

HEMOGLOBIN REMOVAL BY DIALYZERS OF DIFFERENT PERMEABILITY PROFILES

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Introduction and Aims

Release of hemoglobin from mechanically stressed erythrocytes into plasma is a general side effect of extracorporeal therapies, like extracorporeal membrane oxygenation and hemodialysis. Dialysis patients often show elevated cell-free plasma hemoglobin levels due to repeated mechanical impact of erythrocytes. Cell-free plasma hemoglobin reacts with nitrogen oxide, which plays a role in cardiovascular signaling, and reduces its bioavailability. The purpose of this study was to measure cell-free plasma hemoglobin clearance of conventional high-flux dialysis filters, high-flux filters with extended permeability and high cut-off dialyzers and to evaluate the opportunity of reducing cell-free plasma hemoglobin levels.

Methods

Polyflux Highflux 170H (Gambro), FX CorDiax 80 (Fresenius) and four different MCO high-flux dialyzers with extended permeability (Gambro) were tested on AK 200 Ultra with QB 400, QD 500 ml/min and UF 0 ml/min. In each experiment 1 L of bovine blood was spiked with about 1 g hemoglobin and dialysis treatments were simulated in a recirculating blood loop. Plasma samples were collected from the blood pool after defined intervals. Changes in cell-free plasma hemoglobin levels were measured photometrically at 405 nm detecting the heme-characteristic soret absorption band. Clearance was calculated from the first order kinetics for the variation of hemoglobin. In the analogous way septeX-Sets (Gambro) were tested on a Prismaflex monitor with QB 200 ml/min, QD 2.5 l/h (42 ml/min) and UF 0 ml/min.

In a second set of experiments hemoglobin clearances were measured on the AK 200 Ultra with QB400, QD 700 and UF 0 ml/min in bovine plasma and a recirculation phase of 60 min with closed dialysate compartment prior to the dialysis treatment simulation. Hemoglobin was added after 55 min.

Results

Hemoglobin clearances of septeX are given in the table below as mean values \pm standard error of the mean of 3 independent experiments:

Filter	Whole blood clearance [ml/min] QB200/QD42/UF0
septeX	22.6 \pm 2.9

Hemoglobin clearances of various high-flux membranes are given in the tables below as mean values \pm standard error of the mean of 3 independent experiments:

Filter	Whole blood clearance [ml/min] QB400/QD500/UF0	Plasma clearance [ml/min] QB400/QD700/UF0 after 60 min recirculation
Polyflux Highflux	< 0	< 0
FX CorDiax 80	< 0	< 0
MCO1	5.9 \pm 1.2	5.8 \pm 1.2
MCO2	5.4 \pm 0.6	7.3 \pm 1.0
MCO3	7.5 \pm 0.5	8.8 \pm 0.6
MCO4	11.3 \pm 1.6	12.7 \pm 1.7

Discussion

Cell-free hemoglobin clearance was measured in simulated dialysis treatments. There was no detectable clearance for conventional high-flux filters. However, filters with extended permeability (referred to as "MCO") and the septeX-Set showed significant hemoglobin removal capacity. At the applied hemoglobin concentrations of about 1 g/L and an assumed tetramer-dimer dissociation constant of 0.5 μ M under physiological conditions [based on considerations by Guidotti in JBC 1967, 242:3685-3693] about 10% of the cell-free hemoglobin is $\alpha\beta$ -dimer while 90% are $\alpha_2\beta_2$ -tetramers with subunit molecular weights of about 15.2 and 16.0 kD. These data show that filters with extended permeability and septeX provide opportunities for cell-free hemoglobin removal in a chronic and acute setting.

Summary

- Hemoglobin removal by dialyzers of different permeability profiles was investigated
- In vitro simulations of dialysis treatments were performed
- Dialyzers with high-flux membranes with extended permeability (MCO) showed significant hemoglobin removal
- septeX filter with a high cut-off membrane showed significant hemoglobin removal
- Dialyzers with a conventional high-flux membrane did not show significant hemoglobin removal
- This study demonstrated the possibility of hemoglobin removal in a chronic and acute setting
- Clinical studies are needed to warrant the findings

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