A multicenter randomized controlled study of an extracorporeal cytokine hemoadsorption device in septic patients

D Schädler1, C Porzelius2, A Jörres3, G Marx4, A Meier-Hellmann5, C Putensen6, M Quintel7, C Spies8, C Engel2, N Weiler1, M Kuhlmann8

1Department of Anaesthesiology and Intensive Care Medicine, University Medical Center Schleswig-Holstein, Campus Kiel, Germany
2Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Germany
3Department of Nephrology and Medical Intensive Care, Charité University Hospital Campus Virchow-Klinikum, Berlin Germany
4Department of Intensive Care and Intermediate Care, RWTH University Hospital Aachen, Germany
5Department of Anesthesiology and Intensive Care Medicine, University of Bonn, Germany
6Centre of Anaesthesiology, Emergency and Intensive Care Medicine, University Hospital Göttingen, Germany
7Anesthesiology and Intensive Care Medicine, Campus Charité Mitte and Campus Charité Virchow-Klinikum, Charité - University Medicine Berlin, Germany
8Department of Nephrology, Vivantes Klinikum im Friedrichshain, Berlin Germany

Introduction
A novel sorbent hemoadsorption device for cytokine removal (CytoSorbents, USA) was developed and successfully tested in animal models of sepsis [1,2]. The experience in the clinical setting is still limited to case reports. In this first clinical trial, we tested the hypothesis that treatment with sorbent hemoadsorption could safely and effectively reduce cytokines in septic patients with acute lung injury (ALI).

Methods
Ventilated patients fulfilling the criteria for severe sepsis and ALI were enrolled in this multicenter randomized, controlled, open-label study comparing standard of care with or without hemoperfusion treatment. Primary endpoints were safety and IL-6 reduction. Treated patients underwent hemoperfusion at flow rates of ~200-300 ml/min for 6 hours per day for 7 consecutive days. The overall mean reduction in individual plasma cytokines for the control and treatment groups during the treatment period was calculated using a generalized linear model.

Results
43 patients (18 treated, 25 control) completed the study and were further analyzed. Incidence of organ dysfunction at enrollment (treatment vs. control) was: septic shock (94% vs. 100%, p=0.42), acute respiratory distress syndrome (67% vs. 56%, p=0.33), and renal failure (39% vs. 24%, p=0.54). During 115 treatments no serious device related adverse events occurred. On average, there were no changes in hematology and other blood parameters except for a modest reduction in platelet count (<10%) and albumin (<5%) with treatment. Hemoperfusion decreased IL-6 blood concentration significantly (-49.1%, p=0.01), with similar reductions of MCP-1 (-49.5%, p=0.002), IL 1ra (-36.5%, p=0.001), and IL-8 (-30.2%, p=0.002). 28-day (28% vs. 24% control, p=0.84) and 60-day mortality (39% vs. 32% control, p=0.75) did not differ significantly between the two studied groups.

Conclusions
In this first clinical study of a novel sorbent hemoadsorption device in patients with severe sepsis and ALI, the device appeared to be safe and decreased the blood concentration of several cytokines. Further research is needed to study the effect of the device on the clinical outcome of septic patients.

Literature

Contact
Dr. Dirk Schädler
dirk.schaedler@uksh.de
http://www.uni-kiel.de/anaesthesie/
The study was funded by CytoSorbents Corporation, New Jersey, United States.