Julio, 2019

RECOMENDACIÓN

INFORME DE BÚSQUEDA Y SÍNTESIS DE EVIDENCIA DE EFECTOS DESEABLES E INDESEABLES

Guía de Práctica Clínica de Manejo y tratamiento de la infección crónica por Virus de la Hepatitis C - 2019

A. PREGUNTA CLÍNICA

En personas mayores de 45 años o de cualquier edad con factores de riesgo ¿Se debe "realizar tamizaje (IgG)" en comparación a "no realizar"?

Análisis y definición de los componentes de la pregunta en formato PICO

Población: Personas mayores de 45 años o de cualquier edad con factores de riesgo.

Intervención: Realizar tamizaje (IgG).

Comparación: No realizar.

Desenlace (outcome): Mortalidad, calidad de vida, morbilidad asociada a hepatitis C, aceptabilidad del test, derivación a atención médica, biopsia de hígado.

B. MÉTODOS

Se realizó una búsqueda general de revisiones sistemáticas sobre hepatitis C (ver Anexo 1: estrategia de búsqueda). Las bases de datos utilizadas fueron: Cochrane database of systematic reviews (CDSR); Database of Abstracts of Reviews of Effectiveness (DARE); HTA Database; PubMed; LILACS; CINAHL; PsyclNFO; EMBASE; EPPI-Centre Evidence Library; 3ie Systematic Reviews and Policy Briefs Campbell Library; Clinical Evidence; SUPPORT Summaries; WHO institutional Repository for information Sharing; NICE public health guidelines and systematic reviews; ACP Journal Club; Evidencias en Pediatría; y The JBI Database of Systematic Reviews and Implementation Reports. No se aplicaron restricciones en base al idioma o estado de publicación. Dos revisores de manera independiente realizaron la selección de los títulos y los resúmenes, la evaluación del texto completo y la extracción de datos. Un investigador o clínico experimentado resolvió cualquier discrepancia entre los distintos revisores. Finalmente, se seleccionaron las revisiones sistemáticas (y los estudios incluidos en éstas) correspondientes a la temática y se clasificaron en función de las preguntas a las que daban respuesta.

En las preguntas que comparan tests diagnósticos, se considera necesario distinguir dos enfoques para abordarlas: *impacto diagnóstico* y *exactitud diagnóstica*. Se estableció priorizar estudios que evaluarán el *impacto diagnóstico del test*, es decir aquellos que comparan los resultados en salud de los pacientes diagnosticados/tratados en función a los resultados de un test. En caso de no encontrar este tipo de estudios, se utilizan estudios que evalúan la *exactitud diagnóstica del test*, es

decir aquellos que miden qué tan bien el test clasifica a los pacientes respecto a si tienen o no una condición.[1]

Los resultados se encuentran alojados en la plataforma Living Overview of the Evidence (L·OVE), sistema que permite la actualización periódica de la evidencia.

C. RESULTADOS

Resumen de la evidencia identificada

Se buscaron revisiones sistemáticas que analizaran estudios en adultos sin diagnóstico conocido de hepatitis C, en quienes se comparara el impacto de un tamizaje dirigido a grupos de riesgo versus no tamizaje. Se identificaron 6 revisiones sistemáticas que incluyen 113 estudios primarios, de los cuales 6 corresponden a ensayos aleatorizados. Para más detalle ver "*Matriz de evidencia*"[2], en el siguiente enlace: Tamizaje focalizado para hepatitis C.

Tabla 1: Resumen de la evidencia seleccionada

Revisión sistemática	6 [1-6]
Estudios primarios	6 ensayos [7-12], 107 estudios observacionales [13-119]

Selección de la evidencia

Se realizó un análisis de la matriz de evidencia, identificándose 4 revisiones sistemáticas [1,2,4,5] que incluyeron 6 ensayos que responden la pregunta de impacto diagnóstico, por lo que se decidió omitir la evidencia que responde a la exactitud diagnóstica del test para la estimación del efecto. Sin embargo, sólo dos revisiones sistemáticas [1,5] con tres ensayos [8,10,12] fueron relevantes para la estimación del efecto, ya que abordan específicamente los componentes de la pregunta priorizada por el panel. El resto de los ensayos aleatorizados fueron excluidos ya que uno de ellos fue realizado en población con factores de riesgo comparado con entregar folletos [7] y dos ensayos utilizaron muestra seca para la detección del virus [9, 11].

Estimador del efecto

Al analizar la evidencia identificada, se concluyó que ninguna revisión sistemática cumple con todos los requisitos metodológicos establecidos para el presente informe, es decir, incluir los estudios primarios relevantes y entregar un estimador agregado del efecto para los desenlaces de interés. Por lo tanto, se decidió rehacer el metanálisis directamente a partir de los estudios primarios para construir la tabla de resumen de resultados.

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[1] Schünemann HJ, Schünemann AHJ, Oxman AD, Brozek J, Glasziou P, Jaeschke R, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ [Internet]. 2008 May 17 [cited 2018 Aug 1];336(7653):1106–10.

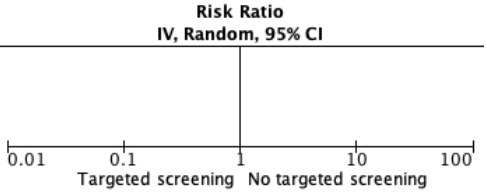
[2] **Matriz de Evidencia**, tabla dinámica cuyas filas representan las revisiones sistemática y en las columnas los estudios primarios que responden una misma pregunta. Los recuadros en verde corresponden a los estudios incluidos en las respectivas revisiones. La matriz se actualiza periódicamente, incorporando nuevas revisiones sistemáticas pertinentes y los respectivos estudios primarios.

Metanálisis

Mortalidad

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cullen 2006	0	104	0	92		Not estimable
Total (95% CI)		**104**		**92**		**Not estimable**
Total events	0		0			

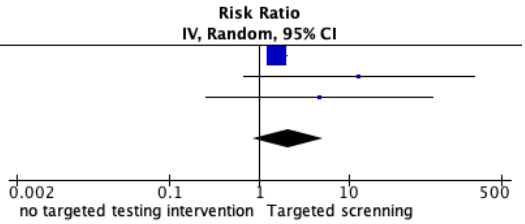
Heterogeneity: Not applicable
Test for overall effect: Not applicable



Casos de anticuerpos de VHC detectados (evidencia indirecta para morbilidad asociada a hepatitis C)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cullen 2006	73	104	41	92	83.0%	1.58 [1.21, 2.04]
Sahajian 2011 a	3	222	0	405	8.4%	12.74 [0.66, 245.62]
Sahajian 2011 b	4	784	0	406	8.6%	4.67 [0.25, 86.46]
Total (95% CI)		**1110**		**903**	**100.0%**	**2.06 [0.84, 5.07]**
Total events	80		41			

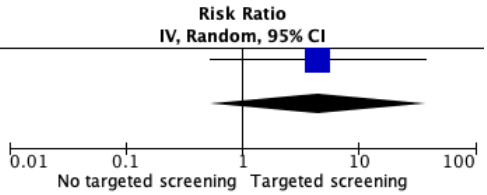
Heterogeneity: $Tau^2 = 0.24$; $Chi^2 = 2.42$, df = 2 (P = 0.30); $I^2 = 17\%$
Test for overall effect: Z = 1.57 (P = 0.12)



Inicio de terapia antiviral (evidencia indirecta para morbilidad asociada a hepatitis C)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cullen 2006	5	104	1	92	100.0%	4.42 [0.53, 37.17]
Total (95% CI)		**104**		**92**	**100.0%**	**4.42 [0.53, 37.17]**
Total events	5		1			

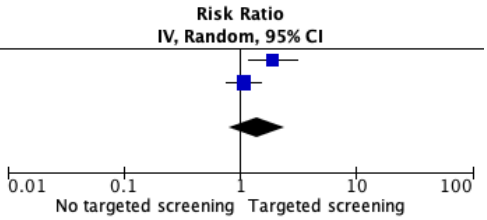
Heterogeneity: Not applicable
Test for overall effect: Z = 1.37 (P = 0.17)



Derivación a atención médica

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cullen 2006	44	73	13	41	45.4%	1.90 [1.17, 3.09]
Rosenberg 2010	17	21	12	16	54.6%	1.08 [0.76, 1.53]
Total (95% CI)		**94**		**57**	**100.0%**	**1.40 [0.80, 2.42]**
Total events	61		25			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 3.42$, df = 1 (P = 0.06); $I^2 = 71\%$
Test for overall effect: Z = 1.18 (P = 0.24)



Biopsia de hígado

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio IV, Random, 95% CI
Cullen 2006	18	104	7	92	100.0%	2.27 [1.00, 5.20]
Total (95% CI)		**104**		**92**	**100.0%**	**2.27 [1.00, 5.20]**
Total events	18		7			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.95 (P = 0.05)

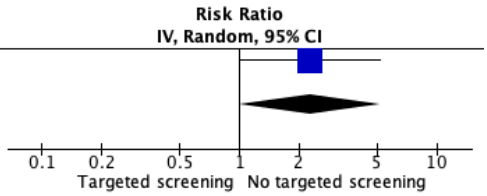


Tabla de Resumen de Resultados (Summary of Findings)

TAMIZAJE EN PERSONAS CON FACTORES DE RIESGO PARA HEPATITIS C						
Pacientes	Personas mayores de 45 años o de cualquier edad con factores de riesgo.					
Intervención	Realizar tamizaje (IgG).					
Comparación	No realizar.					
Desenlaces	**Efecto relativo (IC 95%) -- Estudios/ pacientes**	**Efecto absoluto estimado***			**Certeza de la evidencia (GRADE)**	**Mensajes clave en términos sencillos**
		SIN tamizaje	**CON tamizaje**	**Diferencia (IC 95%)**		
Mortalidad Seguimiento: 6 meses	-- 1 ensayo/196 pacientes [12]	No se observaron muertes en ninguno de los grupos.			⨁⨁◯◯[1] Baja	Realizar tamizaje podría tener poco impacto en mortalidad en personas con factores de riesgo para hepatitis C, pero la certeza de la evidencia es baja.
Calidad de vida	El desenlace calidad de vida no fue medido o reportado por los estudios.				--	--
Morbilidad asociada a hepatitis C Seguimiento: Entre 9 y 18 meses	No se encontraron estudios que evalúen morbilidad asociada a hepatitis C. Sin embargo, se identificó evidencia indirecta: En dos ensayos [8,12] (2.013 pacientes), se pesquisó un mayor número de casos (anticuerpos VHC; RR 2,06; IC 0,84 a 5,07), y en un ensayo [12] aumentó el número de personas que inició terapia antiviral (RR 4,42; IC (0,53 a 37,17).				⨁⨁◯◯[2,3] Baja	Realizar tamizaje podría disminuir la morbilidad en personas con factores de riesgo para hepatitis C, pero la certeza de la evidencia es baja.
Aceptabilidad del test Sin seguimiento	Un estudio observacional [27] reportó que el 86% de los pacientes (37/43) estaban satisfechos con la decisión tomada por el test y un 14% no (6/43).				⨁◯◯◯[1,6] Muy baja	Realizar tamizaje podría ser aceptable por las partes interesadas. Sin embargo, existe considerable incertidumbre dado que la certeza de la evidencia es muy baja
Derivación a atención médica** Seguimiento: Entre 6 y 18 meses	RR 1,40 (0,80 a 2,42) -- 2 ensayos/151 pacientes [10,12]	439 por 1000	614 por 1000	Diferencia: 175 más (88 menos a 623 más)	⨁◯◯◯[2,4,5] Muy baja	Realizar tamizaje podría aumentar la derivación a atención médica en personas con factores de riesgo de hepatitis C. Sin embargo, existe considerable incertidumbre dado que la certeza de la evidencia es muy baja
Biopsia de hígado Seguimiento: 6 meses	RR 2,27 (1,00 a 5,20) -- 1 ensayo/196 pacientes [12]	76 por 1000	173 por 1000	Diferencia: 97 más (0 a 320 más)	⨁⨁⨁⨁ Alta	Realizar tamizaje lleva a un aumento en el número de biopsias de hígado realizadas en personas con factores de riesgo para hepatitis C.

IC 95%: Intervalo de confianza del 95% // RR: Riesgo relativo.
GRADE: Grados de evidencia Grading of Recommendations Assessment, Development and Evaluation.
* El **riesgo SIN tamizaje** está basado en el riesgo del grupo control en los estudios. El **riesgo CON tamizaje** (y su intervalo de confianza) está calculado a partir del efecto relativo (y su intervalo de confianza).
**Derivación a atención médica cuando el anticuerpo de VHC es positivo.
[1] Se disminuyó dos niveles de certeza de evidencia por imprecisión, ya que es estudio único con bajo tamaño muestral para predecir la mortalidad y satisfacción.
[2] Se disminuyó un nivel de certeza de evidencia por imprecisión, ya que cada extremo del intervalo de confianza conlleva una decisión diferente.
[3] Se disminuyó un nivel de certeza de evidencia por ser indirecta, ya que los desenlaces reportados corresponden a desenlaces sustitutos de morbilidad asociada a hepatitis C.
[4] Se disminuyó un nivel de certeza de evidencia por riesgo de sesgo ya que en uno de los ensayos [10] no está claro el ocultamiento de la secuencia aleatoria. Además, el ensayo no fue ciego.
[5] Se disminuyó un nivel de certeza de la evidencia por inconsistencia, debido a que se observó heterogeneidad significativa entre los estudios (I2=71%)

[6] Diseño observacional.
Fecha de elaboración de la tabla: Julio, 2019.

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ANEXO 1: ESTRATEGIA DE BÚSQUEDA

#1 HCV*
#2 (Hepatitis AND C)
#3 "hepatitis-C"
#4 "hep C"
#5 "hep-C"
#6 NANBH
#7 nonAnonB
#8 ("non-A" AND "non-B")

#9 (nonA AND nonB)
#10 ("non A" AND "non B")
#11 (C AND virus)
#12 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13 test*
#14 suspect*
#15 suspicion
#16 detection
#17 diagnos*
#18 sensitivity
#19 sens
#20 specificity
#21 spec
#22 "predictive value"
#23 PPV
#24 NPV
#25 accuracy
#26 likelihood
#27 LR
#28 screening
#29 #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
#30 #12 AND #29