. Gejala klinis dikibatkan oleh hemoroid interna dan hemoroid eksterna.

Gejala gejala akibat hemoroid interna :[1,2,4]

Perdarahan peranum, darah segar merah terang, menetes setelah buang air besar (BAB). Tidak disertai sakit dan pruritus. Perdarahan masif dapat terjadi bila bantalan prolaps dan terbendung oleh sfingter ani. Perdarahan dapat terjadi diluar defekasi, terutama pada orang tua, karena bantalan anus hanya ditutupi mukosa diluar anus.

Pembengkaan anus dan prolaps anus. Harus dibedakan dengan trombosis perianal, skin tag yang mengalami edem atau polip rektum.

Nyeri dan tak nyaman, terjadi bila prolaps, trombosis, atau ada penyakit lain misalnya fisura ani, abses atau keganasan. Disertai rasa tak puas saat defekasi dan tak nyaman sekitar perineum.[1.2.5]

Gejala dari hemoroid eksterna: trombosis akut menyebabkan rasa sakit pada benjolan hemoroid ekterna, juga bisa terjadi perdarahan bila ada laserasi, bisa juga terjadi abses.[5]

Komplikasi: Trombosis, edem dan inflamasi bantalan anus interna, terjadi bila prolaps hemoroid interna terbendung oleh sfingter ani. Trombosis dan edem menetap diluar. Tekanan diluar dan didalam kanalis anus menyebabkan sakit, hingga penderita menghindari duduk dan defekasi. Bila terjadi penyembuhan setelah 14 hari akan menyisakan polip fibrosis atau skin tag.[1.5] Anemia berat defisiensi besi terjadi karena perdarahan yang sering terjadi, Hb dapat sampai kurang dari 4 gr %.[1.4] Trombosis hemoroid eksterna terlihat benjolan licin, keras dan nyeri, berwarna kebiruan, terletak diluar kanalis anus dan tak berhubungan dengan hemoroid interna.[1] Dermatitis peri anal akibat kebersihan yang buruk, adanya skin tag, dan alergi obat obat topikal.[1]

Diagnosis

Diagnosis hemoroid ditegakan dengan : anamensa yang cermat, pemeriksaan fisik dan pemeriksaan penunjang. Anamnesa yang cermat dari gejala klinis hemoroid. Perlu pula ditanyakan kemungkinan adanya penyakit lain yang mempunyai gejala yang hampir sama dengan hemoroid. Kemungkinan adanya fisura ani, keganasan anorektal, abses anus.[1.2.8] Pemeriksaan fisik inspeksi sekitar anus, colok dubur. Pada colok dubur perlu diperhatikan 3 posisi hemoroid utama dilateral kiri, anterior kanan dan posterior kanan. Umumnya letak benjolan hemoroid di tempat tersebut. Jika ada nyeri hebat dan trombosis peri anal colok dubur tak perlu dilakukan.[1.2]

Pemeriksaan penunjang : pemeriksaan laboratorium darah rutin, tinja rutin, tinja darah samar. Bila bersamaan dengan diare kronis perlu pemeriksaan *C E A dan fecalcalprotectin* untuk mencari kemungkinan keganasan anorektal dan IBD. Pemeriksaan anoskopi untuk melihat heroid interna D I secara visual. Rektoskopi dan kolonoskopi diperlukan bila ada kecurigaan kearah keganasan atau IBD.[2.5]

Penatalaksanaan

Hemoroid yang asimtomatis tidak memerlukan pengobatan. Hemoroid yang simtomatis yang datang ke klinik atau ke UGD penatalaksanaanya bervariasi tergantung dari umur penderita, berat ringanya penyakit dan komorbid serta ketersediaan obat dan alat penunjang. Variasi penatalaksanaan tersebut: Diet dan modifikasi kebiasaan hidup, terapi medika mentosa*, offise procedures* (kamar prosedur) untuk hemoroid interna derajat I, II dan sebagian III. Untuk derajat III dan IV terapi pembedahan.[1.3.5.8]

Diet dan modifikasi kebiasaan hidup :

Diet dan modifikasi kebiasaan hidup diterapkan pada semua derajat hemoroid yang simtomatis meliputi: Mengurangi diet yang dapat menimbulkan konstipasi (diet yang berlemak). Meningkatkan konsumsi makanan berserat kira kira 30 gram tiap hari. Minum yang cukup.Bila masih sulit defekasi, tinja masih keras perlu diberi laksansia laktulosa. Mengurangi makan pedas dan berbumbu (merangsang). Menghindari duduk lama di kloset, tidak mengejan. Memperbaiki kebersihan anus dan sekitarnya serta olah raga. Bagi yang obesitas menurunkan berat badan sampai ideal.[1.3.4]

Terapi medika mentosa:

Obat yang tidak spesifik diberikan untuk memperlancar defekasi: laktulosa. Obat untuk mengurangi rasa sakit pada anus diberikan obat topikal berupa supositoria atau krim yang mengandung anti inflamasi hidrokortison 1-3%, dikombinasikan dengan anestesi lokal. Dapat juga dikombinasikan dengan: Astringen, Protektan Zinc Oxide, Decongesta Phenylephrine. Contoh: Policresulen 50 mg, Lidokain Hydroclorine10 mg. [1.3.4]

Obat obat kusus untuk hemoroid yaitu obat flebotonik atau venotonic. Saat ini yang tersedia *micronized purified flafonoid fraction (MPFF*) *diosmin - hisperidin dan hidrosmin*.

Cara kerja flafonoid pada hemoroid sebagai berikut : [1,3,4]

- Meningkatkan tonus vena dan memperpanjang respons konstraksi terhadap noradrenalin.
- Mengurangi hiperpermeabilitas kapiler serta meningkatkan resistensi kapiler
- Mengurangi mediator inflamasi (PGE2, PGF2a)dan radikal bebas.
- Mengurangi adhesi netrofil pada vena vena post kapiler
- Mencegah dan memperbaiki kebocoran mikrovaskuler serta melindungi mikrovaskuler terhadap mediator mediator inflamasi. Menaikan drainase limpatik.

Efek klinis MPFF :

- Cepat mereduksi serangan akut perdarahan hemoroid.
- Mengurangi intensitas kekambuhan hemoroid.
- Menurunkan derajad hemoroid secara signifikan.
- Menurunkan resiko kambuhnya hemoroid setelah operasi hemoroid.

- Efektif dan aman untuk wanita hamil dengan hemoroid setelah trimester pertama.

Pada penelitian M Cospite 1994[9] dengan Double Blind Placebo Controlled. Terhadap 100 penderita hemoroid yang mengalami perdarahan akut berat yang berjalan 1 sampai 3 hari di klinik atau di RS. 50 penderita diterapi dengan Daflon 500mg (D 500) dan 50 diberi plasebo Kedua group memenuhi kriteria inklusi dan eksklusi. Daflon berisi diosmin 90% dan hesperidin 10%. Dosis yang diberikan: 2x3 tablet (1500mg) selama 4 hari. 3 hari berikutnya diberikan 2x2 tablet (1000 mg).

Hasilnya sebagai berikut : perbaikan simptom di hari ke 2-7 terjadi pada kedua group, tetapi pada group D500 lebih cepat dan lebih baik. Perdarahan peranum, rasa tak enak di sekitar anus sakit waktu defekasi, pada kedua group membaik, tetapi group D500 jauh lebih baik ($p<0,001$). Inflamasi, kongesti, edem, dan prolaps jauh lebih cepat membaik pada group D500. dibanding plasebo. Pemakaian obat analgetik topikal menurun pada kedua group, tetapi pada group D500 jauh lebih menurun , pada hari ke 4 sudah tidak memakai lagi ($p<0,001$).

Kesimpulanya terapi dengan D500 pada perdarahan akut hemoroid , perbaikan klinis lebih baik dari plasebo.[9]

Penelitian oleh Shelygin Y et all 2016 pada penderita hemoroid yang mengalami perdarahan akut diberikan MFPP tablet 1000 mg dan tablet 500mg sehari dengan dosis yang sama : 3 gram dalam 4 hari diteruskan 2 gram selama 3 hari. Setelah 7 hari pemberian pada kedua group sama efektifnya dan tidak memberikan efek yang jelek dengan dosis 1 tablet 1000 mg. [10]

Pemberian Daflon 500mg 2x 1tb sehari selama 8 minggu efektif menurunkan simptom dan perjalanan klinis serta menurunkan drajat hemoroid.[1,11]

Hidrosmin: merupakan derifat diosmin yang larut dalam air, mempunyai efek venotropik (venotonik) yang lebih baik dari diosmin. Disamping efek yang sama dengan diosmin, hidrosmin mempunyai efek hematologik dapat mengurangi viskositas darah dengan memperbaiki deformitas eritrosit. Selain dalam bentuk kapsul hidrosmin ada dalam sediaan krim dan tetesan. Kandungan dalam krim: Hidrosmin

5g, menthol 2g, cairan ektrak hammamelis 3 gram, lidokain HCl 1,5 gram dapar sampai 100 gram.

Hidrosmin drop 100mg dalam 1cc sediaan. Dosis umumnya 3x2 capsul.[1,12]

Terapi non bedah lain (dalam kamar prosedur)

Pada beberapa pasien hemoroid derajat I dan II serta derajat III yang terseleksi yang diobati dengan diet dan modifikasi gaya hidup, tidak berhasil, dapat diterapi lebih efektif dengan prosedur terapi dalam kamar prosedur. Dapat dikerjakan : skleroterapi*, rubber bend ligation* , koagulasi bipolar, hemoroidolisis, foto koagulasi sinar infra merah. [1,3,4]

Skleroterapi dengan suntikan etoksi sklerol 1,5% pada hemoroid interna derajat I dan II. Letak hemoroid dilihat dengan anoscop, suntikan pada sub mukosa intra hemoroid atau para hemoroid , dengan tujuan terjadi sklerosis pembuluh darah tersebut. Terjadi fibrosis dan fiksasi hemoroid ke kanalis ani. Dapat diberikan pada pasien dengan pemberian antikoagulansia. Keberhasilan prosedur ini 70%. Komplikasi kadang terjadi tidak nyaman dan perdarahan. [1,3,4]

Rubber band ligation (RBL)

Diindikasikan pada hemoroid derajat II dan III yang terpilih. Kontra indikasi pada pasien koagulopati dan pasien yang mendapat antikoagulansia kronik. Dengan protoskopi kusus, karet pengikat ditempatkan kira kira ½ cm diatas linea dentata pada hemoroid interna yang menonjol. Ligasi (ikatan) yang kuat pada hemoroid ini menyebabkan aliran darah ke hemoroid berhenti, terjadi nekrosis, setelah 1-2 minggu jaringan yang nekrosis lepas. Dapat dilakukan ligasi 2-3 sekaligus. Efektifitasnya 60-80 %. Komplikasi sangat jarang , dapat terjadi rasa sakit, retensi urin, perdarahan yang terlambat, sangat jarang sepsis perineal. [1.3.4]

Koagulasi Bipolar

Bipolar Circumactive Probes (BICAP) dapat digunakan karena memiliki efek koagulasi membran mukus didekat hemoroid. Dilaporkan cukup efektif untuk pengobatan hemoroid interna yang berdarah.[1]

Hemoroidolisis. Menggunakan gelombang galvanik terapeutik secara langsung pada hemoroid, yang menghasilkan suatu reaksi kimia yang akan menyusutkan dan melarutkan jaringan hemoroid. Tehnik ini cukup efektif digunakan pada hemoroid interna.[1]

Fotokoagulasi : *Infrared Coagulation* (IRC)

Tehnik ini menggunakan alat foto koagulator yang memfokuskan sinar inframerah ke bagian hemoroid. Dapat digunakan pada hemoroid derajat I dan II yang mengalami perdarahan aktif.

Pada satu sesi pengobatan selama 2 menit untuk beberapa kali penyinaran terjadi nekrosis hemoroid dan terjadi fibrosis mukosa sehingga terjadi retraksi. Prosedur ini efek sampingnya minimal, rasa sakit dan perdarahan sedikit.(1.3)

Ringkasan

Untuk pengobatan hemoroid semua derajat hemoroid pengobatan dengan diit dan modifikasi kebiasaan hidup.

Derajat I : Medikamentosa, Skleroterapi dan Fotokoagulasi

Derajat II : Medikamentosa, *Rubber band Ligation*, *Coagulation Bipolar*, Skleroterapi

Derajat III : *Rubber band Ligation*, Terapi bedah, Medikamentosa

Derajat IV : Terapi bedah dan Medikamentosa

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Non Surgical Treatment Option For Hemorrhoid

Suyatmi
Divisi Gastroenterohepatologi
Ilmu Penyakit Dalam UNDIP

Hemoroid

- Kondisi medis yang sering dijumpai
- Ditemukan hampir 80% Orang Dewasa ——Asimptomatis.
- Asimtomatis umumnya derajat I-II.
- Derajat III-IV 25% dari seluruh penderita.
- Prevalensi sangat bervariasi dari 4,4% ——12,8%.
- 2,5 juta pasien berobat ke dokter. Tiap tahun
- 160.000 operasi hemoroid tiap tahun
- Insidensi laki laki = Wanita. Tertinggi umur 45- 65 tahun.

Anatomi Hemoroid.

Hemoroid suatu struktur anatomi normal . terdiri 3 komponen:

- Lapisan permukaan (mukosa)
- Stroma : V hemoroidalis. Otot polos. Jaringan Penunjang/ ikat.
- Jaringan ikat dari sfingter ani interna.
- V hemoroidalais inferior dan superior dilatasi ————>
- Membentuk pleksus hemoroidalis (Bantalan Anus)
- Umur bertambah jaringan ikat melemah —>hemoroid menonjol kelumen

Semarang Gastroentero-Hepatology Update 2020

Step Up vs Step Down Management of IBD: How to Start Biologic Agents

Puo-Hsien LE

The past few decades have been revolutionary in IBD care with the growing availability of biological therapies and small molecular drugs in addition to conventional medications. Biologics play an irreplaceable role in the treatment of moderate to severe Crohn's disease and ulcerative colitis. It not only improved the outcomes, but also provided higher deep remission rate. Therefore, the right timing to start biologics is critical issues for every IBD specialist.

Semarang Gastroentero-Hepatology Update 2020

Abstrak Poster

Semarang Gastroentero-Hepatology Update 2020

43 Years Old Woman with Secondary Budd-Chiari Syndrome caused by Hilar Cholangiocarcinoma and Hepatitis C

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Background

Budd-Chiari Syndrome is a rare disease that occurs in about 0,001% of the population and has a variety of potential etiologies.

Case presentation

We report a 43-year-old woman presented with a mass in the right upper quadrant abdomen, abdominal pain, ascites, hepatomegaly, icteric and weight loss. Labs on admission were notable for albumin 2,4 g/dl, bilirubin 0,8 mg/dl, positive anti-HCV, ALP 252 U/L and GGT 81 U/L. Abdominal USG showed hepatomegaly, ascites, intrahepatic bile duct enlargement, hyperechoic mass on the hilus and hepatic vein thrombus. Abdominal CT scan showed inhomogeneous solid cystic mass on the hepatic hilus with intra and extra hepatic bile ducts enlargement. From ERCP, CBD size was normal, right and left IHBD dilated. We did a brush biopsy smear resulting amorphous mass in bile pigments, flattened and columnar epithelium, macrophages, with increased N/C ratio, mild pleomorphic; as described in hilar cholangiocarcinoma. Pathological examination from liver biopsy revealed parenchymal tissue of the liver composed of polygonal cells with oval round nuclei, relatively uniform, eosinophilic cytoplasm, arranged in plates consisting of 1-2 hepatocytes, including sinusoidal centrilobular dilatation and extravasation of erythrocytes with infiltrate neutrophils, lymphocytes, and histiocytes; as described in Budd-Chiari Syndrome.

Discussion

The diagnosis of BCS should be considered in all patients with clinical signs as follow: 1). Abdominal pain, hepatomegaly and ascites that occur rapidly, 2). Massive ascites with slight changes of the liver physiology tests, 3). Fulminant liver failure accompanied by hepatomegaly and ascites, 4). Chronic liver disease whose unclear cause, 5). Liver disease with thrombogenic disease. Advances in imaging have made most BCS diagnosable based on non-invasive imaging studies. In this case, hepatitis C is one of the predisposing factors of hilar cholangiocarcinoma, then hilar cholangiocarcinoma is the cause of Budd-Chiari Syndrome.

Conclusions

Secondary Budd-Chiari Syndrome is present when the hepatic veins are compressed or invaded by a lesion that originates outside of the vein (e.g. a malignancy). In this case, the therapy for this patient is radiotherapy or surgery as well as stenting, providing antivirus for hepatitis c and administration of anticoagulants.

Keywords: Budd-Chiari Syndrome, Hilar Cholangiocarcinoma, Hepatitis C

Atypical Chronic Myeloid Leukemia and Severe Iron Deficiency Anemia in Hepatitis B Related Decompensated Liver Cirhosis: A Case Report

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Abstract

Atypical Chronic Myeloid Leukemia (aCML) is a chronic myeloproliferative disorder with a clinical and haematological picture similar to CML but lacking Philadelphia chromosome and BCR-ABL. ACML is a rare disorder of old adults, no predominance of sex and the incidence is not established. Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury like a viral infections etc. Iron deficiency anemia or IDA is associated with liver disorders.

Case Illustration

A 54-year-old woman has reported a history of hematemesis, melena, refractory ascites, no history of blood cancer, unresponsive to high-dose diuretics and restricted sodium diet. In laboratory findings, Hb : 5,4 g/dl, MCV : 52,5 fl, MCH : 17 pg, SI : 21 µL/dL,TIBC : 328 µL/dL, Ferritin : 13.40 ng/ml, WBC : 89680 /µL, platelet : 1.356.000/µL, HbsAg : Reactive, HBeAg : Reactive, AntiHBV : 72.500, BMP : CML (Chronic Phase), BCR-ABL : Transcription Not Detected BCR ABL. In USG, we found splenomegaly, liver cirrhosis and ascites. During hospital treatment, patient got blood transfusion until Hb > 9gr/dl before takes hydroxyurea. After treatment, platelet and leukocyte are reduced to a normal level. the effects of hydroxyurea in patients are monitored every 3-4 days.

Discussion

Anemia is a frequent manifestation in patients with liver cirrhosis. It is characteristical of moderate severity and may be caused by diverse mechanisms. Iron deficiency appears to be a major mechanism for anemia developed in these patients. The most important approach to management is to identify the underlying disease and treat the cause of anemia. The prognosis aCML is very poor and no guidelines exist on the treatment. Overall survival ranges between 10.8 months and 25 months even 29 months for smaller series. When a patient has suspected CML without confirmation, we initiate hydroxyurea to reduce WBC and platelet counts close to normal levels. We continue hydroxyurea until confirmation of the Philadelphia chromosome. Hydroxyurea is a contraindication in severe anemia.

Keywords : severe anemia, liver cirhosis, aCML

Importance of Skeletal Mass Evaluation on Hepatocellular Carcinoma Patients Treated with Sorafenib: A Literature Review

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Abstract

Background

Sorafenib was known as first-line systemic thrapy for Hepatocellular Carcinoma (HCC). However, recent study has also found that Sorafenib cause decrement of skeletal muscle index (SMI), which leading to sarcopenia. Hence, sarcopenia was found to be correlated with worse outcome on HCC patients. This study aimed to the importance of skeletal muscle mass evaluation on HCC patients treated with Sorafenib.

Methods

A literature search was conducted in the electronic databases (PubMed and ScienceDirect), identifying observational studies from 2015 to 2020 with Skeletal Muscle, Sarcopenia, Sorafenib, and HCC as keywords.

Results

Ten studies consist of cohort and retrospective cohort were included. Sarcopenia / low skeletal muscle mass (SMM) was varriously defined as SMI lower than 36,2-43 cm^2/m^2 for men and lower than 29,6-41 cm^2/m^2 for women. Moreover, one study showed that HCC with and without sarcopenia patients treated with Sorafenib showed a decrease of SMI by 1,07 and 2,14 within 3 months. Low SMM before Sorafenib treatment was correlated with lower overall survival (100,5 days-39 weeks versus

11,7 months-61 weeks) and lower median survival time (MST) (7,6-13,7 months versus 13,4-18,5 months). Moreover, studies showed group with SMI decrement on the third month of treatment showed lower MST, 10,9-11 versus 13,4 months. Decrement more than 5,73 cm^2/m^2 within 120 days also provide worse survival. Hence, survival rate for first, and second year was lower in low SMI group, 39,7% versus 57,6% and 11,3% versus 36%.

Conclusion

Low SMM before and losing SMM during Sorafenib treatment correlated to worse outcome on HCC patients. Evaluating SMI before and after treatment of Sorafenib on HCC patients might play important role to determine patients' survival. Further studies are needed to confirm duration of evaluation and cut off point that might be exclusion for Sorafenib treatment.

Keywords: HCC, Sarcopenia, Skeletal Muscle, Sorafenib

Rapunzel Syndrome

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Abstract

Background

Trichobezoar is a collection of dense mass of hair in stomach. The word trichobezoar is a combination of “trich” meaning hair from Greek and “bezoar” meaning poison in Arabic or Persian[1]. Rapunzel Syndome is a type of trichobezoar with an extension of the hair from stomach into the small bowel. Clinical manifestation is deceptive and ranges form classic gastrointestinal symptoms like nausea and vomitus, abdominal mass, to partial or complete gastric outlet obstruction. Commonly, a gastric trichobezoar has a tail extending to the jejunum, ileum, or the ileocecal junction[2].

Case Description

A 33 year-old female was admitted to Emergency Deparment with complaints of severe abdominal pain and persistent vomiting since 4 days ago. Patient looked malnourished, with BMI only 16.4 kg/m^2. Physical examination revealed epigastric tenderness and a hard and fixated mass . No pathologic findings in laboratory tests, except for iron deficiency anemia. Ultrasonography of abdomen showed echogenic, intraluminal, curvilinear in the stomach suggestive of gastric bezoar (Picture 1). Upper gastrointestinal endoscopy confirmed trichobezoar occupying almost the whole gastric cavity caused pylorus obstruction (Picture 2). Endoscopic removal of the mass was not possiblem hence surgical intervention was planned. Trichobezoar was removed

by anterior gastrotomy (Picture 3). A 30 cms long bezoar weighing 700 grams was removed (Picture 4). The mass was occupying almost the whole stomach and extending up to the duodenum.

Conclusion

Rapunzel syndrome is a rare form of trichobezoar. Mostly, it occurs in psychiatric patients with trichotillomania and trichophagia[3]. There are co-existing factors like mental retardation, family problem/parental discontent, and bereavement[4]. Small trichobezoar can be evacuated by endoscopic removal, but large trichobezoar should be removed by surgery. Psychiatric treatments also needed to prevent its recurrence[5].

Keywords: Rapunzel Syndrome, trichotillomania, trichophagia, gastric obstruction.

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Severe Hepatic Dysfunction in Patient with Graves Disease: A Diagnostic and Therapeutic Challenge

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Background

Hepatic dysfunction in a patient with Graves' disease may result from hyperthyroidism per se, as a side effect of antithyroid drugs, and causes unrelated to hyperthyroidism which sometimes causes diagnostic and therapeutic difficulties.

Case Description

A 44-year-old man presented with hyperthyroidism, a history of jaundice, and had presented to another hospital before admission. Initial testing at this hospital a year before revealed severe hyperbilirubinemia, and negative serologic test results for hepatitis A, B, and C virus infection. He had been prescribed propylthiouracil (PTU) for more than 1 year without any improvement. A cholestatic pattern of jaundice was found on the first-time admission in our hospital (May 2020) and also hyperthyroidism finding, goiter, ophthalmopathy, tachycardia, tremulousness. Steroid therapy was initiated for a presumed diagnosis of autoimmune hepatitis, replace PTU to carbimazole and continuing beta-blocker, these give improvement biochemical parameters after 2 months follow up. However, after these initial improvements, he developed progressively ascites and peripheral edema. Abdominal ultrasound revealed chronic hepatitis with the cirrhotic pattern, portal hypertension, and splenomegaly, grade 3 ascites, without biliary dilatation. Child-Pugh-Tourette scoring giving result 11 (Child pugh C). Abdominal paracentesis was performed to ameliorate abdominal

symptoms, and fluid examination shows SAAG 1,8 (high gradient). The patient was initially treated with intravenous furosemide and cefotaxime, and oral methimazole, propranolol, spironolactone, methylprednisolone, dietary sodium restriction, and discharge after a 5-day treatment.

Conclusion

In this case report, we describe a patient with Graves' disease whose presentation with jaundice and hepatic dysfunction. Decompensated cirrhosis, in this case, maybe caused by hyperthyroidism itself, Thionamide (PTU) hepatotoxicity (drug induced liver injury), and presumed autoimmune hepatitis. It is recommended that liver function should be assessed in all patients with graves disease before and during treatment, and choosing that newer agent such as methimazole may reduce the deleterious side effect.

Keywords: Graves' disease, decompensated cirrhosis, autoimmune hepatitis, PTU, methimazole

Symptomatic Autosomal Dominant Polycystic Liver Disease: Case Report with Updated Diagnostic and Management Approach

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Background

Polycystic liver disease (PLD) is a rare disorder which often mistakenly as benign disease and no treatment required. PLD may be part of autosomal dominant polycystic liver disease (ADPLD) or autosomal dominant polycystic kidney disease (ADPKD); with the latter is more common. Several criteria may be used to distinguish ADPLD with ADPKD. Distinction is important as the monitoring, management, and prognosis may vary greatly.

Case Description

A 73-year-old woman came to emergency department with progressively increased right upper quadrant (RUQ) abdominal pain since 3 months before admission. The pain was rated as six out of ten, according to Visual Analog Scale. Her remarkable past medical history is controlled hypertension. Her family history is unremarkable. On physical examination, she appeared moderately ill with blood pressure of 130/90

mmHg, heart rate of 82 bpm, respiration rate of 20x/minute, body temperature 37.0^{0}C. Abdominal examination showed tenderness on RUQ with hepatomegaly. The laboratory examination showed normal complete blood count and liver function. USG examination demonstrated multiple hepatic cystic lesion on both liver lobes. Contrast abdominal CT-scan result showed multiple simple hepatic cystic lesions with more than 20 cysts on both liver lobes sized 7.5 mm to 74.6 mm. Hepatic cystic lesions were found on all over liver segments except segment number 1. Simple left kidney cyst sized 25.7 mm x 20.6 mm was also detected on CT-scan. Based on CT-scan finding (Figure 1), she was diagnosed for having ADPLD with Schnelldorfer type C and Gigot type II. She was planned for cyst fenestration-deroofing via laparoscopic (Figure 2). The postoperative course was unremarkable and she was discharged on the third day of admission.

Conclusion

Burden of liver cyst should be assessed in every ADPLD patient. Therapy which consists of medical and surgical management should be utilized for symptomatic ADPLD.

A Man With Peritonitis Tuberculosis, Pulmonary Tuberculosis and Hematoschezia Suggestive Colitis Tuberculosis a Case Report

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Abstract

Background: Peritonitis Tuberculosis (PTB) is chronic granulomatous infections caused by gram-positive aerobic intracellular bacilli that slowly multiply and have a long incubation period. Peritonitis is an emergency cause of acute abdominal. Peritoneal Tuberculosis develops as a result of reactivation of latent TB.

Case Description: A 60-years-old man entered Teluk Bintuni Hospital, with chief complaint abdominal pain that felt since 5 days ago, but worsening in the last 2 days. Abdominal pain accompanied by weakness in the entire body until its difficult to walk. Patient also complained mucous cough, intermitten fever, decreased appetite about 1 months before being hospitalized. Patient also have ascites, edema legs, and hematochezia since 3 months ago. The patient's previous medical history was diagnosed with pulmonary tuberculosis but discontinued of treatment. The patient diagnosed with suggestive colitis tuberculosis prevent of hematoschezia and radiologically finding. Physical examination showed weak general condition and the vital sign in normal condition. In general examination revealed crackles from both lungs, lowered bowel sounds, distended abdomen and ascites. The laboratory findings showed anemia, high white blood cell, hypoalbumin, and hyponatremia. The treatment

for the patient was anti tubercular therapy (ATT) 2nd category, antibiotic injection, then correction hypoalbumin and hyponatremia and then decompression.

Discussion : The pathways through which TB infects the peritoneum the bacterial spread is achieved by reactivation of TB in the lungs or other solid organ and subsequent hematogenous or lymphatic spread to the peritoneum. Treatment of peritonitis tuberculosis with anti-tubercular therapy start 2-3 months after ATT and continue with corticosteroid. In this patient was clinical recovery respond with ATT.

Summary: This case emphasizes that clinicians should keep in mind that pulmonary tuberculosis patients can develop peritonitis tuberculosis in the same time. Thus they should be followed up closely and screening once they diagnosed with pulmonary tuberculosis.

Keywords: Peritonitis Tuberculosis, Colitis Tuberculosis, Pulmonary Tuberculosis

The Relationship of Alcohol Consumption with the Occurrence of Erosive Gastritis in Endoscopic Patients

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Background

RISKESDAS 2018 reported North Sulawesi Province had the highest national proportion of alcohol consumption (16%) from total Indonesian population. A high concentration of alcohol can induce and disrupt endothelial vascularization of the gastric mucosal layer. The high number of medical treatment visits in poly gastroenterology may be related to the high number of alcohol consumption in the community.

Method

Descriptive analytic design using a cross-sectional approach in 67 patients aged over 17 years who had been performed esofagoduodenoscopy and diagnosed with *erosive gasttritis* in July to October 2019.

Result

Based on research conducted, from total 67 respondents the frequency of respondents consuming alcohol is 44 respondents (65.7%) with the average frequency of alcohol consumed by respondents consisting of: respondents consuming beer as much as 17 respondents (23.9%), tuak as much as 18 respondents (25.4%), liquor as many as 8 respondents (12.7%), wine was 1 respondent (3.7%). From these results it was found that the frequency of respondents who occurred *erosive gastritis* was 43 respondents (64.2%).

Conclusion

There is a significant relationship between alcohol consumption and the occurrence of erosive gastritis using Chi Square, with a p value of 0,000 and the chance of alcohol consumption become *erosive gastritis* is 27 times greater than that of non-alcoholic consumption.

Keywords: *Alcohol,* Erosive gastritis

Amoebic Liver Abscess after Perforated Appendicitis Laparotomy: A Case Report

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Abstract

Introduction

The incidence of liver abscess in Indonesia hospitals accounts for 5-15% per year. Liver abscess can be classified into two different categories: amoebic and pyogenic liver abscess. The most common symptoms of liver abscess are pain in the upper right quadrant of abdomen, fever, diarrhea and loss of appetite. [1,2,3]

Case Presentation

History

A 32-years old male was present with abdominal pain in the upper right since 2 months before admitted to the hospital. The pain did not spread to another area and accompanied by an enlargement in the upper right, yellowish of the eyes, fever, nausea and vomiting. The patient had a history of laparatomy due to perforated appendicitis one week ago.

Physical examination

Temperature was 38.5 C, conjunctival pallor, scleral icterus, dullness percussion at right hemithorax and decreased breath sound on the right hemithorax starting at the fourth intercostal space. Abdominal examination revealed a mass in the right upper quadrant of abdomen 15x15 cm in size, positive murphy sign and positive ludwig sign.

Diagnostic Testing

Laboratory testing: Leucocytes: 20,300/mm^3, Total Bilirubin: 2.60mg/dL, Direct Bilirubin: 1.70 mg/dL, Indirect Bilirubin: 0.90 mg/Dl

Abdominal Ultrasound : enlarged liver with flat surface, sharp edges, smooth and homogenous parenchym

Thorax X-ray : hazy opacification starting at the fourth intercostal space

Abscess fluid : amoeba visualization

Abdominal CT-scan : Hepatomegaly with right lobe liver abscess

Diagnosis

Giant Amoebic Liver Abscess

Treatment

- Ceftriaxone 2 x 1 g IV
- Metronidazole 3 x 500 mg IV
- Ketorolac 3 x 30 mg IV
- Abscess Drainage

Conclusion

- Amoebic liver abscess is more often associated with acute clinical presentations than pyogenic liver abscess
- Jaundice is a rare finding, when presented it indicates poor prognosis
- Abdominal ultrasound is the first choice for initial testing, because it is non-invasive and has a high sensitivity (80-90%)

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The Role of Oral Zinc Supplementation in Adults with Acute Diarrhea: An Evidence-Based Case Report

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Background

Acute diarrhea in adult is one of the most common diagnoses in general practice, and it remains responsible for high morbidity rates worldwide. Zinc supplementation is proven to reduce the duration and severity of childhood diarrhea in randomized controlled trials. However, its efficacy in reducing diarrhea morbidity in adults remains unknown. The objective of this study is to determine the role of zinc supplementation as adjuvant therapy in adults with acute diarrhea.

Methods

An electronic literature search was conducted on PubMed, ScienceDirect, Google Scholar, and Cochrane according to clinical query terminology. The studies were selected based on inclusion and exclusion criteria, and then critically appraised for their validity, importance, and applicability.

Results

As the result from data extraction process, only one article was found to satisfy the inclusion criteria. Kostermans et al., found that Zinc supplementation significantly reduced the duration of acute diarrhea in adult patients(p=0.027), also reduced nausea in adult patients with acute diarrhea (p=0.032). The positive action by zinc in acute diarrhea derives from a regulation of intestinal fluid transport, stimulates enterocyte

growth and differentiation, reduces intestinal permeability, and positively regulates oxidative stress and inflammation. Research in children suggests that zinc supplementation decreased the risk of dehydration, the duration and severity of the diarrheal episode by an estimated 20% to 40%.

Conclusion

Zinc supplementation can be considered to be an additional therapy in adult acute diarrhea patients. However, further studies with bigger sample size and more centers involved are needed to confirm the finding.

Keywords: Acute diarrhea, Adult, Zinc

Colorectal Cancer Profile at Prof Dr. R. D. Kandou Hospital and Siloam Hospital Manado from 2018 to 2019

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Background

Colorectal cancer is the third most commonly diagnosed malignancy and is the leading cause of cancer deaths in the world. The Global Cancer Observatory (GLOBOCAN) 2018 reports the incidence of colorectal cancer ranked third in the world with 1.8 million cases of all types of cancer. And in Indonesia the number of cases of colorectal cancer has reached 30,017 cases.

Method

Retrospective descriptive study using medical record data at Endoscopy Center Prof. Dr. RD Kandou and Siloam Hospital Manado from January 2018 to December 2019.

Results

In this study there were 233 patients with colorectal cancer, a large number of patients were 126 male patients (54, 1%) and 107 female patients (45.9%). The highest incidence of colorectal cancer is at the age of more than 60 years, where in male 50 patients (21.4%) and in female 41 patients (17.5%). The youngest age is 18 years in female, and in male 24 years. The most common type of pathology is moderately differentiated adenocarcinoma, in which 86 male patients (36.9%) and 69 female patients (29.6%). The least poorly differentiated adenocarcinoma was found, where

in male 2 patients (0.8%) and in female 1 patient (0.4%). The most common locations for colorectal cancer were found in the rectum, where 69 male patients (29.6%) and 43 female patients (18.4%). The fewest locations were found in the hepatic flexure, where in both male and female each was 2 patients (0.8%).

Conclusion

Colorectal cancer is most common among men, over 60 years of age, with the type of adenocarcinoma being moderately differentiated and the most common location in the rectum.

Keywords: Colorectal Cancer

Asymptomatic Non-Alcoholic Fatty Liver Disease (NAFLD) in Young Woman 29 Years Old

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Abstract

Background

Non-Alcoholic Fatty Liver Disease (NAFLD) has become the common cause leading to chronic liver disease recently and known to show a strong association with DM, CKD, cardiovascular disease or cerebrovascular disease as well as high cancer incidence of 1.3 hazard ratio (HR), especially 16.7 HR for hepatocellular carcinoma respectively[1–5]. Early diagnosis is important, as the condition is associated with increased risks of disease progression[6].

Case Description

A woman 29 y.o came to ER with mild head injury without any symptoms. Her blood pressure was 150/90 mmHg with no history of hypertension. The woman neither drank alcoholic beverages nor smoked cigarettes earlier, but still prefer to eat oily snack and food. Her Height was 145 cm, her body weight was 58.4 kg, Her BMI was 27.7 and her waist circumference was 86.5 cm. Her laboratory test was ALT 83 U/L and AST 136 U/L, normal Random Blood Glucose 169 mg/dL, Increased Total Cholesterol 256 mg/dL, low LDL 38 mg/dL, low HDL 22 mg/dL, and excessive increased of triglyceride 1783 mg/dL. Abdominal sonography test found hepatomegaly with sign of fatty liver grade II-III. Her final diagnosed was Non-alcoholic Fatty Liver Disease and Metabolic Syndrome then treated with Fenofibrat 1 x 300mg, Atorvastatin 1 x 20mg, and Livapro 3 x 1 caps.

Conclusion

This case shows that there is an increase in prevalence of NAFLD in young adult without any symptoms with excessive increased of triglyceride. So, Screening and early detection really important to reduce the risk of complication, morbidity, and mortality.

Keyword: Asymptomatic NAFLD, Dyslipidemia, Hypertriglyceridemia, Young Adult

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Characteristic Of Hepatitis C Infection In Regular Hemodialysis Patients: Efficacy Of Direct Acting Antiviral Treatment (Elbasvir/Grazoprevir)

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Abstract

Background

Hepatitis C infection is common in end stage renal disease (ESRD) patients undergoing regular hemodialysis, with prevalence is approximately 10%-20% patients.The emergence of new direct acting antivirals, Elbasvir/Grazoprevir, has studied to be safe and effective for patients with end stage renal disease on regular hemodialysis.

Methods

We conducted retrospective observational (analytic cross-sectional) study involving ESRD patients on regular hemodialysis with Hepatitis C infection treated at Gastro-Hepatology outpatient clinic Sanglah General Hospital from July 2019 until March 2020. We evaluate characteristic of patients including age, gender, initial level of HCV RNA, ALT, AST, platelet count, and degree of fibrosis using APRI score. Efficacy of treatment with Elbasvir/Grazoprevir is evaluated by examining level of HCV RNA 12 weeks post therapy (SVR12). Inclusion criteria are dialysis patient age >18 years old with detectable HCV RNA and seronegative for Hepatitis B and HIV infection.

Results

Total of 30 dialysis patients with detectable HCV RNA is enrolled in this study, with 73.3% patients is male and 60% of patients aged >50 years (mean age 50.77 ±

13.90 (20-85)). We find mean of initial HCV RNA level is 5.66 x 10^6 equivalents/mL ± 1.68 x 10^7 (900-9x10^7), 53.3% of patients have normal ALT level (mean ALT 53.72 U/L ± 51.8 (6.90-237.4)), AST level is elevated in 53.3% of patients (mean AST 39.60 ± 24.05 (6.40-103.7)), 63.3% of patients have normal platelet count (mean 192.40 ± 78.55 (58.80-444.90)), and mean of APRI score 0.76 ± 0.62 (0.10-2.50) with 2 patients have score e”2). We further evaluate correlation of initial HCV RNA level with other laboratory indices and we find significant correlation with AST level (r= 0.439, *p* 0.015), platelet count (r= -0.379, *p* 0.039), and APRI score (r= 0.479, *p* 0,0007). Only 9 out of 30 patients (30%) that have completed therapy with Elbasvir/Grazoprevir for 3 months due to limited drug distribution, 8 patients (26.6%) had therapy for 1 month, 4 patients (13.3%) had 2 months of therapy, and 9 patients still haven’t start therapy yet. All patients who completed 3 months of therapy have achieved SVR12 (100%).

Conclusion

Regular hemodialysis patients with Hepatitis C infection in our outpatient clinic in majority is elder male with high viral loads, elevated AST level, significant degree of fibrosis, and normal level of ALT and platelet count. Treatment with Elbasvir/Grazoprevir is effective in achieving SVR12 in patients who have completed course of therapy.

Hyperbaric Oxygen Therapy Improved the Histopathological Features of Gastric Mucosa in Aspirin-induced Wistar Rats

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Background

Gastritis, inflammation or erosion of the lining of the stomach, may cause someone to seek medical help. One of the most frequent causes of gastritis is the consumption of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin. Aspirin exerts its anti-inflammatory effects through inhibition of cyclooxygenase enzymes (COX), resulting in reduced blood flow and increased reactive oxygen species (ROS). Hyperbaric oxygen therapy (HBOT) could promote tissue survival by modifying ischemia and ROS activity. The aim of this study was to determine the effects of HBOT on the histopathological features of gastric mucosa in aspirin-induced Wistar rats.

Methods

This study was an experimental study with a randomized posttest only control group design using on three groups of Wistar rats, and each group consisted of seven rats. P1 was the negative control group without aspirin induction, P2 was the positive control group with aspirin induction. P3 was the treatment group with aspirin induction and HBOT (at chamber) of 2.4 ATA with 98% O_2 in three sessions, 30 minutes / session, and air break for five minutes between each session for the period of 10 days. Aspirin was administered at 20mg/kg body weight. Histopathological slide of

gastric mucosa was done with HE staining and the feature of gastric epithelium was analyzed based on *Barthel Manja* modification. The comparison of features in the three groups were analyzed using Kruskal-Wallis and Mann-Whitney U tests.

Results

Groups P1 and P2 were terminated on the 10^{th} day, while group P3 was terminated on the 20^{th} day. Normal histological feature was seen in P1. P2 showed acute gastritis features, such as infiltration of PMN inflammatory cells in the mucosa to serous layers, submucosa edema, and capillary dilatation. P3 showed decreased PMN inflammatory cells in mucosa and submucosa, compared to P2. The Kruskal Wallis test showed a significant value of $p = 0.003$, and Mann-Whitney U test with $p = 0.042$)

Conclusion

The administration of HBOT improved the histopathological feature of gastric mucosa in aspirin-induced Wistar rats.

Keywords : Gastric mucosa (sub mucosa) erosion, aspirin, hyperbaric oxygen therapy.

Proton Pump Inhibitor as Gastrointestinal Bleeding Management in Percutaneous Coronary Intervention Case: A Systematic Review and Meta-Analysis

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Abstract

Background

Percutaneous coronary intervention (PCI) is a standard treatment in patients with acute coronary syndrome. Studies have shown that administering Dual Antiplatelet Therapy (DAPT) can increase bleeding incidence especially gastrointestinal bleeding (GIB). The objective of this study is to synthesize the evidence of the effect of PPI on gastrointestinal bleeding outcomes in a PCI patient population.

Methods

We conducted a systematic literature review for studies reporting clinical outcomes in patients who underwent a PCI and were initiated on DAPT with or without a PPI. Studies were included in the analysis if they reported at least one of the clinical outcomes of GIB on patients with acute coronary syndrome who underwent coronary stenting. We excluded studies that were not exclusive to PCI patients or had no PCI subgroup analysis. Medline and Cochrane were searched from 2005 to 2020 for matching randomized control trials. Statistical analysis was done using RevMan version 5.4.

Results:

Six studies with 6934 patients (3451 on PPI with DAPT and 3483 with only DAPT) were included. Our analysis showed that PPI significantly reduced the incidence of gastrointestinal (GI) bleed [35 vs. 97, odds ratio (OR)= 0.37, confidence interval (CI)= 95%, Pd" 0.00001, I2 =0%]. There was an insignificant difference in unstable

angina pectoris adverse events, myocardial infarction adverse events, cerebrovascular events, target vessel revascularization events, all-cause of mortality, and major adverse cardiovascular events endpoint.

Conclusion

Concomitantly administered PPIs with DAPT have a significant protective effect on the GI bleeding events.

Keyword: gastrointestinal bleeding, proton-pump inhibitors, percutaneous coronary intervention, acute coronary syndrome

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Acute Liver Failure on 23 Years Old Man and Acute Kidney Injury Due to Hepatitis C Virus

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Introduction

Acute liver failure (ALF) is characterized by acute liver injury, hepatic encephalopathy, and an elevated prothrombin time/international normalized ratio (INR).The accuracy of diagnosis and management acute liver failure is crucial**,** viral hepatitis is the most common cause of ALF. Around 40-60% of patients with ALF suspected having a viral infection. The examination was found negative in serological markers for hepatitis A virus (HAV) and hepatitis B virus (HBV), being classified as non-A non-B (NANB) hepatitis which are now called Hepatitis C Virus-Associated Liver Failure.[2]

Case Report

A 23 years old male was admitted to Rumah Sakit Umum Daerah Kabupaten Bekasi with history of jaundice, fever, encephalopathy, coagulopathy, and renal failure. He had no history of any comorbidities. He was having jaundice and flapping tremors. He was anuria, his laboratory examination showed AST 461 U/L, ALT 1383 U/L, total bilirubin 2.7 mg/dl, albumin 3 g/dl, PT prolonged 2 sec, glomerular filtration rate (GFR) 5.2 ml/min/L, D-Dimer 4.0, and thrombocytes 70.000/uL. His viral screen revealed positive anti HCV. N-Acetylsistein and supportive hemodialysis were done and patient improved gradually.

Conclusion

Determining the etiology of acute liver failure requires a combination of history taking, laboratory tests, and imaging studies. Because patients may decompensate rapidly, the initial evaluation should be broad, even in patients with a presumed cause for their acute liver failure. A broad evaluation is required to identify a cause of the acute liver failure and holistic management should be done

Key Findings: Acute Liver Failure, Hepatitis C Virus, Hepatitis

A 28 Years Old Woman P2A0 Post Caesarean Section ec Fetal Distress, Gastric Varices ec Non Cirrhotic Portal Hypertension ec Splenic Vein Stenosis

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Background

Non-cirrhotic portal hypertension is a portal hypertension without cirrhosis, it happen in 10% of patients with portal hypertension. Most common complication of NCPH are oesophageal varices and gastric varices which also most common cause of death. It is difficult to diagnose because of the low prevalence and many clinical manifestations, commonly found are oesophageal varices, gastric varices, splenomegaly, and anaemia. In ultrasound and liver biopsy the result is normal. The therapy for NCPH is beta-blocker to lower portal tension, endoscopic therapy for oesophageal varices, and surgery.

Case Description

We show a case about 28 years old woman with history of two times pregnancy resulting with fetal distress. She also had gastric varices from non-cirrhotic portal hypertension. Patient came to the clinic because of the vomiting of blood and black stool within pregnancy and resulted in anaemia and thrombocytopenia. From physical examination, splenomegaly was found. From the gastroscopy, isolated gastric varices was found. From angioportal MSCT, thrombus of portal vein, hepatic vein, and splenic vein enlargement were not found. From splenoportography splenic vein stenosis at the level of spleen hillus was found.

Discussion

We found that the cause of multiple pregnancy with fetal distress was anaemia from vomiting blood and black stool caused by gastric varices. From gastric varices we found the main problem was the splenic vein stenosis at the level of spleen hillus. We planned splenectomy for the patient so the patient can get normal pregnancy.

Conclusion

Non-cirrhotic portal hypertension is a portal hypertension without cirrhosis, it happen in 10% of patients with portal hypertension. In this case, 28 years old woman with history of two times pregnancy resulting with fetal distress from splenoportography splenic vein stenosis at the level of spleen hillus was found. We planned splenectomy for the patient so the patient can get normal pregnancy.

Case Report : 30 Year Old Male present with Idiopathic Non Cirrhotic Portal Hypertension

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Abstract

Background

Idiopathic Non Cirrhotic Portal Hypertension (INCPH) is a hepatic presinusinoidal cause of portal hypertension with unknown causes, which is characterized by the features of portal hypertension and splenomegaly. Even though this disease has worldwide distribution, it is more likely happened in Asia. Which is usually happened in low socioeconomically people, which usually live in low hygiene and living standards. This disease were characterized with clinical signs of portal hypertension and some histological findings. There is still no specific guideline to treat INCPH.

Case report

30 year old male come to Emergency Department with hematemesis and melena. Patient had already three times bloody vomiting before come to the hospital. Patient also had black stool since three days before came to the hospital. The patient had no history of hepatitis, alcohol abuse, drugs abuse, and HIV. He lived in a densely populated area with low hygiene.

Form the physical examination, the patient looked weak, completely aware. He had no breathing difficulties, and had no fever. His conjunctiva looked pale, and his sclera looked icteric. There were no liver enlargement. But we found splenomegaly as large as Hackett 2. Form the laboratory examination the patient had anemia, and had slight increase on liver function. The serologic test for hepatitis B, C and HIV were

negative. The ANA test was slightly increased. The USG examination only showed splenomegaly. And the endoscopic examination showed Esophageal Varices grade 2 and gastropathy portal hypertension

Conclusion

INCPH is a rare disorder which consisting of intrahepatic portal hypertension with no evidence of intrinsic liver disease and/or splanchnic vein thrombosis. The diagnosis were made through exclusion of other liver disease. The treatment is focused on managing the complications of portal hypertension and PVT. The 5 years prognosis of this disease is nearly 100%.

Keywords: INCPH, portal hypertension

Challenges in Diagnosis and Treatment of Peritonitis Related Tuberculous Appendicitis with Additional Burdens Faced Amid COVID-19 Pandemic: A Case Report

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Abstract

Introduction

Tuberculosis remains as global burden for decades, moreover in endemic countries such as Indonesia. Out of total TB cases, up to 20% cases are extrapulmonary TB, among which, abdominal TB has contributed in 11% of its incidence**.** The possibility of tuberculous abdominal is often overlooked. Diagnosis and treatment of this disease had become even more challenging during COVID-19 pandemic.

In this article, we present a case of tuberculous appendicitis induced peritonitis admitted to our center during COVID-19 pandemic. We would like to emphasize on the challenges and additional burdens we found, given this trying time.

Case Description

A 12-year old girl came to our surgery department with chief complaint of abdominal pain for 2 weeks. Abdominal ultrasonography revealed a lot of free liquid in peritoneal cavity with prominent McBurney area, highly suggestive of perforated appendicitis. Patient's hemoglobin was low, therefore surgery was delayed after transfusion with targeted hemoglobin level of 10 g/dl. During surgery we found adhesion on gut lumen alongside multiple easily bleeding granulomatous studded on colon surface. Histopathology of specimen revealed multinucleated giant cell *Datia Langhans,* signified the possibility of tuberculous appendicitis. Patient was discharged on anti-

tuberculous treatment. However, a week after, patient was re-admitted with unknown etiology of bloody diarrhea and severe anemia. Referral was unlikely, due to the unattainable fast rapid and swab result.

Conclusion

Despite its rare occurrence, tuberculosis of appendix should always be considered, moreover in patients residing in endemic area. To date, histopathological finding remains reliable and effective for diagnosis. Surgery should be prioritized in our patient regarding the disadvantageous signs of perforation.

During COVID-19, many unfamiliar procedures need to be routinely carried out to prevent transmission of disease. Blood shortage, delayed referral, patient's reluctance to go to the hospital had cost greater risk of unfavorable result in our patient. This novel state required healthcare providers to be very vigilant, as well as efficient, and more adaptable than ever.

Case Report: Recurrent Non-Variceal Upper Gastrointestinal Bleeding

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Abstract

Introduction

Gastrointestinal Bleeding (GIB) is an emergency case that often found in the condition. In Indonesia, the prevalence of GIB in the population is still unknown. The most common cause of gastrointestinal bleeding is peptic ulcer, which is followed by erosive gastritis. *Helicobacter pylori* infection is a major factor in the development of ulcers, both duodenal and gastric ulcers. Acute gastrointestinal bleeding due to hookworm infections was rarely described previously. However, in developing countries especially in the tropics, worm infection should be considered an important cause of obscure acute gastrointestinal bleeding

Presentation of Case

A 57-year-old female presented with recurrent upper gastrointestinal bleeding. Endoscopy revealed Gastroduodenopathy erosive and helminthiasis. Suspect *H. pylori* was confirmed from biopsy.

Discussion

Early evaluation and resuscitation are important measures that should be carried out for patients with GIB. *H. pylori* test is recommended in all patients with peptic ulcer bleeding. The test is subsequently followed with eradication therapy for all patients who have positive results. Literature mentions that Hookworms may cause clinic

conditions such as gastrointestinal bleeding, and severe anaemia. According to CDC, Hookworm infection is treated with albendazole, mebendazole, or pyrantel pamoate

Conclusion

Endoscopy has important role for identification of the source of GIB. In developing country, very important to consider and remember helminths in differential diagnoses during daily routines.

Keywords: upper gastrointestinal bleeding, h. pylori, helminthiasis

Administration of Tranexamic Acid and Vitamin K in Recurrent Upper Gastrointestinal Bleeding Case: Does it Reduce Rebleeding and the Need for Blood Transfusion?

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Background

The use of Tranexamic Acid (TXA) and Vitamin K (Vit K) in Upper Gastrointestinal Bleeding (UGIB) is still controversial. Some studies claim to reduce mortality rates while some claim to be no. Despite all that, TXA and Vit K is readily available drug, widely used in resource poor areas.

Case Description

A 65-year-old man came to the ER of the PMC Hospital with complaints of heartburn since 3 days ago and had black stools since 1 month ago. While in the ER, the patient vomited blood once ± ¾ glass. The patient appears pale and limp. Previously, the patient routinely took uric acid medication but did not remember the name of the medication. The patient was treated in 2015 and 2016 with the same complaint. On physical examination, the conciousness is compos mentis, BP 80/43 mmHg, RR 20x/i, pulse 108x/i, temperature 36.8p C, VAS 6, pale inferior conjunctival palpebra, epigastric tenderness in abdomen, four extremities acral are cold and CRT <2 “. Blood test shows Hb level was 8.9 g/dl. Patients were given loading RL 500cc and NaCl 500cc, Pantoprazole injection 2x40mg then 40mg/5 hours, TXA Injection 3x500mg, Sucralfate syrup 3xCth2, Vit K 3x1 tab. Twelve hours later, the Hb level was 8.6g / dl. On the second day of treatment, the patient vomited blood again ± half a glass. The second, third and fourth day of treatment there was a decrease in Hb levels, respectively 8.4 g/dl, 8.2 gr/dl and 7.9 gr/dl. Then the patient was given a blood transfusion of 1 unit /day for 2 unit. Post transfusion on the fifth and sixth day

of treatment, the Hb level increased in the numbers 9.2 g / dl and 10.9 g / dl. Clinical symptoms began to improve on the fifth day. The patient was discharged on the seventh day of hospitalization.

Conclusion

Early administration both of TXA and Vit K in this case could possibly reduce the duration and amount of bleeding at presentation and the risk of re-bleeding. This could reduce mortality and the need for blood transfusion.

Keyword: Tranexamic Acid, Vitamin K, Upper Gastrointestinal Bleeding

Evidence of Microalbuminuria and Estimated Glomerular Filtration Rate Decline as Chronic Kidney Disease Risks in Non-alcoholic Fatty Liver Disease Patients: Systematic Review and Meta-Analysis of Cohort Studies

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Background

Non-alcoholic fatty liver disease (NAFLD) has been the most prevalent chronic liver disease that may lead to cirrhosis and hepatocellular carcinoma. Recent evidences showed association between NAFLD and extrahepatic manifestations include chronic kidney disease (CKD) although the result is still inconsistent. This study aims to measure the association of microalbuminuria and estimated glomerular filtration rate (eGFR) decline as CKD risks in NAFLD patients.

Methods

Comprehensive searching using predefined queries was done through online databases Pubmed, EMBASE, ScienceDirect, and The Cochrane Library for all literature until July 2020. We included all cohort studies met inclusion criteria of NAFLD patients diagnosed by ultrasonography (USG), commutated tomography (CT), or scoring system fatty liver index (FLI) which reports microalbuminuria and eGFR decline below 60 ml/min/1.73m^2. Bias risk was assessed by The Newcastle-Ottawa Scale for cohort studies. Analysis of this study was performed using Review Manager (RevMan) version 5.3 to provide hazard ratio (HR) with 95% confidence interval (CI) using random effect heterogeneity test.

Results

We included 9 cohort studies met our criteria. Analysis of 6 NAFLD cohort studies diagnosed by USG is significantly associated with eGFR decline (pooled HR=1.54 95%CI 1.13-2.11 p=0.006 I^2=88%), while overall analysis combined with other diagnostic modalities showed significant association between NAFLD and eGFR decline (pooled HR=1.53 95%CI 1.29-1.80 p<0.00001 I^2=82%). Microalbuminuria risk is increased in NAFLD patients although not statistically significant (pooled HR=1.49 95%CI 0.94-2.38 p=0.09 I^2=79%). Surprisingly, NAFLD patients whose increased gamma-glutamyltransferase (GGT) has higher eGFR decline risk (pooled HR=1.73 95%CI 1.02-2.92 p=0.04 I^2=78%).

Conclusion

Microalbuminuria and eGFR decline has significant association in NAFLD patients as risks for CKD development. However, further studies are still needed to establish causality.

Keywords: non-alcoholic fatty liver disease, NAFLD, microalbuminuria, chronic kidney disease.

Amoeba Liver Absess with Lung Empiema : A Case Report

*** Jona August, ** Budiman Sujatmika Sulaiman**

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Abstract

The extraintestinal infection of Entamoeba histolityca is most commonly amoebic liver abscess. The most dominant symptoms are dull right upper abdominal pain and fever. The most frequent complication of amoebic liver abscess is rupture and through the diaphragm causing amoebic empyema. In this case report, we report a 45 year old man presented with a complaint of shortness of breath 1 week before being admitted to the hospital, shortness of breath accompanied by right chest pain and coughing. No fever, no coughing up blood, no weight loss, no defecation and bowel problems. Past disease history of pulmonary TB with OAT category I 2 months. Blood pressure 93/58, pulse 134 beats per minute, breathing 30 times per minute, temperature 36.1. on physical examination of the chest, it was found that the lung sound decreased by 1/3 of the basal lung. From the laboratory results obtained leukocytosis (29,300 / uL), negative smear results, ADA results (adenosine deaminase) 232.5U / I and antibody E. Histolytica OD unit 1.98 (negative <0.4; positive> 0.4), liver function, kidney function and value electrolytes within normal limits. X-rays and chest x-rays, plural right encapsulated effusion, bronchopenumonia, upper abdominal ultrasound results: 2.4x4.2 cm clear borderline cystic lesions, contrast upper abdominal msct results: cystic lesions of the right hepatic border were enlarged by contrast. Management by installing WSD for drainage of plural effusions, administration of antibiotics, meropenem and metronidazole for 7 days and OAT category I continued

Keyword : Amoeba Liver Absess, Lung Empiema

The Seroprevalence of Hepatitis C Positive in Donors of Indonesian Red Cross Blood Bank Semarang, Central Java

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Abstract

Background

The Asia-Pacific region has the highest prevalence of HBV and HCV infections in the world with 74% of lethal liver complications occuring in Asia. In 2012, Indonesia had a prevalence of 0,39% HCV infections, according to a data taken from Unit Transfusi Darah Pusat. It is a target by WHO to reduce new viral hepatitis infections by 90% and to reduce deaths due to viral hepatitis by 65% by 2030.

Methods

This was an observational descriptive study conducted in Semarang from September 2019 – February 2020. Data were obtained through patient's medical records from January 2009 – December 2019. Subjects who had been a donor in the Indonesian Red Cross Semarang, had an HCV-reactive screening result, and had their basic demographic data taken were included to the study.

Results

The seroprevalence of Hepatitis C reactive were 2267 donors from a total of 710.778 (0.3%) during the ten-year cohort. The highest prevalence was found in 2009 (0.6%) with the lowest were in 2018 and 2019 (0.2%). In 2011 through to 2015 and 2017 the prevalence was 0.3%. In 2010 and 2016, the prevalence was 0.4% respectively. This showed a trend of decreasing prevalence during this ten-year cohort. The mean age of reactive donors was 33.88 (SD 11.45) with a range of 16 – 67. Among the reactive donors, 79.8% were males and 20.2% were females. These donors mostly domicile in the region of Semarang (74.6%). The most prevalent occupation was people worked in the private sectors (55.5%).

Conclusions

HCV infection among blood donors remains an important public health concern. It has been discovered that the trend of infection has decreased but has not yet reached the designated target. Greater efforts of management need to be implemented and maintained in order to achieve the target of reducing new viral hepatitis infection.

Clinical Characteristics and *Helicobacter pylori* Infection in Chronic Kidney Disease Patients with Gastrointestinal Event (Clinical Study in Kariadi General Hospital Semarang)

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Background

astrointestinal event (GI event) is one of the complications that occurs in patients with chronic kidney disease (CKD), with a variety of symptoms ranging from mild nausea-vomitus, to severe bleeding. The pathogenesis of gastrointestinal disorders in CKD patients is multifactorial; uremic toxin retention, chronic inflammation, iatrogenic and motility disorders. It is not yet known about clinical feature of GI events that occur in patients with CKD, endoscopic and histopathological decriptions of gastrointestinal lesions, and *H. pylori* infection.

Methods

This study was an analitical observational study with cross sectional approach. The samples were CKD patients aged 18 years or above who experienced GI events and underwent gastrointestinal endoscopy at dr. Kariadi General Hospital Semarang, both inpatient or outpatient during the period of January 2018-January 2020. Classification of the severity of CKD based on creatinine clearance (*Cockcroft-Gault*) is divided into stages 1 to 5. Endoscopic and histopathological imaging data are drawn from the conclusions of the examination. Analysis of finding correlation between the severity of CKD with several variables; type of GI event, endoscopic features and *H.pylori* infection.

Results

A total of 104 CKD patients, the majority of whom were inpatients with GI events had undergone gastrointestinal endoscopy, ages ranging from 22-87 years, mean age of 52.26 years, 54.8% male and 45.2% female, the majority are patients in stage 5 CKD (61.5%). Types of GI events are based on the highest order, namely; melena (56.7%), dyspepsia (25%), hematemesis (12.5%), abdominal pain (3.8%) and hematoschezia (1.9%). The features from gastrointestinal endoscopy were ulcers (38.5%), inflammation (29.8%), erosions (26.9%) and polyps (4,8%). The location of GI lesions mostly in the stomach 66.3%. The histopathological feature mostly of active chronic inflammation 78.8% and the incidence of *Helicobacter pylori* infection is 24.4%. The results of the analysis finding correlation between the severity of CKD with several variables; type of GI event (p= 0.18), endoscopic features (p= 0.75) and *H. pylori* infection (p= 0.073).

Conclusion

The majority of GI events in CKD occur in stage 5 CKD patients, with melena as the most common presenting symptom, ulcer was the most commonly detected lesion and stomach as the most commonly affected site. There are no correlations between the severity of CKD with types of GI event, endoscopic features and *H. pylori* infection.

Keywords: gastrointestinal event, chronic kidney disease, endoscopy, *H.pylori*

Abstract

Geographic Distribution and Clinical Characteristics of Hepatocellular Carcinoma Patients Etiology of Hepatitis B Viruses in Dr. Kariadi Hospital Semarang

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Background

Hepatocellular carcinoma (HCC) ranks highest from all malignancy levels in the world. HCC is 10-20% of all liver diseases in Indonesia. There is no patient's geographic distribution data of Hepatitis B virus etiology in Central Java.

This study aims to analyze geographic distribution and the correlation between patient's place of origin with clinical characteristic of HCC with Hepatitis B virus as etiology in RSUP Dr Kariadi Semarang.

Methods

Retrospective study through RSUP Dr Kariadi HCC patient's medical record in 2013-2015. Analyzed variables were distribution of patient's place of origin (urban/rural), clinical characteristic: age, sex, severity: child-pugh score, BCLC staging, and AFP level. The data was processed with SPSS program, with significant value $p<0,05$.

Results

There were 103 HCC patients with most place of origin included Demak(22,3%), Semarang (17,5%), Grobogan(14,6%). Male : female ratio, 4,4 : 1, Group age mean 47±12,8, Child-Pugh A, 14 (13,6%) , Child-Pugh B, 54 (52,4%), Child-Pugh C 35 (34,0%) , 7 (6,8%) BCLC A (early stage), BCLC B *(intermediate stage)*41 (39,8%) .

BCLC C *(advanced stage)* 21 (20,4%) . BCLC D *(terminal stage)* 34(33%) . AFP 70% > 400. There's no significant correlation between geographic distribution with clinical characteristic and severity.

Conclusion

There's a description of the geographic distribution of patients with HCC who seek treatment at Dr Kariadi Hospital with the 3rd largest order of Demak, Semarang, and Grobogan. There's no significant correlation between geographic distribution with clinical characteristic and HCC's severity (age, sex, BCLC staging, Child-Pugh level, and AFP level).

Key words: hepatocellular carcinoma, geographic distribution, severity index

Case Report of Decompensated Liver Cirrhosis with Alcohol Risk Factor: Diagnostic and Therapeutic Challenge in Primary Hospital

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Introduction

Liver Cirrhosis is a chronic liver disease characterized by irreversible fibrosis, lobular structure and vascular disorganization. There are many causes of cirrhosis include chemicals (such as alcohol), hepatitis viruses, toxic metals, and autoimmune liver disease.

Case Illustration

Male, 60 years old, present with abdominal bloating, black stools, bloody vomiting and history of alcohol consumption for 10 years. Physical examination revealed anemic conjunctiva, ascites, splenomegaly and bilateral legs edema. Laboratory examinations showed anemia, thrombocytopenia and hypoalbuminemia. AST, ALP and Bilirubin level were increased. Abdomen USG showed characteristic of liver cirrhosis. Diagnosis of liver cirrhosis was made based on clinical, laboratory, and radiologic findings.

Discussion

Diagnosis of alcoholic liver disease was made based on the presence of excessive alcohol consumption history, presece of sign and symptoms of liver disease, and absence of other etiology of liver injury. Physical examination may range from normal to the presence of signs of cirrhosis. There is no single definite laboratory marker which can determine alcohol as the etiology of liver disease. Imaging studies did not have specific role in determining alcohol as the specific etiology of liver disease. In the presence of complications such as ascites, a history of hematemesis melena

indicates that liver cirrhosis in this patient has entered the decompensated stage. Cessation of alcohol consumption is the most important thing in therapy and early management of alcohol abuse in patients with alcoholic liver disease**.**

Conclusion

Alcohol consumption with long periode can be caused irreversible liver damage (hepatic cirrhosis) with its complication. Decompensated cirrhosis are nearing end-stage liver failure and are usually candidates for a liver transplant.

Keyword: *Decompensated Liver Cirrhosis, Alcohol Risk Factor*

Abstract

Liver Involvement and Severity in Patients with COVID-19

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Introduction

In March 2020 Pantiwilasa dr Cipto Hospital first discovered patients suspected to have COVID-19. Some evidence suggested extra-pulmonary involvement in COVID-19 patients, including liver injury. We aimed to quantify the effects of COVID-19 on the liver.

Methods

We extracted data regarding patients with PCR-confirmed COVID-19 whom admitted to our hospital from March to August 6th, 2020. Obtained data included age, sex, liver function test result, severity, and comorbidities. Age were categorized as 0-18 years old, 19-30 years old (young-adults), 31-40 years old, 41-50 years old, 51-60 years old, and >60 years old (geriatry). Sex were men and women. The regular liver function tests were AST and ALT. The upper limit of normal for liver transaminases in female and male were 19 U/L and 30 U/L, respectively. Severity was rated by ARDS (acute respiratory distress syndrome), which was measured by SpO2/FiO2 d”315.

Results

Altogether, 178 patients were enrolled, with 88 men and 90 women. The prevalence of patients with increased AST in the male and female group were 90,91% and 96,97%, consecutively.

There were 68,18% of men and 77,78% of women who had elevated ALT.

The patients were mostly in the sixth decade and above (33,70%). There was only 1 patient under 18 years old, who was a thirteen years old girl with elevated liver transaminases. The highest prevalence of patients with abnormal AST (97,38%) was noted in the 41 to 50 years age group. The prevalence of patients with increased ALT not differ much between the consecutive age groups; 19-30 years old (87,50%) ; 31-40 years old (85,00%) ; and 41-50 years old (84,20%).

ARDS was found in 58 of 178 patients (32,58%). The geriatry group marked the most with ARDS (46,55%), followed by the age group of 51 to 60 years old (34,48%). The prevalence of patients with increased AST and ALT were higher in the ARDS group (96,55% and 75,86%) than in Non-ARDS group (92,50% and 71,67%).

There were only 1 patient in 41-50 years age group , 1 patient in 51-60 years age group, and 2 patients in the geriatry group who fall into ARDS without having comorbidites. The most found comorbidities in ARDS patients were chronic heart failure (28), hypertension (22), diabetes mellitus (18), and chronic kidney disease (8). Researchers were unable to confirm the pre-existing chronic liver disease in all patients due to limitation of laboratory and physical diagnosis. However, the medical records reported one ARDS patient with liver cirrhosis and one ARDS patient with first grade fatty liver.

Conclusion

Liver injury is not uncommon in patients with COVID-19. Higher prevalence of liver involvement were found in patients with ARDS than Non-ARDS.

The Role of Aspirin in the Prevention of Hepatitis B Virus-related Hepatocellular Carcinoma Development and Recurrence: A Systematic Review

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Introduction

Hepatocellular carcinoma (HCC) is one of the most prevalent cancer worldwide. Chronic hepatitis B (CHB) is a major risk factor of HCC development. Hepatitis viral status is also linked to tumor recurrence. Another effective therapy to reduce HCC risk in this population is needed since antiviral therapy for preventing HCC has limitations. A less costly drug, aspirin, has been reported to have chemo-preventive effects on HCC.

Methods

PubMed, Cochrane, and DOAJ databases were searched for English language studies published in the last 5 years reporting the association between aspirin-use and the HCC development or recurrence risk in patients with hepatitis B virus (HBV) infection. Data about participants, study design, aspirin administration, and outcomes were extracted. Newcastle-Ottawa Assessment Scale (NOS) was used to assess the quality of cohort studies.

Results

Three studies were eligible for this review. Two cohort studies reported that aspirin-use was associated with lower risk of HCC development in CHB patients. In one cohort study, lower risk of HCC recurrence was observed among aspirin-users with hepatitis B virus-related HCC after surgical resection.

Conclusion

Aspirin has a potential role for preventing the development and recurrence of HBV-related HCC. Further larger-scale and high-quality studies with better design are needed to evaluate aspirin use, particularly in HBV-related HCC.

Keywords: aspirin; hepatocellular carcinoma; hepatitis B

Anticoagulant Therapy for Cirrhosis-related Portal Vein Thrombosis: A Meta-Analysis

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Backgrounds

Portal Vein Thrombosis (PVT) remains a devastating complication in liver cirrhosis (LC) patients. It is associated with poor outcome and high short-term mortality rates, as it may enhance the risk of bleeding aside from the already established mechanism; portal hypertension. Treating cirrhosis-related PVT with anticoagulants is difficult because of the patient's nature of coagulopathy-related disorders. Thus, a systematic review and meta-analysis was done to assess the efficacy and safety of anticoagulant in cirrhosis-related PVT.

Methods

A search on PUBMED and EMBASE was conducted. The efficacy and safety outcomes were any recanalization (partial and total) and variceal bleeding, respectively. Data were pooled to determine the odds ratio (OR) and its 95% CI.

Results

One RCT and 8 observational studies comprising 516 patients were included. Pooled analysis showed that recanalization was more likely to happen in patients who received anticoagulants than in no treatment group (OR=6.59; 95%CI=3.18-13.64). Occurence of variceal bleeding was lower in the anticoagulant group (OR=0.5; 95%CI=0.25-0.97; p=0.04).

Conclusion

Preliminary analysis showed that anticoagulant therapy may be beneficial and safe for cirrhosis-related PVT. Further studies with RCT-design and bigger samples are needed to better elucidate its efficacy and safety.

Expanding the Potential Benefits of Vitamin E in NAFLD Patients: A Meta-Analysis of Randomized Controlled Trials

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Background

Non-alcoholic fatty liver disease (NAFLD) is characterized by lipid deposition in the liver parenchyma without significant history of alcohol consumption or other secondary causes. Disease presentation of NAFLD ranges from asymptomatic disease to cirrhosis with the complication of liver failure and hepatocellular carcinoma. Insulin resistance and oxidative stress play a vital role in the progression towards NAFLD in all age groups. Currently, there is no established treatment for this disease. Several pilot studies have provided evidence that antioxidants such as vitamin E improve clinical and histologic features of NAFLD. Vitamin E is considered a chain-breaking antioxidant in free radical reactions such as lipid peroxidation.

Methods

We searched PUBMED and EMBASE from their inception to November 2019. The outcomes were as follows; ALT, AST, GGT, ALP, BMI, steatosis score, lobular inflammation, ballooning, and fibrosis. Using random-effects meta-regression model, data were pooled to determine the weighted mean difference (WMD) of the outcomes. The meta-analysis was conducted using Revman 5.3 software.

Results

A total of 8 randomized controlled trials involving 539 NAFLD patients were included in the analysis. The pooled analysis showed that, comparing with the control group, patients treated with vitamin E had significant improvement in ALP of -9.42 U/L, fibrosis of -0.43, lobular inflammation of -0.18, and steatosis of -0.62.

Conclusion

Vitamin E as adjuvant therapy has potential benefits in NAFLD patients by significantly improving biochemical and histological changes.

Probiotic to Treat Irritable Bowel Syndrome Associated with Constipation: An Evidence-based Case Report

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Abstract

Background

Irritable bowel syndrome (IBS) is affecting quality of life for a lot of people due to its exaspereting symptoms. Constipation (IBS-C) is one associated symptom of IBS, the other being diarrhea (IBS-D), and mix symptoms of both (IBS-M). Treatment options for IBS-C includes strict diet, psychological stress control, and drugs to alleviate symptoms. We present a case, an adult woman with chronic abdominal discomfort that meets Rome III criteria for IBS, where constipation predominates. Beneficial effects of probiotic for IBS-C has been a debatable issue. Some studies, guidelines, and expert opinions recommend the use of probiotic in such patient.

Method

In August 13th, 2020, we performed systematic search on Pubmed, Embase, and Cochrane Library following a predefined clinical question. Keywords include; probiotic, functional, chronic, constipation, and irritable bowel syndrome. We screened through title and abstract with inclusion and exclusion criteria, filtered double, and finally read full text articles. The process yielded five useful articles that correspond to our case. This evidence-based case report critically appraised the articles for its validity, importance, and applicability based on the guideline from Oxford's Center of Evidence-Based Medicine treatment worksheet guideline.

Result

All articles are randomized placebo-controlled trial, with outcome observation point at 3 to 12 months. Probiotic strain varies. Four articles use multistrain probiotics in their treatment group including; *L acidophilus, L reuteri, L plantarum, L rhamnosus, B animalis, B breve, B bifidum, and P freudenreichii.* All articles are considered valid and all support the use of probiotics to alleviate symptoms in IBS-C patient ($p < 0,05$). Outcome were measured by irritable bowel syndrome - severity scoring system (IBS-SSS).

Conclusion

We recommend the use of probiotic as treatment options for patient with irritable bowel syndrome where constipation predominates. Further study needed to appraise the correct strain combination and dosage to achieve best symptoms control result.

Duration of Hemodialysis and Hepatitis C Seroprevalence in Chronic Kidney Disease Patients Underwent Hemodialysis

Abstract

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Background

Hepatitis C Virus (HCV) infection increase morbidity and mortality in Chronic Kidney Disease (CKD) patients who undergoing hemodialysis. On the other hand, patients with HCV seropositive are carrier and have the potential to transmit HCV to the surrounding environment, including other patients. The purpose of this study was to determine the relationship between duration of hemodialysis and hepatitis C seroprevalence in CKD patients who undergoing hemodialysis.

Methods

This case control study was conducted in January 2020 in Semarang. The sample was selected by total sampling methods with inclusion criteria : undergoing hemodialysis for e”3 months, the frequency of hemodialysis is twice a week and willing to participate in this study. Patients whose data was incomplete, anti-HIV +, HbsAg +, history of making tattoos and piercings, and a history of high-risk lifestyle were excluded from the study. Of them, 95 respondents joined in this study. Respondents were divided into two groups : group 1 included respondents who had HCV seropositive and group 2 included respondents who had HCV seronegative. Then, duration of hemodialysis were compared between these two groups.

Results

It was found that 38,9% of respondents had hepatitis C seropositive. The duration of hemodialysis in months were 36,4±22,4 in group 1 and 16,6±13,5 in group 2. From Mann Whitney U Test we found a significant relationship between duration of hemodialysis and hepatitis C seroprevalence (p value 0,000).

Conclusion

There is a significant relationship between duration of hemodialysis and hepatitis C seroprevalence in CKD patients undergoing hemodialysis.

Keywords. Hepatitis C, Seroprevalence, Hemodialysis, Duration of Hemodialysis, Chronic Kidney Disease

Proton-pump Inhibitors Use as the Risk of *Clostridium difficile* Infection: A Systematic Review and Meta-analysis

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Background

Proton-pump inhibitors (PPIs) have become the most widely prescribed agents throughout the world since their release. They are highly effective in treating gastric acid-related disorders but are often overprescribed without a clear indication both in hospitalized patients and outpatients. Nevertheless, like in the case of other drugs, PPIs are not as safe as it has been thought. Several studies have reported conflicting results regarding the association between PPIs use and increased risk of *Clostridium difficile* infection (CDI). Thus, a systematic review and meta-analysis was carried out to analyze the correlation between PPIs use and the risk of CDI.

Methods

The following electronic databases were searched from PubMed, Medline, EMBASE, and Cochrane Library. A meta-analysis was conducted using RevMan 5.3 software to identify the association between PPI use and risk of CDI, analyzing the odds ratio (OR) with 95% confidence intervals (95% CIs) using a random-effect model.

Results

19 cohorts and 54 case-control studies comprising 535,112 patients were included in the analysis. Pooled analysis showed that PPIs use was associated with higher risk of CDI (OR=1.92; 95%CI=1.67-2.21; p<0.00001). Risk of CDI was even higher in

the inpatient group than in ICU and community (OR=2.01; 1.72-2.34 vs OR=1.24; 0.83-1.86 dan OR=1.81; 1.17-2.81).

Conclusion

PPIs use was associated with higher risk of CDI, with the highest risk in an inpatient setting.

Research Report

Prevalence and Risk Factors as Sociated with Hepatitis DrugInduced (HDI) in TB-HIV Coinfection Patients in Perifer Regional Hospitals

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Introduction

Abstract

Until now, TB is still the first rank in mortality due to infectious diseases, namely 27.8%. TB-HIV co-infection is the main cause of mortality for people with HIV. A low immune system in HIV infection increases the risk of new TB infection and reactivation of latent TB by 20 times. TB is the most opportunistic infection among people living with HIV/AIDS, namely 49%.[1] Hepatitis drug induced (HDI) is a serious side effect of consuming OAT which causes patients to stop treatment. The incidence of HDI is 8-39%.[2]

Objective

To assess the prevalence and risk factors associated with HDI in TB-HIV coinfection

Methods

A retrospective cross-sectional study was carried out by tracing the medical records of TB patients with reactive HIV status from July 2019 to December 2019. The results of the analys is of the study used the chi square test on 40 patient medical record data as a sample, consisting of 8 cases of HDI and 32 not HDI with assess risk factors for HDI in patients co-infected with TB-HIV.

Result

HDI was found in 8(20%) TB-HIV coinfected patients. The prevalence of men compared to women who experience HDI is 3:1. Risk factors that had a significant relationship in HDI ($p<0.05$) were age >35 years ($p=0.01$), combination ARV Duviral and Nevirapin ($p=0.04$), alcohol consumption ($p=0.038$), BMI <18.5 kg/m^2 ($p=0.04$), hypoalbumin ($p=0.01$), and CD4<100 ($p=0.01$).

Conclusion

The prevalence of HDI is quite high in TB-HIV co-infected patients. Monitoring of HDI risk factors such as liver function should still be done to evaluate patients who have risk factors for HDI.

Keywords: Hepatitis drug induced (HDI), co-infection, tuberculosis, Human Immunodeficiency Virus.

Original Research Report

Plain Photographs of Thorax Covid-19 Patients with Gastrointestinal Manifestations in the Peripheral Region

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Background

Abstract

Covid-19 became a global pandemic due to more aggressive transmission. Indonesia is ranked as the third highest in ASEAN contributors to the Covid-19 case. East Nusa Tenggara is also experiencing the effects of this global pandemic. Covid-19 manifestations not only affect breathing but also gastrointestinal. Chest radiography has a very important role especially in screening and establishing diagnosis of Covid-19 especially in helping covid-19 patients with more dominant gastrointestinal manifestations.

Methods

Descriptive research conducted retrospectively with sampling in the form of total sampling techniques. This type of sample was taken from covid-19 patients who had gastrointestinal manifestations at the Kupang Wirasakti Army Hospital in the period April 2020 to July 2020 and had performed plain chestradiographs as anexamination for diagnosis of the disease.

Results

16 people with as uspected covid-19, 8 patients were confirmed covid-19 and there maining 8 were rapid reactive. Each of these groups had 3 patients with gastrointestinal manifestations. Gastrointestinal manifestations experienced by covid-

19 patients were 37.5% and the most manifestations were diarrhea by 25%. The prevalence of males compared to females is higher at 56%. The largest age distribution group is the age range of 20-29 years (25%). Occupational groups at risk of exposure to co-19 (31.25%) are traders and health workers. 33% of covid-19 patients with more dominant gastrointestinal manifestations show abnormalities in their plain photo chest radiology. The most common pattern of abnormality is un ilateral sub pleural GGO with a mild severity. While in moderate and severe cases there is a picture of consolidation of unilateral peripheral middle and bilateral multifocal peripheral lobes.

Conclusions

Chest radiological examination can help with screening and diagnosis of covid-19 in peripheral areas, especially for health facilities that do not have imaging tools. About 33% of covid-19 patients show abnormalities in their gastrointestinal manifestations.

Keywords: Thorax Radiography, Covid-19, Gastrointestinal

The Efficacy of Obeticholic Acid for Improving Liver Histology in Patients with Non-AlcoholicSteatohepatitis (NASH): A Systematic Review

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Abstract

Background

Non-alcoholic steatohepatitis (NASH) is an increasingly common cause of chronic liver disease, which can progress to cirrhosis, hepatic decompensation, hepatocellular carcinoma, and liver-related death. Currently, there are no approved therapeutic options for NASH. Recent studies showed that obeticholic acid improved liver histology of NASH, including fibrosis.

Objective

To evaluate the efficacy of obeticholic acid in improving liver histology (fibrosis, steatosis, or other parameters) of NASH patients.

Methods

We searched PubMed, CENTRAL, and Springer and included randomized controlled trials (RCTs) involving patients aged e"18 years old with NASH comparing efficacy of obeticholic acid and placebo in improving liver histology; irrespective of publication status, year of publication, and language.

Results

Two RCTs were included. One study reported significant improvement of fibrosis with no worsening NASH ($p<0.001$, RR 1.9, 95% CI 1.4-2.8), significant improvement in

lobular inflammation (p<0.05, RR 1.2, 95% CI 1.0–1.5), and significant improvement In hepatocellular ballooning (p<0.001, RR 1.5, 95% CI 1.2–2.0) in obeticholic acid group compared to placebo. The second study reported significant improvement of liver histology score defined as a decrease in NAFLD Activity Score (NAS) by at least 2 points without worsening of fibrosis (p<0.001, RR 1.9, 95% CI 1.3 to 2.8), significant improvement in steatosis (p<0.05, RR 1.7, 95% CI 1.2 to 2.3), significant improvement in hepatocellular ballooning (p<0.05, RR 1.5, 95% CI 1.0 to 2.1), and significant improvement in lobular inflammation (p<0.01, RR 1.6, 95% CI 1.1 to 2.2) in obeticholic acid group compared to placebo. All studies reported decrease serum aminotransferase, c-glutamyl transpeptidase and increase serum alkaline phopatase, LDL cholesterol from baseline in obeticholic acid group.

Conclusion

Obeticholic acid significantly improved liver histology in NASH patients, including fibrosis, lobular inflammation, and hepatocellular ballooning. Further studies are needed to determine long-term benefits and safety in NASH patients.

Keywords. NASH, obeticholic acid, liver histology, fibrosis, steatosis

Unusual Clinical Presentation of Covid-19 with Severe Chest Pain From Gerd: A Case Report

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Abstract

Background

The outbreak of COVID-19 has declared as pandemic by WHO and become a great danger to global health. This infection mainly manifest in respiratory problem such as cough, fever and dyspnea. But recently, evidence revealed COVID 19 might present as extra-respiratory symptoms including gastrointestinal symptoms

Case description

We report a unique case of 26 years old female with intense bilateral chest pain aggravated by swallowing who later confirmed positive nasopharyngeal swab for COVID 19. Abnormalities findings were not found in electrocardiography. Chest x-ray didn't show any signs of pneumonia or any respiratory distress. Esofagoduodenoscopy revealed esophagitis Los Angeles grade A and anthral gastritis. Histological examination presented with plasma cell, lymphocytes infiltration and erosion. Helicobacter pylori were absent in the specimens. The main complaint resolved after treated with lansoprazole 8mg/ hour for 24 hours. Therefore the diagnosis was consistent with GERD.

Conclusions

Our case possessed an unusual manifestation of COVID-19 presented with severe chest pain from GERD while esophagoduedenoscopy findings were inconsistent with pain degree suffered.


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