LETTER TO EDITOR

Colloids Use in Asian ICU Patients: Do not Mix Oranges with Apples. Consider the Proven Concerns on Hydroxyethyl Starch Use in ICU Patients

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Dear Editor,

We read with great interest the article by Jacob et al. aimed to evaluate the characteristics of Asian intensive care unit (ICU) patients, *"with a focus on fluid and volume therapy."*[1] In this prospective observational study, the authors compared two groups of ICU patients: one receiving crystalloids together with colloids, including hydroxyethyl starch (HES), albumin and gelatin, and the other one receiving only crystalloids. A total of 3,187 patients (India: 18 centers, 2,404 patients; Malaysia: four centers, 394 patients; Taiwan: two centers, 389 patients) were prospectively enrolled in the study and 2,621 were included for multivariate analyses. The primary outcomes were 90-day mortality ($n = 2,472$), acute kidney injury (AKI) ($n = 2,621$) and the use of renal replacement therapy (RRT) ($n = 2,621$). For the 90-day mortality outcome, the authors also compared three subgroups based on the day of the initial colloid dose administration during their ICU stay: day 1, day 2, or day 3. The authors concluded that in critically ill patients the use of colloids, received on day 1 of the ICU stay, was associated with a reduced risk of 90-day mortality and that the initial colloid dose was not associated with an increased risk for AKI or for the use of RRT.

After that evidence of higher mortality and AKI in critically ill patients that received HES led to the restrictions by FDA and European Medicines Agency (EMA), the potential for *"... intensification of efforts to market HES in low-income and middle-income countries, and that this will mean vulnerable patients [...] will bear the highest burden as a consequence"* was reported to the Director-General of the World Health Organization in 2018.[2-4] It is therefore not surprising that a group of eminent German scientists that reported no conflict of interest in this trial sponsored by Fresenius Kabi—an HES producing company—coauthored this interesting prospective observational study.

A major limitation in interpreting presented data is that the authors pooled evidence collected in patients that received HES—a starch containing colloid—with those of other synthetic and natural colloids. According to the presented data patients treated with HES are consistently a minority: proportions range approximately from one-fifth in the Indian experience to one-tenth in the Malaysian population. How can the authors conclude that *"The Rational Fluid Therapy in Asia (RaFTA) registry showed that colloid use was not associated with an increased risk of mortality or AKI but might even be correlated with a survival benefit in the Asian ICU population"* when the presented data include mixed evidence from colloids with no reported harm and HES, that is proven to associate with increased mortality and AKI?

We wonder which are the current regulatory rules for HES use in the countries where this study was set, and how patients have been informed on the possible and proven risks?[5]

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