



Randomized Controlled Trial of Medium Cut-Off versus High-Flux Dialyzers on Quality of Life Outcomes in Maintenance Hemodialysis Patients

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BACKGROUND

Patients on maintenance hemodialysis suffer from symptoms such as fatigue, generalized weakness, and pruritus. These subjective conditions are assumed to be related to the accumulation of middle molecules that are not cleared by conventional hemodialysis (HD). Middle molecules have molecular weights (MWs) ranging between 500 and 60,000 Daltons, and their size is a barrier to removal with dialyzers. The accumulation of middle molecules is associated with specific complications such as amyloidosis, inflammatory reactions, oxidative stress, and endothelial dysfunction. Consequently, middle molecules contribute to morbidity and mortality and poor quality of life (QOL) in patients with end-stage renal disease (ESRD).

Compared with high-flux dialyzers and hemodiafiltration (HDF), medium cut-off dialyzers may improve the removal of middle molecules due to their higher permeability and increased convective transport, but clinical data on the effects of **MCO** dialyzers on patient-reported outcomes are lacking.

OBJECTIVE

This study aimed to investigate potential QOL improvement using **MCO** dialyzers in patients undergoing maintenance HD with a high-flux dialyzer. This study also sought to evaluate the effect of **MCO** dialyzers on the removal of middle molecules and pre-dialysis plasma concentrations.

METHODOLOGY

Study Design

This study was a randomized, prospective, controlled, open-label, phase 4 trial in patients treated with maintenance HD at a national university hospital in South Korea. Patients aged 18 years or older, had been receiving maintenance high-flux membrane HD for more than three months, had vascular access by arteriovenous fistula/graft and adequate dialysis were enrolled.

Patients were randomly assigned into **MCO** dialyzer and high-flux groups at 1:1 ratio. Patients and physicians were unblinded to the assignment. The **MCO** dialyzer group switched from a high-flux membrane (Fx CorDiax 60 or 80; Fresenius Medical Care Deutschland, Bad Homburg, Germany) to a **Theranova** 400 dialyzer (Baxter International Inc., Hechingen, Germany) and the high-flux group continued with a high-flux membrane.

Data Collection and Analysis

Patients completed the Kidney Disease Quality of Life-Short Form (KDQOL-SF) questionnaire. Uremic pruritus was assessed using the modified scoring questionnaire consisting of severity, distribution, and sleep disturbance categories. Questionnaires about QOL and pruritus were completed at baseline and at 12 weeks. Blood samples to identify middle molecule removal were obtained before and at the end of dialysis.

Study Outcomes

The primary outcomes were the KDQOL-SF and pruritus assessment. For the KDQOL-SF, analysis identified differences between the **MCO** dialyzer and high-flux groups, pre- and post-dialysis, in the questionnaire's 26 categories. For pruritus assessment, analysis identified differences in questionnaire responses between the two groups, pre- and post-dialysis, on severity and distribution by time of day (morning, afternoon), sleep disturbance, and scoring of responses to a visual analog scale.

The secondary outcomes were pre-dialysis plasma concentrations and reduction ratios (RRs) of middle molecules at baseline and 12 weeks after randomization. Analysis identified differences between the **MCO** dialyzer and high flux groups, pre- and post-dialysis, in levels of three middle molecules: β 2-microglobulin [molecular weight (MW) 11.8 kDa], a small middle molecule, and kappa free light chain [κ FLC] (22.5 kDa) and lambda free light chain [λ FLC] (45 kDa), larger middle molecules.

Study Limitations

This study has several limitations. The sample size was small, and the study duration was insufficient to evaluate definite effects of the **MCO** membrane. The **Theranova** 500 dialyzer, which has a greater surface area (2.0 m²) than the **Theranova** 400 dialyzer (1.7 m²), was not applied in the **MCO** dialyzer group because the **Theranova** 500 dialyzer has not yet been introduced in South Korea. The actual extent of solute removal could not be estimated, or the exact pathophysiologic correlations proven between middle molecules and the physical components of QOL and uremic pruritus.

RESULTS

Patient Characteristics

A total of 50 patients were enrolled and one patient withdrew consent, resulting in 49 patients who completed the study. Twenty-four patients were in the **MCO** dialyzer group and 25 were in the high-flux group. No significant between-group differences in age, sex, body mass index, dry weight, daily urine volume, vascular access, baseline dialyzer, and dialysis vintage were observed.

Comparison of QOL Scores

The baseline perceptions of QOL assessed by the KDQOL-SF were similar in both groups. After 12 weeks, the physical function domain score was better in the **MCO** dialyzer group than in the high-flux group and the role-physical function domain score was also higher in the **MCO** dialyzer group. See Table 1. The effect of the **MCO** dialyzer on QOL is likely related to the better removal of middle molecules compared to high flux dialyzers. The improvements in the physical components of the QOL questionnaire over a relatively short exposure period occurred concurrently with the change of the dialyzer.