Comparison of Hemodialysis with Medium Cut-Off Dialyzer and On-Line Hemodiafiltration on the Removal of Small and Middle-Sized Molecules

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BACKGROUND

Recent data suggest that the use of medium cut-off dialyzers in hemodialysis (HD) promotes greater clearance and reduction ratio (RR) for myoglobin (17 kDa) and other large-sized molecules than on-line hemodiafiltration (ol-HDF), but its effects on β2-microglobulin (11.8 kDa) are not clear.

The association of high serum levels of middle-sized toxins, particularlyβ2-microglobulin, with inflammation, immune dysfunction, and patient survival has been established in several studies. The removal of middle-sized toxins such as β2-microglobulin (11.8 kDa) and myoglobin (17 kDa) depends on both dialyzer permeability and treatment modalities. Ol-HDF, combining the use of a high-flux dialyzer, ultrapure dialysis fluid and extensive convective fluid exchange is currently considered as the new standard for highly efficient renal replacement therapy (RRT), achieving the best extraction of small and middle-sized molecules.

Theranova dialyzer (polyarylethersulfone/ polyvinylpyrrolidone, Gambro Dialysatoren GmbH, Hechingen, Germany) is a novel-generation **MCO** dialyzer designed to remove molecules over 25 kDa. Recent clinical data on the use of **MCO** dialyzer in HD patients have shown efficient removal of β2-microglobulin (11.8 kDa), myoglobin (17 kDa), k free light chains (FLC) (22.5 kDa)1, λFLCs (45 kDa)1 complement factor D (24 kDa)1, and α1-microglobulin (33kDa)1.

OBJECTIVE

The aim of the study was to compare high-flux ol-HDF with the **MCO** dialyzer with respect to removal of small (<500 Da) and medium-sized molecules (>500 Da) and nutritional parameters.

METHODOLOGY

The study was a retrospective analysis of ten stable patients on post-dilution ol-HDF using high-flux dialyzer for at least 6 months. These patients were then switched to HD with the **Theranova**-500™ **MCO** dialyzer (Gambro Dialysatoren GmbH, Hechingen, Germany) for a 6-month period.

Before switching to the **MCO** membrane-HD, all patients were on ol-HDF using a **Polyflux**-210H (Gambro Dialysatoren GmbH, Hechingen, Germany) or an Elisio-21H (Nipro Europe, Zaventem, Belgium) dialyzer.

All patients had negligible residual renal function. Pre-and postdialysis serum levels of small molecules (urea (60.055 Da2), creatinine (113.12 Da3)) and middle-sized molecules (β2-microglobulin (11.8 kDa) and myoglobin (17 kDa)) measured during the first mid-week session on 2-month intervals, were compared in each patient during treatments with ol-HDF and the **MCO** membrane-HD. A total of 28 sessions for each treatment period were available for analysis.

Limitations

Limitations of the study included its retrospective design without randomization, small number of analyzed patients, calculation methods without dialysate concentration measures, and the use of slow-flow methods in patients with catheters.

RESULTS

Safety

There was no statistical significance for mean number of inter-dialytic hypotensive episodes requiring fluid volume expansion between high-flux ol-HDF and the **MCO** membrane-HD period. There were no clinically relevant adverse events reported with use of the **MCO** membrane-HD.

Renal Replacement Therapy Characteristics

There was no significant change between the high-flux ol-HDF and the the **MCO** membrane-HD period regarding blood flow rate, ultrafiltration rate, session length, ionic dialysance, or KT/V monitor. See Table 1.

	High-flux ol-HDF	MCO-HD	p
Blood flow rate (mL/min)*	346 ± 27	338 ± 23	.097
Dialysate flow rate (mL/min)	600	500	NA
Ultrafiltration (L)*	1.79 ± 0.66	1.66 ± 0.71	0.58
Session length (min)*	231 ± 6	233 ± 7	0.52
Ionic dialysance* (mL/min)	217 ± 26	218 ± 30	0.52
KT/V monitor*	1.41 ± 0.2	1.40 ± 0.2	0.165
Convection volume (L)*	2.44 ± 0.2.38	NA	NA

TABLE 1. RRT characteristics. *Data are expressed as mean ± standard deviation (SD). Abbreviations: RRT: renal replacement therapy; ol-HDF, on-line hemodiafiltration; **MCO** membrane-HD, medium-cut off hemodialysis; NA, not applicable. Adapted from Belmouaz et al.

Biological, Nutritional and Inflammatory Parameters

Median serum albumin (65 kDa)1, serum prealbumin, normalized protein catabolic rate (nPCR), c-reactive protein (CRP) levels did not change significantly between the high-flux ol-HDF and the **MCO** membrane-HD period. Median serum β2-microglobulin and myoglobin levels before and after dialysis also did not change significantly between the high-flux ol-HDF and the the **MCO** membrane-HD period. See Table 2.

	High-flux ol-HDF	MCO-HD	p
Albumin (g/L)*	37.8 (5)	38 (6.4)	.029
Prealbumin (mg/L)*	0.28 (0.08)	0.26 (0.14)	.025
nPCR*	0.9 (0.3)	1 (0.4)	0.95
CRP (mg/L)*	8 (9.0)	7 (6.5)	0.35
β_2-microglobulin			
Before*	27.5 (4)	28 (3.0)	0.63
After*	5.6 (1.6)	6.2 (0.9)	0.56
Myoglobin (μg/L)			
Before*	164 (81)	184 (151)	0.67
After*	79 (51)	76 (64)	0.72

TABLE 2. Biological, nutritional, and inflammatory parameters. *Data are expressed as median interquartile rate (IQR). Abbreviations: nPCR, normalized protein catabolic rate; CRP, c-reactive protein; ol-HDF, on-line hemodiafiltration; **MCO** membrane -HD, medium cut-off hemodialysis. Adapted from Belmouaz et al.

Small and Middle-Sized Molecule Removal

Similar urea and creatinine reduction ratios (RRs) of 79% and 71% respectively, were found using both techniques. Other parameters of removal of these small molecules (KT/V, eKT/V, and ionic dialysance) were similar during the high-flux ol-HDF and the **MCO** membrane-HD periods (see Table 3) despite a difference in dialysis flow rate (600 mL/min for high-flux ol-HDF vs 500 mL/min. for the **MCO** membrane-HD. See Table 1.

There was no significant difference between the high-flux ol-HDF and the **MCO** membrane-HD for mean β2-microglobulin and myoglobin RR, as well as mean β2-microglobulin and myoglobin Kd. See Table 3. The similar efficacy of the **MCO** membrane-HD for β2-microglobulin and myoglobin RR are probably related to diffusive transfer, supplemented by uncontrolled convection arising from the process of internal filtration and backfiltration.

	High-flux ol-HDF	MCO-HD	p
eKT/V*	1.49 ± 0.19	1.52 ± 0.19	0.06
Overall reduction ratio (%)			
Urea*	79 ± 4	79 ± 3	0.09
Creatinine*	71 ± 5	71 ± 3	0.26
β_2-microglobulin	81 ± 5	81 ± 6	0.72
Myoglobin*	60 ± 9	61 ± 7	0.59
Overall clearances (mL/min)			
β_2-microglobulin	91 ± 11	84 ± 10	0.24
Myoglobin*	51 ± 10	50 ± 10	0.92

TABLE 3. Small and middle-sized molecule removal. *Data are expressed as mean ± standard deviation (SD). Abbreviations: ol-HDF, on-line hemodiafiltration; **MCO** membrane-HD, medium-cut off hemodialysis. Adapted from Belmouaz et al.

CONCLUSION

This study is the first evaluating efficacy and safety of the **MCO** membrane-HD with the new-generation **Theranova**-500 dialyzer in HD over a 6-month period, showing similar removal for small molecules, β-2 microglobulin and myoglobin when compared to ol-HDF, with good tolerance profile and without modification of nutritional status. In addition, median serum albumin levels did not change significantly between the high-flux ol-HDF and the **MCO** membrane-HD period.

Although the study has several limitations, the **MCO** membrane-HD may provide a useful alternative to high-flux ol-HDF for middle-sized molecule removal. The **MCO** membrane-HD has been suggested to more efficiently remove k and λFLCs than high-flux HD and HDF, which have little impact on the removal of molecules beyond 30 kDa. However, the efficacy of this strategy compared to online high efficiency ol-HDF remains to be assessed by clinical trial.

The use of MCO dialyzer produced similar removal of urea, creatinine, β2-microglobulin and myoglobin as ol-HDF with good tolerance profile and without modification of nutritional status.

References:

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