The Medium Cut-Off Membrane Does Not Lower Protein-Bound Uremic Toxins

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BACKGROUND

The concentration of gut-derived protein-bound uremic toxins (PBUTs) is increased in the circulation of patients with chronic kidney disease (CKD) due to alterations caused by uremic conditions. Some PBUTs such as indoxyl sulfate (IS) and p-cresyl sulfate (pCS) are associated with increased cardiovascular disease in CKD.

Even though PBUTs are small (<500 Da), they tend to bind to larger-sized proteins, particularly albumin, and this bound form is difficult to remove by diffusive dialysis. IS and pCS are classified as PBUTs that are strongly bound to albumin (>90%), with a very small fraction as free form.

The kidney primarily removes PBUTs by tubular secretion via organic anion or cation transporters. Conventional hemodialysis (HD) partially replaces glomerular filtration but cannot reproduce tubular function, therefore PBUTs build up in the plasma of patients on HD despite HD therapy. Free forms of PBUTs are easily removed by HD, however they represent a small fraction. Various HD strategies have been investigated to remove PBUTs, for example, prolonged HD duration using nocturnal dialysis eliminated PBUTs to a greater extent. Adding a convective method with hemodiafiltration (HDF) enhanced the removal of middle molecular uremic toxins, but did not consistently remove PBUTs. A recently developed medium cut-off (**MCO** dialyzer) selectively removes larger-sized uremic toxins, but the efficacy of PBUT removal remains unclear.

OBJECTIVE

This study was performed to test the effectiveness of high-flux HD (HF-HD), high-volume post-dilution online HDF (post-OL-HDF), and **MCO** membrane-HD dialysis for removing PBUTs.

METHODS

Study Design

This was a prospective, randomized, cross-over study conducted at three tertiary dialysis centers in Korea.

Participants

The study included adult patients who were anuric, had permanent vascular access, and received maintenance HDF 3x/week for >3 months. Patients were excluded if they had residual urine of more than 100 cc/day, were pregnant, received dialysis with a catheter, had malignancy, congestive heart failure, or hemodynamic instability.

Treatments

Patients received all dialysis treatments: HF-HD, post-OLHDF, and **MCO** membrane-HD 3x/week for three consecutive weeks each. The order in which patients received the treatments was randomly assigned. Plasma and dialysate samples were collected during the mid-week treatment in the third week. The dialysis duration was 4 h, with a dialysate flow of 500 mL/min and a blood flow of 250–320 mL/min. HDF was performed in post-dilution mode with a target convective volume of >23 L.

Characteristics of the dialyzers tested are shown in Table 1. Please note the difference in surface area of the membranes used with the **MCO** membrane having the smallest surface area.

Outcomes

The following plasma levels were measured before and after dialysis:

- Blood urea nitrogen (BUN, 60 Da)
- ƛ-free light chain (ƛ -FLC, 45,000 Da)
- ß2-microglobulin (ß2MG, 11,800 Da)
- Albumin and protein levels

Pre-dialysis serum concentration, post-dialysis concentration, reduction rate (RR), dialysate mass removal and clearance were measured for IS and pCS.

	HF-HD	Post-OL-HDF	MCO-HD
Dialyzer	Fx CorDiax 80	Fx CorDiax 800	**Theranova** 400 dialyzer
Inner diameter (μm)	185	210	180
Wall thickness (μm)	35	35	35
Membrane polymer	polysulphone-PVP blend	polysulphone-PVP blend	polyarylethersulphone-PVP blend
Effective surface area (m2)	1.8	2.0	1.7
Sieving coefficients of albumin	<0.001	<0.001	0.008
Clearance of inulin	135	178	183
UF coefficient (mL/h/mmHg)	64	62	48

PVP, polyvinylpyrrolidone; UF, ultrafiltration.

TABLE 1. The characteristics of the dialyzers