

## Commentary

# High-volume hemofiltration in septic shock

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See related research article by Ratanarat *et al.*, in this issue [<http://ccforum.com/content/9/4/R294>]

### Abstract

In the past decade we have learned a lot about the pathophysiology of septic shock. A lot of experimental research has been performed *in vitro* and *in vivo*, showing that hemofiltration can improve hemodynamics and survival. With modern machines, hemofiltration is becoming a sepsis treatment in patients.

Since continuous haemofiltration (HF) was first described by Kramer as a new form of renal replacement therapy [1], it has undergone many changes, making it a widely accepted treatment modality for acute renal failure in critically ill patients. Concomitantly, new insights into the pathogenesis of severe sepsis and septic shock recently led to new forms of immunomodulatory therapy for septic shock. A number of clinical trials investigating the effect of antiendotoxin or anticytokine interventions were unable to demonstrate a consistent improvement in survival of patients with sepsis or septic shock. Another possible immunotherapy is removal of various inflammatory substances, including endotoxin, cytokines, oxygen-free radicals and arachidonic acid metabolites, by HF.

In this issue of *Critical Care* Ratanarat and coworkers [2] report the results of an observational study in patients with septic shock who were treated with 'pulse high volume hemofiltration'. Ratanarat and colleagues utilized a HF rate of 85 ml/kg per hour for 6–8 hours, followed by a more conventional rate of 35 ml/kg per hour. It is indeed now accepted that 35 ml/kg per hour should be used in patients with acute renal failure who are treated with HF [3].

Bearing in mind that removal of the so-called 'middle molecules' is a convective process, Grootendorst opted to apply much higher volumes of ultrafiltration (UF). Grootendorst and coworkers [4] introduced the concept of high-volume haemofiltration (HVHF) in a pig endotoxin model, in

which they demonstrated improvement in haemodynamics in the study animals as compared with controls. Moreover, infusion of the ultrafiltrate from the endotoxic animals into healthy ones induced the same symptoms as in the endotoxic group [5]. In another study [6] the same group examined a bowel ischaemia–reperfusion model. HVHF started before the mesenteric artery was clamped significantly diminished bowel damage and prevented haemodynamic deterioration. These studies established that convective removal of septic mediators can be performed when sufficiently high UF rates are applied.

Several studies have confirmed these findings. In all of these a similar improvement in haemodynamics was found, and some even reported an increase in survival [7-9]. In one study [8], different UF rates were compared in a clinically representative model of severe pancreatitis in pigs. HVHF at a rate of 100 ml/kg per hour was better than low-volume HF. Frequent filter change, allowing more adsorption of cytokines, was also better than no change. These data were confirmed in a very recent study conducted in the same model [10].

Several studies have examined the effects of HVHF in patients. In one study [11] HVHF was performed during cardiopulmonary bypass in children undergoing cardiac surgery, which resulted in a blunted inflammatory response, reduction in postoperative blood loss and improved oxygenation. In a prospective cohort analysis [12], in which 306 critically ill patients with acute renal failure were treated with an UF rate of 3.8 l/hour, the observed survival rates were significantly better than predicted. In a small trial of 11 patients with shock and multiple organ dysfunction syndrome [13] the authors compared an UF rate of 1 l/hour with 6 l/hour using a crossover design. HVHF resulted in a significant reduction in vasopressor requirements and a greater reduction in levels of complement 3 and 5. In another

study conducted in 20 patients with refractory septic shock, Honoré and coworkers [14] gave a 4-hour treatment with HVHF, followed by conventional continuous venovenous haemofiltration. Eleven patients responded to the treatment with increases in cardiac index, venous oxygen saturation and arterial pH, and a decrease in norepinephrine requirement. Of these responders, nine out of eleven survived to 28 days; all of the nonresponders died.

Ratanarat and coworkers [2] show that HVHF, following its birth as a theoretical concept and subsequent experimental research in animals, is progressing toward the bedside of our critically ill patients. This modality is feasible with modern HF machines and the available fluids, and can be performed without major side effects.

It is increasingly accepted that the 'renal dose' of HF is not the same as the 'septic dose'. We must define those patient populations that may require this form of treatment and those that can be treated with more conventional renal replacement therapy. Despite initial scepticism, we are beginning to learn that HF for severe sepsis and septic shock is more than bloodletting, 21st century style.

## Competing interests

The author(s) declare that they have no competing interests.

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