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Hydroxy-ethyl-starches: are the conclusions always evidence-based?

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Sir: Study design has considerably improved, especially statistical analysis. However, conclusions should focus on results only, not on one's own beliefs, a recurrent problem with fluid resuscitation. Important papers have recently been published in this field, especially the VISEP study [1] and the paper from Schortgen et al. [2]. An accompanying editorial, and recent correspondence [3] point towards potential bias, but we wish to formulate supplementary observations.

(1) Despite a prospective cohort of 822 patients, Schortgen's study solely proves a link between hyperoncotic albumin use and probability of renal replacement therapy. Confidence intervals overlap (Fig. 2) shows that there are no differences among the other groups. So is Schortgen's conclusion not evidence-based when she states that the "study shows a strong association between hyperoncotic colloids and kidney dysfunction".

(2) The main design problem is that rather planning a randomisation, the authors based their analysis among an arbitrary pooling of fluids.

In their discussion, Schortgen et al. mentioned their precedent study and

the VISEP study which authors pretended they used a "modern hydroxy-ethyl-starch (HES), designed to have fewer side effects". In fact they used a hyperoncotic 10% HES (200/0.5), which in no way can be considered a modern HES.

Similarly, Schortgen's study pooled dextrans, HES (130/0.4) and older HES solutions in a so-called "artificial hyperoncotic colloids" group. This may be misleading.

Because criticisms towards a first study where they wrote that even modern HES persist in tissues for months, which is not factual [4], Schortgen et al. build a new hypothesis about HES toxicity: the putative role of oncotic pressure. The problem is that discussing of HES, mix-up seems more common than clinical "misuse" is. Although macromolecule accumulation may induce osmotic-nephrosis-like lesions, HES widely differ in their physicochemical characteristics: mean molecular weight (Mw), substitution and concentration. The 6% (130/0.4) solution has a measured oncotic pressure of 36 mmHg: it cannot be assimilated with 10% solutions and considered hyperoncotic, but isoncotic.

(3) The statistical analysis is modern and sophisticated. But the consequence of analysing a priori defined groups was the necessity of "several statistical methods", that carry the risk of majoring the first type error. Last, but not least, although a computed χ^2 comparing (130/0.4) and older HES gave a *P* value of 0.51, the study was not fitted to distinguish between incidences of renal adverse events in these groups of 119 and 270 patients (risk of type 2 error).

As a matter of fact, the influence of HES on renal function remains controversial. Apart from being an efficient plasma-volume expander, HES has been associated with a reduction of endothelial damage

during inflammation and sepsis. Gelatins are less efficacious and carry a fourfold greater risk of allergic reactions. So, there is for the present no evidence-based demonstration that we must banish a careful use of HES of low Mw from our medical armamentarium. The further step in improving our scientific knowledge [5] would perhaps be focusing our discussions on facts, not on our own convictions.

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