Impact of Medium Cut-Off Dialyzers on Patient-Reported Outcomes (PROs): COREXH Registry

Alarcon JC, Bunch A, Ardila F, et al. Impact of Medium Cut-Off Dialyzers on Patient-Reported Outcomes (PROs): COREXH Registry. *Blood Purif* 2020. <u>doi: 10.1159/000508803</u>.

BACKGROUND

Health-related quality of life (HRQoL) is a patient reported outcome (PRO) that considers the subjective point of view of the patient and supports the evaluation of outcomes and healthcare quality. Patients on dialysis experience poor HRQoL due to the symptoms of end-stage renal disease (ESRD) and the physical and psychosocial burdens of their treatments.

The impact of contemporary renal replacement therapies on a patient's perceived HRQoL is critical to treatment success. While hemodialysis (HD) therapy removes small solutes, the removal of larger molecules >25 kDa (often termed large middle molecules) is limited. Hemodiafiltration (HDF) therapy can remove middle molecules more effectively than HD. However, the effect of an improved uremic environment resulting from the clearance of middle molecules remains unclear based on randomized studies.

Advances in membrane technology have led to the development of novel medium cut-off membranes that have enhanced selectivity and increased permeability to conventional and large middle molecules. This results in a steep sieving curve in which the molecular weight retention onset and molecular weight cut-off are very close to each other while remaining lower than that of albumin, mimicking the filtration profile of the native kidney. The application of these membranes in clinical dialysis is known as expanded hemodialysis therapy due to the enhanced clearance of large middle molecules, which are associated with cardiovascular disease, immune modulation, and protein-energy wasting. Initial studies have demonstrated that the **MCO** membrane removes toxins at least as effectively as a hemofilter used in HDF mode. The goal is that this enhanced removal will improve PROs and QoL for dialysis patients.

OBJECTIVE

The goal of this study was to determine the impact of the **MCO** membranes on PROs, including HRQoL, presence and severity of symptoms, as well as diagnostic criteria of restless legs syndrome (RLS) in a large multicentric cohort of patients in the Expanded Hemodialysis Registry Protocol in Colombia (COREXH).

METHODOLOGY

Study Design and Patients

The study was a prospective, multicenter, observational cohort study of 992 patients undergoing dialysis from 12 renal clinics in Colombia who were switched from high-flux HD to **HDx** therapy with **MCO** membrane and observed for 12 months. Patients with chronic kidney disease (CKD) aged 18 or older who had been undergoing HD therapy for more than 90 days at a **Renal Therapy Services** network clinic were invited to participate. Patients received HD therapy using the **MCO** dialyzer (**Theranova**, Baxter, Deerfield, IL, USA) three times a week for a minimum of 4 hours. Patients diagnosed with an active infection within the last 4 weeks or had a life expectancy less than 6 months were excluded. Eligible patients were prospectively followed for 12 months from enrollment.

Assessments

Baseline (before switching to therapy with the **MCO** dialyzer) demographic and disease characteristics were collected. HD treatment parameters, including session duration, number of sessions per week, blood flow, dialysate flow, and type of vascular access were recorded. Baseline values of Kidney Disease Quality of Life 36-Item Short Form Survey (KDQoL-SF36), Dialysis Symptom Index (DSI), and diagnostic criteria for RLS were captured and repeated at 6 and 12 months.

RESULTS

Patient Profile

A total of 992 patients from 12 clinics were included in the baseline, with 638 remaining at 12-month follow-up. Patients had been receiving high-flux HD for a median of 3.7 years at the time of enrollment.

Kidney Disease Quality of Life 36-Item Short Form Survey

After 12 months of therapy with the **MCO** dialyzer, three of five KDQoL domains improved compared with baseline, with the most pronounced improvements found in the kidney disease effects domain. Significant increases in KDQoL-36 mean scores from baseline were also observed for symptoms/problems and burden of kidney disease. No significant changes in scores for mental and physical domains were found (see Table 1). The effect size was modest but consistent across the full 12-month follow up period, suggesting that the expanded clearance of large molecules may be associated with improvements in QoL. In addition, contrary to the expected outcomes for patients receiving chronic dialysis, QoL trended towards improvement over the course of follow-up.

Decreases in the physical and kidney disease components of KDQoL-36 had been associated with increased adjusted mortality risk. The Convective Transport Study (CONTRAST) demonstrated that decreases in physical function, emotional health, and social functioning were significantly associated with mortality over 2 years and were independent of age. Thus, the positive impact of the expanded removal of large middle molecules on QoL measures observed in this study is encouraging.

KDQoL-36 Domain	Statistic	Baseline n = 971	6 months n = 808	12 months n = 642	P value*
Symptoms/problems	Mean	78.6	81.0	81.5	<0.0001
	SD	15.8	15.4	14.9	
Effects of kidney disease	Mean	69.7	72.8	75.1	<0.0001
	SD	22.3	22.0	21.0	
Burden of kidney disease	Mean	46.2	48.9	50.2	<0.0001
	SD	27.5	29.9	32.3	
SF-12 Physical	Mean	41.1	41.0	41.7	0.3
	SD	11.1	11.2	10.5	
SF-Mental	Mean	51.1	51.9	52.3	0.02
	SD	11.6	11.3	11.1	

TABLE 1. Change of Kidney Disease Quality of Life 36-Item Short Form Survey (KDQoL-36) Score Over 12 Months of Follow Up. *For hypothesis testing, type-1 error/p value significance was set at p=0.01. Abbreviation: SD, standard deviation. Adapted from Alarcon et al.

Restless Legs Syndrome Diagnostic Criteria

The proportion of patients meeting RLS diagnostic criteria significantly decreased (54.6%) over the follow-up period. See Figure 1. Combined with the difficulties in correlating uremic toxin removal with RLS occurrence as well as the consistent, yet limited, data indicating HD has minimal impact on RLS, results suggest that the expanded clearance of large middle molecules with the **MCO** membrane comparable with the natural kidney) may alleviate the development and impact of RLS.
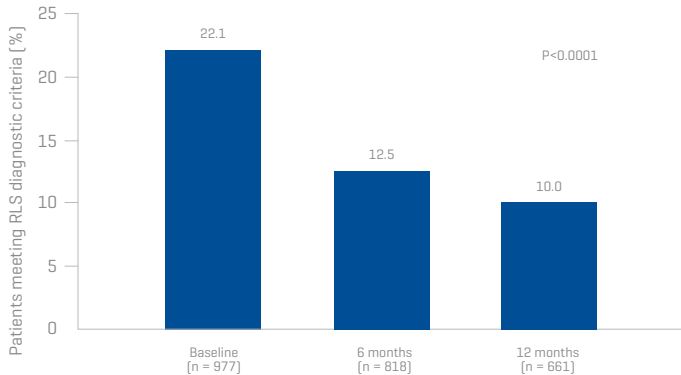
FIGURE 1. Longitudinal Changes in Patients Meeting Restless Legs Syndrome (RLS) Diagnosis over 12 Months of Follow Up. Abbreviation: RLS, restless leg syndrome. Adapted from Alarcon et al.

Dialysis Symptom Index

No significant differences in the mean number of symptoms from baseline were observed at 6- and 12-month follow up. However, a significant decrease in mean severity scores from baseline were observed at 6 and 12 months. See Table 2. All 30 DSI items, each of which target a specific physical or emotional symptom, were reported at a lower frequency at 6 and 12 months than at baseline, with marginally significant reductions in shortness of breath, dizziness/light-headedness, and difficulty falling asleep. The decrease in the proportion of patients with difficulties falling asleep, as well as in the presence of dizziness/light headedness was likely related to improvements in RLS and sleep pattern, which has been previously linked to the clearance of middle molecules in literature.

Strengths and Limitations

The study strengths included its prospective observation, enabling the longitudinal measurement of outcomes and comparison with historical baseline values, and its large cohort of patients (n=992) from multiple clinics. The study limitations included no randomization as a registry, or blinding to the intervention, as well as no comparator group.

DSI Domain	Statistic	Baseline n = 977	6 months n = 813	12 months n = 642	P value
Number of symptoms	Mean	10.3	10.3	10.0	0.1[a]
	SD	6.6	6.7	6.6	
	Mean	9	9	9	
	IQR	10	10	9	NA
Symptom severity score	Mean	30.7	29.9	28.5	0.0009[b]
	SD	22.3	32.0	21.7	
	Mean	26	26	23	
	IQR	32	30	31	NA

TABLE 2. Changes in Dialysis Symptom Index (DSI) Over 12 Months of Follow Up.
a. by Friedman's test. b. by ANOVA. Abbreviations: ANVOA, analysis of variance; DSI: dialysis symptom index; IQR, interquartile range; SD, standard deviation. Adapted from Alarcon et al.

CONCLUSION

Significant improvements were observed in three of the five HRQoL domains measured by KDQol: symptoms/problems; effects of kidney disease; and burden of kidney disease.
A significant decrease was also shown for the percentage of patients meeting the diagnostic criteria for RLS at 12 months. Expanded clearance of large middle molecules provided by the **MCO** membrane (closer to the natural kidney) may be associated with improvements in patient's QoL and may alleviate the development and impact of RLS.

Expanded clearance of large-middle molecular uremic toxins with the **MCO** membrane may improve patient reported kidney disease quality of life outcomes including symptom burden, and Restless Leg Syndrome (RLS) criteria.

The **Theranova** dialyzer is indicated for patients with chronic kidney failure who are prescribed intermittent hemodialysis. It provides an expanded solute removal profile with increased removal of various middle molecules (up to 45 kDa) that may play a pathologic role in the uremic clinical syndrome. The **Theranova** dialyzer is not intended for hemofiltration or hemodiafiltration therapy. The total extracorporeal blood volume for the **Theranova** dialyzer and the set should represent less than 10% of the patient's blood volume. For single use only.

Rx only. For safe and proper use of these devices refer to the Instructions for Use.