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CLINICAL RESEARCH

A Pilot Study on the Safety and Adequacy of a Novel Ecofriendly Hemodialysis Prescription–Green Nephrology

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Introduction: Hemodialysis (HD) units require large quantities of water. To reduce water consumption without compromising the adequacy and safety of dialysis, we studied a novel HD prescription with high temperature and low flow dialysate.

Methods: This was a single-center nonrandomized open-label cross-over pilot trial in patients with end-stage kidney disease on maintenance HD. Each participant was subjected to 3 different dialysis prescriptions for 1 month each as follows: (i) normal temperature with normal flow dialysate (NTNF prescription), (ii) high temperature with normal flow dialysate (HTNF prescription), and (iii) high temperature with low flow dialysate (HTLF prescription). The primary outcome, assessed at the end of each dialysis session, was the delivery of "adequate" dialysis, as defined by a single-pool Kt/V (spKt/V) ≥1.2. Outcomes were evaluated by comparing the NTNF and HTLF prescriptions.

Results: A total of 863 sessions of HD were performed in 30 patients over 3 months, with 287 to 288 sessions in each of the 3 dialysis prescriptions. The primary outcome was not significantly different between the NTNF prescription (202 sessions [70.14%]) and the HTLF prescription (198 sessions [68.75%]) (odds ratio, 1.07; 95% confidence interval, 0.75 to 1.52; $P = 0.45$). The mean spKt/V and urea reduction ratio (URR) were not significantly different. Clinically evident hemodynamic instability occurred in only 1 dialysis session in the HTNF prescription.

Conclusion: Increasing dialysate temperature while reducing dialysate flow rate (Q_D) can be used as a water conservation strategy without compromising the adequacy and safety of dialysis in young and hemodynamically stable patients. Reducing the Q_D from 500 ml/min to 300 ml/min reduces water consumption by 40%.

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HD is the most widely used mode of kidney replacement therapy. Worldwide, 89% of patients with end-stage kidney disease receive HD.[1] In recent years, HD services have expanded considerably in low and low-middle-income countries. However, HD is a resource-intensive therapy, utilizing large quantities of water and power, and generating significant biomedical waste. On average, a 4-hour session of HD using a dialysate flow rate (Q_D) of 500 ml/min would require 120 litres of purified water.[2]

With increasing emphasis on the concept of "Green dialysis," a number of dialysis facilities use the reject water for irrigation, laundry, and sanitation, or for the generation of steam for sterilization of hospital instruments. Even the spent dialysate is recycled with reverse osmosis and nano filters and made suitable for irrigation.[3]

Solute clearance in conventional HD primarily depends on the blood flow rate, Q_D, and the K_0A of the dialyzer. Any increase in solute clearance therefore requires up-titration of 1 of these 3 parameters, or an increase in the treatment time.

Reduction in the Q_D could result in substantial water conservation. Lowering the Q_D, however, reduces the delivered spKt/V.[4] We hypothesized that this could be

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counterbalanced by raising the temperature of the dialysate. We therefore conducted a trial to study the safety and adequacy of a dialysate prescription with HTLF, as compared with NTNF.

METHODS

Trial Design

This was a single-center non-randomized open-label cross-over pilot trial in which 3 different HD prescriptions were compared in patients with end-stage kidney disease on maintenance HD. The study was conducted at the Institute of Nephrology, Madras Medical College, India, between February and June 2022, approved by the Institutional Ethics Committee, and registered in the Clinical Trials Registry of India (CTRI/2022/01/039108). All patients provided written informed consent for participation in the study.

Participants

Eligible patients had end-stage kidney disease and were undergoing twice-weekly or thrice-weekly maintenance HD through an arteriovenous fistula. Patients were ineligible if they had an ejection fraction of less than 40%, recurrent intradialytic hypotension, clinical evidence of autonomic neuropathy, or if they had been on dialysis for less than 3 months.

Run-In Period and Dialysis Protocols

After enrollment, patients underwent a run-in phase of 1 month, whereby all patients had their dry weights optimized and their antihypertensive medication titrated. Any patient who developed recurrent intradialytic hypotension during this period was excluded from the study.

All patients underwent twice-weekly or thrice-weekly 4-hour dialysis sessions with a Fresenius 4008S HD machine and a Fresenius F6HPS polysulfone dialyzer (surface area 1.3 m^2, K_{UF} 13 ml/hr/mm Hg, K_0A 731 ml/min). The dialysis unit was air-conditioned, with the temperature set to 25 ^{o}C. The blood flow rate was kept at 300 ml/min for all the sessions, and unfractionated heparin was used for anticoagulation. Dialyzers were reused for up to 8 sessions but were discarded earlier if the fiber bundle volume was $<$80%. Patients received intravenous iron sucrose, subcutaneous erythropoietin, and oral phosphate binders, as required, for the duration of the trial.

The temperature of the patient was measured at the beginning and end of the dialysis session using a noncontact infrared thermometer (Beurer infrared thermometer FT65). Pre-dialysis and post-dialysis blood pressure and temperature were recorded, and automated blood pressure monitoring (using the Fresenius 4008S HD machine blood pressure module) was done every 30 minutes throughout the dialysis session. All adverse events that occurred during the dialysis session were recorded.

Interventions

Each participant was sequentially subjected to 3 different dialysis prescriptions, with each prescription lasting for 1 month (i.e., 8–12 sessions of dialysis, depending on whether the patient was on twice-weekly or thrice-weekly dialysis). The prescriptions studied were as follows:

(i) NTNF prescription: dialysate temperature of 37 ^{o}C, with a Q_D of 500 ml/min
(ii) HTNF prescription: dialysate temperature of 38.5 ^{o}C, with a Q_D of 500 ml/min
(iii) HTLF prescription: dialysate temperature of 38.5 ^{o}C, with a Q_D of 300 ml/min

All participants received the NTNF, HTNF, and HTLF prescriptions for 1 month each, in that order. Because there is unlikely to be a carry-over effect for the primary outcome that was studied (see below), there were no washout periods between crossovers.

Monitoring of Dialysis Adequacy

Adequacy of dialysis was monitored using the spKt/V and the urea reduction ratio (URR), during every session of dialysis, for the entire 3-month period when the study was conducted.

To calculate the URR, blood samples for urea measurement were taken pre-HD and post-HD in every dialysis session. The pre-HD blood sample was taken from the arterial sampling port of the dialysis circuit at the start of the dialysis session. The post-HD blood sample was taken 30 minutes after the end of the 4-hour dialysis session, through the dialysis access (the venous needle was retained *in situ* for 30 minutes after completion of dialysis, to facilitate sampling). The URR was calculated using the formula:

$$URR = (1 - [C_t / C_0]) \times 100$$

(where C_t and C_0 are the post-dialysis and pre-dialysis blood urea levels[5])

The spKt/V was estimated using the online clearance monitoring tool on the Fresenius 4008S HD machine, which measures the effective ionic dialysance of sodium during the dialysis session.[6] The total body water or urea distribution volume, which is required for online clearance monitoring, was estimated using Watson's formula.[7]

Outcomes

The primary outcome, assessed at the end of every dialysis session, was the delivery of "adequate" dialysis, as defined by a spKt/V $\geq$1.2. Secondary outcomes

studied were the absolute achieved spKt/V and URR at every dialysis session, the change in body temperature and systolic blood pressure during every dialysis session, and the occurrence of any hospitalization or death during the study period.

Prespecified Exploratory Analysis

The primary objective of the study was to compare the NTNF and HTLF prescriptions. However, the HTNF prescription was included in the protocol to serve as a proof-of-concept that raising the dialysate temperature would improve clearance. It was hypothesized that the clearance achieved (in terms of spKt/V and URR) would be higher with the HTNF prescription than with the NTNF prescription due to the effect of a high dialysate temperature. Similarly, it was hypothesized that the clearance achieved would be lower with the HTLF prescription than with the HTNF prescription due to the low Q_D. Appropriate statistical tests were therefore used to make these comparisons.

Sample Size

We assumed that 90% of sessions with the NTNF prescription would achieve an spKt/V of ≥1.2, and that 80% of the sessions with the HTLF prescription would achieve an spKt/V of ≥1.2. It was calculated that 199 sessions of dialysis would be required in each arm, in order to achieve a power of 80% with an alpha error of 5%, to detect a difference of 10% in the proportion of dialysis sessions achieving an spKt/V >1.2 between the treatment and control arms. Assuming an attrition rate of 10%, the final sample size was calculated to be 219 dialysis sessions in each arm. With a minimum of 8 sessions of HD per subject in a month, it was planned to recruit 30 patients.

Statistical Methods

Quantitative variables were expressed as mean±SD or median (interquartile range) and categorical variables were expressed as number (percentage). Statistically significant differences between dialysis prescriptions were assessed using the McNemar's test for categorical variables and the one-way repeated measures analysis of variance for quantitative variables. Because all sessions except one were completed as assigned, a per-protocol analysis was done. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Enrollment and Patient Characteristics

A total of 30 patients were enrolled in the trial (Figure 1), with a mean age of 37 ± 12 years, and 83% of them were men. They had a median dialysis vintage of 38 months (±27) at the time of enrollment. The

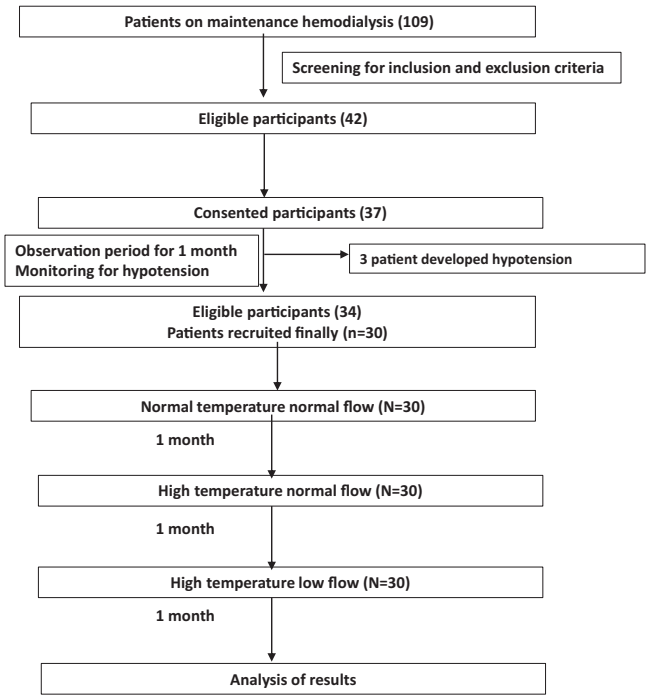

Figure 1. Participant flow diagram.

baseline characteristics of the enrolled patients are described in Table 1 and Supplementary Table S1. A total of 863 sessions of HD were performed on 30 patients over 3 months. Of these, 288 sessions were with the NTNF prescription, 287 sessions with the HTNF prescription, and 288 sessions with the HTLF prescription. The clinical characteristics of the patients during the 3 prescriptions are described in Supplementary Table S2. There was no loss to follow-up during the study period.

Primary and Secondary Outcomes

The primary outcome, defined as the delivery of an spKt/V ≥1.2, was achieved in 202 sessions (70.14%)

Table 1. Baseline characteristics of the study population

Characteristics	Total (*N* = 30)
Age, yr, mean±SD	37 ± 12
Male gender, *n* (%)	25 (83)
Type of AV access, *n* (%)	
• Radiocephalic fistula	22 (73.3)
• Brachiocephalic fistula	8 (26.6)
Dialysis vintage, months, median (IQR)	36 (18–60)
Patients receiving thrice-weekly dialysis, *n* (%)	12 (40)
Diabetes mellitus, *n* (%)	4 (13)
Hypertension, *n* (%)	26 (87)
Systolic BP, mm Hg, mean±SD	156 ± 22
Diastolic BP, mm Hg, mean±SD	90 ± 10
Hemoglobin, g/dl, mean±SD	8 ± 1.6
Albumin, g/dl, mean±SD	3.3 ± 0.3
Ejection fraction, %, mean±SD	57 ± 6
Urea distribution volume, L, mean±SD	34 ± 7

AV, arteriovenous; BP, blood pressure; IQR, interquartile range.

Table 2. Analysis of the primary outcome

Primary outcome	NTNF prescription (n = 288)	HTLF prescription (n = 288)	Odds ratio (95% CI)	P-value
Dialysis sessions with spKt/V ≥1.2	202 (70.14%)	198 (68.75%)	1.07 (0.75 to 1.52)	0.45

CI, confidence interval; HTLF, high temperature low dialysate flow; NTNF, normal temperature, normal dialysate flow; spKt/V, single-pool Kt/V (by online monitoring).

with the NTNF prescription, and in 198 sessions (68.75%) with the HTLF prescription (odds ratio, 1.07; 95% confidence interval, 0.75 to 1.52; $P = 0.45$) (Table 2).

The secondary outcomes were compared between the NTNF prescription and the HTLF prescription and are described in Table 3. There was no significant difference in the achieved mean spKt/V or mean URR between the 2 prescriptions (Figures 2 and 3). There was a mean increase in body temperature with the HTLF prescription by 0.066 °C (95% confidence interval, 0.040 to 0.093; $P < 0.001$). The change in systolic blood pressure during the dialysis session was not different between the 2 groups.

Safety

One session with the HTNF prescription was terminated due to symptomatic hypotension. No other clinically significant hypotensive episodes or serious adverse events were noted. None of the patients volunteered any sensations of discomfort or warmth during the dialysis sessions.

Prespecified Exploratory Analyses

All 3 dialysis prescriptions were compared with each other in terms of the primary and secondary outcomes, and the results are presented in Table 4. Notably, the results of this prespecified exploratory analysis are compatible with our initial hypothesis as discussed in the Methods section, that raising the dialysate temperature increases clearance.

DISCUSSION

This cross-over study suggests that urea clearance was not significantly different between the HTLF prescription as compared to NTNF. The HTLF prescription's advantage is that reducing the Q_D from 500 ml/min to 300 ml/min reduces water consumption by 40%. For a single 4-hour dialysis session, the requirement of purified water is reduced from 120 l to 72 l. If this were to be extrapolated to an average dialysis unit with 3 shifts of 10 patients each, the daily requirement of purified water is reduced from 3600 l to 2160 l, thus saving 1440 l of water per day. Assuming that the reverse osmosis membrane operates at a ratio of rejection water to purified water of 3:1, then the amount of raw water saved per day increases to 4320 l. Additional indirect benefits would include a reduction in the energy consumed by the reverse osmosis water pump; as well as an improvement in the life of the pretreatment filters, micron filters, and even the reverse osmosis membrane (because this is directly related to the quantum of water processed), all of which ultimately impact the carbon footprint.

The mechanism by which raising dialysate temperature improves urea clearance is currently unknown; however, there are several plausible explanations. First, increasing the temperature of a fluid would increase the Brownian movement of the particulate matter contained within it.[8] In HD, this would increase the bombardment of molecules on the dialyzer membrane, thus increasing diffusion across the membrane and resulting in an increased clearance of low-molecular-weight solutes.[9] Second, higher temperatures have been shown to reduce total peripheral vascular resistance, and this is largely accounted for by an increase in skin blood flow, from 250 ml/min in normothermic environments to up to 8 l/min in conditions of severe heat stress.[10] The skin contains 10% to 15% of the total body water, and hence urea. Thus, better perfusion would be expected to reduce urea compartmentalization and thereby increase clearance.[11] Third, increasing

Table 3. Analysis of the secondary outcomes

Secondary outcomes	NTNF prescription (n = 288)	HTLF prescription (n = 288)	Mean difference (95% CI)	P-value
Mean spKt/V	1.32 ± 0.24	1.31 ± 0.25	−0.003 (−0.012 to 0.007)	0.57
Mean URR	68.15 ± 6.58	68.17 ± 5.35	0.018 (−0.545 to 0.582)	0.95
Difference between predialysis and postdialysis body temperature, °C, mean±SD	0.06 ± 0.16	0.12 ± 0.15	0.066 (0.040 to 0.093)	<0.001
Difference between predialysis and postdialysis systolic blood pressure, mm Hg, mean±SD	4.51 ± 9.13	4.38 ± 8.11	−0.139 (−1.50 to 1.22)	0.84
Difference between predialysis and postdialysis diastolic blood pressure, mm Hg, mean±SD	3.23 ± 6.05	2.99 ± 5.67	−0.24 (−1.22 to 0.732)	0.62
Hospitalization or death	0	0	-	-

CI, confidence interval; HTLF, high temperature, low flow dialysate; NTNF, normal temperature, normal flow dialysate; spKt/V, single-pool Kt/V (by online monitoring); URR, urea reduction ratio.

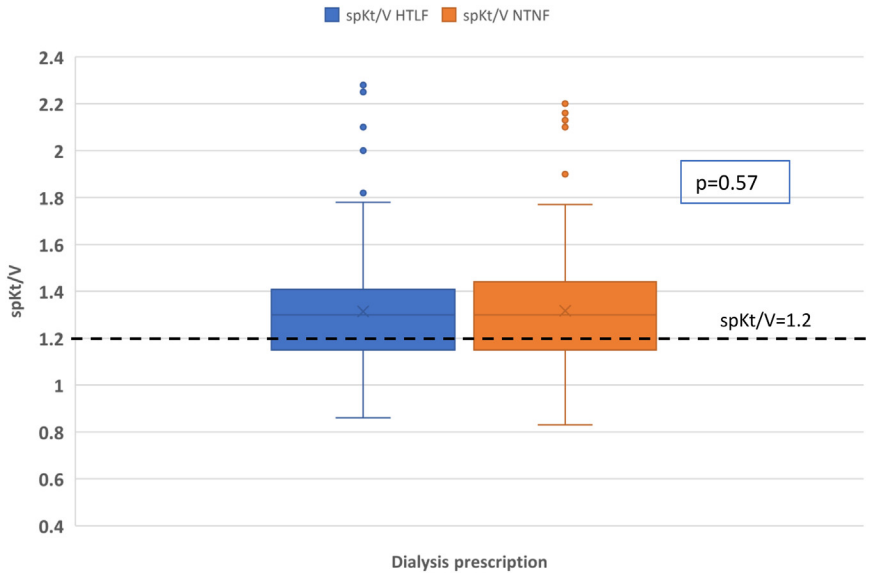

Figure 2. Box and whisker plot comparing the achieved spKt/V between HTLF and NTNF prescriptions. HTLF, high temperature, low flow dialysate; NTNF, normal temperature, normal flow dialysate; spKt/V, single-pool Kt/V (by online monitoring).

dialysate temperature may reduce the viscosity of the blood, favoring diffusive transport, as predicted by the Stokes-Einstein equation.[12]

To clarify whether the increase in solute clearance takes place due to increased urea diffusion at the dialyzer or due to mobilization of compartmentalized urea through peripheral vasodilation, requires the application of mathematical equations (viz. the Michaels equation[13] that relates Q_D and clearance, and the Stokes-Einstein equation that relates dialysate temperature, blood viscosity and diffusion[14]), as well as measurement of skin blood flow. Given that our study was designed as a proof-of-concept pilot trial to assess the effect of manipulating dialysate temperature in a real-world setting, we did not attempt to collect the data required to perform such calculations, and therefore cannot provide mechanistic insights regarding the increase in clearance.

Nevertheless, irrespective of the mechanism at play, an increase in clearance clearly exists when the dialysate temperature is increased. This is evident in the comparison between the NTNF and HTNF prescriptions (Table 4); both arms had the same Q_D; however increasing the dialysate temperature in the HTNF arm resulted in a statistically significant increase in the number of dialysis sessions achieving an spKt/V $\geq$1.2.

A previous study by Yu *et al.*[11] did not note an increase in urea clearance despite raising the dialysate temperature to 37.5 °C. However, this was from a

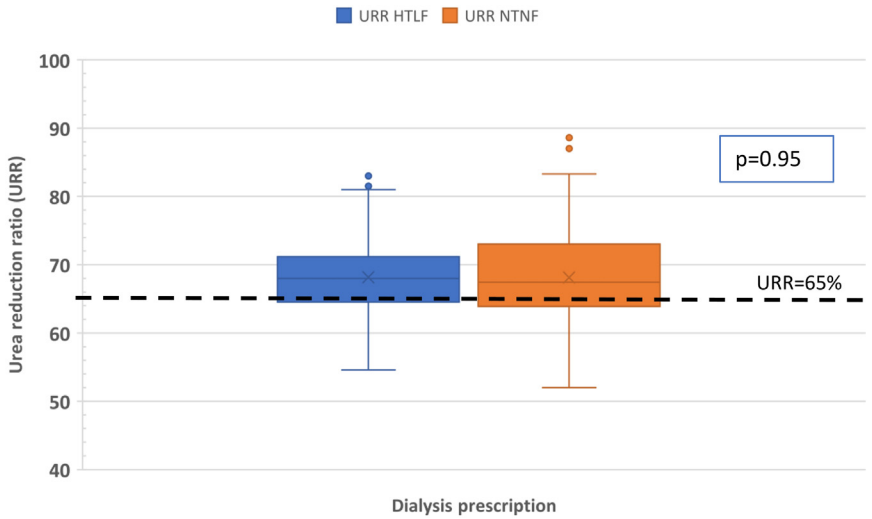

Figure 3. Box and whisker plot comparing the urea reduction ratio between HTLF and NTNF prescriptions. HTLF, high temperature, low flow dialysate; NTNF, normal temperature, normal flow dialysate; URR, urea reduction ratio.

Table 4. Prespecified exploratory analysis comparing all 3 dialysis prescriptions

Primary outcome	NTNF prescription (n = 288)	HTNF prescription (n = 287)	HTLF prescription (n = 288)	Unadjusted odds ratio (95% CI)	*P*-value
Dialysis sessions with spKt/V ≥1.2		222 (77.35)	198 (68.75)	1.55 (1.07 to 2.25)	<0.001
	202 (70.14)	222 (77.35)		0.69 (0.47 to 1.00)	<0.001
	202 (70.14)		198 (68.75)	1.07 (0.75 to 1.52)	0.45
Secondary outcomes	**NTNF prescription (n = 288)**	**HTNF prescription (n = 287)**	**HTLF prescription (n = 288)**	**Mean difference (95% CI)**	***P*-value**
Mean spKt/V	1.32 ± 0.24	1.39 ± 0.28		0.068 (0.055 to 0.082)	<0.001
	1.32 ± 0.24		1.31 ± 0.25	−0.003 (−0.012 to 0.007)	0.57
		1.39 ± 0.28	1.31 ± 0.25	0.071 (0.060 to 0.083)	<0.001
Mean URR	68.15 ± 6.58	69 ± 6.86		0.856 (0.167 to 1.544)	0.015
	68.15 ± 6.58		68.17 ± 5.35	0.018 (−0.545 to 0.582)	0.95
		69 ± 6.86	68.17 ± 5.35	0.84 (0.22 to 1.46)	0.008
Difference between pre- and post-dialysis body temperature, °C, mean ±SD	0.06 ± 0.16	0.11 ± 0.15		0.057 (0.033 to 0.081)	<0.001
	0.06 ± 0.16		0.12 ± 0.15	0.066 (0.040 to 0.093)	<0.001
		0.11 ± 0.15	0.12 ± 0.15	0.009 (−0.014 to 0.033)	0.43
Difference between predialysis and postdialysis systolic blood pressure, mm Hg, mean ±SD	4.51 ± 9.13	5.45 ± 10.01		0.94 (−0.56 to 2.43)	0.22
	4.51 ± 9.13		4.38 ± 8.11	−0.14 (−1.50 to 1.22)	0.84
		5.45 ± 10.01	4.38 ± 8.11	1.08 (−0.37 to 2.52)	0.14
Difference between predialysis and postdialysis diastolic blood pressure, mm Hg, mean±SD	3.23 ± 6.05	3.92 ± 6.80		0.69 (−0.35 to 1.73)	0.19
	3.23 ± 6.05		2.99 ± 5.67	−0.24 (−1.22 to 0.73)	0.62
		3.92 ± 6.80	2.99 ± 5.67	−0.94 (−1.92 to 0.05)	0.06

CI, confidence interval; HTLF, high temperature, low flow dialysate; HTNF, high temperature, normal flow dialysate; NTNF, normal temperature, normal flow dialysate; spKt/V, single-pool Kt/V (by online monitoring); URR, urea reduction ratio.

single dialysis session performed on 9 participants. Furthermore, the upper limit of "normal" body temperature (defined as 2 SDs above the mean) has recently been studied[15] and found to be around 37.5 °C. Given that we wished to study the effect of dialysate temperature that was slightly higher than the normal body temperature, we used a dialysate temperature of 38.5 °C in this trial. This is higher than the dialysate temperature studied by Yu *et al.*[11] and is possibly one reason for the improvement in urea clearance noted in our study.

Earlier reports suggest that warmer dialysate is associated with greater hemodynamic instability.[11] However, when there is temperature-mediated peripheral vasodilation resulting in a reduction in central blood volume, there is a reflex stimulation of cardiopulmonary baroreceptors, which abolish the peripheral vasodilatory activity and reduce skin blood flow, even in the face of heat stress.[16] Therefore, while using higher dialysate temperatures, though cautious monitoring is warranted, severe hemodynamic instability is not necessarily the rule. In our study, all patients entered a run-in phase during enrollment, and patients with recurrent intradialytic hypotension were excluded. Except for one dialysis session in the HTNF arm where clinically significant intradialytic hypotension occurred, no other serious adverse effects were observed.

Two cohort studies have previously suggested that the use of cooler dialysate is associated with improved cardiovascular mortality.[17,18] However, a recent cluster-randomized controlled trial found no cardiovascular benefit to reducing dialysate temperature.[19] Similarly, higher temperatures have been associated with hemolysis in several case reports from the 1970s and 1980s, but only at dialysate temperatures of >42 °C, which is higher than the upper limit of the temperature alarm in most modern dialysis machines.[20,21]

The rise in body temperature during dialysis was higher in the HTLF prescription (0.12 ± 0.15 °C) than in the NTNF prescription (0.06 ± 0.16 °C) (Table 3). However, this small difference (0.066 °C) could well have occurred by chance, given that the clinical bias in noncontact infrared thermometers ranges from just under −0.9 °C to just over 0.2 °C.[22] Furthermore, the temperature of the dialysate and the outflow (venous) blood entering the patient access are not equal, because the latter is dependent on multiple factors, including blood flow, environmental temperature, length of the outflow (venous) line, and its insulation characteristics. In fact, the temperature of the blood in the outflow (venous) line has been reported to be up to 1 °C lower than the dialysate temperature.[23]

Since the 1960s, dialysate flow rates have conventionally been maintained at 500 ml/min, and this has become the standard-of-care. However, over the past

half-century, improvements in the design of dialyzers have improved the flow distribution of dialysate. This has been achieved through changes in the fiber packing density and design, and the inclusion of spacer yarns in the fiber bundle. It is therefore possible that lower dialysate flow rates than those used in the 1960s may not have as large an effect on solute clearance as previously presumed.[24]

In fact, some investigators have studied the effect of reducing Q_D to 400 ml/min, and found that this has not resulted in a significant reduction in urea clearance.[25,26] The strategy studied in our current study balanced any potential loss of clearance due to reduced Q_D by increasing dialysate temperature, and resulted in significant savings in the amount of water consumed. Although HD remains far from an ecofriendly therapy, small interventions to reduce its impact on the environment, when applied broadly, can cumulatively have an enormous benefit on our carbon footprint.

Strengths

Compared to previous studies done to assess clearance and hemodynamic stability in patients with a high-dialysate temperature prescription, ours had a larger sample size and was adequately powered to assess the intended primary outcome.

Limitations

Most patients were young and none of them had previous recurrent intradialytic hypotensive episodes. These entry criteria likely selected for an overall healthier group of subjects than the general dialysis population. The results of this study, particularly with respect to hemodynamic stability during dialysis, may not be generalizable and require confirmation in elderly subjects.

Urea distribution volume was estimated using the Watson formula, which may not have been as accurate as more sophisticated methods such as bioelectrical impedance spectroscopy and isotope dilution techniques. Measurement of skin blood flow (which would require venous occlusion plethysmography or laser Doppler flowmetry) was not performed; therefore, the contribution of temperature-induced peripheral vasodilation to the increase in solute clearance could not be assessed. Finally, dialysis prescriptions were not individualized (with regard to K_0A of the filter, duration of dialysis, and blood flow rates); thus, some patients did not achieve spKt/V of 1.2 even at baseline.

Conclusion

In this pilot study of young, hemodynamically stable patients, a dialysis prescription with a high dialysate temperature of 38.5 °C and a low Q_D of 300 ml/min is a safe and effective alternative to standard dialysis prescriptions with a dialysate temperature of 37 °C and a Q_D of 500 ml/min. Such a strategy decreases water consumption by 40% for each session of dialysis.

DISCLOSURE

All the authors declared no competing interests.

ACKNOWLEDGMENTS

We gratefully acknowledge the contributions of all of our dialysis technicians, who in addition to their regular duties, assisted with data collection and provided essential logistic support for the conduct of this study.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Baseline clinical characteristics in individuals on twice-weekly and thrice-weekly hemodialysis.

Table S2. Clinical characteristics of patients while on each dialysis prescription.

CONSORT 2010 statement: extension to randomized crossover trials.

REFERENCES

1. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. *Nat Rev Nephrol*. 2020;16:573–585. https://doi.org/10.1038/s41581-020-0315-4
2. Tarrass F, Benjelloun M, Benjelloun O. Recycling wastewater after hemodialysis: an environmental analysis for alternative water sources in arid regions. *Am J Kidney Dis*. 2008;52:154–158. https://doi.org/10.1053/j.ajkd.2008.03.022
3. Tarrass F, Benjelloun M, Benjelloun O, Bensaha T. Water conservation: an emerging but vital issue in hemodialysis therapy. *Blood Purif*. 2010;30:181–185. https://doi.org/10.1159/000321485
4. Hauk M, Kuhlmann MK, Riegel W, Köhler H. In vivo effects of dialysate flow rate on Kt/V in maintenance hemodialysis patients. *Am J Kidney Dis*. 2000;35:105–111. https://doi.org/10.1016/S0272-6386(00)70308-8
5. Owen WF, Lew NL, Liu Y, Lowrie EG, Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. *N Engl J Med*. 1993;329:1001–1006. https://doi.org/10.1056/NEJM199309303291404
6. Aslam S, Saggi SJ, Salifu M, Kossmann RJ. Online measurement of hemodialysis adequacy using effective ionic dialysance of sodium—a review of its principles, applications, benefits, and risks. *Hemodial Int*. 2018;22:425–434. https://doi.org/10.1111/hdi.12623
7. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am J Clin Nutr*. 1980;33:27–39. https://doi.org/10.1093/ajcn/33.1.27
8. Srivastava M, Chakraborty D. The effective temperature for the thermal fluctuations in hot Brownian motion. *J Chem Phys*. 2018;148:204902. https://doi.org/10.1063/1.5025762

9. Maheshwari V, Lau T, Samavedham L, Rangaiah GP. Effect of cool vs. warm dialysate on toxin removal: rationale and study design. *BMC Nephrol*. 2015;16:25. https://doi.org/10.1186/s12882-015-0017-5
10. Charkoudian N. Mechanisms and modifiers of reflex induced cutaneous vasodilation and vasoconstriction in humans. *J Appl Physiol (1985)*. 2010;109:1221–1228. https://doi.org/10.1152/japplphysiol.00298.2010
11. Yu AW, Ing TS, Zabaneh RI, Daugirdas JT. Effect of dialysate temperature on central hemodynamics and urea kinetics. *Kidney Int*. 1995;48:237–243. https://doi.org/10.1038/ki.1995.289
12. Roy Y, Warsinger DM, Lienhard VJH. Effect of temperature on ion transport in nanofiltration membranes: diffusion, convection and electromigration. *Desalination*. 2017;420C:241–257. https://doi.org/10.1016/j.desal.2017.07.020
13. Hootkins R. Lessons in dialysis, dialyzers, and dialysate. *Dial Transplant*. 2011;40:392–396. https://doi.org/10.1002/dat.20609
14. Miller CC. The Stokes-Einstein law for diffusion in solution. *Proc R Soc Lond*. 1924;106:724–749.
15. Geneva II, Cuzzo B, Fazili T, Javaid W. Normal body temperature: a systematic review. *Open Forum Infect Dis*. 2019;6:ofz032. https://doi.org/10.1093/ofid/ofz032
16. Kellogg DL Jr, Johnson JM, Kosiba WA. Baroreflex control of the cutaneous active vasodilator system in humans. *Circ Res*. 1990;66:1420–1426. https://doi.org/10.1161/01.res.66.5.1420
17. Dasgupta I, Thomas GN, Clarke J, et al. Associations between hemodialysis facility practices to manage fluid volume and intradialytic hypotension and patient outcomes. *Clin J Am Soc Nephrol*. 2019;14:385–393. https://doi.org/10.2215/CJN.08240718
18. Hsu HJ, Yen CH, Hsu KH, et al. Association between cold dialysis and cardiovascular survival in hemodialysis patients. *Nephrol Dial Transplant*. 2012;27:2457–2464. https://doi.org/10.1093/ndt/gfr615
19. MyTEMP writing committee. MyTEMP writing committee. Personalised cooler dialysate for patients receiving maintenance haemodialysis (MyTEMP): a pragmatic, cluster-randomised trial. *Lancet*. 2022;400:1693–1703. https://doi.org/10.1016/S0140-6736(22)01805-0
20. Fortner RW, Nowakowski A, Carter CB, King LH, Knepshield JH. Death due to overheated dialysate during dialysis. *Ann Intern Med*. 1970;73:443–444. https://doi.org/10.7326/0003-4819-73-3-443
21. Berkes SL, Kahn SI, Chazan JA, Garella S. Prolonged hemolysis from overheated dialysate. *Ann Intern Med*. 1975;83:363–364. https://doi.org/10.7326/0003-4819-83-3-363
22. Sullivan SJL, Rinaldi JE, Hariharan P, et al. Clinical evaluation of non-contact infrared thermometers. *Sci Rep*. 2021;11:22079. https://doi.org/10.1038/s41598-021-99300-1
23. Schneditz D. Temperature and thermal balance in hemodialysis. *Semin Dial*. 2001;14:357–364. https://doi.org/10.1046/j.1525-139x.2001.00088.x
24. Barraclough KA, Agar JWM. Green nephrology. *Nat Rev Nephrol*. 2020;16:257–268. https://doi.org/10.1038/s41581-019-0245-1
25. Albalate M, Pérez-García R, de Sequera P, et al. Is it useful to increase dialysate flow rate to improve the delivered Kt? *BMC Nephrol*. 2015;16:20. https://doi.org/10.1186/s12882-015-0013-9
26. Molano-Triviño A, Meid BW, Guzman G, et al. Effects of decreasing dialysis fluid flow rate on dialysis efficacy and interdialytic weight gain in chronic hemodialysis - FLUGAIN Study. *Nephrol Dial Transplant*. 2018;33(suppl 1):i514–i515. https://doi.org/10.1093/ndt/gfy104.SP491