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Original Article

Internal Medicine Section

The Effect of Dialysate Temperature on Urea Reduction Ratio among Patients Undergoing Maintenance Haemodialysis: A Case Control Study

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ABSTRACT

Introduction: Lowering the dialysate temperature in Intradialytic Hypotension (IDH) prone Maintenance Haemodialysis (MHD) patients, offers better haemodynamic stability. Evidence is lacking relating the effects of low dialysate temperature on urea clearance.

Aim: To study the effect of dialysate temperature on dialysis adequacy in terms of urea reduction ratio in MHD patients.

Materials and Methods: This experimental study was conducted on stable End Stage Renal Disease (ESRD) patients undergoing regular MHD in the age group of 18 to 65 years. The study population (n=118) was randomly divided into two groups. In the control group (n=59), the dialysate temperature was set at 37°C and in the study group (n=59), the temperature was set at 35.5°C. Urea Reduction Ratio (URR) and Online Clearance Monitoring (OCM) Kt/V of individual Haemodialysis (HD) sessions in both the groups were calculated and compared.

Results: The mean pre and post Blood Urea Nitrogen (BUN) values of HD sessions in the control group were 49.95±19.54 mg/dL and 14.17±7.92 mg/dL respectively. The mean pre and post BUN values of HD sessions in the study (low dialysate temperature) group were 50.76±17.67 mg/dL and 21.69±10.96 mg/dL respectively. The mean URR of HD sessions of the control group was 69.08±14.72 and in the study group, it was 56.93±15.85. In the low dialysate temperature group, 43 (72.9%) patients achieved <65% URR and 16 (27.1%) patients achieved >65% URR.

Conclusion: Dialysis with low dialysate temperature was associated with statistically significant reduction of URR. Low dialysate temperature can affect dialysis adequacy in stable MHD patients.

Keywords: Blood urea nitrogen, Cool dialysate, Dialysate temperature, Online clearance monitoring

INTRODUCTION

IDH is a common complication occurring in 20% to 30% of patients undergoing MHD. Recurrent episodes of IDH compromise adequacy in HD patients. Reducing dialysate temperature is one of the commonly utilised option to prevent incidence of IDH [1-3]. In usual circumstances, the dialysate temperature is typically set at 37°C [1-3]. Several studies have shown that cool dialysate provides good haemodynamic stability in patients who are prone to IDH [4,5].

Although haemodynamic stability with lower dialysate temperature is well established, it is still not known if there is a compromise in uraemic clearance with cool dialysate therapy. Inter-compartmental 'resistance' is considered the main barrier for uraemic toxin removal. Small vessel vasoconstriction secondary to dialysate temperature lowering can potentially increase this inter-compartmental resistance. Authors intended to do an experimental study in HD population to find the relationship of cool dialysate with urea clearance.

MATERIALS AND METHODS

It is an experimental study with case control design (1:1 ratio) done at the dialysis unit of Sri Ramachandra Medical Centre, Sri Ramachandra Institute of Higher Education and Research, Chennai. The study was conducted from September 2017 to March 2018. Stable ESRD patients in the age group of 18 to 65 years who were undergoing regular MHD were included in the study. Patients who were getting dialysis for Acute Kidney Injury (AKI) and those prone to IDH were excluded from the study. The sample size was 118 patients (α=0.05 and β=80%) and they were randomly assigned into two groups.

Group 1 patients (n=59) (control group) were dialysed with standard dialysate temperature of 37°C. Group 2 patients (n=59) were the study group and were dialysed with dialysate temperature of 35.5°C. For the study, only one session of dialysis was conducted in a single patient and a total of 118 HD sessions were done in 118 patients. The HD duration was 4 hours for all sessions. All of them were dialysed using Fresenius medical care HD machines with ionic conductance based online clearance monitoring facility. Bicarbonate based dialysate with same electrolyte concentration was used for all the patients.

All the patients had a well-functioning arterio-venous fistula through which HD was done. Blood samples were collected from both groups during the HD session for the estimation of BUN and URR. Pre-dialysis sample was collected from the arterial line before initiation of HD. The post dialysis sample was collected after termination of HD. OCM for Kt/V was also done in addition to URR for assessing dialysis adequacy. Monitoring of blood pressure and body temperature was done for all the patients during dialysis sessions. Informed consent was obtained from all the patients. Institutional Ethical Committee approval was obtained for the study. (CSP/17/MAY/68/164).

Urea is an end product of protein metabolism. BUN is the measure of urea nitrogen in blood. URR is the current primary measure of dialysis adequacy. It is calculated by (Predialysis BUN - Postdialysis BUN)/Predialysis BUN. By convention, this is measured as a percentage. Kt/V is another index of urea removal where the volume of plasma cleared of urea (Kt) (K-dialyser urea clearance, t-dialysis session length) is divided by the urea distribution Volume (V). It is a dimension ratio and values ≥1.2 for a dialysis session is considered adequate for a patient who is on weekly thrice dialysis. Equations have been developed that can translate URR to Kt/V by adjusting for dialysis session urea generation and volume removal. [Kt/V=-ln (R-0.008 *t) + (4-3.5 * R) * 0.55 UF/V (Daugirdas)]. Both URR and Kt/V are determined by pre and postdialysis BUN levels and both are mathematically linked. Neither is superior to the other for measuring outcomes [6].

STATISTICAL ANALYSIS

The data obtained were expressed through mean and standard deviation. Pearson chi-square test was used to compare baseline characteristics and outcomes of both the groups. Student's t-test was used to find difference of mean between the two groups. Data were analysed using SPSS 20. A p-value of <0.05 was considered statistically significant.

RESULTS

Out of 118 patients, there were 83 (70.3%) males and 35 (29.7%) females. In the study (low dialysate temperature) group, 45 (76.3%) were males and 14 (23.7%) patients were females. In the control (standard dialysate temperature) group, 38 (64.4%) patients were males and 21 (35.6%) patients were females. In the study population, 11 (9.3%) patients were between 18-40 years of age, 71 (60.2%) patients were between 41-60 years and 36 (30.5%) patients were more than 60 years. Baseline characteristics of the study and the control groups are described in [Table/Fig-1]. Demographic factors including age and gender distribution, co-morbid conditions including diabetes mellitus and hypertension, Body Mass Index (BMI), dialysis related factors including frequency, blood and dialysate flow rates and dialyser surface areas were comparable between the control and study groups.

The mean pre and post BUN values of HD sessions in the control group were 49.95±19.54 mg/dL and 14.17±7.92 mg/dL respectively. The mean pre and post BUN values in the study group were 50.76±17.67 mg/dL and 21.69±10.96 mg/dL (p<0.001) respectively. The mean URR of HD sessions for the control group was 69.08±14.72 and for the study group, it was 56.93±15.85. (p<0.001). The mean Kt/V (OCM) of HD sessions for the control group was 1.285±0.2467 and for the study group, it was 1.2192±0.1751. (p=0.097).

On analysing the results, it could be interpreted that 43 (72.9%) patients achieved <65% URR and 16 (27.1%) patients achieved >65% URR in the low dialysate temperature (study) group, whereas in the control group, only 19 (32.2%) patients achieved <65% URR. (p<0.001). Overall, 42 (35.6%) patients achieved Kt/V (OCM) of <1.2 and 76 (64.4%) patients achieved >1.2 of Kt/V (OCM). In the low dialysate temperature group, 24 (40.7%) patients achieved Kt/V (OCM) of less than 1.2 and 35 (59.3%) patients achieved more than 1.2 of Kt/V (OCM). In the control group 41 (69.5%) patients achieved Kt/V (OCM) of more than 1.2. (p=0.249) [Table/Fig-2].

All the patients tolerated dialysis well except for two in the low dialysate temperature group, who experienced chillness but not leading to premature termination of the HD session.

	Group 1 (37°C) Control group (n=59)	Group 2 (35.5°C) Study group (n=59)	p-value
Male	38 (64.4%)	45 (76.3%)	0.158
Female	21 (35.6%)	14 (23.7%)	
Age (years)	56.8±11.6	52±11.5	0.026
Age Distribution			
18 to 40 years	4 (6.8%)	7 (11.9%)	0.378
41 to 60 years	34 (57.6%)	37 (62.7%)	
>60 years	21 (35.6%)	15 (25.4%)	
Comorbidities			
Hypertension	33 (55.9%)	38 (64.4%)	0.802
Diabetes mellitus	10 (16.9%)	9 (15.3%)	
Both	13 (22%)	10 (16.9%)	
Others	3 (5.1%)	2 (3.4%)	
Body Mass Index			
(BMI) kg/m^2	24.3±3.6	24.7±4.2	0.602
Body Mass Index			
<18.5	2 (3.4%)	2 (3.4%)	0.414
18.5 to 25	30 (50.8%)	36 (61%)	
25.1 to 30	23 (39%)	16 (27.1%)	
30.5 to 35	4 (6.8%)	3 (5.1%)	
>35.1	-	2 (3.4%)	
Dialysis Frequency			
Weekly thrice	7 (11.9%)	7 (11.9%)	0.900
Weekly twice	49 (83.1%)	50 (84.7%)	
Weekly once	3 (5.1%)	2 (3.4%)	
Blood Flow Rate			
250 mL/min	37 (62.7%)	42 (71.2%)	0.328
300 mL/min	22 (37.3%)	17 (28.8%)	
Dialysate Flow Rate			
500 mL/min	43 (72.9%)	41 (69.5%)	0.684
800 mL/min	16 (27.1%)	18 (30.5%)	
Dialyser Surface Area			
1.3 m^2 (ELISIO 13M)	40 (67.8%)	44 (74.6%)	0.416
1.7 m^2 (ELISIO 17M)	19 (32.2%)	15 (25.4%)	

[Table/Fig-1]: Baseline characteristics of the study population.

	Group 1 (37°C) Control group (n=59)	Group 2 (35.5°C) Study group (n=59)	p-value
Pre BUN (mg/dL)	49.95±19.544	50.76±17.673	0.813
Post BUN (mg/dL)	14.17±7.925	21.69±10.958	<0.001*
URR (%)	69.08±14.716	56.93±15.854	<0.001*
Kt/V (OCM)	1.285±0.2467	1.2192±0.1751	0.097
URR			
<65%	19 (32.2%)	43 (72.9%)	<0.001†
>65%	40 (67.8%)	16 (27.1%)	
Online Kt/V			
<1.2	18 (30.5%)	24 (40.7%)	0.249
>1.2	41 (69.5%)	35 (59.3%)	

[Table/Fig-2]: Comparison of different parameters in group 1 and group 2.
BUN: Blood urea nitrogen; OCM: Online clearance monitoring; URR: Urea reduction ratio
*significant-Student's t-test
†significant- Pearson chi-square test

DISCUSSION

There are several definitions of IDH including a nadir systolic BP <90 mmHg, a decrease in mean arterial pressure by 10 mmHg, a decrease in systolic blood pressure by ≥20 mmHg, or a fall in some percentage of the initial blood pressure [7]. Repeated IDH episodes result in inadequate fluid removal and suboptimal clearance of uraemic toxins, leading to volume overload on subsequent visits. Interventions such as, optimising 'dry' weight, dialysate sodium modelling, lowering dialysate temperature, avoidance of food and antihypertensive agents prior to dialysis and pharmacological agents like midodrine help to prevent IDH in subsequent dialysis sessions [4,8].

During dialysis ultrafiltration, sympathetic overactivity leads to constriction of the dermal capillaries. This leads to impaired heat dissipation and increase in core body temperature. Also, dialysis procedure per se increases heat production in the body. IDH occurs when core body temperature overcomes the initial peripheral vasoconstriction. IDH is an independent risk factor for cardiovascular mortality in MHD patients and has a significant bearing on overall quality of life of the patient. Cool dialysate is associated with better cardiovascular and overall outcomes [9-13]. In a large meta- analysis which included 26 trials and 484 patients, the rate of IDH was reduced by 70% with cool dialysate [5]. There was an increase in mean arterial pressure by 12 mmHg in the study population. Selby NM et al., reported that cooling of dialysate reduced the rate of IDH by 7.1 times as compared to conventional treatment [11]. Also, patients' perceptions were found to be positive with 'cool' dialysis in a small study population [14].

Blood volume monitoring has been shown to be an effective tool to prevent IDH in some studies. A biofeedback system was used in which dialysate conductivity and ultrafiltration rates were constantly adjusted throughout the HD procedure based on input from the measured change in blood volume and/or blood pressure [15]. Such systems may not find wide acceptance in day to day practice, especially in less sophisticated dialysis units. Reduction in dialysate temperature for the prevention of IDH can be practised in all centres because it does not involve additional cost, apparatus or manpower. In addition to better haemodynamics, individualised 'cool' dialysate also abrogates HD induced myocardial stunning without compromising patients' tolerability [16]. Advanced techniques incorporating biofeedback systems where the dialysate temperature is adjusted to keep a constant core body temperature (isothermic dialysis) could also be beneficial in preventing IDH [17].

In the last decade, online monitoring systems of urea clearance based on either urea concentration measurement in dialysate or ultrafiltrate or ionic conductance based systems have been incorporated in dialysis machines and are now widely practised [18,19]. It is still not known whether online monitoring systems are perfect and yield Kt/V results similar to calculation by conventional method. Previously, some studies have compared both Kt/V (Daugirdas) and Kt/V (OCM) for validating accuracy of Kt/V (OCM). Studies so far have yielded discordant results. Kt/V (OCM) overestimated urea clearance in some studies and underestimated in a few as compared to conventional Kt/V measurement, but there was moderate correlation between these two methods in most of the studies [20-24].

There are no large studies which have been done on clearance with low dialysate temperature, and the few available studies are of very small sample size, from which definite conclusions could not be derived [25-27]. Alex WY et al., reported that in a study with nine patients, use of cool dialysate was associated with increased mean arterial pressure and there were no clinically important effects on urea clearance and/or urea rebound [25]. In a similar study with the same number of patients, where high efficiency dialysis using volumetric fluid removal system was performed, results were similar. The mean change in the systemic peripheral vascular resistance index was significantly higher in the cool dialysate group and there was no significant difference in pre and post dialysis urea concentration, urea rebound and equilibrated Kt/V [26]. In another study including 15 patients, cooling of dialysate offered haemodynamic stability without compromising efficacy of dialysis, as estimated by equilibrated Kt/V [27]. Sub-analysis of a large meta-analysis, where adequacy data was available for nine trials, also showed no difference in dialysis adequacy between low dialysate temperature and standard temperature groups [5]. In our study, only 16 (27.1%) patients achieved >65% URR in the low dialysate temperature group, where as in the standard dialysate temperature group, 40 (67.8%) patients achieved >65% URR, suggesting that low dialysate temperature significantly affects urea clearance.

The strength of this study is that this is probably the first one with good sample size and design that has analysed the effect of dialysate cooling on URR. Adequacy was also tested by OCM in the study population.

LIMITATION

The limitation of the study is that it was done in a single centre and patients were randomly allocated to the control and study groups without blinding. Measurement of urea removal per se is not a surrogate marker for uraemic toxin removal, and measurement of other markers such as uric acid, creatinine, phosphate and β2 microglobulin could have predicted dialysis adequacy better. Patients' comfort levels with cool dialysate were not studied, and detailed questionnaire including parameters such as subjective feeling of chills and rigors, post dialysis energy levels could have added value to the study. The study did not include patients prone to IDH because they could have contributed to confounding errors in the interpretation of results.

FUTURE RECOMMENDATIONS OF THE STUDY

The study findings have significant implications in clinical practice and also in designing further clinical trials involving dialysate temperature and dialysis adequacy. Randomised controlled trials including a larger sample size, measurement of solute clearance with all three methods, viz the URR, conventional Kt/V, Kt/V (OCM) and including other uremic toxins such as, creatinine, phosphate and β2 microglobulin for estimating clearance are recommended.

CONCLUSION

In this study, we observed a significant reduction of URR in patients who underwent haemodialysis with lower dialysate temperature. Kt/V (OCM) was also lower in the low dialysate temperature group but it was not statistically significant. Dialysis medical personnel should be aware that IDH precludes uremic clearance and, the reduction in dialysate temperature to prevent IDH can per se lead to less clearance. The new findings from the study should encourage clinicians to carry out similar trials with large randomised sample size with cross over design.

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