ICU MANAGEMENT & PRACTICE

ICU Volume 5 - Issue 3 - Autumn 2005 - Cover Story:Outreach

Pulse High Volume Haemofiltration (PHVHF): Novel Treatment for Sepsis

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Pulse high volume haemofiltration (PHVHF) in the treatment of sepsis may offer a practical, efficacious and relatively inexpensive compromise between continuous renal replacement therapy (CRRT) and high volume haemofiltration (HVHF).

Severe sepsis represents the leading cause of mortality and morbidity in critically ill patients world wide. (Angus et al. 2001; Friedman et al. 1998; Laupland et al. 2004). The cornerstone of therapy continues to be early recognition, prompt initiation of antibiotic therapy, and elimination of the source of infection. Goal-directed haemodynamic, ventilatory, and metabolic support are also crucial. To date, the adjuvant treatment of sepsis remains a major therapeutic challenge. Based on humoral theory of sepsis, both pro- and anti inflammatory factors become upregulated with complex interactions leading to hyperinflammation and/or immunoparalysis. Trials to improve survival with anti inflammatory therapeutic strategies have been disappointing (Wheeler and Bernard 1999). Novel therapies, such as drotrecogin alfa (activated), are promising. Interestingly, these new tools do not act on specific targets, but rather act globally or non-specifically.

Blood purification using continuous renal replacement therapy (CRRT) is theoretically attractive potentially providing a restoration of humoral homeostasis by avoiding both excessive inflammation and counter-inflammation. Non specific and continuous removal of pro- or anti-inflammatory soluble mediators, may be the most logical and adequate approach to a complex and long-running process like sepsis.

CRRT has commonly used three types of mechanisms: convection, diffusion and adsorption. In addition to removing excess fluid, convective modalities have the advantage of removing higher molecular weight substances, which include many inflammatory mediators. Adsorption to the membrane is a process that saturates in a few hours. An increased efficiency can be obtained by increasing membrane sieving or the rate of ultrafiltration (Langsdorf and Zydney 1994) as in a modality called high volume haemofiltration (HVHF).

In vitro studies have shown that haemofiltration is capable of removing nearly every known substance involved in sepsis to a certain degree (De Vriese et al. 1999). Animal studies have shown a beneficial effect of HVHF on survival (Grootendorst et al. 1992; Rogiers et al. 1999; Yakebas et al. 2001), haemodynamics (Bellomo et al. 2000; Rogiers et al. 1999; Yakebas et al. 2001), and improvement in immune cell hyporesponsiveness in endotoxemic models (Rogiers et al. 1999). Human studies have demonstrated that HVHF improves haemodyamics decreasing vasopressor requirement (Cole et al. 2001; Honore et al. 1998; Jannes-Boyau et al. 2004) and survival of septic patients (Jannes-Boyau et al. 2004; Oudemans-van Straaten et al.1999). Because of the requirements of high blood flows, tight ultrafiltration control, and large amounts of sterile fluids, HVHF is difficult to perform over 24 hours. Nevertheless, continuity of treatment seems to be as important as the high volume fluid exchange.

We therefore proposed “Pulse high volume haemofiltration” (PHVHF), which is a daily schedule of HVHF (85 ml/kg/h) for 6-8 h followed by continuous venovenous haemofiltration (CVVH) (at 35 ml/kg/hr) for the remaining time. This leads to a cumulative dose of approximately 50 ml/kg/hr. We studied 15 critically ill patients (7 male, mean APACHE II score 31.2, mean SAPS II 62, mean SOFA 14.2) with severe sepsis (Ratanarat et al. 2005). PHVHF was performed with a blood flow rate of 250-300 ml/min. Bicarbonate-based replacement fluid was used at the ratio of 1:1 in simultaneous pre-post- dilution. No treatment was prematurely discontinued because of extracorporeal circuit clotting. Haemodynamics improved, allowing a significant reduction of noradrenaline dose and this effect was maintained at 6 and 12 h after treatment ($p=0.001$). SBP also improved ($p=0.04$). Mean daily Kt/V was 1.92. Predicted mortality were 72% (APACHE II score) and 68% (SAPS II score), and the observed 28-day mortality was 47%. There is growing evidence for the role of apoptosis in organ injury during sepsis and inflammation. We found that septic plasma had remarkably proapoptotic effect on U937 human monocytic cells compared with control. Pulse HVHF, but not CVVH, significantly reduced the pro-apoptotic plasma activity already at 1h and this was maintained unvaried at 4 and 12h (Brendolan et al. 2004).

In summary, PHVHF appears to be a feasibly promising technique for the treatment of severe sepsis providing haemodynamic benefits, positive biological effects and improved survival while it represents a practical and less expensive compromise between CRRT and HVHF.

Published on : Thu, 20 Oct 2011