10.5152/turkjnephrol.2025.24752

Original Article

Turkish Journal of Nephrology

The Impact of Citrate-Based Dialysis Solution on the Efficacy of Hemodialysis

Kerim Erer[1], Cihan Uysal[2], Oktay Oymak[2]

[1]Department of Internal Medicine, Erciyes University Faculty of Medicine, Kayseri, Türkiye
[2]Division of Nephrology, Erciyes University Faculty of Medicine, Kayseri, Türkiye

ABSTRACT

Objective: The current study focused on the possible effects of citrate-containing acidic dialysis solutions on laboratory parameters and dialysis adequacy.
Methods: Only patients who were undergoing chronic hemodialysis (HD) were enrolled and analyzed. The HD treatment was defined as 3 times per week, with each dialysis session lasting 4 hours. Only the arteriovenous fistula was preferred for vascular access. Dialysis sessions were performed with citrate-containing acidic dialysis solutions for 3 months. Afterward, the outcomes of this period were compared with the prior 3-month period using a standard acetate-containing acidic dialysis solution.
Results: In this study, 80 patients were analyzed. The average Kt/V urea value was 1.47 (1.35-1.80) during the HD with acetate-containing acidic dialysis solution, whereas it was 1.57 (1.38-1.80) during HD with citrate-containing acidic dialysis solution (P = .003). The average urea reduction ratio was 72.1 ± 5.7 during the HD with acetate-containing acidic dialysis solution, while it was 73.5 ± 5.6 during the HD with citrate-containing acidic dialysis solution (P = .015). Lower total serum calcium levels were determined during the citrate-containing acidic dialysis solution period (P < .001). A significant decrease was observed in clotting events during the citrate-containing acidic dialysis solution period (P = .026).
Conclusion: Outcomes underscore that dialysis efficiency could be augmented by using citrate-containing acidic dialysis solution.
Keywords: Anticoagulation, citrate, dialysis solution, hemodialysis

Corresponding author: Kerim Erer ✉ kerimerer@gmail.com **Received:** April 29, 2024 **Revision Requested:** May 30, 2024 **Last Revision Received:** May 30, 2025 **Accepted:** June 16, 2025 **Publication Date:** October 1, 2025

Cite this article as: Erer K, Uysal C, Oymak O. The impact of citrate-based dialysis solution on the efficacy of hemodialysis. *Turk J Nephrol.* 2025;34(4):304-310.

INTRODUCTION

Hemodialysis (HD) is still the most commonly administered kidney replacement therapy worldwide. The survival of dialysis patients is made possible by the removal of uremic solutes by dialysis. Also, dialysis duration can impact survival.[1]

The primary mechanism for the removal of solutes from the blood is diffusion in HD. Substance transport occurs between blood and dialysate through the dialysis membrane. The dialysate is a non-sterile aqueous electrolyte solution that resembles normal electrolyte levels found in extracellular fluid, excluding bicarbonate buffer and potassium.[2]

The dialysate is composed of pure water and a mixture of dialysis solutions. The HD solutions are formed by mixing specific ratios of acidic and alkaline concentrates. Bicarbonate is used as a standard alkaline substance, however, cations such as calcium and magnesium are incompatible with bicarbonate and can lead to precipitation. Therefore, these cations are added to the acidic concentrate solutions, and acetate is mostly used as an acidifier.[3]

This work is licensed under a Creative Commons Attribution 4.0 International License.

Occasionally, citric acid is used as an alternative acidifying agent instead of standard acetic acid. Additionally, citric acid may reduce anticoagulation counts and the risk of clotting in the dialysis set-dialyzer system.[4]

Dialysis adequacy is a concept that encompasses both clinical findings and laboratory parameters. Mathematical formulas have been successfully used to evaluate dialysis dosage and adequacy. The urea kinetic model was first described in 1972, and a simple logarithmic equation was developed using pre- and post-dialysis blood urea nitrogen (BUN) values, ultrafiltration (UF) volume, and body weight.[5] Kt/V is more sensitive than the urea reduction ratio (URR) for dialysis effectiveness.[6] According to the Kidney Disease Outcomes Quality Initiative guidelines, dialysis dose adequacy should be assessed at least once a month in long-term HD patients, and for a patient undergoing HD 3 times a week, the recommended target single-pool Kt/V is 1.2 as a minimum value.[7]

Anticoagulation protocols enhance the effectiveness of dialysis by preventing clotting in the circuit and improving membrane pore patency during HD. Several studies have indicated that the use of citrate-containing acidic dialysis solution may improve the Kt/V values due to their anticoagulant effects.[8] The current study aimed to evaluate the utility of citrate-containing acidic dialysis solution on HD efficiency.

METHODS

Study Design

The study protocol was approved by the Local Ethics Committee of Erciyes University with the decision numbered 2021/699 on November 03, 2021. This clinical investigation was carried out in accordance with the Helsinki declaration.Informed consent was obtained from all participants included in the study.

This study was conducted in a single HD center. Adult chronic HD patients were enrolled and analyzed. Only patients who had an arteriovenous fistula were enrolled to minimize vascular access problems. Patients with acute illnesses, vascular access problems, unstable hemodynamics, or who received chronic anticoagulation therapy for other indications were excluded.

MAIN POINTS

- Citrate-containing acidic dialysis solution improved dialysis efficacy.
- Citrate-containing acidic dialysis solution utilization decreased serum calcium levels; however, symptomatic hypocalcemia was not observed.
- Citrate-containing acidic dialysis solution utilization altered clotting events.

In the dialysis center, all patients underwent HD session with citrate-containing acidic dialysis solution for only 3 months due to technical reasons. All patients then returned to HD with a standard acetate-containing acidic dialysis solution. The laboratory and clinical parameters while using citrate-containing acidic dialysis solution were compared with the prior 3-month period (standard acetate-containing acidic dialysis solution).

Glucose, BUN, creatinine, electrolytes, hemogram, albumin, liver function tests, venous blood gases, Kt/V, URR, heparin dosage, clotting events, and bleeding events were assessed once a month. Parathyroid hormone (PTH) level was measured only 1 time in these 3 months. The average values were used in the analysis for each parameter in 2 periods. Heparin dosage, bleeding, and clotting events were recorded in every HD session as clinical parameters. Also, Kt/V urea <1.2 was defined as dialysis inadequacy (DI) in this study.

Hemodialysis Procedure

Chronic HD treatment was defined as 3 times per week, with each dialysis session lasting 4 hours. The dialysis sessions were performed using a Braun Dialog+© dialysis machine and a high-flux single-use polyethersulfone membrane (Purifier©; H160 or 180 with an effective surface area of 1.6 and 1.8 m^2 and an UF coefficient of 67 and 75 ml/h mmHg, respectively). The blood flow rate was maintained between 300 and 400 mL/min. The dialysate flow rate was maintained stable at 500 mL/min. The initial unfractionated heparin dose was 4.000 IU per HD session, and the dosage was adjusted individually when necessary in follow-up. Acetate concentration was 3.0 mmo/L in a standard acidic dialysis solution. Citrate concentration was 1.0 mmo/L in an acidic dialysis solution. Dialysis solutions were produced by Farmasol© (Türkiye) and the fluid composition was as following; sodium 140 mmol/L, potassium 2.0 mmol/L, calcium 1.25 mmol/L, magnesium 0.5 mmol/L, chloride 111.5 mmol/L, bicarbonate 33 mmol/L, glucose 1.0 g/L, and osmolarity 294.8 mOsm/L. Acidic and basic solutions dilution rate was 1/34.

There were no special changes in dialysis-related nursing behaviors to the patients. The nurse performing dialysis did not implement any different practices regarding the solution used for the patient.

Blood Sampling

Pre-dialysis blood sampling was performed just before the dialysis session. Post-dialysis sampling was performed after the blood pump rate was decreased to 100 mL/min for 15 seconds and stopped. Kt/V was calculated using a second-generation single-pool Daugirdas formula ($Kt/V = -\ln(R - 0.03) + [(4 - 3.5 \times R) \times (UF/W)]$ where R = post-dialysis BUN/pre-dialysis BUN, UF = net UF and W = weight).[5] The URR was calculated using the following formula ($URR = (1 - \text{post-dialysis BUN/pre-dialysis BUN}) \times 100\%$).

Statistical Analysis

SPSS version 22 software (IBM SPSS Corp.; Armonk, NY, USA) was used for data analysis. The Shapiro–Wilk test was employed to assess whether numerical data followed a normal distribution. Numerical data showing a normal distribution were presented as mean ± standard deviation, while non-normally distributed numerical data were presented as median (first quartile-third quartile). Non-numerical (categorical) data were expressed as percentages. The paired *t*-test was used to analyzing normally distributed parameters. The Wilcoxon test was used used to analyzing non-normally distributed parameters. The chi-square test was employed to assess non-numerical data. Results were evaluated at a 95% CI, with significance set at $P < .05$.

RESULTS

The total number of included patients in this study was 80. All patients have fulfilled the study protocol. Among these patients, 54 were males (67.5%) and 26 were females (32.5%). The mean age of the patients was 57.1 ± 11.6 years. The average HD duration for patients was 95.4 ± 61.3 months. The baseline characteristic features of the patients are summarized in Table 1.

Table 1. Baseline Characteristic Features of the Patients

Parameters	Results
Gender	
Male	54 (67.5%)
Female	26 (32.5%)
Age (years)	57.1 ± 11.6
BMI (kg/m^2)	24.8 (22.8-27.6)
Hemodialysis vintage (months)	95.46 ± 61.28
Comorbidities	
Hypertension	35 (43.7%)
Diabetes mellitus	23 (28.7%)
Coronary artery disease	15 (18.7%)
Heart failure	8 (10.0%)
Stroke	3 (3.7%)
Kt/V	1.42 (1.32-1.67)
URR (%)	72.2 ± 6.4
Urea predialysis (mg/dL)	143.2 ± 22.7
Creatinine predialysis (mg/dL)	8.8 ± 2.3
Sodium (mEq/L)	137.2 ± 2.8
Potassium (mEq/L)	5.1 ± 0.7
Calcium (mg/dL)	9.0 (8.5-9.3)
Phosphate (mg/dL)	4.7 ± 0.9
CaXP (mg^2/dL^2)	46.4 ± 11.0
PTH (pg/mL)	351 (226-602)
Albumin (g/dL)	3.8 ± 0.3
Bicarbonate (mEq/L)	22.7 (22.0-24.8)
Hemoglobin (g/dL)	10.9 ± 1.7
Ferritin (ng/mL)	539.0 ± 112.7

Values are expressed as n (%), mean ± standard deviation, median (first-third quartiles).
BMI, body mass index; CaXP, calcium-phosphate products; PTH, parathyroid hormone; URR, urea reduction rate.

The 2 different dialysis solution periods were compared to each other. The results of comparison according to laboratory parameters are summarized in Table 2. Firstly, DI (average Kt/V urea < 1.2) was evaluated. The frequency of DI was 5.4% in the acetate-containing acidic dialysis solution period, and it was 5.0 % in the citrate-containing acidic dialysis solution period.

Solute clearance and dialysis efficiency were analyzed according to acetate and citrate-containing acidic dialysis solution periods. The average Kt/V urea was 1.47 (1.35-1.80) during acetate-containing acidic dialysis solution period, whereas was 1.57 (1.38-1.80) during citrate-containing acidic dialysis solution period. The average Kt/V value was significantly higher during the period using the citrate-containing acidic dialysis solution compared to the period using the acetate-containing acidic dialysis solution ($P = .003$).

The average URR value was 72.1 ± 5.7% during acetate-containing acidic dialysis solution period, while the average for citrate-containing acidic dialysis solution was 73.5 ± 5.6%. The average URR value was statistically significantly increased in the citrate-containing acidic dialysis solution period ($P = .015$). The results are summarized in Table 3. The comparison of Kt/V and URR values according to treatment months was demonstrated in Figure 1.

The median total serum calcium level was 8.9 (8.6-9.3) mg/dL in the acetate-containing acidic dialysis solution period and decreased to 8.6 (8.2-8.8) mg/dL in the citrate-containing dialysate period. The average total serum calcium level was statistically significantly decreased in the citrate-containing acidic dialysis solution period ($P < .001$).

The average phosphate level was 4.7 ± 0.9 mg/dL in the acetate-containing acidic dialysis solution period and increased to 4.8 ± 1.1 mg/dL in the citrate-containing acidic dialysis solution period. The average phosphate level was no statistically significantly increased in the citrate-containing acidic dialysis solution period ($P = .053$).

The median PTH level was 351 (226-602) pg/mL in the acetate-containing acidic dialysis solution period, and it increased to 402.0 (274-718) pg/mL in the citrate-containing acidic dialysis solution period. The average PTH level was statistically significantly increased in the citrate-containing acidic dialysis solution period ($P = .044$).

Table 2. Comparison of the Average Laboratory Results of the Both Dialysis Solution Periods

Parameters	Acetate-Containing Acidic Dialysis Solution Period	Citrate-Containing Acidic Dialysis Solution Period	*P*
Sodium (mEq/L)	137.9 ± 2.1	136.5 ± 2.1	.126
Potassium (mEq/L)	5.2 ± 0.6	5.1 ± 0.5	**.007**
Calcium (mg/dL)	8.9 (8.6-9.3)	8.6 (8.2-8.8)	**<.001**
Phosphate (mg/dL)	4.7 ± 0.9	4.8 ± 1.0	.053
CaxP (mg^2/dL^2)	42.6 ± 8.4	42.9 ± 9.4	.775
PTH (pg/mL)	351 (226-602)	402.0 (274-718)	**.044**
Albumin (g/dL)	3.7 ± 0.2	3.6 ± 0.3	.236
Hemoglobin (g/dL)	10.9 ± 1.5	11.1 ± 1.6	.168
Bicarbonate (mEq/L)	24.0 (22.0-26.0)	21.0 (20.0-23.0)	**<.001**

Values are expressed as mean ± standard deviation, median (first[t]-third quartiles).
CaxP, calcium-phosphate product; PTH, parathyroid hormone. P values in bold indicate statistical significance.

The average bicarbonate level was 24.0 (22.0-26.0) mEq/L in the acetate-containing acidic dialysis solution period, and it decreased to 21.0 (20.0-23.0) mEq/L in the citrate-containing acidic dialysis solution period. The average bicarbonate level was statistically significantly decreased in the citrate-containing acidic dialysis solution period (*P* < .001).

Finally, the patients were analyzed concerning clotting events and anticoagulant therapy. The average heparin dose was 3879 ± 455 IU in acetate-containing acidic dialysis solution period, and 3835 ± 437 IU in citrate-containing acidic dialysis solution period (Figure 2). There was no significant change in heparin dosage between the 2 dialysis solution periods (*P* = .088). Furthermore, no major bleeding events were observed in the patients during both acetate and citrate-containing acidic dialysis solution periods.

The frequency of clotting events during HD sessions was assessed according to the types of dialysis solutions. There was a reduction in the number of clotting events during the citrate-containing acidic dialysis solution period (3.8%) when compared to the acetate-containing acidic dialysis solution period (5.3%), and this was a statistically significant decrease (*P* = .026). The results are summarized in Table 3.

DISCUSSION

The amount of uremic toxins clearance affects mortality and morbidity in dialysis treatment. Kt/V urea is calculated by dividing the plasma volume removed of urea by the urea distribution volume and is an established parameter assess dialysis effectiveness. The current study represents data from a 3-month prescription of citrate-containing acidic dialysis solution with high-flux dialyzers in an outpatient-based dialysis center.

Using citrate-containing dialysate has some effects on dialysis practice. Citric acid has been proposed as an alternative dialysis buffer due to its anticoagulant, anti-inflammatory, and antioxidant properties. In vitro, low concentrations of citrate can reduce complement and granulocyte activation. Also, citrate reduces endothelial cell dysfunction and vascular smooth muscle cell osteoblastic differentiation. Clinically, using citrate-containing dialysate significantly reduces chronic inflammation parameters. Additionally, citrate-containing dialysate may offer greater hemodynamic stability with significantly fewer episodes of arterial hypotension. By chelating ionized calcium in plasma, the use of citrate-containing dialysate decreases thrombogenicity. Citrate has a local anticoagulant effect inside the dialyzer, allowing reduced heparin dosing while maintaining extracorporeal patency and optimizing dialyzer clearances. Lastly, citrate-containing dialysate helps to control acid-base balance by correcting acidosis between sessions and avoiding/reducing post dialysis alkalosis.[9-11] Also, citrate-containing acidic dialysis solution can be used for every patient.

The main outcome of this study was that using citrate in the dialysate as an acidifying agent could augment dialysis efficiency. Also, this improvement was observed in both Kt/V urea and URR. The increment was determined to be 6.8% in Kt/V urea and 1.9% in URR during the citrate-containing acidic dialysis

Table 3. Monthly Results of Dialysis Efficacy and Circuit Clotting for Both Dialysis Solution Periods

Parameters	Acetate-Containing Acidic Dialysis Solution Period			Citrate-Containing Acidic Dialysis Solution Period			*P**
	First	Second	Third	First	Second	Third	
Kt/V urea	1.46 (1.32-1.67)	1.46 (1.31-1.70)	1.49 (1.36-1.80)	1.57 (1.38-1.81)	1.64 (1.45-1.77)	1.49 (1.32-1.80)	**.003**
URR	72.7 ± 6.4	71.9 ± 6.7	73.2 ± 7.0	73.7 ± 6.3	74.0 ± 6.1	72.8 ± 6.6	**.015**
Clotting events (%)	5.2	5.6	5.3	3.8	4.2	3.5	**.026**

Values are expressed as n (%), mean ± standard deviation, median (first-third quartiles). URR: urea reduction rate. * result of overall period comparisons.
URR, urea reduction rate.
*Result of overall period comparisons.

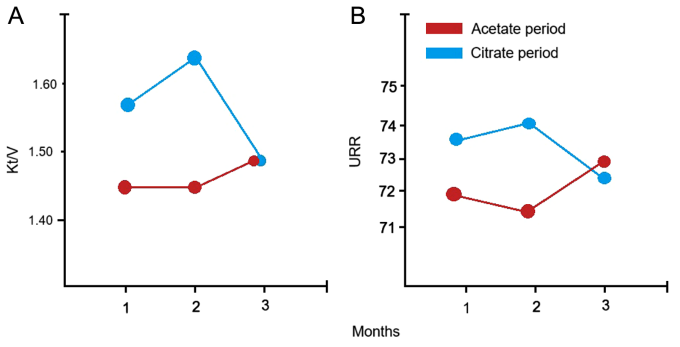

Figure 1. The course of Kt/V and URR values according to treatment months.

solution period. Although there was a decrease in the third month, there was an increase when looking at overall period. The short period of citrate use in the study, three months, prevents an elaborate explanation of this decrease. These results could be explained by the anticoagulant effect of citrate molecules and the prevention of the closing of the membrane pores, which increases dialyzer efficiency. In fact, the results were compatible with previous studies. Kossmann et al[8] used citrate as an acidifying agent in dialysis solution for 147 HD patients over six months. An increase in the Kt/V urea value (from 1.51 to 1.57) of the patients was observed. Also, when the standard acetate-containing acidic dialysis solution was reused, the Kt/V urea value decreased. This impact of citrate was attributed to improving solute clearance.[12] The results of a different study reported that citrate-containing acidic dialysis solution is associated with an increase in dialyzer reuse, reduced clotting, and increased Kt/V urea (1.23 to 1.47).[13]

In addition, fluctuating Kt/V values were observed in the third month of the citrate-containing acidic dialysis solution period, in contrast to stable values in the acetate-containing acidic dialysis solution period. This fluctuation of Kt/V was not easily explained with simple because it was shown that significant variation occurs within individuals. Vascular access efficacy, blood pump rate, time on dialysis, and fluid removal were associated with Kt/V calculation. Also, anticoagulation and circuit

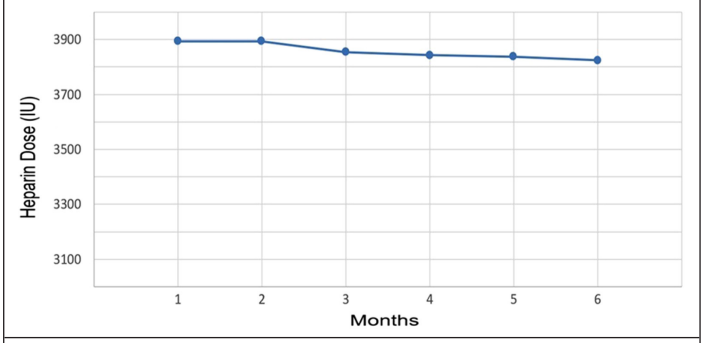

Figure 2. The average administered heparin dose per hemodialysis session according to monthly.

clotting affect the mentioned parameters. Lambie et al[14] investigated intra-individual variation of Kt/V. They also stated that 55% of patients had Kt/V variation that could change their status from adequate to inadequate dialysis within one month. When the medical records of the cohort were examined, hypotension attacks were detected in a few patients whose Kt/V values decreased in the third month. This may have been a factor that reduced dialysis efficacy.

This contribution of citrate to dialysis efficiency was mainly attributed to its anticoagulant features. Blood clotting inhibition in dialysis equipment is an important factor for effective dialysis. Blood comes into contact with intravenous cannulas, dialysis circuits, drip chambers, internal parts of the dialyzer, and the dialysis membrane during HD. Clotting could be initiated by these thrombogenic surfaces and exposure to air in the drip chambers.

Heparin is the most commonly preferred pharmacological agent for anticoagulation. The efficiency of the dialyzer is decreased by clogging of fibers and pores due to blood clots. Microcoagulation of dialyzer fibers and membrane pores frequently occurs during the use of heparin, although it is usually not noticed.[13] This ignored coagulation on pores does not hinder the completion of HD, however, reduces the solute movements and dialysis efficiency. Clotting may also decrease even Kt/V values, which is the indicator of dialysis adequacy. Additionally, heparin had some undesired side effects; such as bleeding risk, thrombocytopenia, hyperkalemia, hypertriglyceridemia, and metabolic bone disease.[15]

Systemic citrate anticoagulation was successfully applied during HD. Also, Mehta et al[16] administered regional citrate for anticoagulation of continuous hemodiafiltration. Citrate administration provided extended filter life and decreased filter clogging during dialysis in critical care patients.[17]

In this study citrate was not used an alternative anticoagulant to heparin. Occasionally, there are dialysate varieties that contain citric acid as an alternative acidifying agent instead of standard acetic acid. Furthermore, it is claimed that the use of citric acid reduces the anticoagulant requirement and the risk of clotting in the dialysis circuit and dialyzer. However, in a study conducted by Leung et al,[18] a statistically significant decrease was not observed in heparin dose with citrate-containing acidic dialysis solution compared to acetate-containing acidic dialysis solution in 20 HD patients. In the observed results, the required heparin dose did not decrease. Also, previous studies revealed that citrate can increase the efficiency of HD by reducing platelet accumulation on the dialyzer membrane.[4]

The outcomes are not surprising because citrate molecules have a limited impact on blood coagulation due to being situated on the dialysate side. Although a small amount of citrate does enter the patient's bloodstream, the concentration in the

patient's blood is only one-sixth of the citrate concentration used for dialysis anticoagulation. Consequently, this does not augment a systemic anticoagulation effect. Calcium-citrate complexes are adequately removed via dialysis procedure. In fact, approximately 75% of the citrate load is removed through both diffusion and convection, enhancing the viability of citrate-based anticoagulation protocols.[19] This increases the applicability of citrate-based anticoagulation protocols.[20] The results from Bakker et al indicated plasma citrate levels lower than 0.29 mmol/L, a value well below the upper safety limit of 0.85 mmol/L.[21]

The potential impact of citrate-containing acidic dialysis solution on metabolic parameters, particularly plasma calcium levels, is a critical clinical concern. Grundström et al[22] conducted a study examining the effects of citrate and acetate containing acidic dialysis solutions on metabolic parameters in HD. In this short-term study, both groups underwent HD using solutions with the same calcium concentration (1.5 mmol/L). The researchers observed a decrease in plasma ionized calcium levels and an increase in PTH levels in the citrate dialysis group. Moreover, there were no discernible differences in plasma levels of inflammation and oxidative stress markers between the 2 groups. Similar findings were reported in another study where additional calcium was introduced into citrate-containing acidic dialysis solution and compared with acetate-containing dialysate. This comparison revealed low calcium levels and elevated PTH levels in the citrate-containing acidic dialysis solution group.[10]

A reduction in serum calcium levels was determined in the patients, aligning with findings in existing literature. Also, there was an increase in PTH levels. However, no significant differences were identified in serum phosphate levels and calcium-phosphate product (CaxP) values between the 2 periods. Despite this statistically significant variance, no clinical signs of hypocalcemia or heightened incidence of dialysis-related cramps were noted. In a separate multicenter randomized study involving 120 patients undergoing HD with a high concentration of (3 mmol/L) citrate-containing acidic dialysis solution, severe hypocalcemia or acid-base disturbances were not reported. These datas conform with the findings. Furthermore, a statistically significant decrease in predialysis venous bicarbonate levels was observed in this study, consistent with the majority of studies in the existing literature.[23,24]

A significant decrease in the frequency of clotting events was observed during the citrate-containing acidic dialysis solution period. Furthermore, there were no serious bleeding events reported during the follow-up period with both citrate and acetate. There was no statistically significant change in the heparin dose for both dialysate periods. It's important to note that no specific reduction in heparin dose was implemented during the citrate-containing acidic dialysis solution period. The primary reason for reducing heparin dose was prolonged post-dialysis vascular access hold time, while increased clotting in the dialysis circuits was the main factor for dose escalation.

Some limitations of the current study, such as the lack of a control group and nursing behavior records, can be mentioned. The main reason for creating a control group was the inability to reach the same number of patients (n = 80) who met the inclusion criteria in the center where the study was conducted. Because the anticoagulant treatments and the presence of dialysis catheters as vascular access were obstacles to the inclusion of the patients in the study. There were no records about nursing behaviors to the patients. However, the nurse performing dialysis did not implement any different practices regarding the solution used by the patient.

Also, the duration of citrate-containing acidic dialysis solution application was as short as 3 months. Extending this period would allow for comprehensive analyzes of clinical parameters. Moreover, this study focused on assessing solute clearance via a small-sized molecule like urea.

CONCLUSION

In conclusion, while acetate-containing acidic dialysis solution is commonly used in HD globally, this study observed enhanced dialyzer function with effective anticoagulation of the extracorporeal system using citrate-containing acidic dialysis solution. Furthermore, the adoption of citrate-containing acidic dialysis solution could yield economic benefits, especially in countries where reused dialyzers are prevalent in HD practice. It would be beneficial to explore the impact of this increased Kt/V urea value on clinical manifestations and overall survival through long-term studies.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erciyes University (Date: 03.11.2021; Number: 2021/699).

Informed Consent: Verbal and written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – K.E., O.O.; Design – K.E., O.O.; Supervision – O.O.; Resources – O.O.; Materials – K.E.; Data Collection and/or Processing – C.U.; Analysis and/or Interpretation – C.U., K.E.; Literature Search – C.U.; Writing Manuscript – K.E., C.U.; Critical Review – O.O.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Lowrie EG, Laird NM, Parker TF, Sargent JA. Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. *N Engl J Med*. 1981;305(20):1176-1181. [CrossRef]
2. Cheung AK, Leypoldt JK. The hemodialysis membranes: a historical perspective, current state and future prospect. *Semin Nephrol*. 1997;17(3):196-213.
3. Novello A, Kelsch RC, Easterling RE. Acetate intolerance during hemodialysis. *Clin Nephrol*. 1976;5(1):29-32.
4. Hofbauer R, Moser D, Frass M, et al. Effect of anticoagulation on blood membrane interactions during hemodialysis. *Kidney Int*. 1999;56(4):1578-1583. [CrossRef]
5. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. *J Am Soc Nephrol*. 1993;4(5):1205-1213. [CrossRef]
6. Eknoyan G, Beck GJ, Cheung AK, et al. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med*. 2002;347(25):2010-2019. [CrossRef]
7. Daugirdas JT, Depner TA, Inrig J. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis*. 2015;66(5):884-930. [CrossRef]
8. Kossmann RJ, Gonzales A, Callan R, Ahmad S. Increased efficiency of hemodialysis with citrate dialysate: a prospective controlled study. *Clin J Am Soc Nephrol*. 2009;4(9):1459-1464. [CrossRef]
9. Huang S, Sandholm K, Jonsson N, et al. Low concentrations of citrate reduce complement and granulocyte activation in vitro in human blood. *Clin Kidney J*. 2015;8(1):31-37. [CrossRef]
10. Sequera P, Pérez García R, Molina Nuñez M, et al. Prospective randomized multicenter study to demonstrate the benefits of haemodialysis without acetate (with citrate): ABC-treat Study. Acute effect of citrate. *Nefrol (Engl Ed)*. 2019;39(4):424-433. [CrossRef]
11. Dellepiane S, Medica D, Guarena C, et al. Citrate anion improves chronic dialysis efficacy, reduces systemic inflammation and prevents chemerin-mediated microvascular injury. *Sci Rep*. 2019;9(1):10622. [CrossRef]
12. Panichi V, Fiaccadori E, Rosati A, et al. Post-dilution on line haemodiafiltration with citrate dialysate: first clinical experience in chronic dialysis patients. *ScientificWorldJournal*. 2013;2013:703612. [CrossRef]
13. Ahmad S, Callan R, Cole J, Blagg C. Increased dialyzer reuse with citrate dialysate. *Hemodial Int*. 2005;9(3):264-267. [CrossRef]
14. Lambie SH, Taal MW, Fluck RJ, McIntyre CW. Analysis of factors associated with variability in haemodialysis adequacy. *Nephrol Dial Transplant*. 2004;19(2):406-412. [CrossRef]
15. Lai KN, Ho K, Cheung RC, et al. Effect of low molecular weight heparin on bone metabolism and hyperlipidemia in patients on maintenance hemodialysis. *Int J Artif Organs*. 2001;24(7):447-455. [CrossRef]
16. Mehta RL, Mcdonald BR, Aguilar MM, Ward DM. Regional citrate anticoagulation for continuous arteriovenous hemodialysis in critically ill patients. *Kidney Int*. 1990;38(5):976-981. [CrossRef]
17. Bihorac A, Ross EA. Continuous venovenous hemofiltration with citrate-based replacement fluid: efficacy, safety, and impact on nutrition. *Am J Kidney Dis*. 2005;46(5):908-918. [CrossRef]
18. Leung KC, Tai DJ, Ravani P, Quinn RR, Scott-Douglas N, MacRae JM. Citrate vs. acetate dialysate on intradialytic heparin dose: a double blind randomized crossover study. *Hemodial Int*. 2016;20(4):537-547. [CrossRef]
19. Ortiz-Melo DI, Kovalik EC. *Methods of Hemodialysis Anticoagulation. Handbook of Dialysis Therapy*. Elsevier; Amsterdam; 2023:118-125.
20. Kozik-Jaromin J, Nier V, Heemann U, Kreymann B, Böhler J. Citrate pharmacokinetics and calcium levels during high-flux dialysis with regional citrate anticoagulation. *Nephrol Dial Transplant*. 2009;24(7):2244-2251. [CrossRef]
21. Bakker AJ, Boerma EC, Keidel H, Kingma P, van der Voort PH. Detection of citrate overdose in critically ill patients on citrate-anticoagulated venovenous haemofiltration: use of ionised and total/ionised calcium. *Clin Chem Lab Med*. 2006;44(8):962-966. [CrossRef]
22. Grundström G, Christensson A, Alquist M, Nilsson L-G, Segelmark M. Replacement of acetate with citrate in dialysis fluid: a randomized clinical trial of short term safety and fluid biocompatibility. *BMC Nephrol*. 2013;14(1):216. [CrossRef]
23. Gabutti L, Lucchini B, Marone C, Alberio L, Burnier M. Citrate-vs. acetate-based dialysate in bicarbonate haemodialysis: consequences on haemodynamics, coagulation, acid-base status, and electrolytes. *BMC Nephrol*. 2009;10:7. [CrossRef]
24. Molina Nuñez M, de Alarcón R, Roca S, et al. Citrate versus acetate-based dialysate in on-line haemodiafiltration. A prospective crossover study. *Blood Purif*. 2015;39(1-3):181-187. [CrossRef]