

LETTER

# Assessment of hemodynamic efficacy and safety of 6% hydroxyethyl starch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: how to guide fluid therapy?

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We argue that assessing the hemodynamic efficacy of hydroxyethyl starch (HES) versus NaCl in patients with severe sepsis requires an algorithm to direct the timing and amount of fluid resuscitation. Such an algorithm may include hemodynamic flow parameters.

In a recent issue of *Critical Care*, Guidet and colleagues [1] reported that a smaller amount of 6% HES 130/0.4 versus 0.9% NaCl was required to achieve hemodynamic stability (HDS) during the initial phase of fluid resuscitation in patients with severe sepsis. The target parameters indicating HDS included central venous pressure (CVP) (8 to 12 mm Hg), a poor indicator of fluid responsiveness [2], and a large urine output (>2 mL/kg per hour), and therefore pose a risk of over-infusion. Other authors have reported that over-infusion, elevated CVP, and excessive fluid resuscitation with HES are associated with increased mortality in patients with sepsis [3,4].

In contrast, after initial HDS was achieved, no such target parameters were defined, and so the cumulative volumes of study drug infused over the course of four consecutive days in the intensive care unit (ICU) were similar for the HES (2,615 mL) and NaCl (2,788 mL) groups. No differences in mortality, hospital length of stay, or kidney function were found. This study may be showing only that, in the absence of an algorithm to guide fluid resuscitation, intensivists use an unvarying amount of fluids, but it is impossible to know whether these fluids were, in fact, indicated. In patients undergoing major abdominal surgery, hemodynamic algorithms that guide the timing and amount of fluid administration have helped determine the clinical efficacy of fluid therapy [5]. The negative results reported by Guidet and colleagues suggest that hemodynamic algorithms for patients with sepsis are urgently required to accurately compare the hemodynamic efficacy, safety, and outcome of HES versus NaCl fluid replacement.

## Author's response

Bertrand Guidet

We thank Hunsicker and Francis for giving us the opportunity to clarify some issues related to fluid replacement and hemodynamic assessment in patients with severe sepsis. When we designed our protocol [1], we used international recommendations that were confirmed by the revision of the Surviving Sepsis Campaign

[6]. Given the multicenter nature of the trial, in which more than 20 ICUs participated, it was impossible to standardize an algorithm that was agreed upon by everybody and feasible 24 hours a day in all ICUs. However, all centers used tools in addition to CVP, urine output, and venous oxygen saturation (SvO<sub>2</sub>) to assess whether a patient was a good candidate for fluid loading.

As a matter of fact, considering the endothelial dysfunction induced by sepsis [7], we strongly advocate the use not only of macrocirculatory parameters (mean arterial pressure and cardiac output) but also of microcirculatory parameters such as mottling score and knee tissue oxygen saturation (StO<sub>2</sub>), as we have shown in

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previous studies that there may be a discrepancy between macro- and microcirculation after initial resuscitation [8,9].

In our study, the baseline values suggested that patients should receive fluid [1], whereas in the study by Perner and colleagues [10], it was only the ICU clinicians who decided, without further information, to give fluid. In this study, less than half the patients had any measure of CVP or SvO<sub>2</sub>. This lack of monitoring might have contributed to a higher volume of fluid infused over the first days in comparison with our study and explain the final results on renal function and mortality. In conclusion, I do agree that an integrative approach should be advocated in order to avoid over-infusion but also under-resuscitation, in particular in the early hours after onset of severe sepsis or septic shock.

#### Abbreviations

CVP, central venous pressure; HDS, hemodynamic stability; HES, hydroxyethyl starch; ICU, intensive care unit; SvO<sub>2</sub>, venous oxygen saturation.

#### Competing interests

The authors declare that they have no competing interests.

Published: 15 November 2012

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doi:10.1186/cc11836

**Cite this article as:** Hunsicker O, Francis RCE: Assessment of hemodynamic efficacy and safety of 6% hydroxyethyl starch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: how to guide fluid therapy? *Critical Care* 2012, **16**:464.