# RECOMENDACIÓN 4

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

Guía de Práctica Clínica Hemodiálisis - 2018

### A. PREGUNTA CLÍNICA

En personas con enfermedad renal crónica etapa 5 en hemodiálisis en tratamiento con eritropoyetina con hemoglobina mayor 12 mg/dL ¿Se debe suspender el uso de eritropoyetina en comparación a mantener el uso de eritropoyetina quincenalmente?

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

**Población:** Personas con enfermedad renal crónica etapa 5 en hemodiálisis en tratamiento con eritropoyetina con hemoglobina mayor 12 mg/dL.

**Intervención:** Suspender el uso de eritropoyetina.

**Comparación:** Mantener el uso de eritropoyetina quincenalmente.

**Desenlace (outcome):** Mortalidad, infarto agudo al miocardio, accidente cerebrovascular.

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

[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.

## C. SÍNTESIS DE EVIDENCIA

### Resumen de la evidencia identificada

Se identificaron 13 revisiones sistemáticas que incluyen 104 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 | 104 ensayos aleatorizados [14-117], 15 observacionales [118-132] |

Además, se analizaron 2 artículos provistos por el equipo de expertos participantes del panel convocado para elaborar la guía [152-153]. También se revisaron las referencias citadas en estos artículos y se buscaron artículos que citaran a los artículos provistos. Sin embargo, no se encontró ningún estudio comparativo que permita estimar el efecto de la intervención.

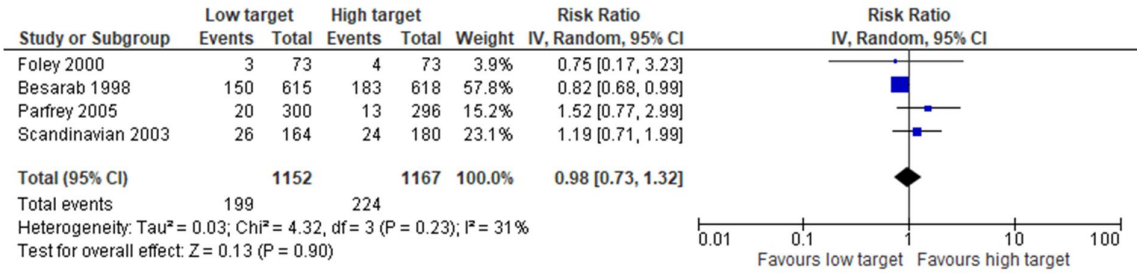
### Estimador del efecto

Del total de estudios identificados, 11 evaluaron metas de hemoglobina en pacientes en hemodiálisis [17, 28, 32, 33, 34, 36, 44, 50, 51, 86, 97], sin embargo, ninguno de ellos analizó las metas relevantes para el presente informe.

En ausencia de evidencia directa, con el fin de informar la decisión concerniente a esta pregunta, se decidió analizar los estudios comparando diferentes metas de hemoglobina/hematocrito en hemodiálisis [17, 28, 32, 33, 34, 36, 44, 50, 51, 86, 97], para esto, se reutilizaron los metanálisis provenientes de una revisión sistemática que incluye todos los ensayos aleatorizados [11].

### Metanálisis

**Mortalidad**

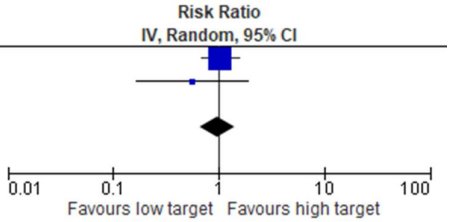



[2] **Matriz de Evidencia**, tabla dinámica que grafica el conjunto de evidencia existente para una pregunta (en este caso, la pregunta del presente informe). Las filas representan las revisiones sistemáticas y las columnas los estudios primarios que estas revisiones han identificado. Los recuadros en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

**Infarto agudo al miocardio**

| Study or Subgroup | Low target Events | Total | High target Events | Total | Weight | Risk Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| Besarab 1998 | 42 | 615 | 41 | 618 | 89.6% | 1.03 [0.68, 1.56] |
| Parfrey 2005 | 4 | 300 | 7 | 296 | 10.4% | 0.56 [0.17, 1.91] |
| **Total (95% CI)** | | **915** | | **914** | **100.0%** | **0.97 [0.65, 1.43]** |
| Total events | 46 | | 48 | | | |

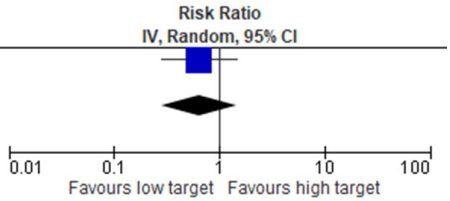
Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.87)




**Accidente cerebrovascular**

| Study or Subgroup | Low target Events | Total | High target Events | Total | Weight | Risk Ratio IV, Random, 95% CI |
|---|---|---|---|---|---|---|
| Besarab 1998 | 9 | 615 | 14 | 618 | 100.0% | 0.65 [0.28, 1.48] |
| **Total (95% CI)** | | **615** | | **618** | **100.0%** | **0.65 [0.28, 1.48]** |
| Total events | 9 | | 14 | | | |

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)



## Tabla de Resumen de Resultados (Summary of Findings)

| SUSPENDER ERITROPOYETINA COMPARADO CON MANTENER EL USO QUINCENALMENTE PARA ENFERMEDAD RENAL CRÓNICA EN HEMODIÁLISIS. | | | | | | |
|---|---|---|---|---|---|---|
| Pacientes | Personas con enfermedad renal crónica etapa 5 en hemodiálisis en tratamiento con eritropoyetina con hemoglobina mayor 12 mg/dL. | | | | | |
| Intervención | Suspender el uso de eritropoyetina. | | | | | |
| Comparación | Mantener el uso de eritropoyetina quincenalmente | | | | | |
| **Desenlaces** | **Efecto relativo (IC 95%) -- Estudios/ pacientes** | **Efecto absoluto estimado*** | | | **Certeza de la evidencia (GRADE)** | **Mensajes clave en términos sencillos** |
| | | **CON mantención** | **CON suspensión** | **Diferencia (IC 95%)** | | |
| Mortalidad | RR 0,98 (0,73 a 1,32) -- 4 ensayos / 2319 pacientes [47, 53, 54, 96] | 192 por 1000 | 188 por 1000 | Diferencia: 4 menos (52 menos a 61 más) | ⊕◯◯◯[1,2,3] Muy baja | Suspender la administración de eritropoyetina en enfermedad renal crónica etapa 5 en hemodiálisis con hemoglobina mayor a 12 mg/dL podría tener poco impacto en mortalidad. Sin embargo, existe considerable incertidumbre dado que la certeza de la evidencia es muy baja. |
| Infarto al miocardio | RR 0,97 (0,65 a 1,43) -- 2 ensayos / 1829 pacientes [47, 96] | 53 por 1000 | 51 por 1000 | Diferencia: 2 menos (18 menos a 23 más) | ⊕◯◯◯[1,2,3] Muy baja | Suspender la administración de eritropoyetina en enfermedad renal crónica etapa 5 en hemodiálisis con hemoglobina mayor a 12 mg/dL podría tener poco impacto en infarto al miocardio. Sin embargo, existe considerable incertidumbre dado que la certeza de la evidencia es muy baja. |
| Accidente cerebrovascular | RR 0,65 (0,28 a 1,48) -- 1 ensayo / 1233 pacientes [47] | 23 por 1000 | 15 por 1000 | Diferencia: 8 menos (16 menos a 11 más) | ⊕◯◯◯[1,2,3] Muy baja | Suspender la administración de eritropoyetina en enfermedad renal crónica etapa 5 en hemodiálisis con hemoglobina mayor a 12 mg/dL podría disminuir el riesgo de accidente cerebrovascular. 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.
GRADE: Grados de evidencia Grading of Recommendations Assessment, Development and Evaluation.
* El **riesgo CON mantención** está basado en el riesgo del grupo control en los estudios. El **riesgo CON suspender** (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 la mayoría de los ensayos no está clara la generación de la secuencia de aleatorización ni el 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.
[3] Se disminuyó dos niveles de certeza de evidencia por indirecto, ya que se utilizó evidencia que proviene de la población más amplia. En el caso de mortalidad, se seleccionó la población en diálisis, por lo que sólo se disminuyó un nivel de certeza de evidencia por la diferencia de la intervención.
**Fecha de elaboración de la tabla:** Octubre, 2018.

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