Prophylactic hemofiltration in severely traumatized patients: effects on post-traumatic organ dysfunction syndrome

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Received: 26 August 1999
Final revision received: 16 October 2000
Accepted: 30 October 2000
Published online: 25 January 2001
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Abstract  Objective: To evaluate the effects of prophylactic veno-venous hemofiltration (CVVH) in the absence of renal failure on multiple organ dysfunction syndrome after severe multiple trauma.
Setting: Prospective, randomized study.
Patients: Twenty-four patients with severe multiple trauma (injury severity score ≥27), no renal failure on admission and no contraindication for moderate heparinization.
Interventions: Twelve patients received conventional treatment while 12 patients were treated additionally with isovolemic CVVH for 5 days starting within 24 h following trauma. Signs of organ dysfunction were assessed daily including monitoring of systemic hemodynamics by means of pulmonary artery catheterization during the first 5 days after trauma.

Measurements and main results: Prophylactic CVVH did not affect the overall severity of organ dysfunction as assessed by MOF or APACHE II scores. However, the pattern of impaired organ systems was influenced by CVVH: while the post-traumatic decrease in platelet count in patients subjected to CVVH was more pronounced than in controls (e.g. day 4: control: 115,080 ± 15,087, CVVH: 57,383 ± 4,201 µl⁻¹; p < 0.05) the development of hyperdynamic circulatory failure was simultaneously attenuated, as reflected by a limited increase in cardiac output and an attenuated decrease in systemic vascular resistance and oxygen extraction ratio (e.g. systemic vascular resistance on day 4: control: 624.3 ± 46.17, CVVH: 842.7 ± 79.24 dyn·s·cm⁻²; p < 0.005).

Conclusion: CVVH blunts the cardiovascular response to multiple trauma and increases tissue oxygen extraction. However, the concomitant decrease in platelet counts represents a limitation for the use of prophylactic CVVH in surgical patients.

Key words  Multiple trauma · Systemic inflammatory response syndrome · Multiple organ dysfunction syndrome · Continuous veno-venous hemofiltration · Oxygen consumption · Oxygen extraction · Prospective, randomized clinical trials

Introduction

Multiple trauma may lead to a non-infectious systemic inflammatory response syndrome (SIRS) or ultimately multiple organ dysfunction syndrome (MODS). Similar to infectious SIRS or sepsis, this inflammatory response is thought to reflect activation of humoral and cellular inflammatory cascades and may be accompanied by alterations in the oxygen extraction capabilities of the tissues and hyperdynamic cardiovascular failure [1]. Nota-
bly, small to middle-sized molecules, such as proinflammatory cytokines or activated complement factors seem to play a key role as humoral mediators in the development of SIRS and MODS [2, 3]. Since MODS is a leading cause of morbidity and mortality in surgical intensive care, attenuation of SIRS by antagonizing [4, 5] or removing [6] potentially involved mediators has attracted great interest as a supportive strategy to prevent organ failure in the critically ill. Unfortunately, therapeutic interventions aiming at neutralizing or antagonizing individual inflammatory cytokines have generally been disappointing [7, 8]. Although anti-mediator strategies are successful in experimental models of endotoxemia, there is an increasing body of evidence that proinflammatory mediators are – in addition to their systemic toxic effects – crucial to mount a local host defense response [9, 10]. Moreover, the simultaneous production of a wide variety of inflammatory mediators sharing many biological activities may limit the use of strategies directed against a single mediator [11].

Hemofiltration, especially continuous veno-venous hemofiltration (CVVH), is a safe and well-established treatment in critically ill patients with renal failure, but has also been used in the treatment of cardiogenic pulmonary edema, acute respiratory distress syndrome (ARDS) and sepsis [12, 13]. Although many of the inflammatory mediators involved in the development of SIRS, ARDS and MODS are known to have a molecular weight well below the cut-off value of hemofiltration membranes, the use of CVVH to attenuate SIRS by eliminating a broad spectrum of small to middle-sized inflammatory mediators has been a source of considerable controversy [6, 13, 14, 15, 16]. In particular, potential targeting of multiple mediators that are released into the systemic circulation without affecting the local host defense response by CVVH is intriguing. However, prospective, randomized and controlled clinical studies assessing the potential effects of prophylactic hemofiltration in patients with severe SIRS, septic shock or multiple organ failure are sparse, although urgently demanded.

The aim of this prospective and randomized single center pilot study, therefore, was to evaluate the influence of prophylactic CVVH, in the absence of renal failure, on the development of post-traumatic MODS in patients with severe multiple trauma.

Methods

Patients and study design

The study design was approved by the local ethics committee and the study was conducted according to the declaration of Helsinki. Twenty-four consecutive patients with multiple trauma and injury severity scores (ISS) of 27 or more were enrolled by drawing one of 24 lots from a box (blinded allocation). Exclusion criteria were:

- age under 18 years, intracranial bleeding, other contraindications for moderate heparinization and established renal failure. The patients were randomly assigned to receive standard ICU treatment (control group) or standard treatment plus CVVH (CVVH group).
- All patients were hemodynamically monitored by means of arterial and pulmonary arterial catheters for at least the first 5 days after trauma. Mechanical ventilation was started in all patients before admission to the ICU and was discontinued when appropriate.
- Crystalloids and colloid were given to achieve a pulmonary capillary wedge pressure (PCWP) of about 12–15 mmHg and a systolic arterial pressure above 100 mmHg. If these goals were not reached by volume administration or transfusion alone, norepinephrine was added to achieve the desired arterial pressure. Of note, no effort was made to increase cardiac output further by means of the administration of inotropic or vasodilating agents. Red packed cells were transfused if necessary to achieve a hemoglobin content between 8 and 10 g/dl. Furthermore, all patients received low-dose heparinization (500 IU/h) of unfractionated heparin to prevent thromboembolic complications. All patients received continuous administration of fentanyl for analgesia and were sedated with midazolam according to clinical requirements.

Performance of continuous veno-venous hemofiltration

The 12 patients randomized to receive CVVH were cannulated with a venous double-lumen catheter via a central vein to allow pump driven veno-venous hemofiltration. CVVH was performed with a blood flow rate of 60–100 ml/min using an AN69 membrane (Hospital, Lyon, France) achieving a passive ultrafiltration rate of about 500 ml/h (not pump controlled). CVVH was strictly isovolemic through substitution of aliquots of a balanced electrolyte solution (SH 05, Schiwa, Glandorf, Germany) to compensate for the withdrawn filtrate. CVVH was started after primary surgery within 24 h after trauma and was continued for 5 days. The filters were replaced daily. To avoid clotting of the dialyzer, the 500 units of heparin per hour administered prophylactically in all patients were added into the inflow line of the extracorporeal circuit in patients subjected to CVVH.

Measurements

Blood samples were taken daily between 7 and 9 a.m. throughout the whole study period for evaluation of blood gases, blood cell counts and chemistry. From the day of admission (at the time of inclusion into the study: “day 0”) up to the 5th day after trauma, the following variables were recorded between 7 and 9 a.m. (“days 1 to 5”): heart rate (HR), mean arterial pressure (MAP), mean pulmonary arterial pressure (MPAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), cardiac index (CI), systemic vascular resistance (SVR), arterial oxygen content (CaO2), mixed venous oxygen content (CVO2), body temperature (BT), respiratory rate (RR) and white blood count (WBC). Oxygen delivery (DO2), oxygen consumption (VO2) and oxygen extraction ratio (OER) were calculated from cardiac output (CO), CaO2 and CVO2 according to the following equations: (i) DO2 = [ml/min] × [CO / [l/min]] × [CaO2 / [ml/100 ml]] × 10; (ii) VO2 = [CO / [l/min]] × [CaO2 / [ml/100 ml]] × [CVO2 / [ml/100 ml]] × 10 and (iii) OER = VO2/DO2. Oxygenation was assessed by calculating the oxygenation index (OI) according to the following equation: OI = PaO2 [mmHg] / FIO2.