Albumin infusion improves endothelial function in septic shock patients: a pilot study

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Geoffroy Hariri[1], Jérémie Joffre[1,2], Stephanie Deryckere[1], Naïke Bigé[1], Guillaume Dumas[1], Jean-Luc Baudel[1], Eric Maury[1,2,3], Bertrand Guidet[1,2,3] and Hafid Ait-Oufella[1,2,4*]

Dear Editor,

Sepsis is a life-threatening condition in response to microbe injury, leading to tissue hypoperfusion, multiorgan failure and death. Human and experimental studies have shown that endothelial dysfunction is involved in microcirculatory blood flow impairment through several mechanisms including vasomotor tone dysregulation, activation of coagulation and glycocalyx damage [1]. Experimental studies suggested that human serum albumin (HSA) could have protective effects on endothelial cells [2], but such a hypothesis has never been directly tested in vivo. The aim of this study was to compare the effect of saline versus HSA bolus infusion on endothelial function in septic shock patients.

Methods

In our intensive care unit, we prospectively included adult patients admitted for septic shock [3]. Standard patient management was guided by international guidelines [4], including fluid resuscitation (30 mL/kg of crystalloids) and norepinephrine infusion, to achieve a mean arterial pressure $\geq$ 65 mmHg. When additional volume expansion was decided by the physician in charge of the patient within the first 24 h, skin endothelial function was measured before and 1 h after volume expansion in the forearm area, as previously described (supplemental material) [5]. The patient received either a 500-mL bolus saline or a 100-mL bolus HSA 20% over 15 min according to physician's decision, based on global hemodynamic parameters and tissue hypoperfusion markers. Decision on the fluid type was made on physician´s discretion. Endothelial function measurements were performed only in stabilized patients whose vasopressor dose was unchanged during the last 2 h.

The protocol was approved by our institution's ethical committee, Comité de Protection des Personnes (CPP Saint-Louis, Paris, France). The study required no other specific intervention. Acetylcholine iontophoresis and quantification of endothelial reactivity were performed blindly by a third party. Results were expressed as median (25th–75th percentiles) and quantitative data comparisons used the Mann–Whitney test.

Results

Thirty-five patients were included during a 4-month period, 3 patients were excluded because of agitation and 2 because of poor non-pulsatile blood flow signal. Among the 30 patients included in the study, 15 received saline and 15 received HSA. Median SAPS II was 42 (37–58) and median SOFA score was 7 (4–9). The most frequent primary sites of infection were the lungs (30%) and the urinary tract (27%). The average time between ICU admission and inclusion [14 (11–18) versus 12 (11–17) h; $P = 0.96$], and the infused volume before inclusion [2500 (1500–3500) mL vs 2500 (1750–2500) mL; $P = 0.17$] were not different between groups. Except for age distribution, demographic characteristics and co-morbidities were not different between groups. In addition, hemodynamic parameters and severity scores were similar between groups (Supplemental Table). Skin blood flow, whether at baseline or after fluid infusion, was not different between saline and HSA groups. Before fluid infusion, endothelial response to acetylcholine was not different between groups [AUC 3295 (1148–5938) vs 3082 (879-4902), $P = 0.70$]. Interestingly, endothelial reactivity improved

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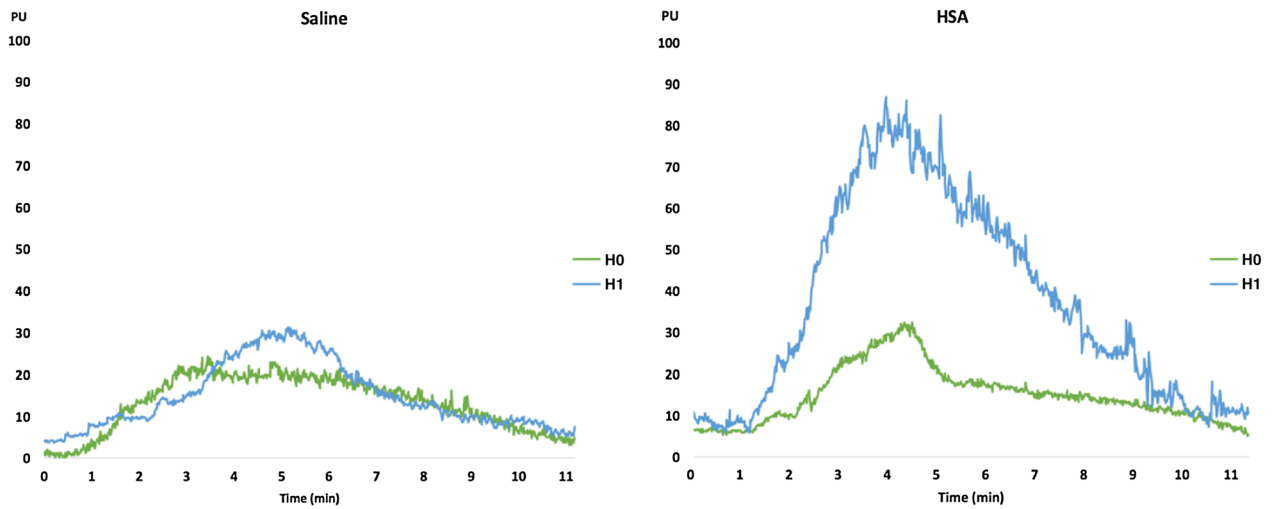

Fig. 1 Examples of microcirculatory blood flow measurements in the skin area in 2 septic shock patients in response to Ach iontophoresis before (Green curve, H0) and after (Blue curve, H1) receiving either saline (Left) or HSA 20% (Right) infusion. PU for Perfusion units

twofold after HSA infusion [AUC 5857 (2888–16679) at H1 vs 3082 (879–4902) at H0, $P = 0.04$], whereas bolus saline infusion had no significant impact on endothelial function [AUC 2388 (1914–10455) at H1 versus 3295 (1148–5938) at H0, P = NS] (Supplemental material), Fig. 1. We did not find any significant correlation between variations of endothelial reactivity between H0 and H1 and norepinephrine dosages for both groups (supplemental material).

Discussion

We found for the first time that HSA infusion had beneficial effects on skin endothelial function in septic shock patients. Variations of both cardiac output and skin blood flow were not different between groups, suggesting that the beneficial effects of albumin could be independent of its oncotic properties. Among the mechanisms that could be proposed to explain the vascular protection of albumin, its anti-oxidant properties may be of paramount importance [2]. Our non-randomized study is limited by potential selection bias such as higher bolus volume in the saline group, which might damage glycocalyx. Our results need to be confirmed in a larger randomized trial.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-018-5075-2) contains supplementary material, which is available to authorized users.

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Author contributions

Study concept and design, all authors. Acquisitions of data, GH, JJ, SD, NB, JLB, and HAO. Drafting of the manuscript, GH, JJ, GD, HAO, EM and BG. Critical revision of manuscript, all authors. Statistical analysis, GH and HAO.

Compliance with ethical standards

Conflicts of interest

B. Guidet has received honorium from LFB biomedicaments and Grifols.

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