RECOMENDACIÓN 1

BÚSQUEDA Y SÍNTESIS DE EVIDENCIA DE EFECTOS DESEABLES E INDESEABLES

Guía de Práctica Clínica Prevención de la progresión de la enfermedad renal crónica - 2018

A. PREGUNTA CLÍNICA

En personas con enfermedad renal crónica (etapa 3 – 4) con diagnóstico de anemia secundaria ¿Se debe realizar tratamiento con eritropoyetina en comparación a no realizar tratamiento con eritropoyetina?

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

Población: Personas con enfermedad renal crónica (etapa 3 – 4) con diagnóstico de anemia secundaria.

Intervención: Eritropoyetina.

Comparación: No usar eritropoyetina.

Desenlace (outcome): Mortalidad, progresión a diálisis, función renal (GFR ml/min), transfusiones, efectos adversos.

B. BÚSQUEDA DE EVIDENCIA

Se realizó una búsqueda general de revisiones sistemáticas asociadas al tema de "Chronic kidney disease". 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 experimentado resolvió cualquier discrepancia entre los distintos revisores. En caso de considerarse necesario, se integraron estudios primarios.[1]

Seleccionadas las revisiones sistemáticas o estudios primarios asociadas a la temática, se clasificaron en función de las potenciales preguntas a las que daban respuesta. Al momento de definir la pregunta la evidencia ya se encontraba previamente clasificada según intervenciones comparadas. Los

[1] Para revisar la metodología, las estrategias y los resultados de la búsqueda, favor revisar el informe "*Búsqueda sistemática de evidencia de los efectos deseables e indeseables*" en la sección de método de la Guía de Práctica Clínica respectiva.

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

C. SÍNTESIS DE EVIDENCIA

Resumen de la evidencia identificada

Se identificaron 13 revisiones sistemáticas que incluyen 138 estudios primarios, de los cuales 123 corresponden a ensayos aleatorizados. Para más detalle ver "*Matriz de evidencia*"[2], en el siguiente enlace: Agentes estimuladores de la eritropoyesis en insuficiencia renal crónica.

Tabla 1: Resumen de la evidencia seleccionada

Revisión Sistemática	13 [1-13]
Estudios primarios	123 ensayos aleatorizados [14-136], 15 observacionales [137-151]

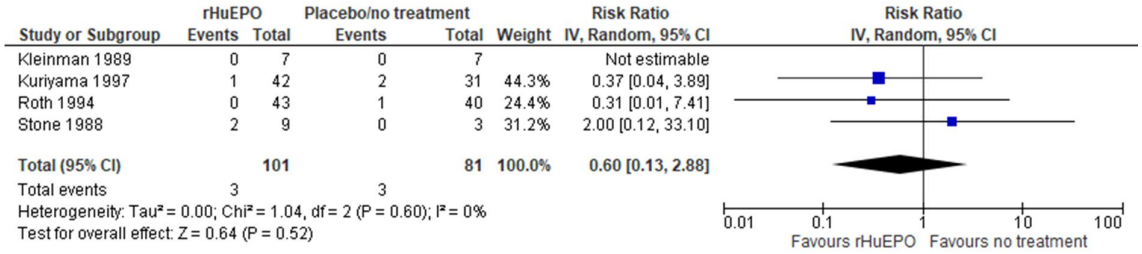
Estimador del efecto

Se realizó un análisis de la matriz de evidencia, decidiendo excluir 32 ensayos [15, 17, 28, 29, 31-34, 36, 39, 42, 46-47, 53, 56, 60, 62, 68, 76, 79, 81, 87, 90-91, 93, 96, 106, 108, 112, 115, 130, 139] que evalúan exclusivamente pacientes en diálisis, cuatro ensayos que evalúan pacientes que han recibido trasplante [38, 43, 128, 129], 2 ensayos [94, 136] que evalúan pacientes con insuficiencia cardiaca (cardiorrenal), un ensayo [78] que no compara contra placebo, 11 ensayos [37, 51, 54, 57, 75, 80, 107, 109, 110, 127, 131] que comparan inicio precoz versus tardío, o metas diferentes, del mismo agente estimulador de eritropoyesis, 14 ensayos [16, 22, 25, 27, 41, 48, 49, 55, 59, 61, 116, 118, 121, 134] que comparan dos agentes estimuladores de la eritropoyesis diferente, 5 ensayos [30, 72, 102, 103, 104] que comparan un agente estimulador de eritropoyesis versus un biosimilar y siete ensayos [24, 44, 88, 89, 95, 97, 114] ya que no presentaron datos para los desenlaces relevantes. Un ensayo potencialmente relevante presentó los resultados como desenlaces compuesto, por lo cual no pudo ser incorporado en el metanálisis [50]. Finalmente, una revisión sistemática [1] incluyó todos los ensayos aleatorizados pertinentes y con datos adecuados, por lo que se decidió reutilizar sus metanálisis para construir la tabla resumen de resultados.

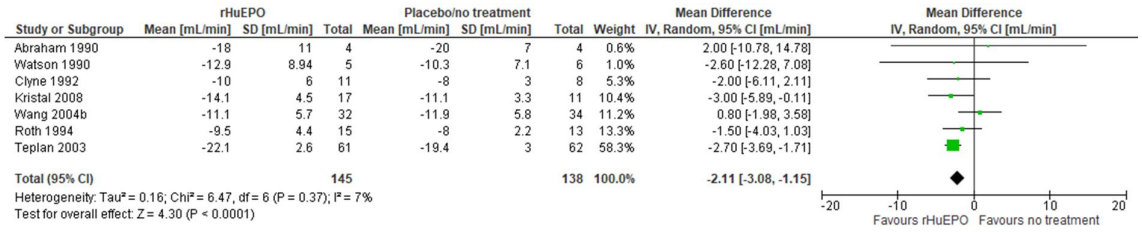
Metanálisis

Mortalidad

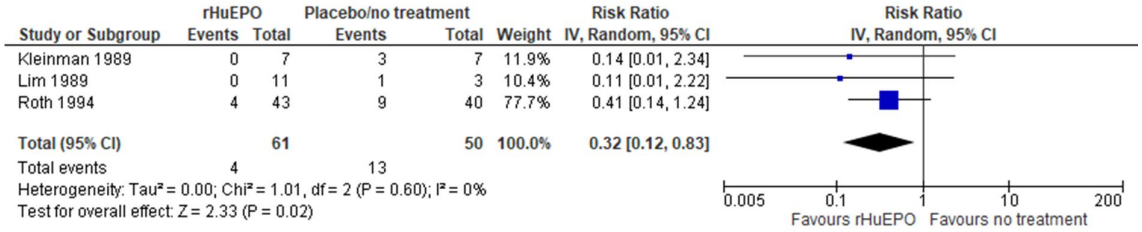
[2] **Matriz de Evidencia**, tabla dinámica que grafica el conjunto de evidencia existente para una pregunta (en este caso, la pregunta del presente informe). Las filas representan las revisiones sistemáticas y las columnas los estudios primarios que estas revisiones han identificado. Los recuadros en verde corresponden a los estudios incluidos en cada revisión. La matriz se actualiza periódicamente, incorporando nuevas revisiones sistemáticas pertinentes y los respectivos estudios primarios.



GFR



Transfusiones



Efectos adversos

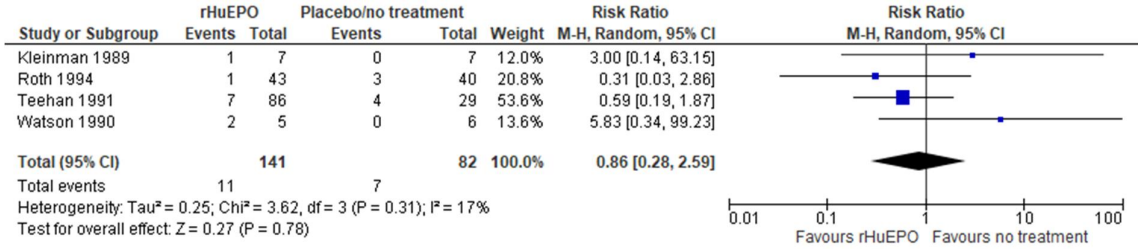


Tabla de Resumen de Resultados (Summary of Findings)

ERITROPOYETINA PARA ENFERMEDAD RENAL CRÓNICA ETAPA CON ANEMIA.						
Pacientes	Personas con enfermedad renal crónica (etapa 3 – 4) con diagnóstico de anemia secundaria.					
Intervención	Eritropoyetina.					
Comparación	No usar eritropoyetina.					
Desenlaces	**Efecto relativo (IC 95%) -- Estudios/ pacientes**	**Efecto absoluto estimado***			**Certeza de la evidencia (GRADE)**	**Mensajes clave en términos sencillos**
		SIN eritropoyetina	**CON eritropoyetina**	**Diferencia (IC 95%)**		
Mortalidad	RR 0,60 (0,13 a 2,88) -- 4 ensayo /182 pacientes	37 por 1000	22 por 1000	Diferencia: 15 menos (32 menos a 70 más)	⨁◯◯ [1,2] Baja	Eritropoyetina podría disminuir la mortalidad, pero la certeza de la evidencia es baja.
Progresión a diálisis	El desenlace progresión a diálisis no fue medido o reportado.				--	--
Función renal (GFR ml/min)	-- 7 ensayos / 283 pacientes	10 ml/min	8 ml/min	DM: 2 ml/min menos (1,15 a 3,08 menos)	⨁⨁◯◯ [1,2] Baja	Eritropoyetina podría acelerar la progresión de la insuficiencia renal, pero la certeza de la evidencia es baja.
Transfusiones	RR 0,32 (0,12 a 0,83) -- 3 ensayos / 111 pacientes	260 por 1000	83 por 1000	Diferencia: 177 menos (44 a 229 menos)	⨁⨁⨁◯ [1] Moderada	Eritropoyetina probablemente disminuye el riesgo de transfusiones.
Efectos adversos	RR 0,86 (0,28 a 2,59) -- 4 ensayos / 223 pacientes [ref]	85 por 1000	73 por 1000	Diferencia: 12 menos (61 menos a 136 más)	⨁◯◯◯ [1,2] Muy baja	Eritropoyetina podría asociarse a menos efectos adversos. Sin embargo, existe considerable incertidumbre dado que la certeza de la evidencia es muy baja.

IC 95%: Intervalo de confianza del 95%.
RR: Riesgo relativo.
DM: Diferencia de medias.
GRADE: Grados de evidencia Grading of Recommendations Assessment, Development and Evaluation.
* El **riesgo SIN eritropoyetina** está basado en el riesgo del grupo control en los estudios. El **riesgo CON eritropoyetina** (y su intervalo de confianza) está calculado a partir del efecto relativo (y su intervalo de confianza).
[1] Se disminuyó un nivel de certeza de evidencia por riesgo de sesgo, ya que en la mayoría de los ensayos no está clara la generación de secuencia de aleatorización ni ocultamiento de ésta.
[2] Se disminuyó un nivel de certeza de evidencia por imprecisión ya que cada extremo del intervalo de confianza conlleva una decisión diferente. En el caso de efectos adversos, el intervalo de confianza es muy amplio.
Fecha de elaboración de la tabla: Octubre, 2018.

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