Performance of Hemodialysis with Novel Medium Cut-Off Dialyzers

Kirsch AH Lyko R, Nilsson LG, et al. Performance of hemodialysis with novel medium cut-off dialyzers. *Nephrol Dial Transplant*. 2017; 32:165-172. doi:10.1093/ndt/gfw310.

BACKGROUND

End-stage renal disease (ESRD) results in the retention of uremic toxins, which is associated with high mortality. Uremic toxins are classified into small (< 500 Da) and middle molecular (500 Da–60 kDa) water-soluble solutes and protein-bound substances. While conventional hemodialysis (HD) modalities remove small solutes and smaller-sized middle molecules, clearance of larger middle molecules and protein-bound substances is poor.

Studies have associated middle molecules to pathological features of uremia, such as immune dysfunction and inflammation, as well as adverse outcomes in dialysis patients. Free immunoglobulin light chains (FLCs) have a molecular weight (MW) of ~22.5 kDa for kappa FLC (κFLC) and 45 kDa for lambda FLC (λFLC). Importantly, FLC levels have been associated with mortality in chronic kidney disease (CKD) cohorts.

Efforts have focused on improving the clearance of larger middle molecules in dialysis. The introduction of more water-permeable high-flux membranes allowed the clearance of middle molecules such as β2-microglobulin (12 kDa) and increasing convection with hemodiafiltration (HDF) considerably enhanced middle molecule clearance. However, high flux dialyzers have cut-off values of ~20 kDa and are thus limited in their ability to remove larger middle molecules κFLC and λFLC. Maintenance HD patients who are at high mortality risk seem to benefit from high-flux HD, but large outcome trials comparing HDF to HD have yielded equivocal results.

Medium cut-off dialyzers utilize a novel class of membranes designed to increase the removal of larger middle molecules in HD, and in contrast to more permeable high cut-off membranes, are intended for routine use in maintenance HD patients.

OBJECTIVES

To compare the performance of three prototypes of **MCO** dialyzers with HD and high-volume hemodiafiltration (HDF) using contemporary high-flux dialyzers. Specifically, these studies compared the clearance of larger middle molecules, including κFLC (23 kDa) and λFLC (45 kDa), considered to be uremic toxins.

METHODOLOGY

Study Design

The two studies were prospective, open-label, 4-arm, randomized, active-control, crossover pilot studies comparing **Theranova** 400 dialyzer (MCO AA; Gambro Dialysatoren GmbH, Hechingen, Germany, a subsidiary of Baxter International Inc.) and two **MCO** dialyzer prototypes (**MCO** BB and CC) with high-flux dialyzers FX CorDiax 80; Fresenius Medical Care Deutschland, Bad Homburg, Germany in studies 1 and 2 and high-volume HDF (FX CorDiax 800; Fresenius Medical Care Deutschland, Bad Homburg, Germany; study 2.

The membranes of the **MCO** dialyzers had increased permeability (AA < BB < CC). **MCO** membranes AA, BB and CC were polyarylethersulfone-PVP blend membrane polymer; Fx CorDiax 80 and Fx CorDiax 800 were polysufone-PVP blend membrane polymer.

Study 1 compared **MCO** membrane AA (**Theranova** 400 dialyzer), BB, and CC with high-flux dialyzers (FX CorDiax 80), while study 2 compared **MCO** membrane AA (**Theranova** 400 dialyzer) and BB with high-flux dialyzers (FX CorDiax 80) and high-volume HDF (FX CorDiax 800).

Study 1 was conducted in the dialysis units of a medical university and a hospital in Austria. Study 2 was performed in a dialysis center in Germany. The dialysis sessions in study 1 were 4 hours with a dialysate flow (Q_D) of 500 mL/min and a blood flow (Q_B) of 300 ± 20 mL/min, while the dialysis sessions in study 2 were 4-5 hours with a Q_B of 400 + 50 mL/min.

Patients

Patients aged 18 years or above, on either HD or HDF treatment for at least 3 months before enrollment, had a κFLC/λFLC ratio of > 0.37 and < 3.1, and no history of monoclonal gammopathy were enrolled and randomized to each study dialyzer treatment. A total of 39 patients were enrolled: 19 in study 1 and 20 in study 2.

Outcomes

The primary outcome was the overall clearance (K_{ovr}) of λFLC using **MCO** dialyzer prototypes in HD mode vs. K_{ovr} using high-flux dialyzers used in HD and HDF. Secondary outcomes were the clearance of other middle molecules and small molecules, as well as safety (albumin removal and treatment tolerance) of **MCO** membrane HD.

RESULTS

Study 1: Free Light Chain Removal During HD Using MCO Dialyzers Compared to a High-Flux Dialyzer

Overall Clearance

In study 1, the λFLC K_{ovr} and the κFLC K_{ovr} with **MCO** membranes AA, BB, and CC were significantly higher than with high-flux HD. See Figure 1A and Table 1A.

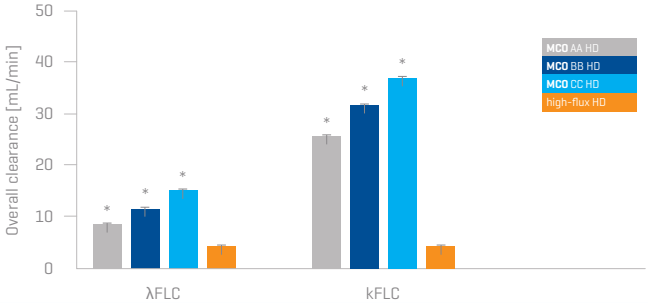

FIGURE 1A. Overall Clearance. Free immunoglobulin light chain removal during hemodialysis with medium cut-off dialyzers and high-flux dialyzer in study 1. Data are least square mean + standard error. *p < 0.001 compared to high-flux dialyzer. Abbreviations: FLC, free light chain; **MCO** membrane, medium cut-off dialyzer; HD, hemodialysis. Adapted from Kirsch et