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Increased bilirubin following fluid resuscitation with albumin: mechanisms behind an important observation

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Dear Editor,
We read with great interest the recent study of albumin versus saline in patients with sepsis from the SAFE study investigators [1]. We were especially interested to note that in septic patients treated with albumin there was a small but significant increase in serum bilirubin leading to an increase in the liver component of the Sequential Organ Failure Assessment (SOFA) score. The authors state that this finding is likely to be due to the presence of bilirubin in the albumin solution and therefore is unlikely to represent an adverse effect of albumin administration per se. We agree that this finding does not reflect an adverse effect of albumin, but we feel the likely explanation is somewhat different.

Albumin has at least two binding sites for bilirubin molecules, and the binding kinetics have been well

characterised [2]. In serum the majority of bilirubin is bound to albumin with a small proportion existing in the unbound form. Current assays for bilirubin measure both fractions. The most likely explanation, therefore, for the findings by the SAFE investigators is that the total bilirubin is raised in the serum as a result of bilirubin moving from tissues to plasma in response to an increased availability of binding sites for bilirubin following albumin administration.

The importance of the albumin binding sites has been investigated in vitro, and this property is exploited clinically by the molecular adsorbent recirculating system (MARS) [3]. The same investigators noticed an increase in serum bilirubin levels following administration of intravenous albumin during abdominal paracentesis, but the bilirubin/albumin ratio (BAR) remained unchanged. Lee et al. [4] observed that pre-treatment BAR is an important factor in predicting the efficacy of MARS.

This mechanism may have relevance in clinical situations where scores that use bilirubin such as Child-Pugh, Model for End-Stage Liver Disease (MELD) and SOFA are used to estimate prognosis. Their prognostic ability may be improved by using BAR rather than bilirubin. Clinicians should be aware of this phenomenon not only in patients with liver disease but also in intensive treatment unit (ITU) patients with sepsis, who frequently have liver test

dysfunction [5], and where use of albumin as resuscitation fluid may cause confusion if the BAR is not calculated.

References

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