

Hydroxyethyl starch: complications

Starches are a synthetic colloid used for volume expansion. They have similar purported benefits to the classic colloid albumin, with a reduced cost and without having to be derived from human plasma. However, hydroxyethyl starches (HES) have had their use restricted by both the FDA and the EMA (the EU's FDA equivalent) due to apparent adverse outcomes. These include:

- An **increase in mortality** (RR 1.31) found in an RCT of >700 patients with severe sepsis. In the interest of completeness, a study of >3000 mixed ICU patients (approximately half surgical) showed no statistically significant increase in mortality.
- An **increase in the incidence of kidney injury and need for renal replacement therapy**. A cochrane review of 42 studies and >11,000 patients showed a RR of 1.31 and 1.59 for renal replacement therapy and kidney failure respectively for patients resuscitated with HES vs. other fluid therapies.
- An **increase in bleeding** caused by decreased factor VII and vWF. A cochrane review of 9 studies and >1,900 patients showed a RR of 1.19 for blood transfusion in patients resuscitated with starches compared to crystalloid. This finding has been corroborated, with a larger effect size, in a meta-analysis of cardiac surgical patients.

There was some initial hope that starches with a lower substitution ratio would avoid the nephrotoxic and coagulopathic effects of older starches, however this does not appear to have panned out. The nephrotoxic and coagulopathic effects may be smaller according to some studies, but ultimately the FDA still labels the approved semisynthetic starches with a boxed warning:

“Use of hydroxyethyl starch (HES) products increases the risk of mortality, kidney injury, and coagulopathy.

Do not use HES products (ie, hetastarch) unless adequate alternative treatment is unavailable.”

Further Reading:

Mutter TC, Ruth CA, Dart AB. Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function. Cochrane Database Syst Rev. 2013 Jul 23;(7):CD007594. doi: 10.1002/14651858.CD007594.pub3. PMID: 23881659.

Lewis SR, Pritchard MW, Evans DJ, Butler AR, Alderson P, Smith AF, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill people. Cochrane Database Syst Rev. 2018 Aug 3;8(8):CD000567. doi: 10.1002/14651858.CD000567.pub7. PMID: 30073665; PMCID: PMC6513027.