Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function

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Authors' objectives
Background: Hydroxyethyl starches (HES) are synthetic colloids commonly used for fluid resuscitation to replace intravascular volume, yet they have been increasingly associated with adverse effects on kidney function. This is an update of a Cochrane review first published in 2010. Objectives: To examine the effects of HES on kidney function compared to other fluid resuscitation therapies in different patient populations.

Search methods: We searched the Cochrane Renal Group's specialised register, the Cochrane Central Register of Controlled Trials (CENTRAL, in The Cochrane Library), MEDLINE, EMBASE, MetaRegister and reference lists of articles. The most recent search was completed on November 19, 2012. Selection criteria: Randomised controlled trials (RCTs) and quasi-RCTs in which HES was compared to an alternate fluid therapy for the prevention or treatment of effective intravascular volume depletion. Primary outcomes were renal replacement therapy (RRT), author-defined kidney failure and acute kidney injury (AKI) as defined by the RIFLE criteria.

Data collection and analysis: Screening, selection, data extraction and quality assessments for each retrieved article were carried out by two authors using standardised forms. All outcomes were analysed using relative risk (RR) and 95% confidence intervals (95% CI). Authors were contacted when published data were incomplete. Preplanned sensitivity and subgroup analyses were performed after data were analysed with a random-effects model.

Main results: This review included 42 studies (11,399 patients) including 19 studies from the original review (2010), as well as 23 new studies. Fifteen studies were excluded from the original review (nine retracted from publication due to concerns about integrity of data and six lacking individual patient creatinine data for the calculation of RIFLE criteria). Overall, there was a significant increase in the need for RRT in the HES treated individuals compared to individuals treated with other fluid therapies (RR 1.31, 95% CI 1.16 to 1.49; 19 studies, 9857 patients) and the number with author-defined kidney failure (RR 1.59, 95% CI 1.26 to 2.00; 15 studies, 1361 patients).

The RR of AKI based on RIFLE-F (failure) criteria also showed an increased risk of AKI in individuals treated with HES products (RR 1.14, 95% CI 1.01 to 1.30; 15 studies, 8402 participants). The risk of meeting urine output and creatinine based RIFLE-R (risk) criteria for AKI was in contrast in favour of HES therapies (RR 0.95, 95% CI 0.91 to 0.99; 20 studies, 8769 patients). However, when RIFLE-R urine output based outcomes were excluded as per study protocol, the direction of AKI risk again favoured the other fluid type, with a non-significant RR of AKI in HES treated patients (RR 1.05, 95% CI 0.97 to 1.14; 8445 patients). A more robust effect was seen for the RIFLE-I (injury) outcome, with a RR of AKI of 1.22 (95% CI 1.08 to 1.37; 8338 patients). No differences between subgroups for the RRT and RIFLE-F based outcomes were seen between sepsis versus non-sepsis patients, high molecular weight (MW) and degree of substitution (DS) versus low MW and DS (<200 kDa and >0.4 DS versus 130 kDa and 0.4 DS) HES solutions, or high versus low dose treatments (i.e. >2 L versus <2 L). There were differences identified between sepsis versus non-sepsis subgroups for the RIFLE-R and RIFLE-I based outcomes only, which may reflect the differing renal response to fluid resuscitation in pre-renal versus sepsis-associated AKI. Overall, methodological quality of the studies was good.

Authors' conclusions: The current evidence suggests that all HES products increase the risk in AKI and RRT in all patient populations and a safe volume of any HES solution has yet to be determined. In most clinical situations it is likely that these risks outweigh any benefits, and alternate volume replacement therapies should be used in place of HES products. US: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007594.pub3/abstract

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