The Effect of Increasing Dialysis Dose in Overweight Hemodialysis Patients on Quality of Life: A 6-Week Randomized Crossover Trial

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Background: Using standard hemodialysis regimens, overweight patients often do not reach Kidney Disease Outcomes Quality Initiatives (KDOQI) Kt/V targets, and this has been associated with lower health-related quality of life (HRQL). Whether increasing dialysis adequacy in large patients not achieving KDOQI targets improves HRQL is unknown.

Study Design: Randomized blinded crossover study.

Setting & Participants: Overweight (>80 kg) underdialyzed patients from 6 dialysis units in 2 Canadian dialysis programs.

Interventions: Six-week treatment periods with a standard dialysis regimen (4 hours 3 times weekly) and 3 augmented regimens: 4.5 hours of hemodialysis, 4 hours of hemodialysis with increased dialysate flow, and 4 hours of hemodialysis with 2 dialyzers in parallel.

Outcomes & Measurements: The End-Stage Renal Disease Symptom domain of the Kidney Disease Quality-of-Life Short-Form questionnaire (primary outcome) and the Health Utilities Index Mark 2 (secondary outcome).

Results: We enrolled 18 patients (mean weight, 109.7 ± 16.2 [SD] kg); 12 completed all 4 regimens. Mean Kt/Vs during the study were 1.27 (95% confidence interval [CI], 1.19 to 1.35), 1.41 (95% CI, 1.32 to 1.50), 1.31 (95% CI, 1.22 to 1.39), and 1.41 (95% CI, 1.33 to 1.49) for patients receiving standard dialysis, 4.5 hours of hemodialysis, hemodialysis with increased dialysate flow, and hemodialysis with 2 dialyzers, respectively. Kidney Disease Quality-of-Life End-Stage Renal Disease Symptom domain and Health Utilities Index Mark 2 scores were 75.9 (95% CI, 70.7 to 81.2) and 0.69 (95% CI, 0.56 to 0.81) for patients receiving standard dialysis, respectively. These did not differ when patients received the 3 augmented dialysis regimens ($P = 0.2$ and $P = 0.5$, respectively).

Limitations: Small sample size and inability to fully blind patients to the treatment they were receiving.

Conclusion: Improving hemodialysis adequacy for large underdialyzed patients did not lead to improved HRQL. Our findings suggest that augmentation of the dialysis regimen is not required for these patients in the absence of overt uremic symptoms.

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INDEX WORDS: Overweight; dialysis adequacy; 2 dialyzers in parallel; Health Utilities Index Mark 2 (HUI2); Kidney Disease Quality of Life Short Form (KDQOL-SF).

The prevalence of obesity is increasing in patients with end-stage renal disease (ESRD),[1] mirroring well-described trends in the general population. Kidney Diseases Outcomes Quality Initiatives (KDOQI) guidelines for dialysis adequacy recommend that delivered single-pool Kt/V be at least 1.2 in patients receiving thrice-weekly hemodialysis.[2] For the increasing number of obese patients on dialysis therapy, achieving this adequacy target is challenging.[3,4] Observational studies indicated that underdialysis (ie, single-pool Kt/V < 1.2) was associated with lower health-related quality of life (HRQL)[5] and other adverse health outcomes, including greater mortality.[6-11]

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It is uncertain whether improving Kt/V from less than 1.2 to greater than 1.2 will result in improvement in clinical outcomes, including HRQL. In the largest prospective study to date, the Hemodialysis (HEMO) Study investigators did not find a mortality benefit comparing a standard dialysis regimen (single-pool Kt/V of 1.25) and a high-dose dialysis regimen (single-pool Kt/V of 1.65).[12] In the HEMO Study, investigators also measured HRQL and did not find clinically significant differences between the standard-dose and high-dose groups.[13] However, patients in the HEMO Study were smaller (mean weight, 69 kg), received shorter dialysis runs on average at baseline, and, to be eligible for the study, had to be able to achieve a minimum equilibrated Kt/V of 1.3 during patient screening. Moreover, mean baseline Kt/V for patients in the HEMO Study was 1.43, and very heavy patients were excluded on the basis of these eligibility criteria.[12]

For underdialyzed patients, less information is available about the impact of improving Kt/V on HRQL. In a prospective unblinded crossover study of 14 large patients, improving Kt/V from 1.16 to 1.34 by using 2 dialyzers in parallel was associated with improved HRQL, measured by using the 36-Item Short-Form Health Survey (SF-36).[14]

There are several potential methods for improving Kt/V in patients who remain underdialyzed despite optimizing their dialysis care within a 4-hour thrice-weekly regimen. Dialysate flow can be increased to greater than 500 mL/min,[15,16] dialysis time can be extended to longer than 4 hours, or patients can be dialyzed using 2 dialyzers in parallel[14,17] or 2 dialyzers in serial.[17,18] Increasing dialysate flow rates is simple, but its impact on dialysis adequacy is limited.[15] Extending the dialysis session is widely practiced in many dialysis centers; however, this often creates difficulty given the current shortage of nurses and dialysis stations in Canada and the requirement to provide 3 dialysis sessions daily in most dialysis units.[19] Use of 2 dialyzers either in parallel or serial can improve delivered Kt/V.[14,17] Importantly, the question of whether improving Kt/V by using any of these methods leads to improved HRQL requires additional study.

Given these uncertainties, we sought to determine whether improving small-solute clearance by using any of these strategies was associated with improved HRQL in large hemodialysis patients with a history of inadequate dialysis adequacy.

METHODS

Patients

We performed a randomized crossover study in 6 dialysis units affiliated with the University of Calgary and University of Alberta. Inclusion criteria were as follows: patients on a stable regimen of hemodialysis for 3 months or longer, dry weight of 80 kg or greater, Kt/V of 1.2 or less on 2 occasions in the previous 6 months or requirement for longer than 12 h/wk of hemodialysis because of a history of inadequate dialysis, and blood flow rate of 350 mL/min or greater through a well-functioning access. Patients were excluded if they had renal transplantation scheduled in the next 6 months, had a contraindication to intradialytic anticoagulation, required longer than 4½ hours of hemodialysis 3 times weekly for the purpose of volume removal because of excessive interdialytic weight gains or intradialytic hypotension/cramping, and failure to provide informed consent. All patients who met inclusion/exclusion criteria and were not already receiving a hemodialysis regimen consisting of 4 hours 3 times weekly were switched to this modality for 4 weeks before entry into the active treatment part of the study.

Study Design

During the study period, each patient received 4 different dialysis modality regimens in a randomized crossover fashion, each lasting 6 weeks. A 6-week duration for each strategy was chosen for convenience and because it previously was suggested that HRQL can change during the course of only 4 weeks in patients receiving increased dialysis adequacy.[14] Although a formal washout period was not included between study periods, because each treatment was administered for 6 weeks and outcomes were measured in the final week of the treatment, it could be considered that we allowed time for washout to occur between treatments. To permit blinding of patients to dialysis treatment modality, all dialysis sessions were 4.5 hours; for the 3 strategies that included active dialysis for only 4 hours, dialysate flow was stopped and no dialysis occurred for the last ½ hour of the run. The standard hemodialysis prescription consisted of 4 hours of hemodialysis 3 times weekly. Hemodialysis was undertaken using a high-flux high-efficiency polysulfone dialyzer (ie, F80A dialyzer; Fresenius Inc, Walnut Creek, CA, or equivalent) with a blood flow of 350 to 400 mL/min and dialysate flow of 500 mL/min. During the increased dialysate flow treatment, patients received standard dialysis for 4 hours 3 times weekly, but dialysate flow rate was 800 mL/min, rather than 500 mL/min. The third modality was increased dialysis time at 4½ hours 3 times weekly. Last, in the final dialysis modality consisting of 2 dialyzers in parallel, patients received hemodialysis for 4 hours 3 times