Impact of expanded hemodialysis using medium cut-off dialyzer on quality of life: application of dynamic patient-reported outcome measurement tool

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BACKGROUND

Many patients with chronic kidney disease (CKD) have retained toxins, particularly larger molecular weight toxins, despite maintenance hemodialysis (HD). These toxins have been associated with cardiovascular disease, chronic systemic inflammation, and increased mortality. Not surprisingly, patients receiving maintenance HD often report significant symptom burden and impaired health-related quality of life (HRQoL). To address this need, medium cut-off dialyzers have been developed that offer the opportunity to remove middle-molecular-weight molecules without removing essential proteins such as albumin and without the need for high-flux hemodiafiltration and its added requirements of infrastructure, costs, and patient selection criteria. Patient-reported outcome measures (PROMs) may help guide clinicians in determining when traditional HD has not sufficiently managed patient symptoms and improved their HRQoL. Theoretically, the use of a rapid, relevant, and repeated PROM tool could guide clinical decisions about the most appropriate dialyzer for a specific patient. The London Evaluation of Illness (LEVIL), is such a PROM instrument. Developed with user input, this tool measures well-being, energy level, sleep quality, bodily pain, appetite, and shortness of breath using visual analog scales. LEVIL takes only seconds to complete, provides real-time monitoring, allows a 24-hour recall period, and is intended for repeated use. An initial study has proven that LEVIL is easy to use, acceptable to patients, and sensitive to clinical changes in the short- and long-term.

OBJECTIVE

This pilot study's main purpose was to establish whether expanded hemodialysis utilizing medium cut-off dialyzers may be associated with changes in HRQoL/symptom burden, whether there may be a dose-dependent response, and whether effects were durable over time, as assessed using LEVIL.

METHODOLOGY

This single-center, unblinded, exploratory pilot study was conducted in the prevalent adult HD population within the London Health Sciences Centre Renal Program in Ontario, Canada. All patients had been receiving thrice-weekly HD for > 3 months. During the 2-week baseline period, patients completed the app-based LEVIL assessment during each of their usual high-flux dialyzer sessions. During the 12-week test period, patients completed LEVIL while receiving HD with a medium cut-off dialyzer that maintained the surface area of the membrane that had been used during the baseline period (i.e., smaller-surface-area dialyzers converted to **Theranova** 400 dialyzer; larger surface dialyzers to **Theranova** 500 dialyzer). Blood work included complete blood cell count, electrolytes, C-reactive protein, β2-microglobulin (B2M), κ- and λ-free light chains (K-FLC, L-FLC), and the free light chain ratio.

A 24-week extension was planned to include a washout phase and a return to high-flux HD for 8 more weeks.

Dialysis treatments were delivered using Fresenius 5008 dialysis monitors, with treatment times between 3.5 and 4 hours. Net ultrafiltration was calculated on an individual basis according to each patient's ideal dry weight. Dialysis prescriptions were unchanged except for the switch between high-flux polysulfone dialyzers and **HDx** therapy. Patients answered 6-question LEVIL surveys via iPad app during each dialysis session. Each participant's LEVIL scores during the first two weeks (i.e., baseline) were averaged to create a collective baseline score that was used to stratify patients into those with high- or low-HRQoL scores. High HRQoL scores were those with an overall average score ≥70; determination of an "acceptable" HRQoL score was based on a survey of 11 study patients.

Primary outcomes were changes in HRQoL and symptoms when patients were treated with **HDx** therapy vs baseline conventional high-flux HD. Secondary outcomes included middle-molecule biomarkers and middle-molecule reduction ratios.

RESULTS

Study Population

Twenty-eight patients consented to participate. One died before study initiation, another died of overwhelming sepsis during the study, one patient was removed due to poor dialysis attendance, and three patients withdrew consent, leaving 22 patients to be analyzed over 12 weeks. Due to limited patient access during the COVID-19 pandemic, only 6 patients were able to complete the 24-week extension program.

Participants' mean age was 65.6 ±14.6 years, with a median time on HD of 55 months. Half of the participants were men, 41% had diabetes mellitus type 2, and 41% of patients had some degree of residual kidney function. Half of the population was treated with **Theranova** 400 dialyzer, half with **Theranova** 500 dialyzer.

Stratification

Sixteen of 22 patients (73%) had a low overall HRQoL baseline. Figure 1A shows how individual participants' HRQoL fell on what survey participants deemed "acceptable" or "unacceptable" for HRQoL scores. Figure 1C shows, at baseline, how many participants had "low" vs "high" HRQoL scores for each domain. Note, for example, that none of the participants ranked energy levels as being at a high HRQoL level. When domain sub-analyses are shown, high and low QoL classifications refer to baseline rankings specific to that domain.

HR-QoL Changes

For the overall HRQoL, the 16 patients with "low" initial overall HRQoL scores and the 6 patients with high initial scores (as shown in Figure 1C) are tracked in Figure 1B and in Table 1 as they received 12 weeks of **HDx** therapy:

- **Low HRQoL group:** The average HRQoL among those with low initial HRQoL increased significantly from baseline to week 8 ($P = 0.001$) and week 12 ($P = 0.001$).
- **High HRQoL group:** Patients who had high initial HRQoL saw no significant changes in HRQoL throughout the study.