



HEPATITIS E CRÓNICA EN PACIENTES INMUNODEPRIMIDOS TRASPLANTADOS DE ÓRGANO SÓLIDO: REVISIÓN A PROPÓSITO DE UN CASO

Antonio Aguilera

Servicio Microbiología CHUS (Santiago de Compostela) antonio.aguilera.guirao@sergas.es

CONFLICTO DE INTERÉS Ayudas para asistencia a congresos y compensación por docencia y asesoría:

Abbott, Abbvie, DiaSorin, Gilead, Hologic, MSD, Roche y Siemens Healthcare

Antonio Aguilera

Servicio Microbiología CHUS (Santiago de Compostela) Departamento de Microbiología USC La infección causada por el VHE es responsable de algunos casos esporádicos de hepatitis crónica que pueden presenta un alto impacto clínico en poblaciones vulnerables como es el caso de los pacientes trasplantados de órgano sólido (TOS).



Se calcula que cada año hay unos 20 millones de casos de infección por el VHE, de los cuales 3,3 millones presentan los síntomas de la enfermedad (OMS, Julio 2019)

El conocimiento de la infección provocada por el VHE ha cambiado enormemente en los últimos años, hasta incluso llegar a considerarse su condición de enfermedad emergente en los países industrializados de nuestro entorno.

EUROPE'S NEW HEPATITIS PROBLEM

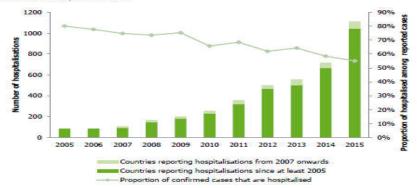
Many get infected with hepatitis E, and a few get very sick. How can the virus be stopped?

By Kai Kupferschmidt



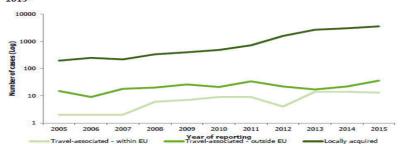
Incremento en los casos diagnosticados de HEPATITIS E en la UE durante los últimos años

Figure 3.5. Number and proportion of hospitalisations among confirmed cases of hepatitis E, EU/EEA Member States, 2005–2015*



^{*} Data available for: Austria, Belgium, Croatia, Czech Republic, Estonia, Germany, Hungary, Italy, Latvia, Poland, Portugal, Slovakia, Slovenia, United Kingdom (Northern Ireland)

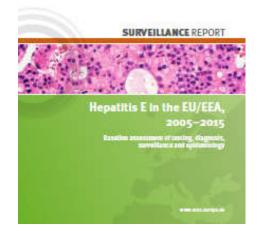
Figure 3.7. Confirmed cases of hepatitis E by travel history and year, EU/EEA Member States, 2005–2015*



*Data on travel history available for: Austria, Croatia, Czech Republic, Estonia, France, Hungary, Italy, Latvia, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, United Kingdom (England, Wales, Northern Ireland);







Cifras significativas de prevalencia de viremia por VHE y de seroprevalencia de Anti-VHE-IgG en donantes de sangre de diferentes países de la UE



Hepatitis E: the current state of play

M. I. Ankcorn^{1,2} & R. S. Tedder^{1,2}

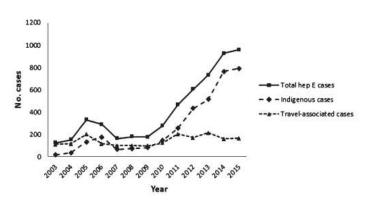


Fig. 1. Reference laboratory-confirmed HEV cases in England & Wales 2003-2015.

Table 2. Prevalence of HEV vitaemia in blood donors and igG scroprevalences in both blood donors and the general population from selected countries where G3 is the dominant genotype. All studies used Wantai IgG assay (Fortress Diagnostics Ltd, Antrim, Northern Ireland, UK). All percentages rounded up to whole numbers

	Country	Blood donors HEV RNA positive	Anti-HEV IgG seroprevalence (blood donors)	Anti-HEV IgG seroprevalence (general population)	Year of sampling
Europe	Austria	1:8416	14%		2013/2014, Fischer et al. (2015)
1.5	England	1:2848			2012/2013, Hewitt et al. (2014)
			12%		2010, Beale et al. (2011)
	France	1:2218	25%		2012/2013, Gallian et al. (2014)
	SW Prance			34%	2010/2011, Mansuy et al. (2011)
			53%		2003/2004, Mansuy et al. (2011)
	Germany	1:1240			2011, Vollmer et al. (2012)
		1:4525			2011, Baylts et al. (2012)
				30%	2010, Wenzel et al. (2013)
	Netherlands	1:762			2013/2014, Hogema et al. (2016)
		1:2671	27%		2011/2012, Slot et al. (2013)
			21%		2011, Hogema et al. (2014)
	Spain	1:3333	20%		2013, Sauleda et al. (2015)
	Sweden	1:7986			2011, Baylts et al. (2012)
North America	USA	1:9500			2013, Stramer et al. (2016)
			16%		2012, Xu et al. (2013)
		0:1939			2011, Baylts et al. (2012)
	Canada	0:5000	6%		2013, Fearon et al. (2014)

La infección por el VHE está "infradiagnosticada"

The Enigma of Hepatitis E Virus

Liza Bronner Murrison, PhD, MPH, and Kenneth E. Sherman, MD, PhD

Table 2. Diagnostic Opportunities and Errors

Clinical Situation	HEV Infection Misdiagnosis		
Subclinical infection: patient does not seek care	No diagnosis made		
Symptomatic infection; practitioner does not consider HEV infection	Non-HEV diagnosis		
Indistinguishable acute HEV infection	Acute hepatitis, cause unknown Chronic liver disease (in a patient with known chronic liver disease) Flare of disease in a patient with chronic autoimmune hepatitis ²⁷ Acute liver injury ²⁶ Liver injury from a drug etiology ²⁸		
Chronic HEV infection	Chronic liver disease due to HBV or HCV Chronic liver disease due to HBV/HIV or HCV/HIV coinfection ¹⁸ Autoimmune hepatitis ¹⁸ Idiopathic hepatitis ¹⁸ Acute cryptogenic hepatitis ^{16,23} Acute cellular rejection		
HEV-induced neuralgic amyotrophy	Neuralgic amyotrophy ⁷⁵		
HEV-associated Guillain-Barre syndrome	Guillain-Barre syndrome, unknown etiology		

HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus.

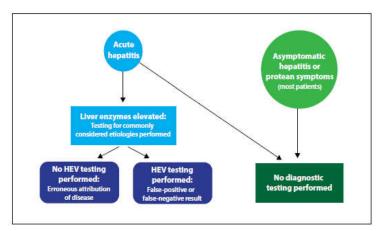


Figure. A flowchart showing the reasons clinicians may fail to diagnose HEV infection. HEV, hepatitis E virus.

Causas: Presentación clínica frecuentemente asintomática, un diagnóstico diferencial erróneo y un diagnóstico microbiológico difícil y exigente.

The Enigma of Hepatitis E Virus

Liza Bronner Murrison, PhD, MPH, and Kenneth E. Sherman, MD, PhD

Table 2. Diagnostic Opportunities and Errors

Clinical Situation	HEV Infection Misdiagnosis		
Subclinical infection: patient does not seek care	No diagnosis made		
Symptomatic infection; practitioner does not consider HEV infection	Non-HEV diagnosis		
Indistinguishable acute HEV infection	Acute hepatitis, cause unknown Chronic liver disease (in a patient with known chronic liver disease) Flare of disease in a patient with chronic autoimmune hepatitis ²⁷ Acute liver injury ²⁶ Liver injury from a drug etiology ²⁸		
Chronic HEV infection	Chronic liver disease due to HBV or HCV Chronic liver disease due to HBV/HIV or HCV/HIV coinfection ¹⁸ Autoimmune hepatitis ¹⁸ Idiopathic hepatitis ¹⁸ Acute cryptogenic hepatitis ^{18,23} Acute cellular rejection		
HEV-induced neuralgic amyotrophy	Neuralgic amyotrophy ⁷³		
HEV-associated Guillain-Barre syndrome	Guillain-Barre syndrome, unknown etiology		

HBV, hepatitis B virus; HCV, hepatitis C virus; HEV, hepatitis E virus;

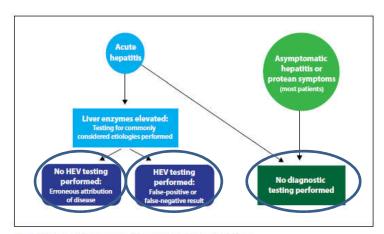


Figure. A flowchart showing the reasons clinicians may fail to diagnose HEV infection. HEV, hepatitis E virus.

GPC para el manejo de la Hepatitis E publicadas en 2018

Clinical Practice Guidelines





EASL Clinical Practice Guidelines on hepatitis E virus infection*

European Association for the Study of the Liver*

Infection with hepatitis E virus (HEV) is a significant cause of ions. Wherever possible, the level of evidence and recommendainfection with Reputits E virus (HBV) is a significant cause of the Monthly American Committee of the Mark Com that HEV is endemic in most high-income countries and is lying evidence. The quality of the evidence in the recommendalargely a zoonotic infection. Given the paradigm shift in our tions has been classified into one of three levels: high (A). understanding of zoonotic HEV and that locally acquired HEV moderate (B) or low (C). The GRADE system offers two grades is now the commonest cause of acute viral hepatitis in many of recommendation: strong (1) or weak (2). Thus, the recom Buropean countries, the focus of these Clinical Practice mendations consider the quality of evidence: the higher the Guidelines will be on HEV genotype 3 (and 4).

hepatikis E virus (HEV) represents an important global public books peoblem. The Sumpson Association for the Study of Live (EASL) invited a panel of experts in the field to develop Clinical Practice Guidelines (OPGs) with a particular focus on HEV geno- Background topo (et) 3. The objective of these CPGs was not to draft a review HEV was discovered in the early 1980s. At that time, Serviet though the supporting evidence may be weak in many cases. and hepatitis II virus (HIV)). A pooled sample of affected solmore detail. In addition, despite the increasing knowledge, areas and named HEV. of uncertainty exist and unanswered questions should be defined. Therefore, cliniciars, patients and public health authorities must continue to make choices on the basis of the evolving

These EASL CPGs have been prepared by a panel of experts invited by the EASL Governing based. The recommendations were approved by the EASL Governing Board. They are based as far as possible on evidence from existing publications and presentations at international meetings as well as, if evidence

* Chical practice patholises pass? Chic Harry S. Satter, Facel monitors: Nation Cames, Sally A. Saplis, Darles Minnelpout, Henor Minhemper, M.S. Greening Stand representative Favorate Props - Corresponding author: Abbrev: European Association for the Study of the Univ



Journal of Reputology 2018 vol. 68 : 1256-1271

was unavailable the experts' personal experiences and onin-© 2018 European Association for the Study of the Liver. Published by is warranted; the greater the variability in values and preferences, or the greater the variability in values and preferences, or the greater the variability in values. recommendation is warranted. It must be noted that only the review of literature was used to inform recommendations. Other criteria or support of recommendations such as cost, fea-As a cause of significant morbidity and most ality, infection with slibility, acceptability, or cost-effectiveness were not considered

article on hepatitis Elect rather to define specific suggestions for troops in Afghanistan were affected by large outbreaks of unex the management of distinct features of HEV infection, even plained hepatitis (testing negative for hepatitis A virus [HAV] in order to leep the manuscript and the reference list to a rea-diers' stook was ingested by a Russian scientist. He developed sonable length, these CPGs frequently refer to previous review a brisk hepaticis, and a rare virus was found in his stook by elecaticles which summarise the evidence on distinct topics in timo microscopy." Subsequently the viral genome was closed









Summary of the British Transplantation Society UK Guidelines for Hepatitis E and Solid Organ Transplantation

Stuart McPherson, MB ChB, MD, FRCP.1 Ahmed M, Eisharkawy, BM, PhD, FRCP.2 Michael Ankcorn, MBBS, MRCP,3 Samreen Ijaz, PhD,4 James Powell, MB ChB, MD, FRCS,5 Ian Rowe, MBChB, MRCP, PhD,⁶ Richard Tedder, MB BChir, FRCP, FRCPath,⁷ and Peter A. Andrews, MD, FRCP⁸

Ab etract: The incidence and prevalence of hepatitis E virus (HEV) infection has increased in many developed countries over the Assumed the includes and presence of the presence of the project of the presence of the presen he olderce relating to the diagnosis and management of persistent hepatitis E in sold organ transplant recipients and the most Recommendation of Persistent on PEV Intercommendations, assessment of Persistent of P mendations. This article includes a summary overview of hepatitis E and transplantation with key references, and the statements of nendation contained within the guideline. It is recommended that the full guideline document is consulted for complete de talis of the relevant references and evidence base. This may be accessed at https://bts.cro.uk/audielines-standards/

(Transplantation 2018;102: 15-20)

he incidence and prevalence of hepatitis E virus (HEV) infection has increased in many developed countries over the last decade, predominantly due to infection with genotype 3 (G3) HEV. Infection with HEV G3 is important in transplant recipients because it can persist in immunosuppessed individuals, leading, if untreated, to the development of chronic hepatitis and significant liver fibrosis. Because there are currently no international guidelines on the man-agement of hepatitis E in transplant recipients, the British Transplantation Society (BTS) has developed guidelines to in form clinical teams and patients about hepatitis E to help

Beneficial 10 hts 2017 Accepted 27 July 2017.

¹ Liver Transglant Unit, The New costle upon Tyree Hospitals NHS Foundation Trust and institute of Calular Microline, New castle University, United Kingdom LiverTransplant Unit, Queen Bhabeth Hospital, Birmingham, United Kingdom ³ Virus Reference Department, National Infection Service, Public Health England? NHS Bined and Transplant, Colindaia London United Knodom * Blood Borne Virus Unit, Virus Reference Department, National Infection Service, PLDE: Health England, Colindale, London, United Ringdom

⁶ Scottin Liver Transplant Unit, Playerinkmary of Edinburgh, Edinburgh, United Hingdom *LiverUnit, St. James' Hospital and University of Leeds, Leeds, UK Division of intection and immunity, University College London and Blood Borne Vision I feet Vision Reference Department National Infection Service, Buildin Health Project College National Control College Colle ⁸ South West Thamps Renal & Transplantation Unit, Surery United Kinodom.

increase the recognition of persistent hepatitis E infection and to provide clear guidance on its management. The follow-ing includes an overview of hepatitis E and transplantation with key references, and the statements of recommendations contained within the BTS guideline.

OVERVIEW OF HEPATITIS E AND SOLID ORGAN TRANSPLANTATION

HEV belongs to the genus Hepevirus in the Hepeviridae family and infects humans and a range of animal hosts. 1 Four major HEV genotypes infect humans (G1 to G4). The

The authors received no succost for the writing of either the BTS quickline or the S.M.P. is a speaker, consultancy or travel support from Abblife, BMS, Glead, MSD

Novets and Rocks. A E is a speaker, consultancy, research grant or travel support from AEDAS, Adalas, SMS, Chies, Cliest and Architic LR is a speaker or travel support from Abble, Bayer, and Norpine. All the other authors deciare no conflicts of interes All sulhors contributed to the BTS guideline document and to this summary of the guideline. All have reviewed and approved the final document. Comespondence: Siturt McPherson, BSc, MB ChB, MD, FRCP, The Liver Unit, Preeman Hospital, Level 6, Freeman Road, Newcastle upon Tyne, NET 7DN, United Kingdom, (bluert-mophes onlikum-ths-uk).

Copyright © 2017 Wolfers Huwer Health, Inc. All rights reserved. BSN 0041-1207/18/10201-0215

Transplantation = January 2018 = Volume 102 = Number 1

www.transplantjournel.com

Copyright @ 2017 Wolfers Kluwer Health, Inc. All rights reserved

CASO CLÍNICO:

HEPATITIS E CRÓNICA EN PACIENTE INMUNODEPRIMIDO TOS



Primeros casos en España de hepatitis crónica E en trasplantados que han sido tratados

VHE

P-51. HEPATITIS E CRÓNICA EN EL TRASPLANTE DE ÓRGANO SÓLIDO: A PROPÓSITO DE UN CASO

A. Aguilera¹, N. Vallejo², A. Vallejo², A.I. Díaz-Mareque², M. Rodríguez-Velasco², E. Molina² y A. Rivero-Juárez³

¹Complexo Hospitalario Universitario de Santiago, Instituto de Investigación Sanitaria de Santiago, Santiago de Compostela; ²Complexo Hospitalario Universitario de Santiago, Santiago de Compostela; ³Hospital Universitario Reina Sofia. Instituto Maimónides de Investigación Biomédica, Córdoba.

Introducción: La infección crónica por el VHE, definida por la persistencia del ARN viral en suero o heces durante más de 6 meses, se ha descrito en pacientes inmunodeprimidos que habían recibido trasplante de órgano sólido y también en otras poblaciones de inmunodeprimidos, como pacientes oncohematológicos o infectados por el VIH. Los pacientes con hepatitis crónica E suelen estar asintomáticos e infectados principalmente por el genotipo 3.

Caso clínico: Paciente asintomático de 35 años, trasplantado renal desde hace seis, que presenta buen estado general pero con alteración de la bioquímica hepática mixta leve desde hace unos siete meses, siendo las analíticas previas normales y sin incidencias hepatobiliares, ni ictérica ni datos de coagulopatía. Desde el inicio de la alteración bioquímica se suspende la medicación que tomaba por sospecha de hepatitis medicamentosa, aunque no se observan cambios al respecto y continúa la ausencia de síntomas. La ecografía abdominal aporta datos de esteatosis hepática en higado normofuncionante sin datos de fibrosis relevante y de etiología indeterminada, por lo que se remite a hepatología para valoración. Con los datos aportados por el laboratorio de microbiología se diagnostica de infección por el VHE con presencia de anticuerpos específicos [gG e IgM y ARN-VHE detectable, categorizada como "hepatitis crónica por VHE sin datos de



Paciente asintomática, 35 años.

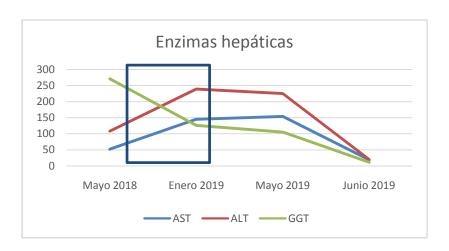
Tx Renal hacía 6 años.

Tratamiento inmunosupresor: (Prednisona, Tacrolimus y Sirolimus)

Alteración bioquímica hepática en los últimos siete meses, con resultado previo normal.

Sin incidencias hepatobiliares.

No ictericia, ni coagulopatía





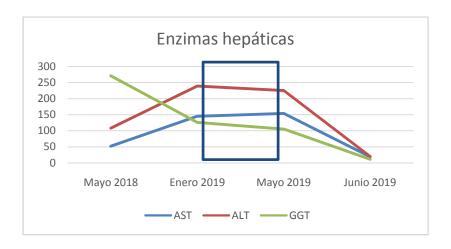
Se suspende medicación (hipolipemiante y anticonceptiva).

Persiste la alteración bioquímica hepática.

Ausencia de infección por VHB y VHC.

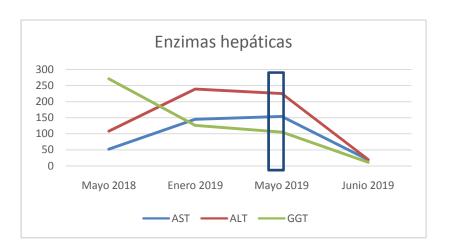
En ecografía abdominal datos de esteatosis hepática en hígado normofuncionante sin fibrosis.

Remisión a hepatología para valoración.





Diagnosticada de infección por VHE por la presencia de anticuerpos IgG/IgM y ARN-VHE. La infección crónica es confirmada al detectar ARN-VHE en una muestra previa de seroteca. Categorizada como Hepatitis E crónica sin datos de gravedad.





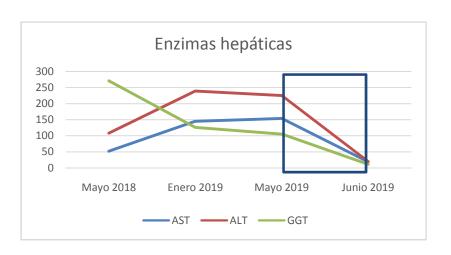
VHE caracterizado como 3f.

Tratamiento antiviral indicado en las GPC (200 mg/8 h) durante 12 s.

Normalización de la bioquímica hepática y ausencia de ARN-VHE en

sangre y heces al finalizar el tratamiento.

Se procede al alta y se confirma la RVS a las 24 s.





A 35-year-old female had a kidney transplant in 2013. After transplantation, the patient experienced acute dysfunction of the graft and drug-related leucopenia was solved. From May 2018, the patient received prednisone (5 mg/day), tacrolimus (1.5 mg/day) and sirolimus (1 mg/day) as immunosuppressive therapy. The patient presented with an elevated level of transaminases in May 2018 and was suspected to have a drug-induced liver injury due to paracetamol, hypolipemiant therapy and contraceptive medication. She was negative for HCV antibodies, sHbAg and anti HBc, but positive for anti-HBs (48 mIU/mL). Viral load for HCV and HBV were also undetectable. Nevertheless, after drug interruption or switching, the elevated level of transaminases parasisted. In March 2019





Case Report

effects associated with the medication. At the end of therapy, the HEV viral load was negative in the plasma and feces, and the patient continues to have a negative viral load 24 weeks after the completion of therapy.

HEPATITIS E CRÓNICA EN PACIENTES INMUNODEPRIMIDOS TRASPLANTADOS DE ÓRGANO SÓLIDO: REVISIÓN





Viral Hepatitis E and Chronicity: A Growing Public Health Concern

Vikram Thekur", Radha Kenta Ratho ", Swatentra Kumar", Shallendra K. Sawena', Ishani Bora: and Pryanka Thakur Department of Virology, Post Gustasia Institute of Medical Education and Research, Chandigarh, India, ⁷ Centre for Arthurs and Change of Changle of Marketing Witter Course to Market all Assessed American Section





Clinical Manifestations, Pathogenesis and Treatment of Hepatitis E Virus Infections

Sébastien Lhomme 1,2,3,* , Olivier Marion 2,3,4 , Florence Abravanel 1,2,3 , Jacques Izopet 1,2,3 and Nassim Kamar 2,3,4,*(3)





Advances in Hepatitis E Virus Biology and Pathogenesis

Shaoli Lin D and Yan-Iin Zhang * D



Submit a Manuscript: https://www.f6publishing.com

DOI: 10.3748/wjg.v26.i37.5543

ISSN 1007-933

Hepatitis E virus: Epidemiology, diagnosis, clinic il estations. and treatment

Abdullah Tarık Aslan, Hatice Yasemin Balaban

Seminar

JOURNAL OF CLINICAL AND EXPERIMENTAL HEPATOLOGY

Chronic Hepatitis E Virus Infection and Treatment

Nassim Kamar*,†,‡, Jacques Izopet†,‡,§, Harry R. Dalton

*Department of Nephrology, Dialysis and Organ Transplantation, CHU Ranguell *INSERM U1043, IFR-BMT, CHU Purpan *Université Paul Sabatier Spepartment of Virology, CHU Purpan, Toulouse, France and Cornwall Gastrointestinal Unit, Royal Cornwall Hospital and European Centre of Environment and Human Health, University of Exeter Medical School, Truro, UK



World J Gestroenterol 2021 March 28; 27(12): 1240-1254

DOI: 10.3748/wjg.v27.i12.1240

1950\ 1007-9327 (print) ISSN 2219-2840 (online)

SHEETH-AWACTST

Hepatitis E in solid organ transplant recipients: A systematic review and meta-analysis

Panupong Hansrivtiit, Angkawipa Trongtorsak, Max M Puthenpura, Boonphiphop Boonpheng, Charat Thongprayoon, Karn Wijarnpreecha, Avishek Choudhury, Wisit Kaewput, Shennen A Mao, Michael A Mao, Caroline C Jadlowiec, Wisit Cheungpasitporn

Hepatitis

Nicole Pavio³. Rakesh Aggarwal⁴. Alain Labrique⁵. Heiner Wedemey y R. Dalton⁷

ED REVIEW

atures and determinants of chronicity in hepatitis E

hivakumar Narayanan¹ | Ameer Abutaleb^{1,2} | Kenneth E. Sherman³ | Shyam Kottilil¹ 🗓

frontiers in Microbiology

published: 29 September 2000 dot: 10.3389/fritob.2000.677388

Viral Hepatitis E and Chronicity: A **Growing Public Health Concern**

Vikram Thakur!*, Radha Kanta Ratho!*, Swatantra Kumar!, Shallendra K. Saxena!, Ishani Borat and Pryanka Thakur

American Journal of Transplantation 2012; 12: 2281–2287 Wiley Periodicals Inc.

Copyright 2012 The American Society of Transplantation and the American Society of Transplant Surgeons

Minireview

doi: 10.1111/i.1600-6143.2012.04078.x

Hepatitis E Virus: What Transplant Physicians Should Know

N. Kamara, b,c, *, F. Legrand-Abravanelb,c,d, J. Izopetb, c,d and L. Rostainga,b,c

HEV3 and HEV4, have been reported. However, recent data suggest that some areas of the developed world have hyperendemics, for example, the South of France

INFECCIÓN CRÓNICA POR VHE EN EL TOS: INTRODUCCIÓN

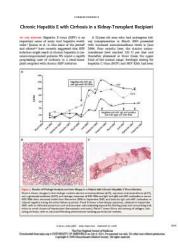
Los primeros casos de infección crónica por VHE se comunican en el año 2006



- Banas B, Tausch U, Hofstadter F, et al. Infection with hepatitis E virus: first report of a chronic case and molecular characterization of the virus. J Clin Virol 2006;36:Suppl 2:S162. abstract.
- Kamar N, Peron JM, Ouezzani L, et al. Hepatitis E virus infection can evolve to chronic hepatitis in organ-transplant patients. J Hepatol 2007;46:Suppl 1:S70-S71. abstract.









INFECCIÓN CRÓNICA POR VHE EN EL TOS: DEFINICIÓN

En el contexto del trasplante de órganos, se observó que no se producía aclaramiento espontáneo del VHE entre los 3 y 6 meses después de una fase aguda, lo cual propició que se considerase infección crónica cuando la replicación viral persistía por más de 3 meses.

American Journal of Transplantation 2013; 13: 1935–1936 Wiley Periodicals Inc. © 2013 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1002/ajt.12253

Letter to the Editor

How Should Hepatitis E Virus Infection Be Defined in Organ-Transplant Recipients?

In this cases series, no HEV clearance was observed between months 3 and 6 after infection. Hence, chronic HEV infection can be defined as persisting HEV replication beyond 3 months after infection, at least in SOT patients.

N. Kamar^{1,2,3,*}, L. Rostaing^{1,2,3},
F. Legrand-Abravanel^{2,3,4} and J. Izopet^{2,3,4}

¹Department of Nephrology, Dialysis and Organ
Transplantation, CHU Rangueil, Toulouse, France

²Université Paul Sabatier, Toulouse, France

³INSERM U1043, IFR-BMT, CHU Purpan,
Toulouse, France

⁴Department of Virology, CHU Purpan, Toulouse, France

* Corresponding author: Nassim Kamar,
kamar, n@chu-toulouse, france

INFECCIÓN CRÓNICA POR VHE EN EL TOS: CARACTERIZACIÓN

La infección crónica por VHE se ha descrito en pacientes infectados por genotipos diferentes al 3

Rat Hepatitis E Virus as Cause of Persistent Hepatitis after **Liver Transplant**

Siddharth Sridhar, Cyril C.Y. Yip, Shusheng Wu, Jianpiao Cai, Anna Jin-Xia Zhang, Kit-Hang Leung, Tom W.H. Chung, Jasper F.W. Chan, Wan-Mui Chan, Jade L.L. Teng, Rex K.H. Au-Yeung, Vincent C.C. Cheng, Honglin Chen, Susanna K.P. Lau, Patrick C.Y. Woo, Ning-Shao Xia, Chung-Mau Lo, Kwok-Yung Yuen

All hepatitis E virus (HEV) variants reported to infect hu- been reported to infect humans belong to Orthohepevirus The zoonotic potential of the species Orthohenevirus C from HEV-A, is unknown. We report a liver transplant recipi-ent with hepatitis caused by HEV-C infection. We detected HEV-C RNA in multiple dinical samples and HEV-C antigen also a potential threat to the blood product supply.

can occur in HEV-infected immunocompromised patients nomic, and serologic features of this new zoonosis. who acquire infection by eating undercooked pork, rabbit deer, camel, or boar meat (2-6). HEV transmission through blood product transfission also has been described (7).

The diverse Hepeviridae family, which incorporates Study Population all HEV variants, includes members whose primary host We conducted this study in Queen Mary Hospital, a 1,700species are terrestrial mammals (genus Orthohopevirus) bed tertiary care hospital in Hong Kong. We assessed 518 and fish (genus Piscihepevirus) (8). The Orthohepevirus solid-organ transplant recipients (kidney, liver, lung, and

Author affiliations: The University of Hong Kong, Hong Kong, China (S. Sridhar, C.C.Y. Yip, S. Wu, J. Cal, A.J.-X. Zhang, K.-H. Leung, T.W.H. Chung, J.F.W. Chan, W.-M. Chan, J.L.L. Teng, R.K.H. Au-Yeung, V.C.C. Cheng, H. Chen, S.K.P. Lau, the upper limit of the reference level for a continuous period P.C.Y. Woo, C.-M. Lo, K.-Y. Yuen): The University of Hong Kong-Shenzhen Hospital, Shenzhen, China (J.F.W. Chan, C.-M. Lo, K.-Y. Yuen); Xlamen University, Xlamen, China (N.-S. Xla)

DOI: https://doi.org/10.3201/eld2412.180937

Emerging Infectious Diseases - www.cdc.gov/eid - Vol. 24, No. 12, December 2018

mans belong to the species Orthohepevirus A (HEV-A). A (HEV-A). Five genotypes within HEV-A (HEV-1-4 and -7) cause hepatitis in humans, and 3 genotypes (HEV-3, -4, (HEV-C), which circulates in rats and is highly divergent and -7) can cause chronic hepatitis in immunocompromised

In addition to HEV-A, the Orthohepevirus senus in in the liver. The complete genome of the HEV-C isolate had cludes 3 other species; Orthohopwirus B circulates in chick-93.7% nt similarity to an HEV-C strain from Vietnam. The patient had preexisting HEV antibodies, which were not protective against HEV-C infection. Ribavirin was an effective E virus, shares only 50%-60% at identity with HEV-A (8). of HEV-C viremia. Testing for this zoonotic virus should be cal infection have not been reported. The substantial phyloperformed for immunocompromised and immunocompetent genetic divergence between HEV-A and HEV-C, especially patients with unexplained hepatitis because routine hepati-in critical receptor binding domains, forms a theoretical speis E diagnostic tests may miss HEV-C infection. HEV-C is cles barrier (11). Serologic and molecular tests for HEV are designed primarily to detect HEV-A, and they might miss HEV-C infections. Therefore, the threat to human health, Hepatitis E virus (HEV) infects 20 million humans world-wide annually (1). HEV-infected persons usually have unknown. We aimed to prove definitively that HEV-C can self-limiting acute hepatitis. However, persistent hepatitis infect humans and describe the clinical, epidemiologic, ge-

genus is classified into 4 species; HEV variants that have heart transplant) who were followed up in Queen Mary Hospital for persistent biochemical hepatitis from January 1, 2014, or date of transplant (whichever date was later) through December 31, 2017. We defined persistent hepatitis as elevation of alanine aminotransferase (ALT) >1.5 times of ≥6 weeks. For patients whose ALT met this definition, we reviewed clinical records, ultrasonogram results, endoscopic retrograde cholangiopancreatography results, and laboratory results to identify the likely cause of hepatitis. We

JOURNAL OF CLINICAL AND EXPERIMENTAL HEPATOLOGY

with acute-on-chronic liver failure (ACLF) as per the Asian

Pacific Association for the Study of the Liver (APASL) defi-

nition. The acute decompensation was precipitated by the

henatitis II virus (HIIV) related to acute henatitis with nos-

itive IgM anti-HEV antibodies in the serum. Because of his

womening liver failure, he underwent un-eventful living-

and since then was on immunosuppression with predniso-

A month after the liver transplantation, he developed a

mild elevation of serum transaminases (2-3 times higher

esonance cholangiopancreatography showed mildly

dilated intrahepatic biliary radicals, a biliary stricture was

suspected and a stent was placed across the bile duct anas-

tomosis. However, there was only a partial reduction in

transaminases and alkaline phosphatase. An alternative

A liver biopsy was performed, which suggested modes

are acure cellular rejection (ACR: Figure 1, biopsy 1); how-

ever, despite the administration of 2 pulses of

methylprednisolone and the histological resolution of

ACR on the repeat liver biopsy (Figure 1, biopsy 2), his

jaundice continued to increase with a maximum bilirubit

of 58 mg/dl. On further work-up, he was found to be now

itive for JeM anti-HEV antibodies, and negative for hepati-

ris B surface antigen, anti-heparitis C virus antibodies, and

autoimmune markers. Markers for the cytomegalovirus,

Epstein-Barr virus, and herpes simples virus were also

negative. HEV RNA was detectable both in serum and in

than the normal), along with an elevation of alkaline phos-

pharase (2 times higher than the normal). Initial magnetic

donor liver transplantation after a month of his illness

lone, tacrolimus, and mycophenolate moferil.

pathology was therefore suspected.

Chronic Hepatitis E With Genotype 1 - Masquerading as Allograft Rejection After LiverTransplantation

Sahaj Rathi", Ajay Duseja", Vikram Thakur I, Radha K. Ratho", Mini P. Singh J, Sunit Taneja", Ashim Das I, Rakesh Aggarwal L. Radha K. Dhiman ", Yogesh K. Chawla

Department of Hispatology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, 1 Department of Visuage, Postgraduate Institute of Medical Education and Research (PCIMER), Chandigari, India, 1 Department of Hatiquathology, Postgraduate Institute of Medical Education and Research (PCIMER), Chandigari, India and 1 Department of Gastroonterology, Santar Gandy Postgraduate Institute of Admitted Science (SGPGB, Lucknew, Litter Products, India

Hepatitis E is one of the leading causes of acute viral hepatitis worldwide. Chronic infection with hepatitis E is less common and limited to immunosuppressed patients and is usually due to genotype 3 of the virus. Genotype 1, the most prevalent strain in the South Asian region, is seldom known to be associated with chronic bepatitis. Here we describe a case of chronic hepatitis E with genotype 1 in a pose-liver transplant setting. In the index case, previously compensated cryptogenic circhosis was decompensated by an acute hepatitis E infection, which necessituted liver transplantation because of acute chronic liver failure. This later progressed to chronicity. This case may have significant implications in management, especially in the post-liver transplant setting. () Cox Exe HIGHTOL MONGAMONA)

epatitis E is one of the leading causes of acute viral hepatitis worldwide, which is more in developing Lountries. A genotypic dichotomy is seen in the geographical distribution of this infection, where geno-I and 2 are mainly seen in developing conwith high endemicity, often being responsible for epi-demics. Genotypes 3 and 4 are predominantly seen in areas of low endemicity. The classic presentation ranges from acute hepatitis with self-limiting course to acute liver failure in 1-2% cases."

Rarely, an indolent, chronic hepatitis is seen with heparitis E. This is largely restricted to those with compromised immunity such as those with HIV, post-chemotherapy, and post-transplant setting. Genotype 3 of the virus is the most non offending agent for chronic hepatitis E (CHE), and a few cases with genotypes 4 and 7 have also been reported. 22 Genotype 1, which is the most prevalent strain in the South Asian region, is almost never known to cause chronic heparitis. Here we describe a case of CHE with genotype I in a post-liver transplant patient, who evaded the nitial diagnosis masqueradine as allograft rejection.

Krywerde chronic hepatitis II, gruntype I, post-leve transplant, ribaritin Burnol 30.3-2020, Accepted 12.7-2020, Appliebt orders no Address for correspondence. Dr. Ajay Disseja, MD, DM, FAMS, FAASLD, FACC, PSGIII, Professor, Department of Hepatology, Pangraduate Institute of Medical Education and Research, Chundigath, Sector 12, 160012, ledia, Tel.: +91 172 2734793; Fax: +91 172 2744401.

Adventure ACLP attream-frome liver falsasy ACR acute official rejection; CHP chronic hepatitis E; HIV: hepatitis E virus; CHP; open reading frame; Billips RNA-dependent RNA polymerasa

© 2020 Indian National Association for Study of the Liver, Published by Elsevier B.V. All rights reserved.

Journal of Clinical and Experimental Reputings | ■ xxxx | Vol. xxx | No. xxx | xx.

of Clearal and Experimental Heparology, https://doi.org/10.1016/j.jceh.2020.07.000

BRIEF REPORT

and Milk

Chronic Infection With Camelid Hepatitis E Virus in a Liver Transplant Recipient Who Regularly Consumes Camel Meat

Guan-Huei Lee, 1,2,3 Boon-Huan Tan, 4 Esmeralda Chi-Yuan Teo, 5 Seng-Gee Lim, 1,2,3 Yock-Young Dan, 1,2,3 Aileen Wee, 1,6 Pauline Poh Kim Aw,7 Yuan Zhu, Martin Lloyd Hibberd, 7,8 Chee-Kiat Tan, 9,10 Michael A. Purdy, 11 and Chong-Gee Teo1

Yang Loo Lis School of Medicine, "Saw Swee Hock School of Public Health, National University of Singapore," Department of Medicine, "Department of Particloge, National University Health System, Singapore, "National University Corrier for Organ Transplantation, National University Corrier for Copy and Transplantation, National University Health Syngapore," Evolution of Health Syngapore, "London School of Hygiene and Tiopidal Health Syngapore, "Security Medical School, Singapore, "London School of Hygiene and Tiopidal Medicine, London, University Medical School, Singapore," "Lindon National Syndapsis, Center and Copy a for Disease Control and Prevention, Atlanta, Georgia

See Covering the Cover synopsis on page 291.

There have been increasing reports of food-borne zoonotic transmission of hepatitis E virus (HEV) genotype 3, which causes chronic infections in immunosuppressed patients. We performed phylogenetic analyses of the HEV sequence (partial and full-length) from 1 patient from the Middle East who underwent liver transplantation, and compared it with other orthohepevirus A sequences. We found the patient to be infected by camelid HEV. This patient regularly consumed camel meat and milk, therefore camelid HEV. (Figure 1B). Acute cellular rejection-like features and central which is genetype 7, might infect human beings. Our finding links consumption of camel-derived food products to post-transplantation benefitie E which if detected at early stages, can be cured with antiviral therapy and (HEV) IgM but not IgG was detected in serum. After reduced administration of immunosuppressive agents.

Keywords: Case Study; Liver Disease; Zoonosis; Viral Infection.

55-year-old Somalian man from the United Arab A Emirates underwent living-donor liver transplantation in Singapore in 2010 for hepatitis B cirrhosis and hepatocellular carcinoma. After recuperating well, he returned to the United Arab Emirates 3 months later with normal liver enzyme levels.

At month 17 after transplantation, he returned to Singapore with the following abnormal serum liver test results: alanine aminotransferase level of 118 U/L, aspartate aminotransferase level of 104 U/L, alkaline phosphatase level of 132 U/L, and y-glutamyltransferase level of 324 U/L. Total bilirubin level was normal. He denied alcohol consumption, noncompliance or alternative use of medica tion, or contact with persons with viral hepatitis.

IU/mL Serologic tests for active infection with human immunodeficiency virus, hepatitis A virus, hepatitis C virus, cytomegalovirus, and Epstein-Barr virus were negative Tacrolimus level was less than 2.0 ug/L. Liver radiology was

unremarkable. The initial differential diagnosis included mild acute cellular rejection and drug-induced liver injury from ezetimibe and alfuzosin. Both these drugs were dis

Gastroenterology 2016;150:355-357

continued and the dosages of the immunosuppressants were increased. However, moderate transaminitis persisted (Figure 1A) leading to suspicion that an infection may be Liver biopsy specimens at 17, 19, and 20 months afte transplant showed increasing interface hepatitis with mild

Johnson recroinflammation (METAVIR scores A2 A2 and A3 respectively), with F2 grade portal and focal septal fibrosis perivenulitis with hepatocytic dropout were seen in the biopsy specimens at 19 and 20 months, respectively. At 22 month after transplant anti-henstitic E virus

contemporary reports were published of chronic hepatitis E in solid-organ transplant patients, polymerase chain reaction (PCR) for HEV RNA in serum was conducted, which confirmed its presence. Infection by HEV belonging to genotype 3 was presumed. The patient was started on oral ribavirin 600 mg/d for 12 weeks, together with reduction of suppression. Liver test results rapidly normalize (Figure 1A). Eight weeks after therapy (24 months after transplant), HEV became undetectable

A retrospective analysis of a stored plasma sample collected at month 19 after transplant showed a HEV RNA concentration of 8.34 × 106 IU/mL, and the presence of

To date HEV responsible for chronic henatitis in organ transplant patients has been reported to be transmissible from pigs and boars, and less extensively from deer, Because the patient is a Muslim, the route of HEV

His serum hepatitis B virus-DNA level was less than 13.5

Abtreviations used in this paper: HEV, hepatitis E virus PCR, polymerase than 13.5

than reaction.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: DIAGNÓSTICO MICROBIOLÓGICO

El diagnóstico microbiológico se basa exclusivamente en la presencia de marcadores de detección directa (ARN-VHE y/o Ag). Las pruebas serológicas que detectan anticuerpos específicos de tipo IgG y/o IgM frente al VHE nunca se pueden usar solas para diagnosticar o excluir la enfermedad crónica.

GASTROENTEROLOGY 2011;140:1481-1489

Factors Associated With Chronic Hepatitis in Patients With Hepatitis E Virus Infection Who Have Received Solid Organ Transplants

Table 2. HEV Serologic and PCR Results at Diagnosis in 85 Solid Organ Transplant Patients With HEV Infection

HEV diagnostic test	No. tested	No. positive	Percent
Anti-HEV IgM ^a	78	32	41.0
Anti-HEV IgG®	78	63	80.8
Serum HEV PCR	82 ^b	82	100
HEV genotyping	64	59°	c

^aA wide range of differing commercial and in-house assays were used, and these differed from center to center.

bThree patients were not tested for HEV RNA by PCR. The diagnosis of HEV infection in these cases was based on an increased IgM and IgG level.

[°]All 59 patients in whom HEV was genotyped were infected with HEV genotype 3. In 50 of these cases, HEV subtyping was performed and showed infection with the following subtypes: 3f, n=37; 3c, n=12; 3e, n=1. In 5 patients, genotyping was not possible due to failure to amplify HEV.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: DIAGNÓSTICO DIFERENCIAL

Los receptores de TOS con niveles de transaminasas hepáticas por encima del límite superior de la normalidad o con síntomas sugestivos de infección se deben de analizar para detectar VHE.

Toward Systematic Screening for Persistent Hepatitis E Virus Infections in Transplant Patients

Michael J. Ankcom, MBBS, MRCP, DTM&H, 1,2 Samreen Ijaz, PhD, 1 John Poh, PhD, 1 Ahmed M. Elsharkawy, BM, PhD, FRCP, 3 Erasmus Smit, FRCPath, 4,5 Robert Cramb, MB, FRCPath, 6 Swathi Ravi, 7 Kate Martin, MSc, BSc, 8 Richard Tedder, MB, BChir, FRCP, FRCPath, 1,2,9 and James Neuberger, DM3

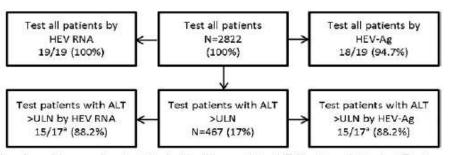


FIGURE 4. Consideration of possible screening strategies for identifying persistent HEV in a transplant cohort. The transplant cohort considered included heart, lung, kidney and stem cell recipients. ALT data missing for two viraemic patients. ULN, Upper limit of normal.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: SEROPREVALENCIA E INCIDENCIA (I)

La incidencia y la seroprevalencia de la infección por el VHE en la población de TOS son difíciles de estimar con precisión, debido a la gran variabilidad dentro de las poblaciones estudiadas con TOS y también a los diferentes ensayos serológicos y moleculares utilizados en estos estudios.

Table 1 Prevalence of hepatitis E virus infection defined by detection of HEV RNA.

Study	Country	Number	Transplanted organs	Prevalence
Legrand- Abravanel et al ⁹	France	700	KT, LT, SPK	3.2%
Legrand- Abravanel ¹⁰	France	171	KT, LT	3.5%
Moal et al ¹⁶	France	1350	KT	1.2%
Pischke et al ¹¹	Germany	226	LT	0.9%
Pischke et al ¹²	Germany	274	HT	1.5%
Haagsma et al ¹³	The Netherlands	285	LT	1.75%
Pas et al ¹⁴	The Netherlands	1200	SOT	1%
Riezebos- Brilman et al ¹⁷	The Netherlands	468	Lung transplantation	2.1%

Abbreviations: KT, kidney-transplant; LT, liver transplant; SPK, simultaneous pancreas-kidney-transplant; HT, heart transplant; SOT, solidorgan transplant.

Study	Number	Organ transplant	Serology tests	Anti-HEV IgG prevalence (%)	HEV RNA prevalence (%)	HEV RNA incidence (%
Abravanel et al. [72]	700	KT/LT/SPK	Adaltis	12.7	-	3.2
Abravanel et al. [73]	263	KT/LT	Wantai	38.4	-	2.6
Buffaz et al. [74]	206	LT	Wantai	29	-	-
Buni et al. [75]	108	KT/LT	Biokits	2.3	-	-
Haasgsma et al. [76]	285	LT	Genelabs	3,5	1.75	-
Koning et al. [77]	145	LT	Wantai	42	0	-
Laverdure et al. [78]	96	LT	Wantai	8,3	-	-
Moal et al. [79]	1350	KT	-	-	1.2	-
Moal et al. [80]	578	KT	Wantai	43	-	1
Magnusson et al. [81]	62	Lung T	Mikrogen	13	0	-
Naik et al. [82]	205	KT	Wantai	20.5	0	-
Pas et al. [83]	1200	SOT	Wantai	-	1	-
Pischke et al. [84]	226	LT	Abbot	4.4	0.9	-
Pischke et al. [85]	274	HT	Genelabs	11,3	1.5	-
Pischke et al. [86]	95	Lung T	MP	5,3	3.2	-
Riezebos et al. [87]	468	Lung T	_	-	2.1	-
Sherman et al. [88]	53	KT	Wantai	19.5	0	-
	113	LT		18.9	0	-

HEV/hepstitis E virus, KT kidney transplant, LT liver transplant, SPK simultaneous pancreas-kidney transplantation, HT heart transplant, Lung T lung transplant

INFECCIÓN CRÓNICA POR VHE EN EL TOS: SEROPREVALENCIA E INCIDENCIA (II)

El ensayo de Roche para el equipo Cobas 6800 es una poderosa herramienta en términos de robustez, reproducibilidad, sensibilidad (6 UI/mL) en un sistema de PCR RT completamente automatizado, lo que lo convierte en una alternativa viable para un gran volumen de pruebas.

Journal of Clinical Virology 129 (2020) 104525





Performance of Roche qualitative HEV assay on the cobas 6800 platform for quantitative measurement of HEV RNA



Viktoria Thodou^{e,*}, Birgit Bremer^a, Olympia E. Anastasiou^b, Markus Cornberg^c, Benjamin Maasoumy^a, Heiner Wedemeyer^d



Thodou V et al. J Clin Virol 2020; 129: 104525

INFECCIÓN CRÓNICA POR VHE EN EL TOS: SEROPREVALENCIA E INCIDENCIA (III)

GEHEP 016 tiene previsto analizar la prevalencia, la incidencia (anual y al final del estudio) y la tasa de cronificación de la infección por VHE en pacientes inmunodeprimidos incluyendo TOS.



SOLICITUD DE PROYECTO DE INVESTIGACIÓN

PROYECTO GEHEP 016

1. Datos del proyecto:

Título del proyecto: Hepatitis E en pacientes inmunodeprimidos y trasplantados de órgano sólido: Situación actual de la infección en España

Investigador principal: Antonio Aguilera Guirao

Entidad Solicitante: Complexo Hospitalario Universitario de Santiago.

Instituto de Investigación Sanitaria de Santiago (IDIS)

Responsable de la entidad: Isabel Lista García

Dirección: Travesia A Choupana s/n

Ciudad: Santiago de Compostela

Tfno: 981955308

2. Resumen del proyecto:

Importancia: La infección por el virus de la Hepatitis E (VHE) presenta un peor pronóstico en pacientes immunodeprimidos, condicionando la aparición de efectos deletéreos asociados a la propia infección y al origen de la immunosupresión. Objetivo primario: Evaluar la prevalencia de infección por el VHE en pacientes

inmunodeprimidos.

Objetivo secundario: evaluar el desarrollo de infección crónica del VHE en pacientes

inmunodeprimidos.

Diseño: Estudio longitudinal prospectivo.

Ámbito: Unidades de Microbiológía en colaboración con Enfermedades Infecciosas, Digestivo/Hepatológía, Nefrológía y Reumatológía de los Hospitales participantes en el proyecto.

Pacientes: inmunodeprimidos por infección por el VIH, trasplantados de órgano sólido (hígado y riñón) y pacientes en tratamiento inmunosupresor.

Variable desenlace: infección por el VHE, definida como presencia de ARN viral en sangre periférica.

Variable desenlace secundaria: infección crónica por el VHE, definida como persistencia de ARN viral en sangre periférica durante más de 3 meses.

Intervención: realización de PCR frente al VHE anual en todos los pacientes incluidos en el estudio.

Análisis: se realizará análisis de prevalencia (basal) e incidencia (anual y al final del estudio) de la infección por el VHE en el total de la población y en cada subpoblación de pacientes. Se evaluará la tasa de cronificación de la infección por el VHE en el total de la población y en cada una de las subpoblaciones de pacientes.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: TRANSMISIÓN DEL VHE

En pacientes inmunodeprimidos con TOS, el VHE se transmite a través de los mismos modos que en la población general. Además, en estos pacientes el VHE también puede transmitirse nosocomialmente.

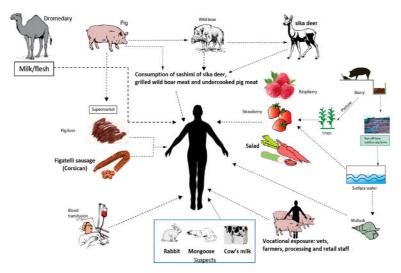


Figure 5. Zoonotic transmission of hepatitis E in developed and many developing countries.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: PREVENCIÓN

Es aconsejable que los pacientes con TOS no coman carne poco cocida, ya que el VHE solo se inactiva con temperaturas superiores a 70º C. Por otra parte, la transmisión nosocomial se evita aislando los casos de infección por VHE que estén ingresados en el hospital.



Recommendations

- The prevention of HEV infection should be based on offering information aimed at avoiding contact with sources of infection (AII).
- · On trips to developing countries, to avoid contact with HEV, general hygienic practices should be adopted, such as washing the hands with clean or sanitised water before handling food, Do not drink water or consume ice of unknown purity. The consumption of fruit not peeled by oneself and of raw foods in general should be avoided (All).
- In addition to adopting the basic hygienic measures recommended for the general population, people at high risk of developing a severe course of infection or the chronification of it (cirrhotic and transplanted) must be specifically informed of the risk involved in eating pork products and undercooked game animals, including sausages, and to avoid the consumption of these products (AII),
- People at high risk of developing a severe course of infection or the chronification of it should subject food to cooking-heating at a temperature > 70 °C for a minimum of 30 min (Al).

INFECCIÓN CRÓNICA POR VHE EN EL TOS: REINFECCIÓN

Aunque los anticuerpos inducidos por la inmunización activa o pasiva protegen frente a la reinfección, la concentración protectora mínima aun no se ha determinado. Se han informado casos puntuales de reinfección en pacientes TOS, seropositivos para el VHE (<7 UI OMS/mL), alguno de los cuales desarrolló hepatitis crónica.

Hepatitis E Virus Reinfections in Solid-Organ-Transplant Recipients Can Evolve Into Chronic Infections

Florence Abravanel, ^{1,2} Sebastien Lhomme, ^{1,2} Sabine Chapuy-Regaud, ^{1,2} Jean-Michel Mansuy, ² Fabrice Muscari, ⁴ Federico Sallusto, ³ Lionel Rostaing, ^{1,3} Nassim Kamar, ^{1,3} and Jacques Izopet ^{1,2}

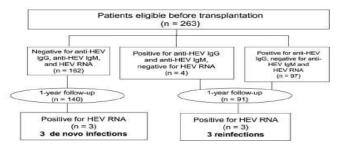


Figure 1. Hepatitis E virus (HEV) markers in 263 recipients of solid-organ transplants. Abbreviations: IqG, immunoglobulin G: IqM, immunoglobulin M.

Abravanel F et al. J Infect Dis 2014; 209: 1900-6

INFECCIÓN CRÓNICA POR VHE EN EL TOS: HISTORIA NATURAL (I)

Sólo 1/3 de los pacientes con TOS infectados por el VHE presentan síntomas, principalmente fatiga, mientras que los niveles de las enzimas hepáticas aumentan de una manera mucho más moderada que los observados generalmente en pacientes inmunocompetentes.

GASTROENTEROLOGY 2011;140:1481-1489

Factors Associated With Chronic Hepatitis in Patients With Hepatitis E Virus Infection Who Have Received Solid Organ Transplants

NASSIM KAMAR, "-5 CYRIL, GARROUSTE, "I ELZABETH B. HAAGSMA," VALÉRIE GARRIGUE, "SVEN RSCHIE;" GEGLE CHAUPET, "I JERCOME DUMORTIER, "8 AMELIE CANNESSON, "I ELISABETH CASSICIORIER, "9 FIRE PROPERTIES PLOMENS CONTI," PAGAZAL LEBRAY, ""HARRY T, DALTON, "9 FODERT SANTELLA, "III ANNE MARIE ROQUE-APONSO, \$500, MACQUES COPET, "55 and LIONEL ROCTAINS," 150

Table 4. Patient Characteristics at Diagnosis of HEV Infection

Variables	Resolving group (n = 29)	Chronic group (n = 56)	P value
Time since transplant (mo)	70.3 ± 52.8	41.4 ± 38	.005
Symptoms at presentation (%)	31	32	NS
AST level (IU/L)	107 (16-1571)	94 (21-436)	.02
ALT level (IU/L)	263 (24-2675)	135 (28-874)	.001
γ glutamyl transpeptidase level (IU/L)	244 (28-2337)	173 (25-3482)	NS
Alanine phosphatase level (IU/L)	251 (66-1924)	172 (46-7775)	NS
Bilirubin level (µmol/L)	16 (6-75)	7 (5-277)	NS
Peak AST level (IU/L)	223 (31-1571)	147 (39-874)	.001
Peak ALT level (IU/L)	272 (29-2675)	167 (32-522)	.005
Serum creatinine level (µmol/L)	168 ± 69	130 ± 51	.005
Hemoglobin level (g/dL)	13.1 ± 1.85	12.9 ± 1.56	NS
White blood cell count (/mm³)	7253 ± 2834	6122 ± 2370	NS
Lymphocyte count (/mm³)	1414 ± 684	1399 ± 702	NS
Platelet count (/mm³)	225,655 ± 62,521	190,384 ± 79,903	.04
Calcineurin inhibitors (%)	75.9	83.9	NS
Cyclosporin A/tacrolimus	9/13	4/43	.003
Cyclosporin A (mg · kg ⁻¹ · day ⁻¹)	1.9 ± 0.5	2.24 ± 1.2	NS
Cyclosporin A trough level (ng/mL)	88 ± 82	183 ± 106	NS
Cyclosporin A C2 level (ng/mL)	543 ± 155	352 ± 248	NS
Tacrolimus (mg · kg ⁻¹ · day ⁻¹)	0.06 ± 0.03	0.09 ± 0.09	NS
Tacrolimus trough level (ng/mL)	8.7 ± 3.2	10.1 ± 4.3	NS
Belatacept (%)	3.4	0	NS
mTOR inhibitors (%)	24	19.6	NS
Sirolimus trough level (ng/mL)	7.8 ± 4.3	8.7 ± 3.6	NS
Everolimus trough level (ng/mL)	10.5 ± 7.07	12.1 ± 6.3	NS
Mycophenolic acid (%)	79.3	69.6	NS
Mycophenolic dose (mg · kg-1 · day-1)	19.2 ± 7.6	20.1 ± 8.07	NS
Azathioprine (%)	0	7.1	NS
Corticosteroids (%)	72.4	69.6	NS
Corticosteroid dose (mg · kg ⁻¹ · day ⁻¹)	0.08 ± 0.04	0.1 ± 0.09	NS
Anti-HEV IgG P/Nº (%)	32.1	46	NS
Anti-HEV IgM P/Nº (%)	84.6	78.8	NS
HEV RNA concentration (copies/mL) ^b	1,927,500 (500-71,440,000)	1,248,500 (35,600-71,000,000)	NS

C2, concentration 2 hours after intake; mTOR, mammalian target of rapermycin; N, negative; P, positive.
PAnti-HEV IgG and IgM were studied in, respectively, 28 and 28 patients from the resolving group and 50 and 52 patients from the chronic group.
*Data were available for 18 patients from the resolving group and 26 patients from the chronic group.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: HISTORIA NATURAL (II)

Aproximadamente ½ de los pacientes infectados por el VHE y con TOS eliminan espontáneamente el virus sin reactivación en los primeros 3 meses posteriores al diagnostico, mientras que los ¾ restantes desarrollaron hepatitis crónica E.

GASTROENTEROLOGY 2011;140:1481-1489

Factors Associated With Chronic Hepatitis in Patients With Hepatitis E Virus Infection Who Have Received Solid Organ Transplants

NASSIM KAMAR,**-5 CYRIL GARROUSTE,**| ELIZABETH B. HAAGSMA,*| VALÉRIE GARRIGUE,* SVEN PISCHKE,**
CÉCILE CHAUVET,**- JÉROME DUMORTIER,55 AMÉLIE CANNESSON,III ELISABETH CASSUTO-VIGUIER,*II
ERIC THERVET,**- FILOMENA CONTI,**- PASCAL LEBRAY,***+ HARRY R. DALTON,595 ROBERT SANTELLA,III
NADA KANAAN,**II MARIE ESSIG,****- CHRISTIANE MOUSSON,***- SYLVIE RADENNE,***+**
ANNE MARIE ROQUE-AFONSO,5959 JACQUES IZOPET,**-51 and LIONEL ROSTAING**-*-5

In conclusion, this is the largest series to assess the occurrence of chronic HEV infection after solid organ transplant. Approximately 60% of solid organ transplant patients infected with HEV developed chronic hepatitis. The use of tacrolimus rather than cyclosporin A and low platelet count were the main independent factors associated with chronic HEV infection.

Review

Clinical Manifestations, Pathogenesis and Treatment of Hepatitis E Virus Infections

Sébastien Lhomme 1,2,3,*,0, Olivier Marion 2,3,4,0, Florence Abravanel 1,2,3, Jacques Izopet 1,2,3,0 and Nassim Kamar 2,3,4,*,0

7. Pathogenesis of Chronic Infection in Immunocompromised Patients

Most studies on the pathogenesis of chronic HEV installation have focused on SOT recipients. The incidence of HEV infection in these patients varies from 0.9% to 3.5%, based on detecting HEV RNA, and acute infections become chronic in ~60% of them [48]. Other studies that were interested in the seroconversion rate among transplant recipients have reported rates of progression to chronicity ranging from 21% to 50% [156–158].

INFECCIÓN CRÓNICA POR VHE EN EL TOS: HISTORIA NATURAL (III)

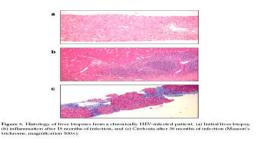
En torno al 10% de los pacientes con TOS e infección crónica por el VHE presentan en mayor o menor medida una rápida evolución de la fibrosis hepática a formas más graves como cirrosis y cirrosis descompensada. No se han informado hasta el momento casos de hepatitis fulminante.

Review

Clinical Manifestations, Pathogenesis and Treatment of Hepatitis E Virus Infections

Sébastien Lhomme ^{1,2,3},*©, Olivier Marion ^{2,3,4}©, Florence Abravanel ^{1,2,3}, Jacques Izopet ^{1,2,3}© and Nassim Kamar ^{2,3,4},*©

Nearly 10% of SOT patients with HEV develop cirrhosis within 3 to 5 years after the primary infection (Figure 5). Progression to liver fibrosis seems to be associated with the slow diversification of the P domain of the capsid [160]. More aggressive variants may be selected in fibroses, although this needs confirmation in a larger cohort.



INFECCIÓN CRÓNICA POR VHE EN EL TOS: FACTORES DE RIESGO (I)

No existen muchos estudios que hayan evaluado los factores de riesgo de la infección crónica por el VHE en el TOS y los mecanismos implicados en la persistencia del VHE no se conocen con exactitud.

Received: 25 May 2018 Accepted: 25 October 2018

DOI: 10.1111/jvh.13059

NON-COMMISSIONED REVIEW

WILEY

Clinical features and determinants of chronicity in hepatitis E virus infection

Shivakumar Narayanan¹ | Ameer Abutaleb^{1,2} | Kenneth E. Sherman³ | Shyam Kottilil¹

Narayanan et al. J Viral Hep 2019; 4:414-21

GASTROENTEROLOGY 2011:140:1481-1489

Factors Associated With Chronic Hepatitis in Patients With Hepatitis E Virus Infection Who Have Received Solid Organ Transplants

NASSIM KAMAR,**-5 CYRIL GARROUSTE,*-1 ELIZABETH B. HAAGSMA,*1 VALÉRIE GARRIGUE,* SVEN PISCHKE,**
CÉCILE CHALVET,**- JÉROME DUMORTIER,55 AMÉLIE CANNESSON,*** LISABETH CASSUTO-VIGUIER,**1
ERIC THERVET,*** FILOMENA CONTI,*** PASCAL LEBRAY,***+ HARRY R. DALTON,555 ROBERT SANTELLA,***
MADA KANAAN,****1 MARIE ESSIG,**** CHRISTIANE MOUSSON,**** SYLVIE RADENNE,****
ANNE MARIE ROQUE-AFONSO,5555 JACQUES IZOPET,**5.1 and LIONEL ROSTAING****5

INFECCIÓN CRÓNICA POR VHE EN EL TOS: FACTORES DE RIESGO (II)

Factores propuestos con mayor o menor evidencia:

Factores del huésped:

Alteración de la respuesta inmune del huésped innata y adaptativa.

Factores del virus:

Mayor diversidad de cuasiespecies del VHE en las regiones ORF1 y ORF2 durante la fase aguda.

El genotipo del VHE y las diferencias epidemiológicas entre las infecciones por diferentes genotipos.

Otros factores:

Uso de Tacrolimus y recuento bajo de plaquetas.

GASTROENTEROLOGY 2011;140:1481-1489

Factors Associated With Chronic Hepatitis in Patients With Hepatitis E Virus Infection Who Have Received Solid Organ Transplants

NASSIM KAMAR, *-16 CYRIL GARROUSTE. *1 ELZABETH B. HAAGSMA, *1 VALÉRIE GARRIGGUE, * SVEN REGHE, **
GÖLLE CHAUPET, *1 JÉGÖME DUMORITER, *2 AMÉLIE CANNESSONI, *1 ELSABETH CASSUTO-VIGUER, *1*
ERIC THERVET, *1 LOMENA CONTI, **1 PASCAL LEBRAY, *15 HARRY R. DALTON, *15 FODGERT SANTELLA, III
FINAL THERVET, *1 LOMENA CONTI, *10 PASCAL LEBRAY, *15 HARRY R. DALTON, *15 FODGERT SANTELLA, III
ANNE MARIE ROQUE. *4 CONTI, *10 PASCAL LEBRAY, *15 HARRY R. DALTON, *15 FODGERT SANTELLA, III
ANNE MARIE ROQUE. *4 CONTI, *10 PASCAL LEBRAY, *15 HARRY R. DALTON, *15 FOTGERT SANTELLA, III
ANNE MARIE ROQUE. *4 CONTI, *10 PASCAL LEBRAY, *15 HARRY R. DALTON, *15 FOTGERT SANTELLA, III

**TOTAL THE TOTAL RESPONSABILITY OF THE TOTAL RESPONSABILIT

Reniem

Clinical Manifestations, Pathogenesis and Treatment of Hepatitis E Virus Infections

Sébastien Lhomme 1,2,3,* , Olivier Marion 2,3,4 , Florence Abravanel 1,2,3 , Jacques Izopet 1,2,3 and Nassim Kamar 2,3,4,*

Receival: 25 May 2018 | Accepted: 25 October 2018

DOI: 10.1111/n-13059

NON-COMMISSIONED REVIEW

Clinical features and determinants of chronicity in hepatitis E virus infection

Shivakumar Narayanan¹ | Ameer Abutaleb^{1,2} | Kenneth E. Sherman³ | Shyam Kottillil¹

INFECCIÓN CRÓNICA POR VHE EN EL TOS: TRATAMIENTO (I)

Aunque la reducción de la terapia inmunosupresora, especialmente la dirigida a las células T, puede lograr la eliminación del VHE en casi un tercio de los pacientes, el tratamiento antiviral es necesario en quienes no lo consiguen.

Las indicaciones terapéuticas recogidas en las GPC son eficaces en el tratamiento de la infección crónica por VHE; sí bien una de ellas está contraindicada en receptores de trasplante de riñón, páncreas, corazón y pulmón al aumentar el riesgo de rechazo.





Review

Treatment of HEV Infection in Patients with a Solid-Organ Transplant and Chronic Hepatitis

Nassim Kamar ^{1,2,3,*}, Sébastien Lhomme ^{2,3,4}, Florence Abravanel ^{2,3,4}, Olivier Marion ^{1,2}, Jean-Marie Peron ^{3,5}, Laurent Alric ^{3,6,7} and Jacques Izopet ^{2,3,4}

INFECCIÓN CRÓNICA POR VHE EN EL TOS: TRATAMIENTO (II)

La monoterapia con el antiviral indicado prioritariamente en las diferentes GPC, en ciclos de 12 semanas (la duración óptima se desconoce) y con dosis ajustada a peso (media de 600 mg/día) es altamente eficiente (RVS del 78% a un ciclo y 90% a dos) en el tratamiento de la infección crónica por VHE en receptores de TOS.

Clinical Infectious Diseases

MAJOR ARTICLE







Kamar N et al. Clin Infect Dis 2020; 71:1204-11.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: TRATAMIENTO (III)

Las diferentes GPC contemplan opciones de tratamiento y algoritmos similares





Stuart McPherson, MB ChB, MD, FRCP, Ahmed M, Elsharkawy, BM, PhD, FRCP, Michael Ankcom, MBBS, MRCP, Samreen Ijaz, PhD, 4 James Powell, MB ChB, MD, FRCS, 5 Ian Rowe, MBChB, MRCP, PhD, 5 Richard Tedder, MB BChir, FRCP, FRCPath, 7 and Peter A. Andrews, MD, FRCP8

between The incidence and presenting of injection for a Big Infection the invested in many developed countries one for a but of countries on a but of countries on a but of countries one for a but of countries on a but of countries on a but of countries one for a but of countries of the development of chronic lengths and significant hard to be for a but of countries of the countries of countries of countries of the development of chronic lengths and significant hard to be foreign the countries of the countries of the countries of countries of the countr the evidence relating to the diagnosis and management of persistent hepatitis E in solid organ transplant recipients and the methods of prevention of HEV infaction. In line with previous guidelines published by the BTS, the guideline has used the Grading of Recommendations, Assessment, Development and Evaluations (GPADE) system to rate the strength of evidence and recommendations. This article includes a summary overview of hepatitis E and transplantation with key references, and the statements of recommendation contained within the guideline. It is recommended that the full guideline document is consulted for complete details of the relevant references and evidence base. This may be accessed at https://bts.org.uk/guideline-standards/.

contained within the BTS guideline

TRANSPLANTATION

OVERVIEW OF HEPATITIS E AND SOLID ORGAN

HEV belongs to the genus Hepevirus in the Hepeviridae family and infects humans and a range of animal hosts.³

Four major HEV genotypes infect humans (G1 to G4). The

The authors received no support for the writing of either the BTS guidaine or this

S.M.P. is a speaker, consultancy or travel support from AbbVis, BMS, Glead, MSD

Noverts and Floche, A.E. is a speaker, consultancy, research grant or travel support from Abbies, Ansies, BMS, Chies, Glassd and MSCs. If it is a speaker or travel support from Abbies, Bayer, and Neighe. All the other authors declare no conflicts of interest.

All authors contributed to the BTS guideline document and to this summary of the guideline. All have reviewed and approved the final document. Correspondence: StuartMcPherson, BSc, MB ChB, MD, PRCP, The Lier Unit Reaman Hospital, Lavid S, Fraeman Road, Newcastle upon Tyne, NET 7DN Uritad Kingdom, (stuart-mophes on@nuth.rhs.uk).

Copyright © 2017 Wolfars Riuwer Health, Inc. All rights reserved 65N 0041-1937/18/10201-0015

DOI: 10.1097/TP.000000000001900

(Transplantation 2018;102: 15-20)

The incidence and prevalence of hepatitis E virus (HEV) increase the recognition of persistent hepatitis E infection infection has increased in many developed countries and to provide clear guidance on its management. The follow-over the last decade, predominantly due to infection with ge-notype 3 (G3) HEV, Infection with HEV G3 is important in with key references, and the statements of recommendations transplant recipients because it can persist in immunosuppressed individuals, leading, if untreated, to the development chronic hepatitis and significant liver fibrosis. Because there are currently no international guidelines on the management of hepatitis E in transplant recipients, the British Transplantation Society (BTS) has developed guidelines to inform clinical teams and patients about hepatitis E to help

Accepted 27 July 2017. 1 Liver Transactional Lines The Managember from Time Absorbinis MAC Department Trans and institute of Cellular Medicine, Newcastle University, United Kingdom. *LiverTranscript Link, Queen Filtsbeth Hospital Riminoham, Linked Kinodom ³ Virus Reference Department, National Infection Service, Public Health England? NHS Blood and Transplant, Colindaia, London, United Mingdom.

*Bood Borne Virus Unit, Virus Reference Department, National Infection Service, Public Health England, Collection, United Ringdom ⁶ Scottsh Liver Transplant Unit Player Informacy of Edinburgh, Edinburgh, United Mingdom. *Libert Int. St. brees' Physipi and Lisbersty of Leads, Leads, LIK

⁷ Division of infection and immunity, University College London and Blood Borne Visus Unit, Visus Parlierance Department, National Infection Service, Public Health England, Colindale, London, Utilitad Kingdom. 8 South West Thames Rend & Transplantation Unit, Surrey, United Kingdom

Transplantation # January 2018 # Volume 102 # Number 1





Treatment of HEV Infection in Patients with a Solid-Organ Transplant and Chronic Hepatitis

Nassim Kamar 1,2,3,*, Sébastien Lhomme 2,3,4, Florence Abravanel 2,3,4, Olivier Marion 1,2, Jean-Marie Peron 3,5, Laurent Alric 3,6,7 and Jacques Izopet 2,3,4

Kamar N et al. Viruses 2016: 8.222.



Executive summary: Consensus document of the diagnosis. management and prevention of infection with the hepatitis E virus: Study Group for Viral Hepatitis (GEHEP) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

Antonio Rivero Juárez 3-4, Antonio Aguilera 3, Ana Avellón 4, Miguel García Deltoro 4, Federico García 5, Christian Gortazar^f, Rafael Granados^g, Juan Macías^h, Nicolás Merchante^h, José Antonio Oteo María Teresa Pérez Gracia¹, Juan Antonio Pineda^h, Antonio Rivero², David Rodriguez-Lazaro^k, Francisco Téllez¹, Luis E. Morano Amado¹⁰, Grupo redactor de GeHEP/SEIMC¹

Historical Universitatio Relina Jodia de Córdoba, Sustituto Malmonator de Europapación Monádica de Córdoba (MHRC), Universitad de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba (MHRC), Universitad de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba (MHRC), Universitad de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba, Cordoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba, Cordoba, Sustituto Malmonator de Europapación Relinador de Córdoba, Cordoba, C

*Conspine Margini data Unite estate Sentingo (CUUS) & Universited da Sentingo, Sentingo de Compostinia, Quini
Como Marcinal de Altri Assissingia, función de de Santa Como III, Mair de L. Spoto
Como de Como de Bospina Universitato de Valencia, Valencia, Spoto
Plangual de Universitato Sentino de Valencia, Valencia, Spoto
Plangual de Universitato Sentino Collo, función de Inventigación de Instanta III, Controla, Spoto
Plangual de Universitato Sentino Collo, Bospina (Paris Collo, Octobro Del Paris Collo Del Paris C

Magnital Universitario de Cran Canaria Dr. Negris, Las Pelmas de Cran Canaria, Spain Hespital Universitario Vigen de Valme, Instituto de Biene dicina de Seville (1815), Sevilla, Spain

H espital Universitario San Pedro, Logrotio Centro de Investigación Biomédica de La Rioja (CIBIR). Spain Instituto de Clencias Biomédicas, Facultad de Ciencias de la Salud, Universidad CEU Cardenal Herrero, V

Foculted de Clencias, Universidad de Burges, Per ges, Spoits Hospital Universitario Átraro Cumpunho, Instituto de Investigación Sanitario Galicia Sur, Vigo, Spoin

ARTICLE INFO

Hepatitis E virus (HEV) infection is one of the main causes of acute hepatitis in both developed and Republic Is virus (RW) infection in one of the main cause of acute bepaties in both developed and exclusive in index of the control program of the control progr

© 2018 Elsevier España, S.L.U. and Sociedad Española de Enfermedades Infecciosas y Microbiologi

all com (A.R. hužova).

0213-06SQ © 2018 Elsevier España, S.L.U. and Sociedad Española de Enfermedades Infecciosas y Microbiologia Clinica. All rights reserve

Please cite this article in press as: Juárez AR, et al. Executive summary: Consensus document of the diagnosis, management and prention of infection with the hepatitis Evinus: Study Group for Viral Hepatitis (GEHEP) of the Spanish Society of Infectious Dise nical Microbiology (SEMC). Enferm Infect Microbiol Clin. 2017, https://doi.org/10.1016/j.eimc2018.06.014

Copyright © 2017 Wolfers Kluwer Health, Inc. All rights reserved

INFECCIÓN CRÓNICA POR VHE EN EL TOS: TRATAMIENTO (IV)

Consideraciones al tratamiento antiviral indicado prioritariamente en las GPC:

Predictores de respuesta: Existen discrepancias en el valor predictivo del aclaramiento viral al mes de iniciar el tratamiento; sin embargo si que consideran como tales el bajo recuento de linfocitos al inicio del tratamiento, la necesidad de reducción de la dosis y el requerimiento de transfusión por la mala tolerancia hematológica.

Rango terapéutico: Para el antiviral indicado prioritariamente en las GPC, las concentraciones plasmáticas en el estado estacionario son significativamente más altas en los respondedores clínicos (1,96 vs 0,48 mg/L)

Mutaciones: Las mutaciones de polimerasa viral (Y1320H, K1383N, D1384G, K1398R, V1479I, G1634R) previas al tratamiento y/o de novo con esta indicación, no tienen impacto negativo en la eliminación del VHE.

Retrasplante: En pacientes TOS con infección crónica por VHE y disfunción del aloinjerto es apropiado el tratamiento antes de considerar el retrasplante para evitar recurrencias.

Rescate: No hay opciones alternativas, que puedan recomendarse, al tratamiento antiviral indicado prioritariamente en las diferentes GPC, excepto para el escenario específico de trasplante de hígado.

Kamar N et al. Clin Infect Dis 2020; 71:1204-11.



Nassim Kamar ^{1,2,3,*}, Sébastien Lhomme ^{2,3,4}, Florence Abravanel ^{2,3,4}, Olivier Marion ^{1,2}, Jean-Marie Peron ^{3,5}, Laurent Alric ^{3,6,7} and Jacques Izopet ^{2,3,4}

Mulder MB et al. J Viral Hep 2021; 28: 431-5.

INFECCIÓN CRÓNICA POR VHE EN EL TOS: NOVEDADES Y DILEMAS

Diferentes estudios han encontrado que durante el tratamiento de la infección crónica por VHE, la persistencia viral en el eyaculado superó en más de nueve meses la duración de la viremia

Research Article



Hepatitis E virus persists in the ejaculate of chronically infected men

Thomas Horvatits^{1,2,*}, Jan-Erik Wißmann³, Reimar Johne⁴, Martin H. Groschup^{2,5}, Ashish K. Gadicherla⁴, Julian Schulze zur Wiesch^{1,2}, Martin Eiden^{2,5}, Daniel Todt^{3,6}, Rudolph Reimer⁷, Lisa Dähnert^{2,5}, Anja Schöbel⁸, Karoline Horvatits¹, Rabea Lübke¹, Christine Wolschke⁹, Francis Ayuk⁹, Meike Rybczynski¹⁰, Ansgar W. Lohse^{1,2}, Marylyn M. Addo^{1,2}, Eva Herker⁸, Marc Lütgehetmann^{2,11,1}, Eike Steinmann^{2,3,†}, Sven Pischke^{1,2,†}

Horvatis T et al. J Hepatol 2021; S0168-8278(21)00025-8...

Los pacientes con infección crónica por VHE albergan variantes virales recombinantes del huésped, que incluyen fragmentos de genes humanos de origen variable.

Review

Clinical Manifestations, Pathogenesis and Treatment of Hepatitis E Virus Infections

Sébastien Lhomme ^{1,2,3,*}, Olivier Marion ^{2,3,4}, Florence Abravanel ^{1,2,3}, Jacques Izopet ^{1,2,3} and Nassim Kamar ^{2,3,4,*}

INFECCIÓN CRÓNICA POR VHE EN EL TOS: EPÍLOGO

DISCUSIÓN Y CONCLUSIONES

Las diferentes guías de práctica clínica (GPC) para el manejo de la hepatitis E (BTS, EASL y GEHEP) recomiendan el cribado del VHE en trasplantados receptores de órgano sólido y pacientes inmunodeprimidos con los niveles de transaminasas por encima del límite normal, además de en todos los casos de hepatitis medicamentosa y de origen incierto. Sin embargo, estas recomendaciones no se están llevando a la práctica como lo demuestra el caso presentado en un receptor de trasplante renal. Se hace por tanto necesario recomendar explícitamente el cribado periódico del VHE en todos los pacientes trasplantados de órgano sólido con alteraciones de la bioquímica hepática con independencia del tipo de órgano trasplantado.

NOS WEBMOS EN GRANADA



Gracias por su atención

Antonio Aguilera

Servicio Microbiología CHUS (Santiago de Compostela) Departamento de Microbiología USC antonio.aguilera.@usc.es





