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## REVIEW ARTICLE

# Colloids versus crystalloids in objective-guided fluid therapy, systematic review and meta-analysis. Too early or too late to draw conclusions



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Colloids;  
Hydroxyethyl starch;  
Crystalloids;  
Systematic review;  
Meta-analysis

### Abstract

**Introduction:** Several clinical trials on Goal directed fluid therapy (GDFT) were carried out, many of those using colloids in order to optimize the preload. After the decision of European Medicines Agency, there is such controversy regarding its use, benefits, and possible contribution to renal failure. The objective of this systematic review and meta-analysis is to compare the use of last-generation colloids, derived from corn, with crystalloids in GDFT to determine associated complications and mortality.

**Methods:** A bibliographic research was carried out in MEDLINE PubMed, EMBASE and Cochrane Library, corroborating randomized clinical trials where crystalloids are compared to colloids in GDFT for major non-cardiac surgery in adults.

**Results:** One hundred thirty references were found and among those 38 were selected and 29 analyzed; of these, six were included for systematic review and meta-analysis, including 390 patients. It was observed that the use of colloids is not associated with the increase of complications, but rather with a tendency to a higher mortality (RR [95% CI] 3.87 [1.121–13.38];  $I^2 = 0.0\%$ ;  $p = 0.635$ ).

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**PALAVRAS-CHAVE**

Hidratação;  
 Hidratação guiada  
 por objetivos;  
 Coloides;  
 Derivados de  
 Hidroxietyl Amido;  
 Soluções Isotônicas;  
 Revisão sistemática;  
 Metanálise

**Conclusions:** Because of the limitations of this meta-analysis due to the small number of randomized clinical trials and patients included, the results should be taken cautiously, and the performance of new randomized clinical trials is proposed, with enough statistical power, comparing balanced and unbalanced colloids to balanced and unbalanced crystalloids, following the protocols of GDFT, considering current guidelines and suggestions made by groups of experts.  
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**Coloides versus cristaloides em fluidoterapia guiada por objetivos, revisão sistemática e metanálise. Demasiadamente cedo ou demasiadamente tarde para obter conclusões**

**Resumo**

**Introdução:** Foram realizados múltiplos ensaios clínicos em fluidoterapia guiada por objetivos (FGO), sendo muitos deles com o uso de coloides para otimização da pré-carga. Após a decisão da Agencia Europea de Medicamento, existe ainda controvérsia sobre sua utilização, benefícios e possível contribuição para a falência renal. O objetivo desta revisão sistemática e metanálise é comparar o uso de coloides de última geração, derivados de milho, com cristaloides em FGO para determinar as complicações e a mortalidade associadas.

**Métodos:** Realização de uma busca bibliográfica em MEDLINE Pubmed, EMBASE e Biblioteca Cochrane comprovando ensaios clínicos aleatórios nos quais se comparam cristaloides com coloides dentro de FGO para cirurgia não cardíaca de grande porte em adultos.

**Resultados:** Foram obtidas 130 referências das quais se selecionaram 38 e 29 foram analisadas; destas, seis foram incluídas para revisão sistemática e metanálise, incluindo 390 pacientes. Observou-se que o uso de coloides não está associado a um aumento de complicações mas sim com uma tendência a maior mortalidade (RR [IC 95%] 3,87 [1,121-13,38];  $I^2 = 0,0\%$ ;  $p = 0,635$ ).

**Conclusões:** Devido às limitações desta metanálise em decorrência do número escasso de ensaios clínicos aleatórios e pacientes incluídos, os resultados devem ser usados com cautela, e propõe-se a realização de novos ensaios clínicos aleatórios, com potência estatística suficiente naqueles em que se comparam coloides balanceados e não balanceados com cristaloides balanceados e não balanceados, dentro de protocolos de FGO, respeitando as indicações atuais e as sugestões emitidas pelos grupos de especialistas.

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**Introduction**

Recently, several clinical trials have been published, as well as meta-analysis<sup>1-11</sup> in which it was demonstrated that the use of perioperative goal-directed fluid therapy (GDFT) decreases post-surgical<sup>2-9,11</sup> complications, hospital stay<sup>2,3</sup> and mortality.<sup>1,7,8</sup> The GDFT is based on preload optimization with the use of fluids, inotropes and/or vasoconstrictors through algorithms designed for this purpose, to achieve a particular target of stroke volume (SV), cardiac index or oxygen delivery. The ultimate goal of this optimization is to avoid fluid overload, as well as hypoperfusion and hypoxia.<sup>12</sup>

From a pathophysiological point of view, hemodynamic stabilization with colloids should result in a smaller amount of liquid administered,<sup>13</sup> and a shorter time in which the patient would find him/herself in a relative position of hypovolemia and possible tissue hypoperfusion.<sup>14</sup>

After examining the available evidence, and based mainly on 3 studies,<sup>15-17</sup> in June 2013 the Pharmacovigilance Risk

Assessment Committee of the European Medicines Agency concluded that the benefits of the use of colloids (hydroxethylstarches [HES]) were smaller than their risks,<sup>18</sup> in the same way as the Food and Drug Administration recommended to avoid its use in patients with sepsis and in patients with renal insufficiency (RI).<sup>19</sup> These conclusions were based on studies of patients with sepsis, not in the context of intraoperative hemodynamic stabilization from bleeding or relative hypovolemia, and the possibility of extrapolating the findings is debatable. Recently Gillies et al.,<sup>20</sup> after performing a systematic review and meta-analysis in which colloids were compared with different kinds of liquids, concluded that the use of HES did not increase mortality, hospital stay, RI or the need for extrarenal clearance<sup>20</sup>; however, in this meta-analysis colloids are not compared with crystalloids in studies which used a GDFT algorithm and included only three randomized controlled trials (RCTs), in which colloids were compared to crystalloids in noncardiac surgery.<sup>21-23</sup> The objective of

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