



# Medium Cut-Off Dialyzers in a Large Population of Hemodialysis Patients in Colombia: COREXH Registry

Bunch A, Sanchez R, Nilsson LG, et al. Medium cut-off dialyzers in a large population of hemodialysis patients in Colombia: COREXH Registry. *Ther Apher Dial.* 2020; 1-11. doi: 10.1111/1744-9987.13506.

## BACKGROUND

Recent advances in technology have introduced expanded hemodialysis utilizing medium cut-off membranes with high retention onset membranes. The **MCO** membrane easily clears conventional and large middle molecules with acceptable levels of albumin removal (2-4 g/session), which maintains serum albumin levels within the normal range.

Middle molecules, which accumulate during hemodialysis (HD) are considered to be inflammatory mediators. Inflammation also contributes to decreased serum albumin levels. Importantly, a lower serum albumin level is associated with increased mortality. The higher mortality rate associated with low serum albumin levels has been reported to be dependent on inflammation as assessed by high sensitivity C-reactive protein (hsCRP) levels.

**Renal Therapy Services (RTS)** is a nationwide provider in Colombia partially owned by Vantive that serves over 9000 patients who are undergoing HD or peritoneal dialysis. RTS dialysis units provide HD to over 5500 patients, accounting for approximately 29% of patients receiving HD in Colombia.

There is a paucity of longitudinal data regarding the clinical outcomes and safety of the **MCO** membrane, especially in the current practice setting.

## OBJECTIVE

To describe the outcomes and trends in serum albumin levels among a large cohort of patients switched from conventional high-flux HD to **HDx** therapy utilizing an **MCO** membrane and document the long-term safety.

## METHODOLOGY

Expanded Hemodialysis Registry Protocol in Colombia (COREXH) is a prospective, observational, multicenter cohort study of patients undergoing **HDx** therapy in Colombia. Between September 4, 2017 to November 30, 2017 prevalent HD patients (receiving HD therapy for at least 90 days at an RTS renal clinic) were invited to participate in the registry. Patients were required to be at least 18 years of age and receiving **HDx** therapy for a minimum of 4 hours, 3 times per week using an **MCO** membrane (**Theranova** dialyzer, Vantive, Deerfield, IL). Patients with life expectancy less than 6 months or those with an active infection diagnosed within the previous 4 weeks were not invited to participate. Baseline data were obtained of the last seven days before switching to **HDx** therapy and represent the initial state of the patient's health, serum albumin levels, and other laboratory parameters. Patients were prospectively followed for one year from enrollment into the registry.

## RESULTS

### Patients

One thousand (1000) patients at 12 clinics across Colombia were invited to participate. A total of 992 patients met the participation criteria and were included in the intention to treat (ITT) group. The majority (62%) of the patients were men, and at enrollment the mean age was 60 years. Over 90% of the patients had a history of hypertension and nearly 50% had a history of diabetes. Two-thirds (67%) of patients had chronic kidney disease (CKD) attributed to hypertension (28%) or diabetes (39%). A total of 638 patients were eligible for the 1-year follow up assessment.

### Albumin Levels

The cumulative change in serum albumin levels in the ITT population during the follow-up was -1.8%. See Table 1. A total of 468 patients in the per protocol (PP) population had all six serum albumin measurements taken during **HDx** therapy. The changes in serum albumin levels was less pronounced, with an accumulated change of -1.2%. See Table 2.

While a slight decrease in albumin over 12 months of observation was statistically significant in the large cohort study, this should be considered clinically insignificant. At all times, the observed variability of serum levels was within 5% from baseline and the mean serum albumin concentration remained within the normal ranges (3.5-5.5 g/dL).

Follow-up	n	Marginal mean <sup>a</sup> (g/dL)	Change from baseline (%)	Change from previous <sup>b</sup> (%)	Cumulative change(%)
Baseline	992	4.05 (4.04-4.07)	-	-	-
15 days	938	3.98 (3.97-4.00)	-1.7	-1.7	-1.7
1 month	951	4.00 (3.98-4.01)	-1.2	0.3	-1.4
3 months	883	3.91 (3.90-3.93)	-3.5	-2.0	-3.5
6 months	728	3.94 (3.92-3.96)	-2.7	0.7	-2.8
9 months	735	3.94 (3.92-3.96)	-2.7	0	-2.8
12 months	587	3.98 (3.96-4.00)	-1.7	1.0	-1.8

**TABLE 1.** Change in serum albumin levels over time (ITT population). Abbreviation: ITT, intention to treat. <sup>a</sup>Marginal mean is the means estimation based on the fitted model in repeated measures and are presented as 95% confidence interval. <sup>b</sup>The percentual change from the last measurement value Table adapted from Bunch, et al.



Follow-up	n	Marginal mean <sup>b</sup> (g/dL)	Change from baseline (%)	Change from previous <sup>c</sup> (%)	Cumulative change(%)
Baseline	468	4.03 (4.01-4.05)	-	-	-
15 days	468	4.00 (3.98-4.02)	-0.9	-0.9	-0.9
1 month	468	3.98 (3.96-4.00)	-1.3	-0.4	-1.3
3 months	468	3.93 (3.91-3.95)	-2.7	-1.4	-2.7
6 months	468	3.95 (3.93-3.97)	-2.0	0.7	-2.0
9 months	468	3.96 (3.94-3.98)	-1.9	0.0	-2.0
12 months	468	3.99 (3.97-4.01)	-1.2	0.8	-1.2

**TABLE 2.** Change of serum albumin levels over time (PPa). Abbreviation: PP, per-protocol defined as patients who received all treatments with the **MCO** membrane during the follow-up period or until hospitalization that involved >12 dialysis sessions without the **MCO** membrane or death. <sup>a</sup>Only patients in the PP population who had baseline and all six scheduled serum albumin measurements during **HDx** therapy were included in the analysis. <sup>b</sup>Marginal mean is the means estimation based on the fitted model in repeated measures and are presented as 95% confidence interval. <sup>c</sup>The percentage change from the last measurement value. Table adapted from Bunch et al.

While a slight decrease in albumin over 12 months of observation was statistically significant in the large cohort study, this should be considered clinically insignificant. At all times, the observed variability of serum levels was within 5% from baseline and the mean serum albumin concentration remained within the normal ranges (3.5-5.5 g/dL).

### Patient Outcomes

Seventy-four (8%) patients died during 866 patient-years (PY) of follow-up; the mortality rate was 8.54 deaths/100 PY (95% confidence interval (CI), 6.8-10.7). There were 673 hospitalization events with a rate of 0.79 events/PY (95% CI, 0.73-0.85) with 6.91 hospital days/PY (95% CI, 6.74-7.09). The observed mortality rate, hospitalization rate, and number of hospital days were lower than previous experiences with the **RTS Network** in Colombia.

### Dialysis Parameters

**HDx** therapy adequacy, as measured by single-pool Kt/V and serum phosphorus. Single pool Kt/V was 1.68, which is considered a very good level of adequacy for small-molecule reduction and is well above the minimum 1.2 Kt/V per HD session for patients treated 3x weekly, as is recommended by the (US) National Kidney Foundation's Kidney Disease Outcomes Quality Initiative. Serum phosphorus levels remained relatively constant throughout the 12 months, with a mean of 4.55 mg/dL at month 12, which is below the recommended level of 5.5 mg/dL.

### Safety

During the follow-up period, there were 1019 adverse events during 866 person-years of follow-up for a rate of 1.18 adverse events (AE) per PY (95% CI, 1.10-1.25). For comparison, 130,601 sessions were performed with **MCO** membranes. A total of 667 (66.4%) AEs were serious, and of these, 91 (8.9%) resulted in withdrawal from the study. No AEs during **HDx** therapy were deemed related to **MCO** membrane use, according to investigator and techno-surveillance evaluation. AEs numbering 146 were deemed related to the dialytic procedure, which represents 0.17 events per PY (95% CI, 0.14-0.20), equivalent to 1.12 events per 1000 HD sessions (95% CI, 0.90-1.30).

### Strengths and Limitations

Strengths of the present study include the prospective collection of current practice data, an analysis of nearly 1000 patients undergoing **HDx** therapy, over 130,000 sessions performed, with baseline information and a follow-up for 12 months. Limitations of the study include the absence of a comparison group, which diminishes the strength of adjudging causality to the observed effects. A positive selection bias cannot be excluded, although given the large number of patients and renal clinics involved, it does not appear that the population in this analysis differs much from the general prevalent HD population in the **RTS Network** in Colombia.

### CONCLUSIONS

No adverse events were related to the **MCO** membrane. **HDx** therapy using an **MCO** membrane maintains serum albumin levels within the normal range among patients undergoing expanded hemodialysis with nonoccurrence of dialyzer related adverse effects.

**The MCO membrane is safe and preserves serum albumin levels within the normal range among patients undergoing HDx therapy.**