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Comparison of Citrate and Heparin for Continuous Renal Replacement Therapy in Pediatric Intensive Units

Çocuk Yoğun Bakım Ünitelerinde Sürekli Renal Replasman Tedavisinde Sitrat ve Heparinin Karşılaştırılması

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Abstract

Introduction: The choice of anticoagulation in continuous renal replacement therapy (CRRT) is very important for circuit life and bleeding complications. The primary outcome of our study was circuit lifespan. Secondary outcomes, we aimed to identify metabolic complications.

Methods: This retrospective study was conducted in our pediatric intensive care unit between November 2019 and March 2021.

Results: The study included 35 patients, 19 with regional citrate anticoagulation (RCA) and 16 with heparin anticoagulation (HA). The patient's pediatric risk of mortality III score was similar in both groups (p=0.76); also, p-SOFA score was higher in the RCA group and was significant [(HA: 6.43±5.24, RCA: 10.21±3.96, p=0.024)]. 100 hemofilter were used in all therapies (total CRRT times 4115.50 h), 43 in HA and 57 in the RCA group. Median circuit life and total CRRT duration were longer for RCA [(33.0; 3.0-168.0) (30.5; 9.0-520.0) (14.0; 0.75-285.0) (94.0; 11.0-394.0) (p=0.043\0.021)] than for HA. Hypocalcemia was detected 9/19 in the RCA and 4/16 in the HA (p=0.021). HA was preferred in 3 patients and RCA in 4 patients who needed ECMO simultaneously with CRRT. The most common reason for circuit change in RCA groups is patient-related and clotting in the heparin group. Mortality rates were not the same in both groups (p=0.012).

Conclusion: Citrate 18/0 has better safety and efficacy with a long filter life and easily manageable systemic complications. In addition, anticoagulation with RCA may be preferred in patients monitored with ECMO and in need of CRRT.

Keywords: Heparin, regional citrate anticoagulation, citrate 18/0, continuous renal replacement therapy, pediatric intensive care unit

Öz

Giriş: Sürekli renal replasman tedavisinde (CRRT) antikoagülasyon seçimi devre ömrü ve kanama komplikasyonları için çok önemlidir. Çalışmamızın birincil sonucu devre ömrü idi. İkincil sonuçlar, metabolik komplikasyonları belirlemeyi amaçladık.

Yöntemler: Bu geriye dönük çalışma, Kasım 2019-Mart 2021 tarihleri arasında çocuk yoğun bakım ünitemizde yapılmıştır.

Bulgular: Çalışmaya 19'u bölgesel sitrat antikoagülasyon (RCA) ve 16'sı heparin antikoagülasyonlu (HA) olmak üzere 35 hasta dahil edildi. Hastanın çocuk ölüm riski III skoru her iki grupta da benzerdi (p=0,76); SOFA puanları da benzer değildi [(HA: 6,43±5,24, RCA: 10,21±3,96, p=0,024)]. Toplam CRRT süresi 4115,50 saat idi. HA grubunda 43 ve RCA grubunda 57 olmak üzere toplam 100 hemofiltre seti kullanıldı. HA grubuna göre; medyan devre ömrü ve toplam CRRT süresi RCA grubunda daha uzundu [(33,0; 3,0-168,0) (30,5; 9,0-520,0) (14,0; 0,75-285,0) (94,0; 11,0-394,0) (p=0,043\0,021)]. Hipokalsemi RCA grubunda daha fazla idi [RCA: 9/19, HA: 4/16 (p=0,021)]. CRRT ile eş zamanlı ECMO ihtiyacı olan 3 hastada HA, 4 hastada RCA tercih edildi. RCA gruplarında devre değişikliğinin en sık nedeni hasta kaynaklı iken heparin grubunda pıhtılaşmadır. Mortalite oranları her iki grupta da aynı değildi (p=0,012).

Sonuç: Sitrat 18/0, uzun filtre ömrü ve kolayca yönetilebilen sistemik komplikasyonlar ile daha iyi güvenlik ve etkinliğe sahiptir. Ayrıca ECMO ile izlenen ve CRRT ihtiyacı olan hastalarda RCA ile antikoagülasyon tercih edilebilir.

Anahtar Kelimeler: Heparin, bölgesel sitrat antikoagülasyon, sitrat 18/0, sürekli renal replasman tedavisi, çocuk yoğun bakım ünitesi

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Introduction

Continuous renal replacement therapies (CRRT) are frequently used in pediatric intensive care units (PICUs). In particular, acute kidney injury, volume overload and multiple organ failure are the most important causes. It has both essential and widespread as well as technical and management difficulties. It has hardly been performed in small children, especially severe clinical status and multi-organ failure due to vascular access and anticoagulation difficulties. In CRRT, anticoagulation is crucial for circuit lifespan and bleeding complications. Circuit runtime is key to the efficacy of treatment.[1] Systemic heparin anticoagulation (HA) is the traditional method because it is cheap and has much experience. However, HA increases bleeding and may cause heparin-induced thrombocytopenia (HIT).[2] Regional citrate anticoagulation (RCA) is an alternative method. Anticoagulation in the RCA is limited to the extracorporeal circuit. This makes RCA a good option in patients at risk of bleeding and in HIT. Moreover, evidence suggests that RCA extends filter lifespan.[3-6]

Few studies compared heparin and citrate efficacy and side effects in children on CRRT.[7] We used prismocitrate 18\0 (Baxter, US®) because, in the literature, there are few studies about prismicitrate 18\0. This study aims to compare the effectiveness of HA and RCA to circuit lifespan, metabolic complications, bleeding, and outcomes in critically ill children on CRRT in our PICU.

Materials and Methods

The study was retrospectively planned and was conducted in our PICU between November 2019 and March 2021. Demographic information, pediatric risk of mortality III (PRISM III) scores, pediatric sequential organ failure assessment (pSOFA) score, indication for CRRT, risk factors of acute kidney injury, CRRT modality (CVVH, CVVHD, CVVHDF) were recorded. We accepted the indication of CRRT as acute kidney injury, fluid overload (FO), electrolyte abnormalities, metabolic acidosis, multi-organ failure, poisoning.

Prismaflex (Baxter, USA) device was used. Hemodialysis catheters between 7F and 12F were preferred based on the age and weight of the child. We preferred that extracorporeal membrane oxygenation (ECMO) circuit connection be used if the patient was under ECMO running. We inserted different central venous catheters for other therapies with or without ECMO patients.

HF 20, M 60, M 100 membranes were used for CRRT circuit. The priming solution selection was based on clinical status, weight and hemoglobin value. For 10 kilograms and below, packed red cells were preferred. Up to 10 kilograms and in circulatory failure, 5% albumin was used. Normal saline was used in non-decompensated patients and patients over 10 kilograms.

We used for anticoagulation heparin or citrate for hemofilter lifespan prolongation. In our PICU, we prefer RCA for patients whom bleeding risks such as thrombocytopenia (<150.000/mm^3) and coagulation troubles. Heparin is chosen in patients with relatively stable and without bleeding risks such as poisoning and inborn metabolic disease crises. Inpatient heparin is preferred for anticoagulation; we also used activated partial thromboplastin time (aPTT) value and activated clotting time (ACT) for effectiveness evaluation. HA group, the patient received an initial intravenous bolus of unfractionated heparin at doses ranging from 20 to 30 IU/kg body weight. This was followed by infusion at a rate of 10 IU/kg/hour. During the procedure, a post-filter ACT of 180 to 220 seconds and aPTT values of 60 to 80 seconds were targeted. MultiBic potassium-free (Fresenius, Germany) was preferred as a dialysate and replacement fluid. Prismocitrare 18/0 (Baxter, USA) solutions were used in the citrate group. The initial citrate infusion rate (mL/h) was determined based on blood flow (Qb×1.6 mL/h). The flow rate was adjusted so that the target post-filter (venous port) ionized calcium concentration was between 0.25 and 0.35 mmol/L. The systemic ionized calcium concentration was targeted at 1.0 to 1.2 mmol/L, and a calcium gluconate infusion (10% calcium gluconate with 5% glucose-0.1 mmol/mL) was administered through the return line of the circuit to maintain it in this range. The citrate effect was neutralized using a continuous calcium infusion. Ionized calcium values were monitored pre and post filtration. Arterial blood gases were closely monitored to determine the acid-base status. Metabolic acidosis with total calcium/ionized calcium ≥2.5 for more than 48 hours and high anion gap is characterized by citrate accumulation CA). The primary outcome of our study was circuit lifespan. Secondary outcomes, we aimed to identify metabolic complications. Clinical complications (bleeding, hemodynamic instability, HIT) and metabolic complications including hypocalcemia (total calcium level <9 mg\dL), hypercalcemia (iCa++>1.25 mmol\L), metabolic acidosis [pH<7.35 or base excess (BE) <-3], metabolic alkalosis (pH>7.45 or BE>+3) and citrate toxicity were noted. HIT diagnostic criteria are shown in Figure 1.[7] The Ankara University Ethics Committee approved the study (number: İ6-441-21).

Statistical Analysis

Statistical Package for Social Sciences (SPSS version 26.0 for Windows, Chicago, IL) was used. Groups were compared using the independent-samples Student's t-test, Mann-Whitney U, chi-squared tests where appropriate. P<0.05 was considered statistically significant.

4 Ts score for estimating the pretest probability of heparin-induced thrombocytopenia (HIT)

4 Ts score parameters:	
Thrombocytopenia:	
▪ PLT decrease >50% **AND** nadir ≥20,000/microL **AND** no surgery within preceding 3 days	2 points
▪ PLT decrease >50% **BUT** surgery within preceding 3 days **OR** any combination of PLT fall and nadir that does not fit criteria for 2 or 0 points (eg, 30 to 50% fall or nadir 10,000 to 19,000/microL)	1 point
▪ PLT decrease <30% **OR** nadir <10,000/microL	0 points
Timing of onset after heparin exposure:	
▪ 5 to 10 days **OR** 1 day if exposure within past 5 to 30 days	2 points
▪ Probable 5 to 10 days (eg, missing PLT counts) **OR** >10 days **OR** <1 day if exposure within past 31 to 100 days	1 point
▪ ≤4 days without exposure within past 100 days	0 points
Thrombosis or other clinical sequelae:	
▪ Confirmed new thrombosis, skin necrosis, anaphylactoid reaction, or adrenal hemorrhage	2 points
▪ Suspected, progressive, or recurrent thrombosis, skin erythema	1 point
▪ None	0 points
Other cause for thrombocytopenia:	
▪ None	2 points
▪ Possible (eg, sepsis)	1 point
▪ Probable (eg, DIC, medication, within 72 hours of surgery)	0 points
Interpretation:	
0 to 3 points – Low probability (<1%)	
4 to 5 points – Intermediate probability (approximately 10%)	
6 to 8 points – High probability (approximately 50%)	

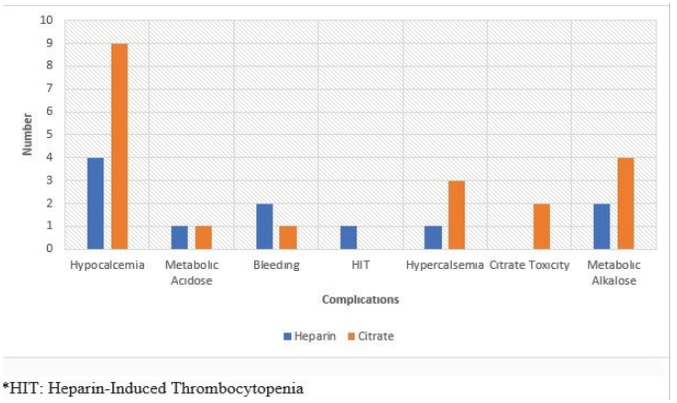
HIT is a clinical and laboratory diagnosis, and this score is not intended to take the place of clinical judgment by a clinician with experience in diagnosing and managing HIT. Refer to UpToDate for details of the evaluation.

PLT: platelet; DIC: disseminated intravascular coagulation.

Adapted from: Lo GK, Juhl D, Warkentin TE, et al. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost 2006; 4:759.

UpToDate®

Figure 1. 4 Ts score for estimating the pretest probability of heparin-induced thrombocytopenia (HIT)



*HIT: Heparin-Induced Thrombocytopenia

Figure 2. Frequency of metabolic complications

Results

Between the dates included in the study, 94 patients were hospitalized in the PICU and 35 (3.8%) required CRRT. Citrate was preferred for anticoagulation in 19 patients and heparin in 16 patients. Twelve (34.3%) patients were female. The mean age was 52.84 months in the HA group and 94.16 months in the RCA group (p=0.96). Also, there was a significant difference between the pSOFA scores as 6.43±5.24 in HA 10.21±3.96 in RCA groups (p=0.024) and PRISM III scores were similar in both groups (p=0.76). The most frequent reason for the need for dialysis was acute metabolic disease attack in heparin group and FO in citrate group. Other indications were hyperammonemia, electrolyte imbalance, acute renal failure, and metabolic acidosis. There was a significant difference in mortality rates between the groups [heparin groups 7/16 (20%) vs. citrate groups 9/19 (45.7%), p=0.012)]. There was no significant difference between the demographic and clinical characteristics of the patients for both groups (Table 1). One hundred hemofilter were used in all therapies (total CRRT times 4115,50 h), 43 in the heparin group and 57 in the citrate group. Median circuit lifetime and total CRRT duration was significantly longer for RCA [(33.0; 3.0-168.0), 30.5; (9.0-520.0)] than for HA (14.0; 0.75-285.0) (94.0; 11.0-394.0) (p=0.043\0.021). CRRT characteristics of patients for both groups are given in Table 2.

Blood parameters before CRRT were similar for both groups. Patients were assessed for side effects developed during CRRT (with a blood sample taken 1, 3, 7, 14 days after CRRT initiation). The frequency of metabolic complications is shown in Figure 2. Hypocalcemia was detected 47.3% (n=9/19) in the RCA and 25% (n=4/16) in the HA (p=0.021). In the RCA group, eight patients (22.8%, n=8/35) and ın HA group 4 patients (11.4%, n=4/35) had an increased liver transaminase enzyme during CRRT. There was no difference in increased liver transaminase enzyme between the two groups (p=0.365).

Only two patients who had citrate toxicity in citrate groups were continued with heparin. In the heparin group, one patient had HIT.

Twenty-eight children (80%) were under mechanical ventilation at the initiation of CRRT. PEX was applied to 17 children with CRRT (48%). HA and RCA were used 3 and 4 patients who had undergone ECMO running together with CRRT. In the HA group, the mean aPTT value of patients on ECMO was 34.1±8.5, and the mean aPTT value of patients who were not on ECMO was 35.5±9.7. There was no significant difference found (p=0.73). In the HA group, bleeding occurred in a patient on ECMO running. There was no significant difference in total CRRT duration (p=0.724), median circuit lifetime (p=0.480), and the number of filters per patient on ECMO (p=0.711) with respect to anticoagulation modality Table 3. There was no significant difference between the two anticoagulation protocols in reasons for circuit failure. In ECMO patients, the most common cause of circuit change in RCA groups is the patient source, and in the heparin groups are clotting Table 2.

Table 1. The demographic and clinical characteristics of patients

	Heparin (n=16)	Citrate (n=19)	p*
Age (months) (mean ± SD)	52.84±67.38	94.16±74.09	0.96
Sex Male, n (%) Female, n (%)	 4 (11.4%) 12 (34.3%)	 8 (22.9%) 11 (31.4%)	0.288
Weight (kg) (mean ± SD)	15.06±12.39	21.89±15.02	0.15
PRISM III, (mean ± SD)	16.1±14.83	19.8±10.9	0.76
pSOFA score	6.43±5.24	10.21±3.96	0.024
Size 5F, n (%) 7F, n (%) 8-12F, n (%) ECMO circuit connection, n (%)	 1 (2.9%) 6 (17.1%) 6 (17.1%) 3 (8.6%)	 0 (0%) 5 (14.3%) 10 (28.6%) 4 (11.4%)	0.574
Length of stay of PICU (days), (mean ± SD)	15.13±14.09	18.47±16.36	0.52
Mechanical ventilation, (n), (%)	10 (62.5)	18 (94.7)	0.701
Mechanical ventilation (days), (mean ± SD)	18.10±10.56	18.56±16.34	0.21
Mortality, n (%)	7 (20%)	16 (45.7%)	0.012
VIS*	60.0 (20-140)	60.0 (10-275)	0.54
Before CRRT, (mean)			
WBC * (mean ± SD)	13533,38±5.731,94	14682,11±14018,74	0.76
Hemoglobin, (median)	9.4 (7.2-12.6)	9.1 (5.7-12.4)	0.707
Platelet count, (median)	276000 (41000-706000)	122000 (24000-532000)	0.145
aPTT, (median)	36.4 (30.4-59.6)	33.0 (24.7-58.0)	0.385
PT, (median)	15.9 (11.4-27.8)	15.0 (12.1-67.2)	0.806
INR, (median)	1.5 (1.04-2.39)	1.33 (1.02-5.89)	0.659
Fibrinogen, (median)	2.39 (0.85-6.89)	2.99 (1.07-4,60)	0.531
BUN (mean)	19.47±16.77	38.96±23.38	0.09
Creatinine (mean)	0.68 (0.18-3.75)	0.89 (0.22-2.41)	0.728
Potassium (mean)	4.02±0.66	3.88±1.08	0.63
Sodium (mean)	142.19±7.82	140.63±10.5	0.62
Albumin (mean)	32.54±6.92	31.01±4.76	0.94
ALT (mean)	218.67±510.35	156.16±380.65	0.685
AST (mean)	295.53±866.86	352.26±914.57	0.855
ALT (during CRRT)	239.33±518.134	229.94±432.647	0.955
AST (during CRRT)	758.33±1521.342	876.44±1984.94	0.852
Indication of CRRT Fluid overload, n (%) Acute renal failure, n (%) Electrolyte imbalance, n (%) Metabolic acidosis, n (%) Acute attacks of inborn metabolic disease, n (%) Hyperammonemia, n (%)	 4 (11.4) 3 (8.6) 1 (2.9) 1 (2.9) 5 (14.3) 2 (5.7)	 10 (28.6) 5 (14.3) 1 (2.9) 2 (5.7) 1 (2.9) 0 (0)	0.163

VIS: Vasoactive inotrop score, BUN: Blood urea nitrogen, WBC: White blood cell, aPTT: Activated partial thromboplastin time, PT: Protrombin time, INR: International normalized ratio, *p<0.05 was accepted statistically significant. Values represent as median (min-max); values represent as number (percentages); "±'' indicate values as mean ± SD, SD: Standard deviation, CRRT: Continuous renal replacement therapy, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, PICU: Pediatric intensive care unit

There were eight patients whose anticoagulation choices changed during the procedure. Because of the bleeding that developed in 4 of these patients, heparin was switched to citrate. In 2 of these patients, citrate was switched from citrate to heparin due to hypocalcemia and citrate toxicity. These values are presented in Table 4.

Discussion

In CRRT, anticoagulation is essential for circuit lifespan and is related to bleeding complications. Few studies compare heparin and citrate anticoagulation in the pediatric population on CRRT. A retrospective study by Sık et al.[4] in critically ill

Table 2. Properties of CRRT in both groups and reasons for circuit failure

	Heparin (n=16)	Citrate (n=19)	p*
Total CRRT duration (hour), median	30.5 (9.0-520.0)	94.0 (11.0-394.0)	0.021
Median circuit lifetime (hour), median	14.00 (0.75-285.0)	33.0 (3.0-168.0)	0.043
Number of filters per patient, median	2.5 (1.0-8.0)	2.0 (1.0-8.0)	0.745
Blood flow rate, median	60.0 (40.0-350.0)	100.0 (40.0-200.0)	0.152
Dialysate flow (ml\H), median	775 (300-1500)	850 (300-2100)	0.690
Citrate dose (Mmol\L), median		511.7	
Calcıum rate (Mmol\L), median		37.08	
Clotting, n (%)	9 (25.7)	12 (34.2)	0.678
Technical reason, n (%)	4 (11.4)	3 (8.5)	0.49
Patient related causes (mortality, for radiology etc..), n (%)	8 (22.8)	14 (40)	0.148
Input negative alarms, n (%)	2 (5.7)	5 (14.2)	0.349

Values represent as median (min-max), *p<0.05 was accepted statistically significant, CRRT: Continuous renal replacement therapy

Table 3. Properties of CRRT in ECMO and non-ECMO groups

	ECMO (n=7)	Non- ECMO (n=28)	p*	ECMO-HA (n=3)	ECMO-RCA (n=4)	p*
CRRT duration, (hour), median	168.0 (72.0-520.0)	46.0 (9.0-393.0)	0.005	138.0 (72.0-520.0)	258.25 (80.0-394.0)	0.724
Circuit lifetime, (hour), median	80.0 (7.0-285.0)	24.0 (0.75-72.0)	0.009	30.0 (7.0-285.0)	105.0 (57.0-168.0)	0.480
Filters per patient, (hour), median	3.0 (1.0-8.0)	2.0 (1.0-8.0)	1.0	3.0 (1.0-3.0)	2.5 (1.0-8.0)	0.711

Values represent as median (min-max), *p<0.05 was accepted statistically significant, CRRT: Continuous renal replacement therapy, ECMO: Extracorporeal membrane oxygenation, HA: Heparin anticoagulation, RCA: Regional citrate anticoagulation

Table 4. Anticoagulation switches for any cause

	Heparin to citrate (n=4)	Citrate to heparin (n=2)	p*
Hemoglobin, (median)	8.5 (8.0-9.0)	9.7 (9.0-10.1)	0.468
Trombosit, (median)	31000 (12000-50000)	45000 (33000-78000)	1.0
aPTT, (median)	42.0 (38.0-46.6)	35.7 (30.0-41.2)	1.0
PT, (median)	22.5 (15.9-29.1)	13.6 (12.4-27.8)	0.248
INR, (median)	2.05 (1.39-2.71)	1.16 (1.03-2.39)	0.245
Fibrinogen, (median)	3.75 (3.72-3.78)	1.59 (0.85-2.63)	0.06

Values represent as median (min-max)
aPTT: Activated partial thromboplastin time, PT: Protrombin time, INR: International normalized ratio

children compared RCA versus HA. In this study, filter lifetime was reported to be significantly higher in RCA, with 12.75 hours (IQR: 40-70). In another study, the median half-life for citrate was 17 hours higher than for heparin.[5] An another study,[8] they were used only prismocitrate 18/0 and reported circuit lifetime was higher in RCA than in HA (p=0.030). In a study in 59 adult patients was used 10\2 formulation in 28 patients and 18\0 formulation in 31 patients and reported median circuit lifetime was higher in 18\0 formulation than in 10\2 formulation (p=0.001). In our study, similar to pediatric studies in the literature, it was shown that the filter lifetime longer in CRRT performed with RCA. Long filter life decreases the possibility of blood loss and hemodynamic instability during circuit replacement.[9] This is important for the risk of bradykinin release syndrome and in children with low blood volume.[10] The longer median circuit lifetime demonstrated in these studies proves the advantages of RCA. However, our study was retrospective and was not double-blind and stratified according to the clinical condition of the patients, which was a major concern when interpreting the results. We choose citrate in case of bleeding risk such as thrombocytopenia. This may cause less clotting in the circuit.

The most important metabolic complication associated with citrate is metabolic alkalosis due to citrate metabolism; a multicenter study by Bunchman et al.[11,12] reported metabolic alkalosis of 11% in patients. Another study by Sık et al.[4] showed that metabolic alkalosis was detected 7.01% in the

citrate group. A retrospective review used only prismocitrate 18/0 of 30 critically ill children[8] metabolic alkalosis observed only in four cases (25%). We used prismocitrate 18\0 in the RCA groups due to problems associated with the use of prismocitrate 10/2 solution, such as hypomagnesemia, hypophosphatemia and the need for additional bicarbonate infusion. However, we reported that the rate of metabolic alkalosis with RCA was 21% higher than literature and similar to that reported by Soltysiak et al.[8] When we notified citrate-induced metabolic alkalosis, we increased the dialysis flow rate or decreased citrate flow rate and observed a high Ca++ level in the extracorporeal circuit.

The most commonly reported metabolic side effect of citrate is hypocalcemia as it affects cardiac contractility; we reported 47.3% hypocalcemia in the citrate group and 25% in the heparin group (p=0.021). Soltysiak et al.[8] reported a similar rate of hypocalcemia in the citrate group with 43.76%. Sık et al.[4] reported a hypocalcemia rate of 12.28% in the citrate group. In our study, the lowest calcium value was 0.45 mmol/L in a patient undergoing RCA. This value was immediately corrected by calcium reinfusion through a line and no cardiac dysrhythmia due to hypocalcemia was observed. Hypercalcemia was reported in 16.6% in the RCA group and 4.1% in the HA-CRRT group. The maximum systemic Ca++ value in the RCA group was 1.41 mmol\L. In our opinion, the main cause of hypercalcemia was due to additional calcium infusion and it is essential to control the composition and infusion rate of all extra fluids such as total parenteral nutrition in the management of hypercalcemia. The electrolyte balance of patients is affected by multiple factors and close follow-up is essential.

HA may increase the risk of bleeding in the critically ill pediatric patient group. Eleven retrospective and prospective observational studies compared the two anticoagulation options for bleeding and found that RCA was safer.[13-15] RCA has been shown to reduce the risk of bleeding with a risk ratio of 0.28 (95% CI: 0.15 to 0.50),[13] and there are studies showing a significant difference between the two groups[5-12] and Liao et al.[16] reported a similar finding in a meta-analysis. In our study, hemorrhagic complications developed in two patients in the HA group and one patient in the RCA group. Especially when performing HA in patients at risk of bleeding, for example in cardiac patients, the heparin dose should be kept comparatively lower to reduce the risk of bleeding. In the heparin group, one patient had HIT and was continued with citrate.

The mortality rate was higher in the citrate group (p=0.012). The pSOFA scores of the patients in the citrate group were also high during their hospitalization (p=0.024). Sık et al.[4] reported that both groups' mortality rates and PRISM scores were similar (p=0.954 and p=0.725). Another study reported mortality rates in the heparin group 25% and the RCA group 25% (p=1.00).[5] To date, there is no safe result that heparin reduces mortality because most studies have included very small groups of patients. In addition, Liao et al.[16-18] found the mortality rate to be similar in the two groups in their meta-analysis for adult patients.

Our study, unlike the literature, can be explained by the high mortality rate in the citrate group, high pSOFA score, and the presence of a patient group, most of whom had bleeding diathesis and multiorgan failure.

We also included patients in need of ECMO in our study. In a study in adult patients, RCA was also used in CRRT cycles in ARDS patients supported with ECMO and treated with HA and analyzed retrospectively. It was reported that the coagulation rate in the CRRT cycle was significantly higher in the HA group (p<0.001).[19-22] We found that the median circuit duration was longer in the ECMO group than in the non-ECMO group with a difference of 56 hours, but there was no significant difference in CRRT duration (p=0.724).

Our study has several limitations. First, the patient number is small. Second, retrospective. However, the superiorities of our study are that we were used only prismocitrate 18\0 for RCA, and we preferred a single CRRT modality (CVVHD), and the second advantage is notified count patients underwent ECMO running.

Conclusion

RCA is a safe and effective method of anticoagulation for CRRT in children as it has no frequent and severe systemic complication; it may be more effective than systemic HA in prolonging the hemofilter lifespan. Citrate is an available and good choice for CRRT. It causes minimal metabolic and electrolyte abnormality that can be easily resolved with good monitoring and interventions. RCA-CRRT in patients followed up with ECMO circuit is possible, safe and effective anticoagulation method.

Ethics

Ethics Committee Approval: The Ankara University Ethics Committee approved the study (number: İ6-441-21).

Informed Consent: Approval was obtained from the family of the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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