Hepatopatía y VIH

PERITONITIS BACTERIANA ESPONTÁNEA
TARV EN HEPATOPATÍA
TRASPLANTE HEPÁTICO EN PACIENTES CON VIH

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Caso Clínico

- SM. 55 años. Procedente de Montevideo, Changas.
- AP. VIH +, Diagnóstico en 11/2015, contexto Pneumocistosis. Recibió

  TMP-SMX con buena evolución.
  - AZT/3TC/EFV en 12/2015, CD4+: 255 cel/mm3 y CV de VIH: 47.787 copias /mm3.
  - No otras Infecciones oportunistas. No coinfecciones.
  - CV (01/2016) CD4+ 248 cel/mm3 y CV 933 copias/mm3.
- Alcoholista de 4 litros de cerveza/día más 1-2 litros de vino/día, de 20 años de evolución. Abstinencia de 3 meses.
- Hepatopatía crónica de etiología alcohólica, diagnóstico en 11/2015.

  No contamos estadificación

  NO descompensaciones previas en lo hepatocelular ni en lo hepatocirculatorio, NO sangrados digestivos, no PBE.

- FI: 17/03.
- Motivo ingreso

  Descompensación de su hepatotopatía crónica a forma de un síndrome hidropígeno edematoso, con ascitis a tensión, grado 3.

Valoración inicial

Regular estado general, gran repercusión proteicocalòrica. Tax 37,7ºC

PP: FR 32 rpm, SatO2 VEA 90%. MAV +/+, no estertores secos ni crepitantes.

CV: RR de 110 cpm, RBG, no soplos, no IY ni RHY. Abdomen:

globuloso, cicatriz umbilical desplegada, matidez. MMII: no

edemas de miembros inferiores.

PNM: no elementos clínicos de encefalopatía hepática. No rigidez de nuca. PC s/p. Motor, Sensitivo parestesias en mmii. Coordinación s/p.

- 17/03 Analítica de laboratorio.

HEMOGRAMA
GB 3790
Linfocitos 360
Neutrófilos 2560
Hemoglobina 11,3
Plaquetas 101,000

FUNCIÓN RENAL E IONOGRAMA
Azoemia 46
Creatininemia 0,88
Na+ 129, K+ 3,7

FUNCIONAL Y ENZIMOGRAMA HEPÁTICO
BT 2,84, BD 1,9
FA 79, GGT 96
TGO 32 , TGP 7
Albúmina 2,4 ,
LDH233
TP 48%

17/3 **Paracentesis diagnóstica y terapéutica.**

Aspecto ligeramente turbio. Proteínas de 26 g/l, Glucosa 1,20 g/l , LDH 207, Amilasa 21, Albumina 11.

Citograma: Leucocitos 420 cel/mm3, 50% PMN, 50% linfocitos. GR 810 cel/mm3.
Bacteriológico de líquido de ascitis: 10,000 UFC de *Enterobacter cloacae*.
Sensible:Ceftriaxona (CIM ≤ 1), Ceftazidime, Piperacilina tazobactam (CIM≤ 4), Carbapenems, Ciprofloxacina (CIM ≤ 0,25), Gentamicina, Nitrofurantoína.
Resistente:Cefalosporinas de 1º y 2º generación, TMP-SMX.

17/3 y 19/3 **Hemocultivos** sin desarrollo.
19/03 **Urocultivo**: más de 100.000 UFC de *Enterobacter cloacae*, con igual perfil de susceptibilidad a los antimicrobianos.

19/03 **Ecografía abdominal**: hígado con superficie nodular, atrofia del lóbulo derecho con hipertrofia compensadora del lóbulo izquierdo. Ascitis de moderada entidad.

Estrategias terapéuticas

Con los planteos diagnósticos de Hepatopatía crónica DESCOMPENSADA, a nivel hepatocirculatorio. COMPLICADA con una PERITONITIS BACTERIANA ESPONTÁNEA.
En un paciente severamente inmunodeprimido.

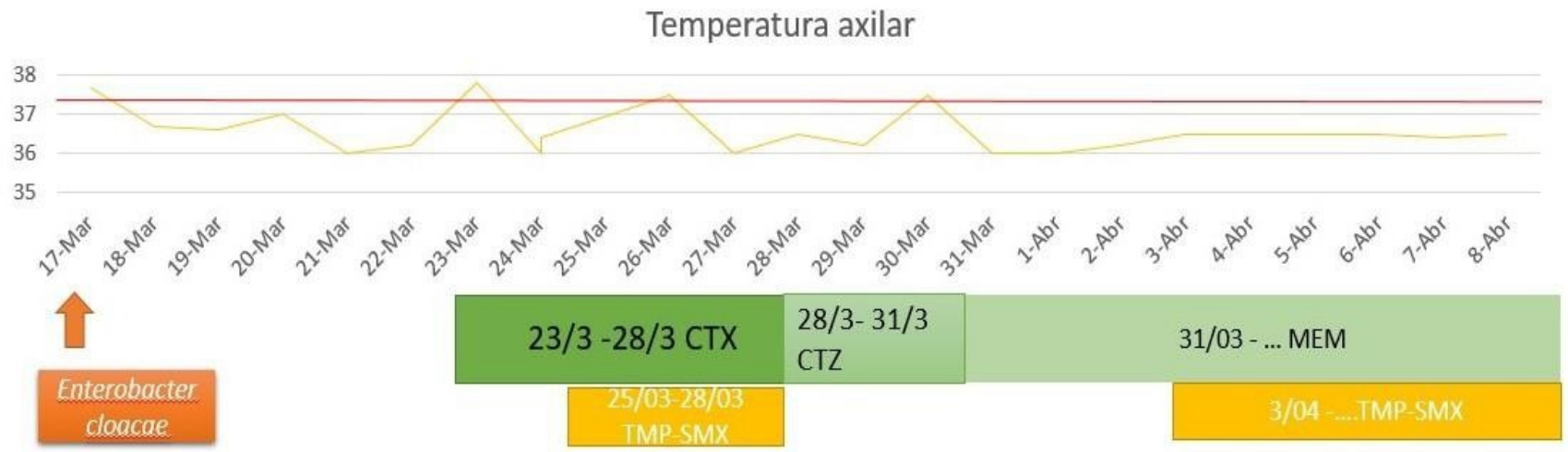
- 1) Paracentesis con criterio terapéutico (17/03, 22/03, 28/03, 29/03, 2/04)
- 2) Tratamiento fisiopatológico

Reposición albúmina.

17/03	22/03	31/03	3/04
30 g	40 g	70 g	40 g c/12hs

- 3) Tratamiento antibiótico

23/03 – 28/03 Ceftriaxona 2g/día
28/03 - 31/03 Ceftazidime 2 g/8 hs
31/03 – 10/04 Meropenem 1g/8 hs



FECHA	17/03	22/03	28/03	29/03	2/04
Aspecto	Ligeramente turbio	Ligeramente hemático	Ligeramente turbio	Turbio	Turbio
Proteinas (g/l)	26	23	18	19	28
Glucosa (g/l)	1,20	0,94	0,77	0,79	1,02
LDH	207	216	154	155	304
Amilasa	21		17		27
Albumina	11	11	9	8	
GB (cel/mm3)	420, 50% PMN	270, 60% PMN		131	
GR (cel/mm3)	810				

Bacteriológicos del líquido de ascitis: 19/03, 22/03, 28/03, 29/03 y 2/04 sin desarrollo

Evolución

- Registros febriles y subfebriles
- Persistencia con IR severa, incluso luego de paracentesis.
  - TC TX 28/03: Áreas parcheadas de aumento de la densidad en vidrio deslustrado, bilateral a predominio periférico asociado a engrosamiento del intersticio peribroncovascular e interlobulillar. DP de distribución típica a izquierda.
  - Se inicia empíricamente TMP-SMX , se suspende por IRA. Se reinicia con la mejoría de la IRA.
- Mala evolución de la hepatopatía.
  - Ascitis refractaria al los tratamientos instaurados. 2/04 Agrega elementos de encefalopatía

Fecha	17/03	26/03	29/03	2/04	3/04	6/04	7/04
BT/BD	2,84/1,9	1,51/0,45	1,77/1,42	2,40/1,42	2,72/2,02	2,45/1,72	
FA/GGT	79/96	116/111	91/75	68/55	56/45		
TGO/TGP	32/7	76/20	22/10	21/6	15/3		
TP	48	44		40	20	20	27
Alb	2,4	2,2	3,0				

- IRA

Fecha	29/03	31/03	2/04	3/04
Azoemia	75	108	109	93
Creatininemia	1,68	3,25	1,91	1,4

Fecha	4/04	6/04	7/04
GB	1770	1650	1150
Neutrofilos	1230	1440	760
Linfocitos	170	223	250
Hemoglobina	7,5	6,8	7,5
Plaquetas	49000	36000	32000

10/04/16 Fallece

Peritonitis Bacteriana Espontánea (PBE)

Infección del liquido de ascitis sin una causa intraabdominal quirúrgicamente tratable.

Cultivo positivo del liquido de ascitis, así como un recuento de PMN en el líquido de ascitis ≥ 250 cel/mm3, excluyendo causas secundarias de peritonitis bacteriana.

Ocurre en pacientes con cirrosis avanzada.

A mayor puntuación en el score de MELD, mayor riesgo de PBE.

Es inusual en ascitis de causa no cirrótica.

Casi siempre se desarrolla en ascitis de gran entidad, clínicamente objetivables.

Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Clinical manifestations. Up to date. Apr 2016. www.uptodate.com

Obstein KL, et al. Association between model for end-stage liver disease and spontaneous bacterial peritonitis. Am J Gastroenterol. 2007;102(12):2732.

Manifestaciones clínicas

Signs and symptoms at the time of diagnosis in 489 patients with spontaneous bacterial peritonitis

Clinical feature	Percent with sign or symptom
Fever	69
Abdominal pain	59
Altered mental status	54
Abdominal tenderness	49
Diarrhea	32
Paralytic ileus	30
Hypotension	21
Hypothermia	17

Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders Company, Philadelphia 1994. p.455.

- Los síntomas y signos en la PBE son discretos al compararse con las PB de causa secundaria (ausencia de ascitis).
- 13% de los pacientes con PBE son asintomáticos al momento del diagnóstico.
- Sospecha baja, paracentesis tardías, detección en etapas avanzadas, mayor mortalidad.

Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Clinical manifestations. Up to date. Apr 2016. www.uptodate.com

-McHutchison Jg, et al. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia 1994. p.455.

-Runyon BA. Monomicrobial nonneutrocytic bacterascites: a variant of spontaneous bacterial peritonitis. Hepatology. 1990;12(4 Pt 1):710.

-Akriviadis EA, et al. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology. 1990;98(1):127.

-Kumar A, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6):1589.

Indications for abdominal paracentesis in a patient with ascites

New onset ascites
At the time of each admission to the hospital
Clinical deterioration, either inpatient or outpatient
Fever
Abdominal pain
Abdominal tenderness
Mental status change
Ileus
Hypotension
Laboratory abnormalities that may indicate infection
Peripheral leukocytosis
Acidosis
Worsening of renal function
Gastrointestinal bleeding (a high risk time for infection)

Reference: Runyon BA, AASLD. Introduction to the revised American Association for the Study of Liver Diseases Practice Guideline management of adult patients with ascites due to cirrhosis 2012. Hepatology 2013; 57:1651.

- Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Clinical manifestations. Up to date. Apr 2016. www.uptodate.com

DIAGNÓSTICO

Paracentesis precoz

-17,711 Pacientes con cirrosis y ascitis con un diagnóstico primario de ascitis o encefalopatía.

-Paracentesis 61%

-Menor mortalidad aquellos a los que se realizó paracentesis.
6,5 % vs. 8,5%

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Paracentesis is Associated with Reduced Mortality in Patients Hospitalized with Cirrhosis and Ascites

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Abstract

Background & Aims—Diagnostic paracentesis is recommended for patients with cirrhosis admitted to the hospital for ascites or encephalopathy. However, it is not known if clinicians in the United States adhere to this recommendation; a relationship between paracentesis and clinical outcome has not been reported. We analyzed a US database to determine the frequency of paracentesis and its association with mortality.

Methods—The 2009 Nationwide Inpatient Sample (which contains data from approximately 8 million hospital discharges each year) was used to identify patients with cirrhosis and ascites admitted with a primary diagnosis of ascites or encephalopathy. In-hospital mortality, length of stay, and hospital charges were compared for those who did and did not undergo paracentesis. Outcomes were compared for those who received an early paracentesis (within 1 day of admission) and those who received one later.

Results—Of 17,711 eligible admissions, only 61% underwent paracentesis. In-hospital mortality was reduced by 24% among patients who underwent paracentesis (6.5% vs 8.5%, adjusted odds ratio [OR], 0.55; 95% confidence interval [CI], 0.41–0.74). Most paracenteses (66%) occurred ≤1 day after admission. In-hospital mortality was lower among patients who received early paracentesis than those who received it later (5.7% vs 8.1%; *P*=.049), although this difference was

Am J Gastroenterol. 2014 Sep;109(9):1436-42. doi: 10.1038/ajg.2014.212. Epub 2014 Aug 5.

Delayed paracentesis is associated with increased in-hospital mortality in patients with spontaneous bacterial peritonitis.

Kim JJ[1], Tsukamoto MM[2], Mathur AK[3], Ghomri YM[3], Hou LA[2], Sheibani S[2], Runyon BA[4].

Author information

Abstract

OBJECTIVES: Spontaneous bacterial peritonitis (SBP) is associated with high mortality. Early paracentesis (EP) is essential for rapid diagnosis and optimal treatment. The aim of the study is to compare the outcomes of patients with SBP who received EP vs. delayed paracentesis (DP).

METHODS: Consecutive patients who were diagnosed with SBP (ascites neutrophil count ≥250 cells/mm(3) and clinical evidence of cirrhosis) <72 h from the first physician encounter at two centers were identified. EP was defined by receiving paracentesis <12 h and DP 12-72 h from hospitalization. Primary outcome was in-hospital mortality.

RESULTS: The mean age of 239 patients with SBP was 53±10 years; mean Model for End-Stage Liver Disease (MELD) score was 22±9. In all, 98 (41%) patients who received DP had a higher in-hospital mortality (27% vs. 13%, P=0.007) compared with 141 (59%) who received EP. Furthermore, DP group had longer intensive care days (4.0±9.5 vs. 1.3±4.1, P=0.008), hospital days (13.0±14.7 vs. 8.4±7.4, P=0.005), and higher 3-month mortality (28/76, 37% vs. 21/98, 21%; P=0.03) compared with the EP group. Adjusting for MELD score ≥22 (adjusted odds ratio (AOR)=5.7, 95% confidence interval (CI)=1.8-18.5) and creatinine levels ≥1.5 mg/dl (AOR=3.2, 95% CI=1.4-7.2), DP was associated with increased in-hospital mortality (AOR=2.7, 95% CI=1.3-4.8). Each hour delay in paracentesis was associated with a 3.3% (95% CI=1.3-5.4%) increase in in-hospital mortality after adjusting for MELD score and creatinine levels.

CONCLUSIONS: Hospitalized patients with SBP who received DP had a 2.7-fold increased risk of mortality adjusting for MELD score and renal dysfunction. Diagnostic paracentesis performed <12 h from hospitalization in patients with cirrhosis and ascites may improve short-term survival.

AJG The American Journal of GASTROENTEROLOGY

Retrospectivo n= 239 pacientes con PBE

Mortalidad fue mayor en los que se realizó paracentesis e/ 12-72 hs después del ingreso

vs.

Los que se realizaron paracentesis dentro de las primeras 12 hs.

(IC 95%, OD 2,7)

Cada hora de retraso en la paracentesis se asoció con un aumento del 3,3 % de la mortalidad.

Paracentesis

Una única dosis de un antibiótico de amplio espectro puede impedir el crecimiento bacteriano en el 86% de los casos, luego de las 6 hs. Procesamiento 1 a 4 horas.

Cultivos.

- Botellas de hemocultivos.

  Monobacteriana, bajo recuento, aumenta las posibilidades de aislamiento.
  Sensibilidad inoculación inmediata 80-100% vs. Retardada 50- 77%.

- Al menos dos botellas (aerobios/ anaerobios)
- Inocular de inmediato, extremas condiciones de esterilidad.
- Al menos 10ml por botella. tasa de cultivo positivo 93% vs. 53%

- Akriviadis EA, et al. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology. 1990;98(1):127.
- Runyon BA, et al. Bedside inoculation of blood culture bottles with ascitic fluid is superior to delayed inoculation in the detection of spontaneous bacterial peritonitis. J Clin Microbiol. 1990;28(12):2811.
- Runyon BA, et al. Optimization of ascitic fluid culture technique. Gastroenterology. 1988;95(5):1351.
- Wong CL, et al. Does this patient have bacterial peritonitis or portal hypertension? How do I perform a paracentesis and analyze the results?. JAMA. 2008;299(10):1166.

Aislamientos frecuentemente hallados

Bacteria isolated from ascitic fluid in 519 patients with spontaneous bacterial peritonitis

Organism	Percent of isolates
Escherichia coli	43
Klebsiella pneumoniae	11
Streptococcus pneumoniae	9
Other streptococcal species	19
Enterobacteriaceae	4
Staphylococcus	3
Pseudomonas	1
Miscellaneous*	10

*In some regions of the world, such as Korea, Aeromonas hydrophila infection is an important cause of SBP, particularly in warm weather months. Affected patients commonly also have diarrhea. [Choi JP, et al. Clin Infect Dis 2008; 47:67.

Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia 1995. p.455.

Bruce A Runyon, MD.Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com

Recuento de PMN

PMN en el líquido de ascitis ≥ 250 cel/mm3

- Si el informe contiene formas evolutivas previas a los PMN, se deben contabilizar.

  El recuento automático es mas rápido y con menor error en recuentos altos, aumenta el error con recuentos de PMN pobre.

  Error: sangre en el liquido de ascitis, hay ingreso de GR y GB.

  - Corrige restando 1 PMN a los PMN totales por cada 250 GR/mm3.

- Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com
- Angeloni S, at el. Validation of automated blood cell counter for the determination of polymorphonuclear cell count in the ascitic fluid of cirrhotic patients with or without spontaneous bacterial peritonitis. Am J Gastroenterol. 2003;98(8):1844.
- Runyon BA. The evolution of ascitic fluid analysis in the diagnosis of spontaneous bacterial peritonitis. Am J Gastroenterol. 2003;98(8):1675.

Criterios De Runyon	PBE	PB secundaria
Proteinas g/dl	<1	>1
Glucosa mg/dl	> 50	< 50
LDH	< Lim sup de normal para suero	> Lim sup de normal para suero
Cultivos	Monomicrobiana	Polimicrobiana

Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com
Akriviadis EA, et al. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology 1990; 98:127.
Runyon BA, et al. Ascitic fluid analysis in the differentiation of spontaneous bacterial peritonitis from gastrointestinal tract perforation into ascitic fluid. Hepatology 1984; 4:447.

Tratamiento PBE

1. Tratamiento antibiótico
2. Suspensión de los betabloqueantes no selectivos.
3. Reposición de albúmina

1- Tratamiento antibiótico

Empírico, lo antes posible.
Previa paracentesis.

Indicaciones de tratamiento, Ascitis mas al menos uno:

Tax mayor 37,8ºC
Dolor abdominal
Confusión u otros elementos de encefalopatía
Líquido de ascitis PMN ≥ 250 células/mm3
*** PMN ≤ 250 células/mm3+ síntomas : Indicación de tratamiento, re valorar a las 48 hs con cultivos.**

1º Cefotaxime 2 g c/ 8 hs i.v , Ceftriaxona 2g /día i.v

Excelentes niveles en líquido de ascitis y en sangre.

2º Fluoroquinolonas. Levofloxacina, Ciprofloxacina.

Bruce A Runyon, MD. Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com

Duración de tratamiento antibiótico

- Cursos cortos son eficaces, la mayoría responde a un curso de 5 días
- Hasta 48 hs posterior a la remisión clínica.

Gastroenterology. 1991 Jun;100(6):1737-42.

Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis. A randomized controlled study of 100 patients.

Runyon BA[1], McHutchison JG, Antillon MR, Akriviadis EA, Montano AA.

Author information

Abstract

In an attempt to determine the optimal duration of therapy of spontaneous bacterial peritonitis, 100 patients with neutrocytic ascites and suspected spontaneous bacterial peritonitis were randomized to short-course vs. long-course treatment groups. Empiric therapy was initiated before the results of ascitic fluid culture were available. Of the 90 patients who met strict criteria for spontaneous bacterial peritonitis or culture-negative neutrocytic ascites, 43 were randomized to a group receiving 5 days and 47 to a group receiving 10 days of single-agent cefotaxime, 2 g IV every 8 hours. Infection-related mortality (0% vs. 4.3%), hospitalization mortality (32.6% vs. 42.5%), bacteriologic cure (93.1% vs. 91.2%), and recurrence of ascitic fluid infection (11.6% vs. 12.8%) were not significantly different between the 5- and 10-day treatment groups, respectively. Recurrence rates were comparable to the values reported in the literature. The cost of antibiotic and antibiotic administration were significantly lower in the short-course group. Short-course treatment of spontaneous bacterial peritonitis is as efficacious as long-course therapy and significantly less expensive.

Ensayo aleatorizado
5 días vs. 10 días
- Tasas similares de curación,
infección recurrente y mortalidad relacionada con la infección.

Runyon BA, et al. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis. A randomized controlled study of 100 patients. Gastroenterology 1991; 100:1737.

Rimola A, et al. Two different dosages of cefotaxime in the treatment of spontaneous bacterial peritonitis in cirrhosis: results of a prospective, randomized, multicenter study. Hepatology 1995; 21:674

Estrategia luego de los 5 días de tratamiento

Mejoría clínica total: SUSPENDER tratamiento
Persiste sintomático: PARACENTESIS

PMN < 250 cel/mm3, Se interrumpe
PMN > valor pre tratamiento, Búsqueda etiología quirúrgica
PMN > 250 cel/mm3 pero < valor pre tratamiento, Tratamiento 48 hs
y nueva paracentesis

En que pacientes se debe prolongar el tiempo de tratamiento?

- MO inusuales. *Pseudomonas spp*
- MO multirresistente a los tratamientos estándar
- MO asociados a endocarditis, *Staphylococcus aureus* o *Streptococcus* del grupo viridans

Bruce A Runyon, MD.Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com

2- Suspender Betabloqueantes

Suspender los betabloqueantes no selectivos, durante el curso de PBE
Uso de betabloqueantes se asocia con peores resultados.

Nonselective β Blockers Increase Risk for Hepatorenal Syndrome and Death in Patients With Cirrhosis and Spontaneous Bacterial Peritonitis

Mattias Mandorfer,[1,2] Simona Bota,[1,2] Philipp Schwabl,[1,2] Theresa Bucsics,[1,2] Nikolaus Pfisterer,[1,2] Matthias Kruzik,[1,2] Michael Hagmann,[3] Alexander Blacky,[4] Arnulf Ferlitsch,[1,2] Wolfgang Sieghart,[1,2] Michael Trauner,[1,2] Markus Peck-Radosav and Thomas Reiberger[1,2]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna Austria; [2]Vienna Hepatic Hemodynamic Lab, Vienna, Austria; [3]Section for Medical Statistics, Center for Medical Informatics, and Intelligent Systems, Medical University of Vienna, Vienna, Austria; and [4]Clinical Institute of Hosp Vienna General Hospital, Vienna, Austria

Gastroenterology

-Retrospectivo
- 607 pacientes con PBE.
- Mortalidad BB vs. NO BB
- BB 58% mas de mortalidad
- Sd hepatorrenal 24% vs. 11 %
- Mayor estancia Hospitalaria

Mandorfer M, Bota S, Schwabl P, et al. Nonselective β blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis.
Gastroenterology 2014; 146:1680.
- Bruce A Runyon, MD.Spontaneous bacterial peritonitis in adults: Diagnosis. Up to date. Apr 2016. www.uptodate.com

3 – Reposición de Albúmina

- De los pacientes con PBE el 30 -40 % desarrollará IRA

Albúmina 1,5 g/kg peso, primeras 6 horas del diagnóstico
Luego 1,0/kg peso, día 3.

Albúmina 0,5-1,0 g/kg peso/día, los primeros 3 días.

Se debe realizar reposición de albumina en todos los pacientes que cursan una PBE independientemente de la función renal

-EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. Journal of Hepatology 2010 vol 53 | 397–417.
http://www.easl.eu/research/our-contributions/clinical-practice-guidelines
-Bruce A. Runyon, Introduction to the Revised American Association for the Study of Liver Diseases Practice Guideline Management of Adult Patients With Ascites Due to Cirrhosis. 2012
http://www.aasld.org/publications/practice-guidelines-0
-http://www.bsg.org.uk/clinical-guidelines/liver/index.html
-Albumin Infusion Improves Outcomes of Patients With Spontaneous Bacterial Peritonitis: A Meta-analysis of Randomized Trials. CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2013;11:123–130
-Albumin infusion in cirrhotic patients with SBP infections: End of the story?'Gastroenterology Report, 3(3), 2015, 216–221

Pronóstico

- Mortalidad de la PBE, es baja, tratamiento bien conducido.
- Mayor mortalidad está condicionada con la IRA y la mayor puntuación MELD.
- Mortalidad Shock séptico asociado a PBE es del 82%.

*Los pacientes que sobrevivieron iniciaron antiobioticoterapia 1,8 hs ingreso vs. 9,5 hs los fallecidos

- Enfermedad hepática grave, mal pronóstico a largo plazo

- Mortalidad no relacionada con la PBE , 20- 40%

- Luego de PBE, mortalidad en el 1er año 70%, aumenta 80% en el 2º año.

***Trasplante hepático debe considerarse siempre luego del episodio de PBE.**

-Navasa M, et al. Randomized, comparative study of oral ofloxacin versus intravenous cefotaxime in spontaneous bacterial peritonitis. Gastroenterology 1996; 111:1011.

-Titó L, et al. Recurrence of spontaneous bacterial peritonitis in cirrhosis: frequency and predictive factors. Hepatology 1988; 8:27.

-Andreu M, Sola R, Sitges-Serra A, et al. Risk factors for spontaneous bacterial peritonitis in cirrhotic patients with ascites. Gastroenterology 1993; 104:1133.

-Runyon BA, et al. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis. A randomized controlled study of 100 patients. Gastroenterology 1991; 100:1737.

TARV en Hepatopatía

Problemas actuales ART y Hepatopatía

- Hepatotoxicidad
- Toxicidad por disminución del metabolismo
- Interacciones con otros fármacos
  Inmunosupresores, tratamiento VHC

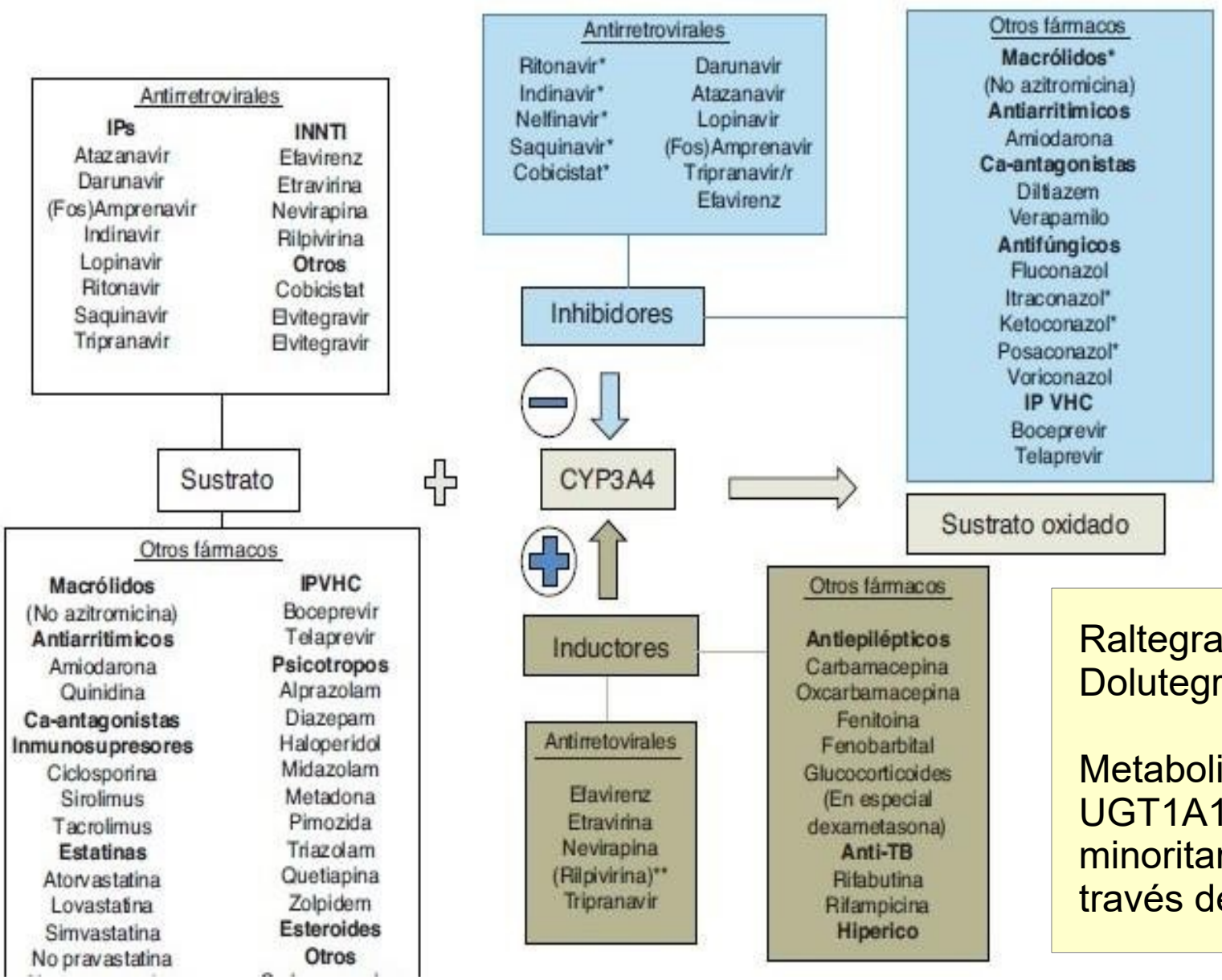
- Escasa evidencia
  Reportes de casos, Opinión de expertos y vigilancia postcomercialización

Espectro del metabolismo de los antirretrovirales es complejo.
Cada fármaco se metaboliza a través de diferentes isoenzimas.

Los citocromos P450 (CYP) son una familia de enzimas responsables de los procesos oxidativos de la mayoría de las sustancias exógenas.

- Mas de 30 subtípos
- CYP3A4 es uno de los mas importantes, responsable del metabolismo del 60% de los fármacos.
- CYP3A4 se sitúa principalmente en hígado.

- C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**:e15–e30



Raltegravir y Dolutegravir

Metabolismo por la UGT1A1 y minoritariamente a través de la CYP3A4

- C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**:e15–e30

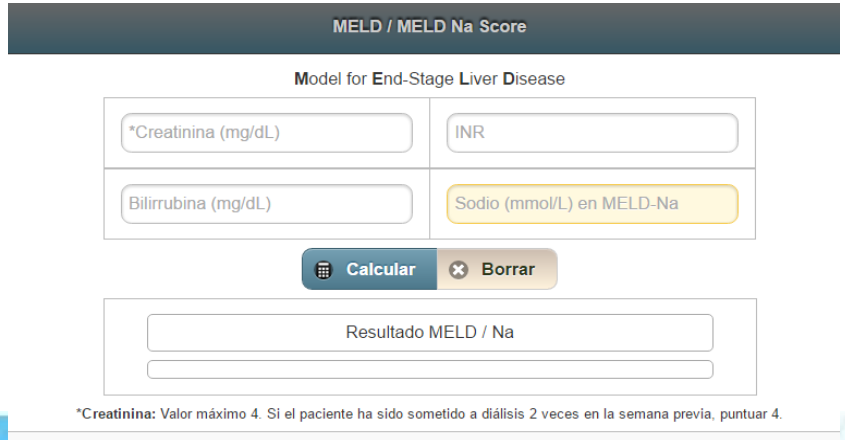
Child-Pugh classification of severity of cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time			
Seconds over control	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Turcotte-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease); 7 to 9 is class B (significant functional compromise); and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85 percent; class B: 80 and 60 percent; and class C: 45 and 35 percent.

Model for End-stage Liver Disease - Sodio (MELD-Na)

MELD Na Score= MELD – Na-(0.025*MELD*(140-Na))+140
MELD Score = 9,6 Ln(Creat)+3,8 Ln(Br) + 11,2 Ln(INR) + 6,4



http://www.aasld.org/publications/hepatology-0

Inhibidores No Nuclesídicos de la Trascriptasa Reversa

- Nevirapina.  Child Pugh A,  Child- Pugh B o C.
Fallo hepático agudo. Hepatotoxicidad.

-Efavirenz.  Child Pugh C. Child Pugh A y B, Datos Contradictorios.

-Etravirina.  Child Pugh A o B, No hay datos disponibles para C.

-Rilpivirina.  Chilld Pugh A o B. No hay datos disponibles para C.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf (Accessed on May 01, 2014).

Schöller-Gyüre M, et al. Effects of hepatic impairment on the steady-state pharmacokinetics of etravirine 200 mg BID: an open-label, multiple-dose, controlled Phase I study in adults. Clin Ther 2010; 32:328.

Inhibidores de la Proteasa

Advertencia para la clase. Deterioro del citocromo CYP3A4

Ritonavir  Hepatitis aguda. Potente inhibidor de esta enzima, y mas aún si hay IH o HVC.

Atazanavir, fosamprenavir  Child Pugh A y B.  Child Pugh C.

Darunavir, tipranavir tienen advertencias específicas por hepatotoxicidad severas.

DARUNAVIR  Child Pugh A .  Child Pugh B y C. Hepatitis aguda.
TIPRANAVIR.

Lopinavir  Child Pugh A.  Child Pugh B y C.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf (Accessed on May 01, 2014).

Amy L Graziani, John G Bartlett, Jennifer Mitty, Dose modification of antiretroviral agents in adults with renal or hepatic dysfunction. Up to date. Apr 2016. www.uptodate.com

Knox TA, Oleson L, von Moltke LL, et al. Ritonavir greatly impairs CYP3A activity in HIV infection with chronic viral hepatitis. JAcquir Immune Defic Syndr 2008; 49:358.

JAMA The Journal of the American Medical Association

JAMA. 2000 Jan 5;283(1):74-80.

Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection.

Sulkowski MS[1], Thomas DL, Chaisson RE, Moore RD.

Author information

Abstract

CONTEXT: Use of antiretroviral drugs, including protease inhibitors, for treatment of human immunodeficienc anecdotally associated with hepatotoxicity, particularly in persons coinfected with hepatitis C or B virus.

OBJECTIVES: To ascertain if incidence of severe hepatotoxicity during antiretroviral therapy is similar for all to define the role of chronic viral hepatitis in its development.

DESIGN: Prospective cohort study.

SETTING: University-based urban HIV clinic.

PATIENTS: A total of 298 patients who were prescribed new antiretroviral therapies between January 1996 a received protease inhibitors as part of combination therapy (median follow-up, 182 days) and 87 (29%) of wh regimens (median follow-up, 167 days). Chronic hepatitis C and B virus infection was present in 154 (52%) a

MAIN OUTCOME MEASURE: Severe hepatotoxicity, defined as a grade 3 or 4 change in levels of serum al aminotransferase, evaluated before and during therapy.

RESULTS: Severe hepatotoxicity was observed in 31 (10.4%) of 298 patients (95% confidence interval [CI]. associated with a higher incidence of toxicity (30%; 95% CI, 17.9% -44.6%). However, no significant differer incidence in other treatment groups, ie, nucleoside analogs (5.7%; 95% CI, 1.2%-12.9%), nelfinavir (5.9%; 9 (5.9%; 95% CI, 0.15%-28.7%), and indinavir(6.8%; 95% CI, 3.0%-13.1 %). Although chronicviral hepatitis w of severe hepatotoxicity among patients prescribed nonritonavir regimens (relative risk, 3.7; 95% CI, 1.0-11. hepatitis C or B virus infection (88%) did not experience significant toxic effects. Rate of severe toxicity with use of any protease inhibitor in patients with hepatitis C infection was 12.2% (13/107; 95% CI, 6.6%-19.9%). In multivariate logistic regression, only ritonavir (adjusted odds ratio [AOR], 8.6; 95% CI, 3.0-24.6) and a CD4 cell count increase of more than 0.05 x 10(9)/L (AOR, 3.6; 95% CI, 1.0-12.9) were associated with severe hepatotoxicity. No irreversible outcomes were seen in patients with severe hepatotoxicity.

CONCLUSIONS: Our data indicate that use of ritonavir may increase risk of severe hepatotoxicity. Although hepatotoxicity may be more common in persons with chronic viral hepatitis, these data do not support withholding protease inhibitor therapy from persons coinfected with hepatitis B or C virus.

Estudio Prospectivo
298 pacientes c/IP

- Sólo el ritonavir se asoció con mayor riesgo de hepatotoxicidad reversible.

- 88% Coinfectados con VHC o VHB toleraron IP sin peoría del fx hepático

Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. JAMA 2000; 283:74.

Inhibidores de CCR5

Maraviroc.

- No Existen recomendaciones específicas para dosificación en la disfunción hepática
- 75% metabolismo por CYP3A4
- Reportes de Hepatotoxicidad grave

Inhibidores de Fusión

Enfuvirtide

NO se recomiendan cambios de dosis para pacientes con disfunción hepática.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf (Accessed on May 01, 2014).

Amy L Graziani, John G Bartlett, Jennifer Mitty, Dose modification of antiretroviral agents in adults with renal or hepatic dysfunction. Up to date. Apr 2016. www.uptodate.com

- Rivero Antonio, Polo Rosa, Pérez José. Documento de consenso de GeSida /Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos INFECTADOS por el virus de la inmunodeficiencia humana. Enero 2016, en http://www.gesida seimc.org/contenidos/guiasclinicas

Inhibidores de la integrasa

Raltegravir, metabolizado por UGT1A1.

- No hay ajustes de dosis recomendados
- No existe evidencia de inocuidad en Child Pugh C.

Elvitegravir, disponible en coformulado (Cobicistat/emtricitabina/tenofovir/Elvitegravir).

- Cobicistat en Child Pugh A y B
- No existe evidencia de inocuidad en Child Pugh C
  No se utilizar en Child C por toxicidad Cobicistat

Dolutegravir,

- No hay ajustes de dosis recomendadas en Child Pugh A y B
- No existe evidencia de inocuidad en Child Pugh C

- Rivero Antonio, and et al. Documento de consenso de GeSida /Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos INFECTADOS por el virus de la inmunodeficiencia humana. Enero 2016, en http://www.gesida-seimc.org/contenidos/guiasclinicas
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf (Accessed on May 01, 2014).

- En pacientes con hepatopatía crónica y función hepática conservada, incluida la cirrosis clase A de Child Pugh, es razonable evitar los dideoxinucleósidos (AIII).

- En pacientes con insuficiencia hepatocelular, los inhibidores de integrasa no precisan ajuste de dosis y son los fármacos de elección.

- Los IP presentan mayor margen terapéutico que los INNTR.

- Monitorización de los niveles plasmáticos, no está disponible en la mayoría de centros.

En Child Pugh C hay menor evidencia ya que son pacientes con indicacion de trasplante hepático.

- Rivero Antonio, Polo Rosa, Pérez José. Documento de consenso de GeSida /Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos INFECTADOS por el virus de la inmunodeficiencia humana. Enero 2016, en http://www.gesida-seimc.org/contenidos/guiasclinicas

Adverse Effect	NRTIs	NNRTIs	PIs	INSTI	EI
Dyslipidemia	d4T > ZDV > ABC: ↑LDL and TG	EFV: ↑TG, ↑LDL, ↑HDL	All RTV-boosted PIs: ↑LDL, ↑TG, ↑HDL LPV/r = FPV/r and LPV/r > DRV/r and ATV/r: ↑TG	EVG/c/TDF/FTC: ↑TG, ↑LDL, ↑HDL	N/A
Gastrointestinal Effects	Nausea and vomiting: ddI and ZDV > other NRTIs Pancreatitis: ddI	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting) Diarrhea: Common with LPV/r, more frequent than DRV/r and ATV/r	Nausea and diarrhea: EVG/c/ TDF/FTC	N/A
Hepatic Effects	Reported with most NRTIs. Steatosis most common with ZDV, d4T, or ddI. ddI: Prolonged exposure linked to non-cirrhotic portal hypertension, esophageal varices. Flares: HIV/HBV-co-infected patients may develop severe hepatic flares when TDF, 3TC, and FTC are withdrawn or when HBV resistance develops.	NVP > other NNRTIs NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 count >250 cells/mm^3 and men with pre-NVP CD4 count >400 cells/mm^3. NVP should **never** be used for post-exposure prophylaxis, or in patients with hepatic insufficiency (Child-Pugh B or C).	All PIs: Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency with TPV/r. IDV, ATV: Jaundice due to indirect hyperbilirubinemia TPV/r: **Contraindicated** in patients with hepatic insufficiency (Child-Pugh B or C)	N/A	MVC: Hepatotoxicity with or without rash or HSRs reported

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, En: http://aidsinfo.nih.gov/guidelines. 01/2016

Tratamiento de la infección por VHC con los nuevos Inhibidores de la proteasa NS3/4A en pacientes coinfectados por el VIH

Tabla 2
Asociaciones entre boceprevir y telaprevir y fármacos antirretrovirales según las recomendaciones de la Agencia Española del Medicamento en pacientes con infección por VIH-1 (asociación permitida), e incluidos en ficha técnica y/o basados en estudios farmacocinéticos en voluntarios sanos (asociación posible)

	Boceprevir	Telaprevir
Atazanavir	Contraindicado	Contraindicado
Atazanavir/r	Contraindicado[a]	Asociación permitida
Darunavir/r	Contraindicado	Contraindicado
Lopinavir/r	Contraindicado	Contraindicado
Fosamprenavir/r	Contraindicado	Contraindicado
Efavirenz	Contraindicado	Asociación permitida[b]
Nevirapina	Contraindicado	Contraindicado
Etravirina	Contraindicado[c]	Asociación permitida
Rilpivirina	Asociación posible[d]	Asociación posible[d]
Raltegravir	Asociación permitida	Asociación permitida
Elvitegravir/cobicistat	Contraindicado[e]	Asociación posible
Dolutegravir	Asociación posible[f]	Asociación posible[f]
Maraviroc	Asociación posible[g]	Asociación posible[g]
Tenofovir	Asociación permitida	Asociación permitida[h]
3TC/Emtricitabina	Asociación permitida	Asociación permitida
Abacavir	Asociación permitida	Asociación permitida
Zidovudina	Contraindicado[i]	Contraindicado[i]

TABLE 3. Antiretroviral drug options for patients taking HCV direct-acting antivirals

	HCV NS34 PIs				HCV NS5A replication complex inhibitor	HCV NS5B polymerase inhibitor
	Boceprevir 800 mg tid	Telaprevir 750 mg tid[a]	Simeprevir 150 mg qd	Faldaprevir 240 mg qd	Daclatasvir 60 mg qd	Sofosbuvir 400 mg qd
HIV PIs						
Lopinavir/ritonavir	Not recommended	Not recommended	Not recommended	No data	No data	Recommended
Darunavir/ritonavir	Not recommended	Not recommended	Not recommended	Recommended at 120 mg qd	No data	Recommended
Atazanavir/ritonavir	Consider on an individual basis	Recommended	Not recommended	Recommended at 120 mg qd	Recommended at 30 mg qd	Recommended
HIV NNRTIs						
Efavirenz	Not recommended	Recommended at 1125 mg tid	Not recommended	Recommended at 240 mg qd	Recommended at 90 mg qd	Recommended
Rilpivirine	Recommended	Caution because of QT prolongation	Recommended	No data	No data	Recommended
Etravirine	Consider on an individual basis	Recommended	No data	No data	No data	No data
HIV InSTIs						
Dolutegravir	Recommended	Recommended	No data	No data	No data	No data
Raltegravir	Recommended	Recommended	Recommended	Recommended	No data	Recommended
Elvitegravir/cobicistat	No data	Recommended	Not recommended	No data	No data	No data
HIV NtRTI						
Tenofovir	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
CCR5 inhibitor						
Maraviroc	Reduce maraviroc to 150 mg bid	Reduce maraviroc to 150 mg bid	No data	No data	No data	No data

HIV, human immunodeficiency virus; HCV, hepatitis C virus; PIs, protease inhibitors; NNRTIs, non-nucleoside reverse-transcriptase inhibitors; InSTIs, integrase strand transfer inhibitors; ARV, antiretroviral; tid, three times a day; bid, twice daily; qd, once daily.
Modified from Karageorgopoulos *et al.* and Antiretroviral Treatment Options for Patients on DAAs - Summary available at http://www.hcvdruginfo.ca (accessed 5 January 2014).
[a]Telaprevir is equally efficacious at a dose of 1125 mg tid in monoinfected patients. However, most drug interaction studies are based on tid dosing.

- C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**:e15–e30
- Miro et al. Infections in SOT HIV-infected patients. Enferm Infecc Microbiol Clin. 2014;20 (7),119–130

Trasplante Hepático y VIH

Excelentes resultados en TH y pacientes con VIH.

- Supervivencia MENOR en coinfectados VIH/VHC en comparación con los monoinfectados con VHC.
  - Recurrencia VHC es mas agresiva en los coinfectados, mayor causa de perdida del injerto y muerte en estos pacientes.

- Riesgo de muerte luego del 1er episodio de descompensación de hepatopatía es mayor VHC/VIH que en VHC.
  - Media sobrevivencia es de 16 y 48 meses respectivamente.

PLANTEARSE LA POSIBILIDAD DE TRASPLANTE HEPATICO LUEGO DE LA PRIMERA DESCOMPENSACIÓN EN PACIENTES CON HEPATOPATÍAS CRÓNICAS.

Pineda JA, and et al. HIV coinfection shortens the survival of patients with hepatitis C virus-related decompensated cirrhosis. Hepatology 2005;41: 779–789. Miro JM, and et al. Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 2015 update. Journal of Hepatology 2015 vol. 62 j 701–711

Selección de pacientes para TH, TH y VIH.

1) Se incluyen pacientes con EO previas, tratadas y con profilaxis efectivas.

*EO sin tratamiento específico o intratables son criterios de exclusión.

*SK compromiso sistémico resuelto, pueden considerarse si la inmunosupresión se realiza con sirolimus.

2) CD4 + mínimo de 100 células / mm3

200 células/mm3 en pacientes con antecedentes de EO (EE.UU. y España), cirrosis compensada clínicamente (Italia), y ausencia de hipertensión portal (Reino Unido).

3) CV para VIH indetectable, en TARV .

Miro JM, et al Quereda C, Laguno M, et al. GESIDA/GESITRA-SEIMC, PNS and ONT consensus document on solid organ transplant (SOT) in HIV-infected patients in Spain (March, 2005). Enferm Infecc Microbiol Clin 2005;23:353–362.
Fox AN, et al. Liver transplantation in HIV patients. Semin Liver Dis 2012;32:177–185.
Miro JM, et al. GESIDA/GESITRA-SEIMC, PNS and ONT consensus document on solid organ transplant (SOT) in HIV-infected patients in Spain (March, 2005). Enferm Infecc Microbiol Clin 2005;23:353–362.
Grossi PA. Update in HIV infection in organ transplantation. Curr Opin Organ Transplant 2012;17:586–593.
O'Grady J, et al . Guidelines for liver transplantation in patients with HIV infection (2005). HIV Med 2005;6:149–153.

Criterios de selección. TH y VIH

Review

CrossMark

EASL JOURNAL OF HEPATOLOGY

Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 2015 update

Table 2. HIV criteria for liver transplantation (LT) in HIV-infected patients in Europe and the USA.

	Spain [13]	France [8]	Italy [14]	UK [15]	US [3]
Previous AIDS-defining events					
Opportunistic infections (OIs)	Some*	Some*	None in the previous year	None after HAART-induced immune reconstitution	Most**
Neoplasms	No	Not defined	No		No**
CD4 cell count/mm^3					
No previous OIs	>100	>100***	>200 or >100 if decompensated cirrhosis	>200 or >100 if portal hypertension	>100
Previous OIs	>200	>100***			>200
Plasma HIV-1 RNA viral load <50 copies/ml on HAART**	Yes		Yes	Yes	Yes

*In Spain and France, patients with previous tuberculosis, *Pneumocystis jiroveci* pneumonia, or esophageal candidiasis can be evaluated for LT.

**In the USA, only progressive multifocal leukoencephalopathy, cryptosporidiosis, multidrug systemic fungal infections, lymphoma, and visceral Kaposi's sarcoma are exclusion criteria.

***Patients under 100 CD4 cells/mm^3 were not excluded in France (case by case evaluation).

****If HIV plasma viral load was detectable, post-LT suppression with HAART should be predicted in all patients.

Miro JM, Stock P, Teicher E, Duclos-Vallée JC, Terrault N, Rimola A. Outcome and management of HCV/HIV coinfection pre- and post-liver transplantation. A 2015 update. Journal of Hepatology 2015 vol. 62 j 701–711

Mortalidad en lista de espera

- A mayor MELD mayor mortalidad en lista de espera.

  Para pacientes VIH:

  Riesgo de muerte aumenta con respecto a pacientes VIH negativos por:

  5,7 para MELD 15-19,
  21,4 para MELD 20-24, y
  101 para 25 MELD.

- La mortalidad en lista de espera en pacientes VIH además se asocia con:
  CV VIH detectables Recuento de CD4+ bajo
  En pacientes con CV para VIH detectables y CD4 cercanos a la línea de base, la mortalidad aumentó un 20% por cada unidad de aumento de MELD.

-Subramanian A, Sulkowski M, Barin B, Stablein D, Curry M, Nissen N, et al.MELD score is an important predictor of pretransplantation mortality in HIV- infected liver transplant candidates. Gastroenterology 2010;138:159–164.

-Miro JM, Stock P, Teicher E, Duclos-Vallée JC, Terrault N, Rimola A. Outcome and management of HCV/HIVcoinfection pre- and post-liver transplantation. A 2015 update. Journal of Hepatology 2015 vol. 62 j 701–711

TARV en Trasplante hepático

- En la era pre TARV altamente eficaz los resultados de los TOS en VIH eran peores en comparación con los VIH negativos.
- La evidencia mas reciente ha demostrado resultados comparables en ambas poblaciones.
- Problemas actuales:
  - Selección de pacientes
  - Interacciones entre ARV y los agentes inmunosupresores
    - Mayor riesgo de rechazo y posibles toxicidades

- C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;33(7):e15–e30
- Castel MA and et al. Heart Transplantation in HIV-infected patients: More cases in Europe. J Heart Lung Transplant.2011;30:1418.
- Roland ME and Stock PG. Solid organ transplantation is a reality for patients with HIV infection. Curr HIV/AIDS Rep. 2006;3:132–8.
- Polak WG and Gladysz A. Solid organ transplantation and HIV infection. Ann Transplant. 2003;8:16–21
- Huprikar S. Solid organ transplantation in HIV-infected individuals: An update. Rev Med Virol. 2009;19:317–23

Inmunosupresores y TARV

- Tacrolimus , sirolimus y Ciclosporina A son sustratos CYP3A4 e inhibidores de la glucoproteína P.
- Micofenolato de mofetilo (MMF) es sustrato de la glucuroniltransferasa.

- **IP** aumentan de forma significativa los niveles de los inmunosupresores, aumentando el riesgo de toxicidad.

- Afectan también la farmacocinética de los GCC y mTOR.

- **INNTR** afectan la eficacia de los inmunosupresores, disminuyendo los niveles plasmáticos.

- Intensidad de la interacción es menor en comparación con los IP .

C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**:e15–e30
Van Maarseveen EM and et al. Drug-drug interactions between antiretroviral and immunosuppressive Agents in HIV-infected patients after solid organ transplantation: A review. AIDS Patient Care STDS. 2012;26:568–81.
Miro JM and et al. Simultaneous pancreas-kidney transplantation in HIV-infected patients: A case report And literature review. Transplant Proc. 2010;42:3887–91. 122.

ARV PREFERIDOS EN TOS

Tenofovir/Emtricitabina/Raltegravir ó Abacavir/ Lamivudina/ Raltegravir (inhibidores calcineurínicos: ciclosporina y tacrolimus).

2 INTR + Dolutegravir. Hace falta mayor evidencia, sobre las interacciones de Dolutegravir e inmunosupresores.

No hay necesidad de de ajustar dosis de inmunosupresores
No hay aumento de la tasa de rechazo del injerto
No hay aumento de la toxicidad por interacciones

-C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**:e15–e30
-Moreno A and et al.Raltegravir-based highly active antiretroviral therapy has beneficial effects On the renal function of human immunodeficiency virus-infected patients after solid organ transplantation. Liver Transpl. 2010;16:530–2.123.
-Tricot L and et al. Safety and efficacy of raltegravir in HIV-infected transplant patients cotreated with immunosuppressive drugs. Am J Transplant. 2009;9:1946–52.

MMF comparte vías metabólicas con el raltegravir.

- Glucuronidación de Raltegravir es catalizada en el Hígado , UGT1A1 y UGT1A9

- MMF se glucuroniza en el hígado a través de UGT1A9

- Datos preliminares de un estudio farmacocinético en 6 pacientes TOS, no han presentado modificaciones en los niveles plasmáticos de ambos, ni rechazo celular, CV para VIH indetectable.

- Recomendación, hasta no obtener datos mas sólidos, monitorizar los niveles de MMF en pacientes con Raltegravir.

- C. Manzardo et al. / Enferm Infecc Microbiol Clin. 2015;**33(7)**
- Miro JM, Manzardo C, Brunet M, Cofan F, Rimola A, Pérez-Villa F. Combination Of raltegravir plus lamivudine or emtricitabine plus abacavir or tenofovir is safe,effective and prevents pharmacokinetic interactions with immunosuppressivedrugs in HIV-infected solid organ transplant recipients. En:18th Conferenceon Retrovirus and Opportunistic Infections. 2011.

Protocolo de Trasplante Hepático en Población VIH positiva.

Unidad Bi Institucional. Programa Nacional de Trasplante Hepático
Hospital Central de las FFAA, Hospital de Clínicas “Dr. Manuel C. Quintela”

HOSPITAL DE CLINICAS Dr.Manuel Quintela

H.C.FF.AA.

UNIDAD BI-INSTITUCIONAL ENFERMEDADES HEPÁTICAS TRASPLANTE HEPÁTICO

Criterios para la indicación

A) Evaluación Psicosocial favorable, abstención de drogas (1 año) y/o consumo de alcohol (6 meses).

B) Idealmente sin enfermedades oportunistas previas.

- CD4+ mínimo 100 células/mm3, en caso de no haber presentado nunca una EO.
- CD4+ entre 100-199, cirrosis compensada y sin Hipertensión portal, es razonable esperar CD4 + mayores 200 células /mm3.
- CD4+ mínimo 200 células/mm3, en caso de haber presentado una EO.

C) CV para VIH en plasma menor a 50 copias/ml.

CONCLUSIONES

1. PBE sospecha y tratamiento precoz en las primeras 12hs.

2. Evaluación de Hepatopatía, diagnóstico de severidad precozmente
   MELD/ Child- Pugh

3. Referir a Trasplante Hepático
   De acuerdo MELD (12-15)
   Primera descompensación de cualquier típo

4. TARV y Hepatopatía.
   Preferir Inhibidores de la Integrasa
   Segunda línea INNTR como Efavirenz.

5. TARV y TH.
   Tenofovir/Emtricitabina/Raltegravir
   Abacavir/ Lamivudina/ Raltegravir


CÁTEDRA DE ENFERMEDADES INFECCIOSAS
1875
Cátedra de Enfermedades Infecciosas, 2016