Letter to the Editor

A different view on human albumin

Boris Nohe*, Hans-Juergen Dieterich

Laboratory for Vascular Biology, Department of Anaesthesiology and Critical Care, University Hospital Tuebingen, Hoppe-Seyler Str. 3, 72076 Tuebingen, Germany

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With great interest we have read the article by Zhang and Frei on the anti-inflammatory effects of human albumin in the September issue of this journal [1]. They report a downregulation of vascular cell adhesion molecule-1 (VCAM-1) on albumin-treated human aortic endothelial cells which supports our previous results of a reduced VCAM-1 expression on TNFα-activated venous endothelial cells (HUVEC) [2]. Nevertheless, their paper warrants further comments since the authors exclusively discuss the beneficial effects of albumin and do not take into account possible risks of albumin supplementation.

Fast infusion of human albumin is well known to cause severe hypotension and flushing. Such reactions are suspected to be caused by impurities of clinically used albumin preparations involving contamination with proinflammatory mediators like kinins [3]. Accordingly, albumin preparations do not always downregulate endothelial cell adhesion molecules but can also upregulate E-selectin and intercellular adhesion molecule 1 (ICAM-1) depending on their manufacture [2]. Upregulation of these molecules affects monocyte adhesion [4] and plays an even more important role during ischemia/reperfusion and systemic inflammation where neutrophils predominate in the microvasculature [5]. Therefore, one should be aware of such effects before favouring human albumin as an anti-inflammatory plasma protein substitute.

Although hypoalbuminemia was associated with increased morbidity and mortality in some clinical studies [6], the effects of albumin substitution are much more controversially discussed in the literature than it seems from the paper of Zhang and Frei. Every meta-analysis on albumin supplementation has been criticized to a considerable extent [7–10]. Even the most recent one that defeated the harmful effects of human albumin documented in the previous Cochrane analysis [7] could not show any benefit for albumin substitution [9]. Far from being beneficial, the study documented an increased relative risk of death of more than 10% overall and up to 76% in subgroups [9,10].

As mentioned by Zhang and Frei, the maintenance of capillary permeability seems to be another physiological function of albumin [11]. In contrast to their paper, a more recent study by Margason and Soni did not confirm a reduction in capillary permeability in septic patients following infusion of human albumin [12].

A striking protection from neuronal injury during ischemia/reperfusion has been reported in models of stroke [13]. Careful review of the experimental design shows that bolus infusion of 25% human albumin was compared to equal volumes of 0.9% saline. The comparison of a hyperoncotic volume therapy with a low volume crystallloid regime results in important confounding effects on flow velocity and shear forces which will influence leukocyte adhesion directly apart from any specific anti-inflammatory effect [14]. In contrast, when human albumin was compared to another colloid in a clinical study on severe sepsis, volume resuscitation with human albumin was accompanied by increased plasma levels of soluble adhesion molecules and a worsened oxygenation index [15]. Manuscripts of basic research are not review papers and do not deal with therapeutic means. However, if the authors suggest “... increasing albumin levels may be an effective strategy to lower cardiovascular risk”, they should also discuss the possible negative aspects of doing so.

References

[3] Turner PJ, Young IF, Marley PB, Herrington RW, Schiff P. Albumin...


