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CORRESPONDENCE

Effects of goal-directed crystalloid vs. colloid fluid therapy on microcirculation during free flap surgery

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Editor,

We read with great interest the article by László *et al.*[1] on the effects of goal-directed crystalloid vs. hydroxyethyl starch (HES) fluid therapy on microcirculation during free flap surgery. In a randomised clinical trial, the authors compared the effect of crystalloids with HES on macrohaemodynamics and microcirculatory effects, in patients undergoing maxillofacial tumour resection and free flap reconstruction, through the use of a multimodal, individualised, approach-based algorithm that was applied to guide haemodynamic support. Recorded endpoints included microcirculatory perfusion as determined by laser-Doppler flowmetry and the amount of crystalloids or HES infused to achieve a predefined haemodynamic goal. The results did not show any difference in microcirculatory perfusion between patients assigned to crystalloids or HES, and a greater amount of crystalloids (1.5 times higher total fluid volume compared with patients treated with HES) was needed to maintain the predefined haemodynamic goal. We would like address to some issues related to this study.

First, because of concerns related to HES treatment, raised since 2013, including an increased mortality and kidney injury in ICU patients, the indication for HES usage has been limited to volume replacement therapy after acute blood loss.[2] Moreover, after a trial on HES safety that started in October 2017, the European Medicines Agency has published more restrictive rules for the use of HES in clinical practice, including a controlled access programme with the obligation for hospitals to be accredited, healthcare professionals to be trained on the safe use of HES solutions and for there to be warnings on the packaging. The European Commission confirmed these restrictions and took a European Union-wide legally binding decision on 17 July 2018. Given this highly disputed safety profile, we were wondering whether the authors had considered the selected endpoints to be adequate to balance out the possible risk for the recruited patients.[3]

Second, in peri-operative fluid management, colloid use in a 'close loop system' relates to the need for smaller fluid volumes but is not associated with lower postoperative complications when compared with crystalloids.[4] We wonder whether the 'smaller volumes' of HES compared with crystalloids needed to achieve a predefined target with the goal-directed fluid therapy, as reported in the study, relate to a clinical benefit?

Third, given the controversies on potential harm it has been claimed that HES use '[...] can only be justified when clinically relevant benefits and safety are established in trials designed and powered to evaluate both outcomes. The absence of harm is insufficient'.[3,5]

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Reply to: effects of goal-directed crystalloid vs. colloid fluid therapy on microcirculation during free flap surgery

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Editor,

We would like to thank Giordano *et al.*[1] for their comments concerning our recently published trial on the

usage of colloid fluid therapy on microcirculation during free flap surgery.[2] They are raising three main issues.

The first is considering the safety of hydroxyethyl starch (HES) in critically ill patients, especially taking into consideration the European Commission's rules and restrictions on HES usage, issued on 17 July 2018.[3] Our study protocol was designed, and the trial started with the recruitment of patients, years before this regulation came into effect. Also, we feel that the decision to erase HES from clinical practice was not supported by very strong evidence as this decision was based on the results of clinical trials that did not apply adequate haemodynamic monitoring and the fluid administration was based on clinicians' intuition or on inadequate indices.[4–6] These trials have an important message: if the current approach in fluid management is used, then normovolaemic patients will be treated with cristalloids or HES, and complications are inevitable. In other words, it may be that it is not the HES, but our current clinical practice that is responsible for the harmful effects of HES observed in these trials. In our study, in contrast to these large trials, we implemented the concept of detailed, multimodal and individualised, haemodynamic monitoring, to maximise the likelihood that only those patients who were most probably hypovolaemic would treated with fluids.[1]

The second question raised by Giordano *et al.* is whether smaller volumes of colloids have any plausible clinical benefit. Although it was not the aim of our study, our data support the theory of Starling's three-compartment model and provided additional information that using colloids may have the benefit of reaching haemodynamic stability two to three times faster compared with crystalloids. This difference could potentially be important during fluid resuscitation. This issue has to be investigated further.

The third issue raised by Giordano *et al.* relates to the use of HES that '[...] can only be justified when clinically relevant benefits and safety are established in trials designed and powered to evaluate both outcomes'.[3,7] Our study was not designed to address safety issues, but to question a specific problem – the effect of different fluids on microcirculation.

Finally, based on the comments depicted above, the colloid vs. crystalloid debate including the effects of HES is far from being closed. It is our strong belief that precision-medicine and personalised-medicine should take over the current 'intuition-based' approach to provide the best and safest treatment for the high-risk patient.

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1 Giordano G, Pugliese F, Bilotta F. Effects of goal-directed crystalloid vs. colloid fluid therapy on microcirculation during free flap surgery. *Eur J Anaesthesiol* 2020; **37**:413.
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Crystalloids should be second choice for goal-directed fluid therapy

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Editor,

I would like to congratulate László *et al.*[1] for their well performed comparison of crystalloid and colloid fluid for goal-directed volume therapy during free flap surgery that was recently published in the *European Journal of Anaesthesiology*. Most evaluations of goal-directed fluid therapy have used colloids but some studies, and many clinicians, have turned to crystalloids. Therefore, László's study is pertinent to the current practice of anaesthesia. However, I still have difficulties in understanding why crystalloids are used for this purpose.

The reason underlying my difficulties in understanding is that the acute rise in cardiac index (CI) induced by a bolus infusion of crystalloid fluid is short-lived. When crystalloid fluid is administered rapidly, within 3 to 5 min, a redistribution phase will be very prominent. Almost half of the induced plasma volume expansion will be lost within 10 min (Fig. 1a). This is the case during general anaesthesia and surgery except when there is a sudden drop in arterial pressure, which transiently stops the redistribution.[2]

The redistribution effect becomes smaller with the infusion time, and is of negligible consequence for lengthy infusions. Then, the rate of elimination is the key factor determining plasma volume expansion, which has in fact