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Original Article

Comparison of Efficacy of Dialysis (Kt/V) and Adverse Effect Profile of Citrate Versus Acetate Based Dialysate Solution

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ABSTRACT

Objective: To compare efficiency of dialysis (Kt/V) and incidence of Intra-Dialytic Hypotension (IDH) and muscle cramps with use of acetate versus citrate-based dialysate solution in patients on maintenance hemodialysis.
Study Design: Quasi-experimental study.
Place and Duration of study: Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, from Mar to Aug 2024.
Methodology: After gaining approval from Ethics Committee and obtaining written, informed consent of all participants, 120 patients were enrolled from Dialysis Unit, PEMH, Rawalpindi, Pakistan. In the first leg, six hemodialysis sessions were done using acetate-based dialysate solution (RenaCarb). Vitals and lab parameters including renal function tests (RFTs), electrolytes and Kt/V, were noted in each session along with reports of Intra Dialytic Hypotension (IDH) and muscle cramp episodes. After 2 weeks, patients were crossed over to the second leg and six sessions of dialysis were done using citrate-based dialysate solution (RenaCit). All data was collected and analyzed using Statistical Package for the Social Sciences (SPSS) Version 22.00.
Results: Mean Kt/V for Leg 1 was lesser than for Leg 2 (1.21 ± 0.08 vs 1.35 ± 0.09) with $p<0.01$, while IDH episodes were also higher in number in Leg 1 than in Leg 2 (34 vs 12) with $p<0.01$ but there were no statistically significant differences in incidence of post-dialysis cramps or bleeding between Leg 1 or 2.
Conclusion: Dialysis sessions with citrate-based dialysate had better dialysis efficacy and lesser number of IDH episodes than with acetate-based dialysate while incidence of muscle cramps was not statistically significant between both dialysate solutions.

Keywords: Acetate Dialysate, Citrate dialysate, Dialysis efficacy, Hypocalcemia

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INTRODUCTION

Kidney Replacement Therapy (KRT) is the mainstay in management of End-Stage Renal Disease (ESRD) patients after hemodialysis, peritoneal dialysis and renal transplantation, with 85% of patients in Pakistan undergoing Hemodialysis[1]. Dialysis involves removal of nitrogenous waste, harmful electrolytes and excess water from blood stream through osmosis and active filtration between blood and a dialysate solution across a semi-permeable membrane within a dialysis machine, with the composition of this dialysate solution including a Part A (acidic) and Part B (basic) solution mixed together inside the dialysis machine to create an osmotic gradient for solutes to be removed from blood, making it one of the major determinants of dialysis effectiveness [2]. Acetate-based Part A solution has been used due to its easy availability and chemical stability, however one of its major side-effects is Intra-Dialytic Hypotension (IDH)[3] due to a greater loss of bicarbonate ions from the blood, leading to worsening of metabolic acidosis, blunting the counter-regulatory mechanisms preventing hypotension[4-5]. Acetate tends to accumulate within the body, causing changes in metabolism,[6] compounded by reduced Left Ventricular Ejection Fraction (LVEF), with ultrafiltration leading to volume depletion, autonomic neuropathy, hypoalbuminemia and poor sodium regulation[7]. Citrate-based Part A dialysate solutions is a natural buffer converted to bicarbonate within the body, which prevents metabolic acidosis, leading to better regulation of blood pressure (BP) during dialysis and reducing IDH[8]. However, post-dialysis hypocalcemia can occur when citrate binds with calcium inside the blood stream and removes it from circulation[9], leading to substantial reduction in blood clotting and significant hypocalcemia, manifested as intra- and post-dialysis muscle cramping, which, in severe cases, may lead to seizures[10]. Our study is aimed at assessing the efficiency of hemodialysis measured via pooled Kt/V and incidence of

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intra/post-dialytic hypotension with hypocalcemic effects of citrate versus acetate-based Part A solution.

METHODOLOGY

This quasi-experimental study was conducted from 1st March to 31st August 2024 at Department of Nephology, Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan, after gaining approval from Ethics Committee via Ltr no A28/ER/162/24, dated 25th Feb 2024. Sample size was calculated using World Health Organization (WHO) sample size calculator, keeping confidence interval of 95%, absolute precision of 5%, number of dialysis dependent patients in Pakistan being 22,000 and frequency of dialysis dependent population at 9.2% of all patients with Chronic Kidney Disease (CKD) [1]. Using non-probability, purposive sampling technique, 120 patients were enrolled from Department of Dialysis after taking written and informed consent from all patients. Basic demographic details of patients, including co-morbidities and baseline lab parameters such as hemoglobin (Hb) levels, renal function tests (RFTs), serum sodium, potassium, calcium, phosphate and intact parathyroid levels, were recorded on a data collection form.

Inclusion Criteria: ESRD patients belonging to either gender, between the ages of 18-70 years and on thrice weekly maintenance hemodialysis for at least 3 months, were included.

Exclusion Criteria: Patients with Acute Kidney Injury (AKI), moderate to severe heart failure (HF) with Ejection Fraction <45%, tertiary hyperparathyroidism or parathyroid levels > 81 ng/dl, bleeding diathesis, uncontrolled diabetes mellitus (HbA1C>6.5%), restless leg syndrome or hypomagnesaemia were excluded.

For the first leg of the study, all patients were placed on thrice weekly maintenance hemodialysis using acetate-based dialysate solution (RenaCarb) for 2 weeks spanning six sessions using Fresenius 4008S dialysis machines. Pulse, blood pressure and O2 saturation, were measured every 30 mins for the duration of dialysis or if the patient became symptomatic. Single session Kt/V was calculated for each session (minimum 3 hours duration) and pooled Kt/V was measured weekly using Daugirda's Equation and mean pooled Kt/V was calculated for each patient after six sessions. IDH episodes (BP<90/60 mmHG, fall in Systolic BP > 30 mmHg or symptomatic hypotension) were documented for each session and any session with 2 or more episodes was taken as significant. Any episode of muscle cramps (as documented by a doctor) occurring during or within 1 hour of completion of dialysis was taken as significant and documented. After 2 weeks, the patients were crossed over to the second leg of the study with citrate-based dialysate solution (RenaCit) for 2 weeks spanning six sessions. This is shown in Figure-1. Adverse event log was maintained for mortality, seizures and significant intra- or post-dialytic bleeding (bleeding from any site requiring stoppage of dialysis session or persistent bleed from arterio-venous access site for 30 mins post-dialysis). Data was analyzed using Statistical Package for Social Sciences (SPSS) version 26.00 frequency and percentage were calculated for qualitative data . Chi-Square test was applied for association between intervention and outcome. Mean with standard deviation was also calculated for quantitative data along with independent samples t-test where $p<0.05$ was taken as significant.

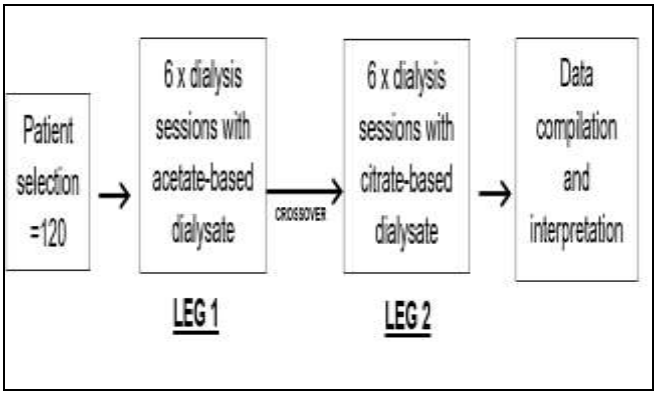

Figure-1: Study Protocol (n=120)

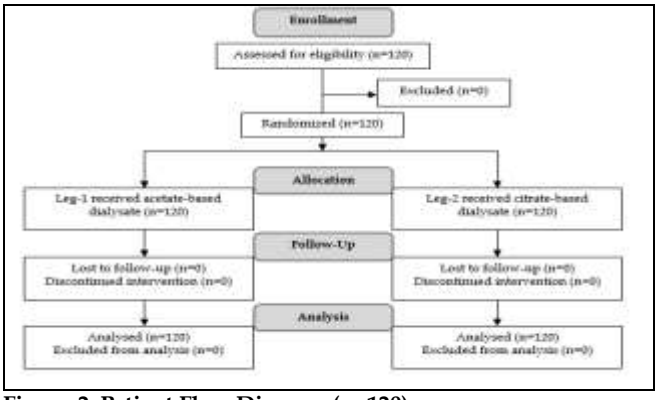

Figure-2: Patient Flow Diagram (n=120)

RESULTS

Total sample size was 120 out of which 78(65.00%) patients were male and 42(35.00%) were female with mean age being 50.93±12.20 years of which 65 patients (56.20%) had diabetes mellitus while

83(69.10%) patients had hypertension. Mean Kt/V for Leg 1 was 1.21 ± 0.08 and for Leg 2 was 1.35 ± 0.09 with p<0.01. Kt/V was higher for Leg 2 than Leg 1, thereby showing that there was a statistically significant improvement in Kt/V with citrate dialysate, as shown in Table-I.

Table-I: Comparison of Mean Kt/V Between Leg 1 (Acetate Dialysate) Versus Leg 2 (Citrate Dialysate) (n=120)

Leg	Mean Kt/V	p-value
1 (acetate dialysate)	1.21 ± 0.08	p<0.01
2 (citrate dialysate)	1.35 ± 0.09	

Intra-Dialytic Hypotension (IDH) occurred in 34 patients in Leg 1 and in 12 patients in Leg 2 with p<0.01, thus, a statistically significant increase in incidence of IDH occurred in Leg 1 than in Leg 2, as shown in Table-II.

Table-II: Incidence of Intra-Dialytic Hypotension (IDH) Episodes in Leg 1 (Acetate Dialysate) Versus Leg 2 (Citrate Dialysate) (n=120)

		IDH		Total	*p*-value
		Yes	No		
Leg	1	34(28.30%)	86(71.70%)	120	*p*< 0.01
	2	12(10.00%)	108(90.00%)	120	

Number of patients experiencing clinically documented muscle cramps in Leg 1 and Leg 2 were 12 and 16, respectively but no statistically significant increase in incidence of muscle cramps between groups was noted, as shown in Table-III.

Table-III: Incidence of Intra- and Post-Dialysis Cramps Between Leg 1 (Acetate Dialysate) Versus Leg 2 (Citrate Dialysate) (n=120)

		Intra- and Post-Dialysis Cramps		Total	*p*-value
		Yes	No		
Leg	1	12(10.00%)	108(90.00%)	120	0.42
	2	16(13.30%)	104(86.70%)	120	

Similarly, the number of patients experiencing significant dialysis associated with a bleeding episode in Leg 1 and Leg 2 were 30 and 35 respectively, with p=0.48, with no statistically significant increase in risk of bleeding in either group, as shown in Table-IV.

Table-IV: Incidence of Intra- and Post-Dialysis Bleeding Between Leg 1 (Acetate Dialysate) Versus Leg 2 (Citrate Dialysate) (n=120)

		Intra- and Post-Dialysis Bleeding		Total	*p*-value
		Yes	No		
Leg	1	30 (25.00%)	90 (75.00%)	120	0.48
	2	35 (29.10%)	85 (60.90%)	120	

DISCUSSION

In patients with dialysis-dependent chronic kidney disease, citrate-based dialysate was associated with better dialysis efficacy (higher mean pooled Kt/V over six sessions) and significantly fewer episodes of intra-dialytic hypotension compared with acetate-based dialysate, although the incidence of post-dialysis muscle cramps did not differ significantly between the two. The risk assessment for citrate-based dialysate safety was assessed in another study and they found that there was no associated higher risk of morbidity than with acetate-dialysate and side effects were much lower when citrate solution was used, with lesser incidence of visible clotting, however this was not measured in our study[11]. Similarly, another study evaluated the efficacy of citrate as a dialysate acidifying agent and found that it resulted in higher Kt/V (1.51 +/- 0.01 vs 1.57 +/- 0.01) than with standard dialysate solution[12] in contrast to another author who observed varying results in their comparison, where citrate-based solutions led to better dialysis efficacy with mean blood pressure lower in patients with citrate solution than with acetate[13] with another study also sharing added beneficial effects by reducing chronic inflammation and chemerin-induced microvascular injury[14]. Another study reported that the substitution of acetate for citrate in dialysis solution improved hemodynamic stability, produced less hypotension and improved nutritional status[15]. Hypocalcemia after dialysis can lead to muscle cramps, tetany and even seizures[16], however the incidence or severity of symptoms does not directly correlate with the degree of hypocalcemia[17] and our study was able to determine that there was no statistically significant increase in incidence of hypocalcemia side effects with either dialysate, which has also been observed in other studies [18-19]. Finally, our study also observed all patients for significant adverse events and there was no mortality during the observation period and the risk of significant intra or post dialysis bleeding was not raised with citrate dialysate, with similar conclusion was also drawn by another author, who observed that additional anti-coagulation was required with citrate-based acidification solution, showing that the requirement of anticoagulation was same with both types of dialysates and there was no added risk of bleeding with citrate dialysate[20].

LIMITATIONS OF STUDY

A key limitation of this study is its quasi-experimental, single-center design, which may restrict generalizability to

other dialysis units with different patient populations and protocols. The relatively small sample size and short follow-up period may not fully capture long-term differences in Kt/V, IDH, or muscle cramps between the two dialysate types. Additionally, the lack of blinding and the potential influence of unmeasured confounders such as comorbidities, fluid status, and medication changes during the crossover period may have affected the observed outcomes. Finally, the study did not assess all possible adverse effects of citrate dialysate (for example, metabolic or coagulation parameters), which limits a comprehensive safety evaluation.

CONCLUSION

A lower incidence of IDH was found when using citrate-based Part A dialysate solution as compared to acetate-based solution with dialysis efficacy, as measured by mean Kt/V, also noted to be higher with no statistically significant difference in the incidence of muscle cramps or bleeding episodes between either solution.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

UIM & SS: Data acquisition, data analysis, critical review, approval of the final version to be published.

MNA & KM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RJA & BR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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