

Analysis of the Effect of High-Dose Segmental Citrate Anticoagulation in High Flux Hemodialysis

Xubo Fu*

The Second People's Hospital of Kunming, Kunming 650000, Yunnan Province China

*Corresponding author: Xubo Fu, fu81822640@163.com

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the clinical effect of high-dose citrate in segmental extracorporeal anticoagulation for high-throughput hemodialysis. *Methods:* The subjects included in this study were admitted to the hospital for maintenance hemodialysis treatment from January 2021 to January 2023. All patients had a high risk of bleeding and received 4% trisodium citrate anticoagulant treatment, administered at a rate of 200 mL/h before and after the dialyzer. The anticoagulant effects achieved by the patients were observed and analyzed. *Results:* The total number of patients who received high-dose segmented citrate extracorporeal anticoagulation dialysis treatment was 50, with each patient undergoing 100 treatments. During the treatment, 2 patients had to end the treatment early due to transmembrane pressure exceeding 30 mmHg and an increase in venous pressure exceeding 250 mmHg; the treatment times for these patients were 20 minutes and 200 minutes, respectively. The remaining patients successfully completed the 4-hour treatment. Blood pH and calcium ion concentration in the venous pot were monitored. It was observed that before dialysis, after 2 hours of dialysis, and at the end of dialysis, the blood pH of the patients remained within a relatively normal range. Although some patient levels changed after dialysis, they remained within the normal range. No adverse reactions (such as numbness of the limbs or convulsions) were observed during the anticoagulant treatment. *Conclusion:* Administering 4% trisodium citrate at a rate of 200 mL/h before and after the dialyzer achieves a good anticoagulant effect, maintains the patient's blood gas levels within the normal range at the end of dialysis, and causes no adverse reactions.

Keywords: High dose; Segmented citrate; High flux; Hemodialysis; Anticoagulation effect

Online publication: June 24, 2024

1. Introduction

The prerequisite and key to the smooth implementation of hemodialysis is an effective extracorporeal anticoagulation effect. Regular dialysis patients may have contraindications to certain drugs, such as low molecular weight heparin, due to factors like active bleeding or perioperative status. In such cases, heparin-free dialysis is the best method, supplemented by rinsing the extracorporeal circulatory pipeline with saline to prevent coagulation of blood *in vitro*.

Citrate implementation can chelate calcium ions, and its use in extracorporeal circulation and infusion after starting hemodialysis can alter calcium ions and impair coagulation factor activation, thereby improving the extracorporeal anticoagulation effect. Initially, using extracorporeal citrate anticoagulation with calcium-free dialysis fluid was ideal for anticoagulation. However, it required constant monitoring of calcium ion content and adjustments to citrate and calcium infusion, making the process cumbersome and prolonging treatment time^[1].

After improvements, conventional calcium-containing dialysis solutions are now widely applied without the need for calcium supplementation. However, the post-dialyzer blood circuit tubing remains highly susceptible to coagulation, which can hinder the smooth progress of dialysis treatment^[2].

In the Second People's Hospital of Kunming, from January 2021 to January 2023, high-dose segmental citrate treatment on maintenance hemodialysis patients with a high risk of bleeding was performed. The results achieved were ideal, demonstrating the effectiveness of this approach.

2. Materials and methods

2.1. General information

The included subjects were admitted with the need to undergo maintenance hemodialysis treatment from January 2021 to January 2023, all of them had the existence of high bleeding risk and received 4% trisodium citrate anticoagulation treatment. There are 30 males and 20 females, aged 35–69 years old, with a mean age of 49.57 ± 10.24 years old. Their disease duration was 1–3 years, with a mean duration of 1.68 ± 0.15 years. Before treatment, the patients' prothrombinogen time was 12.25 ± 1.36 s, activated partial thromboplastin time was 30.19 ± 8.72 s, and platelet count was $(211.35 \pm 50.42) \times 10^9/L$.

Inclusion criteria: (1) The patients' conditions were confirmed by relevant examinations and had indications for maintenance hemodialysis treatment; (2) The patients and their families agreed to join the study.

Exclusion criteria: (1) Those who have difficulty correcting hypoxemia; (2) Those who are combined with cognitive disorders and infectious diseases; (3) Those who are combined with hepatic and renal dysfunction.

2.2. Methods

Hemodialysis treatment was carried out for all patients using a hemodialysis machine. Each treatment session lasted 4 hours, with a blood flow rate of 200 mL per minute. The dialysis fluid temperature was set to approximately 36 degrees Celsius, and the flow rate of the dialysis fluid was 500 mL per minute. The electrolyte concentrations in the dialysis fluid were as follows: (1) Sodium: 135 mmol/L; (2) Bicarbonate: 26–28 mmol/L; (3) Potassium: 2–4 mmol/L; (4) Calcium: 1.5 mmol/L; (5) Magnesium: 0.5 mmol/L; (6) Chlorine: 106–110 mmol/L. A high-flux dialyzer with an ultrafiltration coefficient of 50 mL/h/mmHg and a membrane area of 1.5 m² was used. Before treatment, the blood tubes and dialyzers were rinsed with 1 L of normal saline, and dialysis was initiated. During the operation, 200 mL of 2% trisodium citrate was administered at a rate of 200 mL/h along the arterial and venous blood lines.

2.3. Observation indicators

Two aspects were monitored: venous pressure in the extracorporeal circulation line and transmembrane pressure. Blood samples were collected at different times: before dialysis, after 2 hours of treatment, and 2 hours after treatment was completed. Blood analysis was performed on these samples. Symptoms such as convulsions and limb numbness were observed in each patient during the treatment.

The final step was to assess the dialyzer and other conditions using a grading system: (1) Grade 0: No coagulation present in the bloodline tube or dialyzer; (2) Grade 1: Coagulation in the dialysis fiber, arterial, and venous pot not exceeding one-third; (3) Grade 2: Coagulation in the dialysis fiber, arterial, and venous pot

exceeding two-thirds. This assessment helped determine the effectiveness of the anticoagulation treatment.

2.4. Statistical methods

The processing tool (statistical software) version applied in this study was SPSS 28.0. The *t*-test was performed for the comparison of measurement data (mean \pm standard deviation), and the χ^2 test was performed for the comparison of count data (%). Statistically significant differences in comparisons were expressed as $P < 0.05$.

3. Results

3.1. Statistical analysis of high-dose segmental citrate anticoagulation effect

A total of 50 patients underwent extracorporeal anticoagulant dialysis with a high dose of segmented citric acid, with each patient receiving 100 treatments. Observation of treatment showed that 4 patients had to stop treatment in advance because 2 patients had transmembrane pressure > 30 mmHg while 2 patients had venous pressure > 250 mmHg, and the treatment time was 20 min and 200 min, respectively. The remaining patients successfully completed 4 hours of treatment, and the anticoagulation effect of high-dose segmented citric acid is shown in **Table 1**.

Table 1. Statistical analysis of the anticoagulation effect of high-dose segmented citrate [*n* (%)]

Dialyzer or vascular path location	Level 0	Level 1	Level 2	Level 3
Arterial pot	98 (97.03)	3 (2.97)	0 (0.00)	0 (0.00)
Dialyzer	87 (86.14)	9 (8.91)	2 (1.98)	3 (2.97)
Venous pots	76 (75.25)	19 (18.81)	5 (4.95)	1 (0.99)

3.2. Observation and analysis of the changes in intracorporeal and extracorporeal blood gas parameters

The pH value and calcium ion concentration of the blood in the venous pot were observed during the treatment. It can be seen that the pH value of the blood in the patient was in a relatively normal range before and after dialysis for 2 hours and after dialysis, and some indicators of the patient changed after dialysis, but they were still in the normal range. Citric acid was added to the dialyzer, and then the data in **Table 2** were analyzed. It can be seen that a series of indicators such as pH in the blood in the venous pot were lower than that in the blood in the body after 2 h hemodialysis treatment, and the calcium ion concentration showed an increasing trend ($P < 0.05$). Other data can be seen in **Table 2**.

Table 2. Observation and analysis of the changes in intracorporeal and extracorporeal blood gas parameters (mean \pm SD)

Targets	Pre-dialysis	Dialysis for 2 h		At the end of dialysis
		Venous pot	Vascular	
pH	7.36 \pm 0.04	7.36 \pm 0.15	7.68 \pm 0.15	7.62 \pm 0.05
Ions (mmol/L)	1.16 \pm 0.15	0.46 \pm 0.25	1.16 \pm 0.73	1.16 \pm 0.15
Total calcium (mmol/L)	2.35 \pm 0.19	2.67 \pm 0.19	2.68 \pm 0.34	2.72 \pm 0.19
Free sodium (mmol/L)	137.35 \pm 2.45	145.60 \pm 2.67	143.61 \pm 1.75	144.65 \pm 1.95
Base remaining (mmol/L)	-1.34 \pm 2.47	-3.68 \pm 2.15	1.26 \pm 1.68	1.67 \pm 1.25
Bicarbonate (mmol/L)	19.67 \pm 3.50	24.92 \pm 2.25	25.64 \pm 2.71	25.45 \pm 2.19

3.3. Occurrence of adverse reactions

No adverse reactions (numbness of limbs, convulsions, etc.) occurred during anticoagulation therapy in all patients.

4. Discussion

Due to the effective anticoagulant properties of citrate and the low risk of bleeding in patients, citrate has become an effective anticoagulation method for patients requiring continuous renal replacement therapy and those undergoing regular dialysis^[3].

During practice, it was found that calcium ion, present in conventional dialysis fluid, plays a critical role. When citrate is removed, its presence in the dialyzer significantly decreases, affecting the anticoagulant effect in the post-dialyzer venous pot. This often necessitates early termination of treatment. Therefore, it is essential to improve the method by applying a specific dose of citrate post-dialyzer to avoid significant intra-dialytic citrate loss and to enhance the anticoagulant effect^[4,5].

In this study, 50 patients underwent high-dose segmented citrate extracorporeal anticoagulation dialysis, each receiving 100 treatments. Observations revealed that 4 patients had to end treatment early: 2 due to transmembrane pressure > 30 mmHg and 2 due to an increase in venous pressure > 250 mmHg. The treatment durations were 20 minutes and 200 minutes, respectively. The remaining patients successfully completed the 4-hour treatment.

Blood pH and calcium ion concentration in the venous pot were monitored, as shown in Table 2. Before, during (at 2 hours), and after dialysis, the patient's blood pH remained within a normal range. Although some indicators changed, they remained within normal limits. No adverse reactions (such as numbness of limbs or convulsions) occurred during anticoagulation therapy. These results indicate a definite anticoagulant effect.

Previous studies suggest that a citrate concentration of 3–6 mmol/L in extracorporeal circulating blood can maintain calcium ion levels at no more than 0.35 mmol/L. After adding 4% trisodium citrate at a rate of 200 mL/h, the citrate concentration in the extracorporeal circulating blood after the dialyzer reached 2.7 mmol/L, ensuring effective anticoagulation and enabling patients to complete the 4-hour dialysis treatment. No adverse reactions were observed, and ionized calcium levels remained within the normal range, suggesting rapid decomposition of calcium citrate in the body, promoting calcium ion release into the bloodstream^[6,7].

Post-treatment, citrate is metabolized into bicarbonate. Although calcium ion levels and blood bicarbonate expression increased significantly, practical assessment and analysis indicated they remained normal. This approach allows for adjustments to maintain these indicators within a reasonable range^[8-10]. For patients with high-risk bleeding, short-term citrate anticoagulation can improve physical and mental safety during treatment without interfering with long-term volume control. For patients who struggle with volume control, maintaining volume stability and scientifically managing dialysis frequency is crucial^[11,12].

In conclusion, infusing 4% trisodium citrate at a rate of 200 mL/h before and after the dialyzer promotes effective anticoagulation and helps prevent adverse effects.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Ke X, Li Y, Luo L, 2021, Clinical Observation on the Anticoagulation Effect of High-Dose Segmented Citrate on High-Flux Hemodialysis. *Journal of Clinical Nephrology*, 21(8): 677–680.
- [2] Feng Y, 2022, Clinical Effect of Two-Stage Anticoagulation with Citrate on Maintenance Hemodialysis Patients. *Chinese and Foreign Medical Treatment*, 41(15): 10–14.
- [3] Gao C, Yang W, Wu Y, 2023, Effectiveness of Sodium Citrate Anticoagulation in Patients with High Bleeding Risk Undergoing DFPP. *Chongqing Medicine*, 52(1): 31–38.
- [4] Yu L, Xu X, 2022, Analysis of the Application Effect of Segmental Citrate Anticoagulation in Hemodialysis. *Chinese and Foreign Medical Treatment*, 41(18): 56–68.
- [5] Xi C, Liu T, Cai R, et al., 2022, Clinical Observation on Continuous Venous Hemodialysis Filtration with Calcium-Containing Dialysis Solution and Replacement Solution with Local Citrate Anticoagulation. *China Blood Purification*, 21(8): 576–579.
- [6] Chen J, Sun Y, He L, et al., 2022, Comparison of Anticoagulant Effects of Segmental Anticoagulation Regimens with Different Concentrations of Sodium Citrate in Hemodialysis Patients. *Clinical Blood Transfusion and Laboratory*, 24(4): 469–476.
- [7] Liu Z, Zeng Q, Yuan J, et al., 2022, A Study of Postfiltration Free Calcium Target Correction During Continuous Venovenous Hemodialysis Filtration with Dilution After Simplified Citrate Anticoagulation. *Journal of Clinical Nephrology*, 22(3): 209–213.
- [8] Wang H, Xie P, Jie Z, et al., 2023, Optimization of Calcium Monitoring During Segmental Citrate Anticoagulation for IHD in Patients with High Bleeding Risk. *Chongqing Medicine*, 52(17): 2696–2700.
- [9] Yuan J, 2022, Clinical Comparison of Low Molecular Heparin Sodium and Sodium Citrate on Hemodialysis in Patients with High Risk of Bleeding. *Chinese Journal of Blood Transfusion*, 35(1): 39–42.
- [10] Pu Y, Zhang L, Wang F, et al., 2023, Application of Local Citrate Anticoagulation in Hemoperfusion Combined with Continuous Renal Replacement Therapy. *West China Medicine*, 38(8): 1174–1180.
- [11] Zhang Y, Zhang L, Wang C, et al., 2022, Optimization of Ionized Calcium Monitoring in Continuous Blood Purification Therapy with Local Citrate Anticoagulation. *Nursing Research*, 36(11): 1915–1919.
- [12] Jia H, Li Y, Jin H, 2020, Clinical Observation of Local Citrate Anticoagulation in Hemodialysis in Elderly Patients at High Risk of Bleeding. *Thrombosis and Hemostasis*, 26(4): 549–552.
- [13] Zhang X, Chasng A, Yang Z, et al., 2023, Analysis of the Effect of Using Low-Calcium Versus Standard Calcium Dialysate with Segmented Citrate Anticoagulant Dialysis. *Journal of Dali University*, 8(4): 54–59.
- [14] Wang C, Yu T, Cai G, et al., 2021, Effect of Two Citrate Anticoagulation Methods in Hemodialysis Treatment of Patients After Parathyroidectomy. *Journal of Practical Clinical Medicine*, 25(15): 75–78.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.