




LETTER TO THE EDITOR

Protein loss and medium cut-off haemodialysis

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Haemodialysis (HD) with medium cut-off (MCO) dialyzer allows efficient depuration of middleweight uraemic toxins, with albumin loss similar to that observed with post-dilution online haemodiafiltration (HDF) [1, 2]. We recently conducted a randomized, open-label, crossover study [3] that included 40 patients assigned to receive either 3 months of MCO-HD followed by 3 months of high-flux HD (HF-HD) or vice versa. After 3 months of MCO-HD, we observed a significant decrease in serum levels of albumin, 25-hydroxyvitamin D [25(OH)D] and 1,25-dihydroxyvitamin D [1-25(OH)₂D]. Both 25(OH)D and 1-25(OH)₂D circulate bound at 85–90% to vitamin D-binding protein (VDBP) and at 10% to albumin. VDBP, a 52-kDa glycoprotein synthesized predominantly by the liver, has many important functions, including not only transport of vitamin D metabolites, but also control of bone metabolism, binding of fatty acids and modulation of inflammatory response [4]. Alpha-1 acid glycoprotein (AGP), another 41-kDa glycoprotein synthesized by the liver, is a major member of the positive acute-phase protein family with immunomodulatory properties and an important role in the binding of drugs and steroid hormones [5].

In a secondary analysis of the above-mentioned study [3], predialysis serum levels of VDBP and AGP were measured by enzyme-linked immunosorbent assay (R&D Systems Europe, Abingdon, UK) and immunonephelometry (BNII analyzer, Siemens, Marburg, Germany), respectively. In addition, to estimate the solute dialysate appearance, dialysate collection was performed in 15 patients treated with both MCO-HD and HF-HD using a device inserted into the dialysate outlet line at 1 min (T1), 5 min (T5), 60 min (T60) and 180 min (T180). Albumin, 25(OH)D (LIAISON Total Assay, DiaSorin, Stillwater MN, USA) and VDBP concentration were measured in the dialysate at each

selected time. Patients and dialysis characteristics, the sampling description and statistical analysis were previously reported [3].

We showed for the first time a significant decrease in AGP ($P=0.03$) and a trend towards a decrease in VDBP serum predialysis levels ($P=0.05$) after 3 months of MCO-HD. Dialysate analyses during MCO-HD indicated a greater loss of VDBP at T1, T5, T60 and T180, whereas 25(OH)D (threshold $>5\ \mu\text{g/L}$) was more significantly detected with MCO-HD only at T1 and T5. Dialysate albumin concentration was similar between MCO-HD and HF-HD, probably related to a dilution effect or sensitivity of the measurement technique (Table 1).

Low plasma concentrations of albumin, 25(OH)D, VDBP and AGP related to excessive urinary protein excretion occur during nephrotic syndrome [6]. In HD patients, loss of 25(OH)D and VDBP has been suggested using polymethyl methacrylate adsorption membranes [7]. Although improvement in serum albumin levels consecutive to increased liver synthesis has been described after 1–3 months of dialysis with albumin-permeable membranes [8], similar improvement in VDBP and AGP serum levels in patients undergoing MCO-HD remains to be established.

The strong limitation of this report was the partial, non-continuous and non-proportional dialysate collection method. However, our study showed predominant VDBP and 25(OH)D losses in the first 5 min. This probably resulted from the high transmembrane pressure applied within the first 30 min and to the later occurrence of a fouling phenomenon. Since AGP has a molecular weight lower than that of VDBP, one may argue that the decrease in serum AGP levels after 3 months of MCO-HD was also related to AGP loss in the dialysate.

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Table 1. Serum and dialysate parameters after 3 months of HF-HD versus MCO-HD

Parameters	HF-HD	MCO-HD	P-value
Serum collection (40 patients), mean \pm SD			
Predialysis VDBP ($\mu\text{g/mL}$)	335 \pm 62	316 \pm 72	0.0501
Predialysis AGP (g/L)	1.21 \pm 0.34	1.10 \pm 0.30	0.0305
Partial dialysate collection (15 patients)			
VDBP (ng/mL), median (IQR)			
T1	351 (134–421)	1155 (120–1921)	0.0114
T5	168 (59–221)	1314 (865–3023)	0.0002
T60	28 (14–63)	256 (177–405)	0.0002
T180	23 (14–43)	188 (111–232)	0.0046
Detected 25(OH)D (>5 $\mu\text{g/L}$), n (%)			
T1	1 (7)	7 (47)	0.0143
T5	2 (13)	9 (60)	0.0196
T60	1 (6)	1 (6)	NS
T180	0 (0)	1 (6)	NS
Albumin (g/L), median (IQR)			
T1	0.06 (0–0.08)	0.04 (0–0.08)	NS
T5	0.03 (0–0.07)	0.01 (0–0.09)	NS
T60	0.03 (0–0.09)	0.05 (0–0.08)	NS
T180	0.02 (0–0.07)	0.02 (0–0.07)	NS

NS, not significant.

In conclusion, most studies on HD and HDF have focused on albumin loss, but little attention has been paid to the impact of novel dialyzers on other biologically active proteins involved in the binding of hormones and drugs. The long-term consequences of such modifications and their impact on the management of HD patients deserve further evaluation.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare. M.B. reports having received speaker fees from Baxter, but none related to this study. The study did not receive any funding. The results presented in this article have not been published previously in whole or part, except in abstract format.

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