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Short Communication

Upgrading Renal Replacement Therapy Machines in the ICU: A Comparative Observational Study of Heparin vs. Regional Citrate Anticoagulation

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Deepak Sharma[1], Afelemo Orilade[2], Priyanka Sharma[1], Fahad Zahid[2], Dean Farrington[3]

1. Sandwell & West Birmingham Hospitals NHS Trust, UK; 2. Independent researcher; 3. New York State Department of Health, Albany, United States

Background: Continuous renal replacement therapy (CRRT) requires effective anticoagulation to prevent circuit clotting. This study compared heparin and regional citrate anticoagulation (RCA) in an Intensive Care Unit (ICU), focusing on patient safety, cost-effectiveness, and nursing perspectives.
Methods: This retrospective observational study included ICU patients undergoing CRRT with heparin (December 2021 - March 2022) and RCA (June 2022 - September 2022). Outcomes assessed were CRRT duration per patient, filter set cost, lifespan, and blood transfusion requirements. Data were extracted from electronic health records and analyzed using IBM SPSS Statistics Version 29.
Results: RCA significantly increased CRRT duration per patient (198 vs. 101 hours, $p = 0.037$) and filter lifespan (67 vs. 24 hours, $p < 0.001$) compared to heparin. Filter cost per renal day decreased from £98.05 with heparin to £57.48 with RCA ($p = 0.04$). Blood transfusion requirements reduced from 0.59 to 0.27 transfusions per renal day, lowering daily transfusion costs from £84.96 to £39.58 with RCA.
Conclusion: RCA demonstrated clinical and economic benefits in CRRT compared to heparin, including improved filter longevity, reduced transfusion requirements, and overall cost savings.
Clinical significance: Implementation of RCA in CRRT can enhance treatment efficacy, reduce nursing interventions, and improve resource utilization in ICU settings.

Introduction

Continuous renal replacement therapy (CRRT) is a critical intervention in Intensive Care Units (ICUs) for managing acute kidney injury and fluid overload in critically ill patients. Effective anticoagulation is essential to prevent clotting within the extracorporeal circuit, ensuring continuous function and efficient waste removal. While traditional heparin anticoagulation is effective, it poses risks such as bleeding and heparin-induced thrombocytopenia.

Regional citrate anticoagulation (RCA) has emerged as a promising alternative to heparin, offering potential

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benefits in safety and efficacy. The 2012 KDIGO guidelines weakly recommended RCA as first-line anticoagulation in CRRT, leading to increased adoption in ICUs worldwide. [1] However, the clinical and economic implications of transitioning from heparin to RCA in real-world settings remain a subject of ongoing research and debate.

This study aims to provide observational insights into the comparative performance of heparin and RCA in an ICU setting, focusing on patient safety, cost-effectiveness, and nursing perspectives. By examining key metrics such as CRRT duration, filter lifespan, and transfusion requirements, we seek to contribute to the evidence base guiding anticoagulation strategies in CRRT.

Methods

Study Design and Setting

This retrospective observational study was conducted at Sandwell and West Birmingham NHS Trust, focusing on ICU patients undergoing CRRT. The study period was divided into two phases: December 2021 to March 2022 for heparin anticoagulation, and June 2022 to September 2022 for RCA.

For heparin anticoagulation, we followed the local protocol of administration of an initial intravenous bolus of 5,000 units followed by a maintenance infusion of 18 units/kg/h, targeting an activated partial thromboplastin time (APTT) ratio of 1.8 to 2.6 which was monitored every six hourly.

For RCA also we followed our local protocol and used a citrate concentration of 3.0 mmol/L of blood, titrated to maintain circuit ionized calcium levels between 0.26 to 0.40 mmol/L and systemic ionized calcium levels between 1.01 to 1.20 mmol/L which were monitored every four hourly.

Inclusion and Exclusion Criteria

Patients aged 18 years or older who received CRRT in the ICU during the specified periods were included. Exclusion criteria encompassed incomplete. Also, patients using alternative anticoagulation methods like low molecular weight heparin (LMWH), direct thrombin inhibitors like argatroban or hirudin, or prostacyclin (epoprostenol) were excluded to ensure a direct comparison between heparin and RCA.

Data Collection

Data were extracted from electronic health records and validated by two independent reviewers. The primary outcomes assessed were:

- CRRT duration per patient
- Filter set cost
- Filter lifespan
- Blood transfusion requirements

A 'renal day' refers to a 24-hour period during which a patient receives CRRT. Filter lifespan was determined by measuring the time from initiation of CRRT to when the transmembrane pressure exceeded 300 mmHg or when the filter was changed due to clotting, with a maximum cut-off time as per manufacturer recommendations.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics Version 29. Comparative analyses between the heparin and RCA groups were conducted using appropriate statistical tests, with a significance level set at $p < 0.05$.

Ethical Considerations

The study received approval from the local Research Ethics Committee (Reference 2307 Version 1), with a waiver for informed consent due to its retrospective, observational nature. Patient data were anonymized by removing all personally identifiable information and assigning unique study identifiers to ensure confidentiality.

Results

The implementation of RCA in CRRT demonstrated significant improvements across several key parameters compared to traditional heparin anticoagulation.

CRRT Duration and Filter Lifespan

RCA nearly doubled the average CRRT duration per patient, increasing from 101 hours with heparin to 198 hours ($p = 0.037$). This substantial increase in treatment duration was accompanied by a significant extension in filter lifespan, rising from an average of 24 hours with heparin to 67 hours with RCA ($p < 0.001$).

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Cost-Effectiveness

Cost-effectiveness was determined by comparing the total cost (filter cost + transfusion cost) per patient per hour of CRRT received. The transition to RCA resulted in a marked reduction in filter-related costs. The filter cost per renal day decreased from £98.05 with heparin to £57.48 with RCA ($p = 0.04$). This reduction in daily filter costs represents a significant economic advantage in favor of RCA.

Blood Transfusion Requirements

RCA demonstrated a notable impact on blood transfusion needs. Blood transfusions refer specifically to red blood cell transfusions. The average number of transfusions per renal day decreased from 0.59 with heparin to 0.27 with RCA. This reduction translated to a substantial decrease in daily transfusion costs, from £84.96 with heparin to £39.58 with RCA. No apparent reasons were found for higher transfusion requirements during heparin anticoagulation other than the clotting of the CRRT circuit.

We observed no common complications associated with either heparin or RCA, including bleeding, acid-base disturbances, and severe hypocalcemia.

Discussion

The findings of this observational study provide substantial evidence for the benefits of transitioning from heparin to RCA in CRRT within the ICU setting. The significant improvements observed in CRRT duration, filter lifespan, and cost-effectiveness align with previous research suggesting the potential advantages of RCA. Some studies indicated that RCA prolongs filter life and reduces bleeding episodes, implying cost savings and clinical benefits. [2] However, a population-level study by Doidge JC et al. (2022) found no evidence that RCA improved patient outcomes in England and Wales. [3]

Clinical Implications

The nearly twofold increase in CRRT duration per patient with RCA suggests enhanced treatment efficacy and stability. This extended treatment time may contribute to improved fluid management and solute clearance in critically ill patients. The substantial increase in filter lifespan from 24 to 67 hours not only reduces the frequency of circuit changes but also minimizes treatment interruptions, potentially leading to improved clinical outcomes.

The marked reduction in blood transfusion requirements with RCA is a particularly noteworthy finding. Fewer transfusions not only decrease costs but also minimize the risks associated with blood product administration, such as transfusion reactions and immune modulation.

Economic Considerations

While the initial setup costs for RCA may be higher, our results demonstrate significant cost savings in terms of reduced filter replacements and decreased transfusion needs. It does require more complex setup and additional staff training. Our unit invested in comprehensive training programs to familiarize nurses with the citrate system, which should be considered when implementing RCA. The lower filter cost per renal day and reduced transfusion expenses suggest that RCA may be a more cost-effective option in the long term.

Nursing Perspective

From a nursing standpoint, the transition to RCA offers several advantages that enhance patient care and resource efficiency, although initial staff training needs to be incorporated as well:

- Reduced Interventions: The significant increase in filter lifespan translates to less frequent filter changes and fewer troubleshooting issues with the machine and vascular access. This reduction in interventions not only decreases the workload on nursing staff but also minimizes the risk of complications associated with frequent handling of dialysis equipment.
- Increased Time for Direct Patient Care: With fewer filter changes and a reduced need for blood transfusions, nurses can allocate more time to direct patient care. This shift in time allocation can lead to improved patient monitoring, more patient-centred care, and potentially better overall outcomes.

Limitations and Future Directions

While our study provides valuable insights, it is important to acknowledge its limitations. The retrospective nature of this study introduces potential biases and limits causal inferences. The single-center design may limit generalizability due to institution-specific protocols, patient populations, and resources. Future research should focus on prospective, multi-center studies to further validate these results across diverse ICU settings.

Additionally, while we observed significant benefits in terms of filter longevity and reduced transfusion needs, further investigation into long-term patient outcomes, such as mortality and renal recovery rates, would provide a more comprehensive understanding of the clinical impact of RCA in CRRT.

We were unable to account for potential confounders such as changes in CRRT machines, filter cartridges, or transfusion thresholds during the study period. Additionally, we did not analyse complications related to heparin or citrate use, nor did we track the frequency of CRRT changes due to filter clotting.

Conclusion

This observational study provides strong support for the incorporation of RCA in CRRT within the ICU setting. The significant improvements in filter longevity, reduced transfusion requirements, and overall cost-effectiveness suggest that units upgrading their CRRT machines can expect tangible benefits from transitioning to RCA. Although this is an observational, single center study, these findings align with best practices in critical care management and offer a promising avenue for enhancing the delivery of renal replacement therapy in critically ill patients. Future research should focus on conducting prospective, multi-center studies to validate these findings across diverse ICU settings and explore long-term patient outcomes, including mortality rates and renal recovery progress.

Clinical significance

The implementation of RCA in CRRT has the potential to significantly improve patient care and resource utilization in ICU settings. The extended filter lifespan and reduced need for transfusions not only enhance treatment efficiency but also minimize patient exposure to the risks associated with frequent circuit changes and blood product administration. From a nursing perspective, the reduction in interventions allows for more focused patient care, potentially leading to improved outcomes. Furthermore, the demonstrated cost-effectiveness of RCA may contribute to more sustainable healthcare delivery in resource-constrained environments.

Figures and Tables

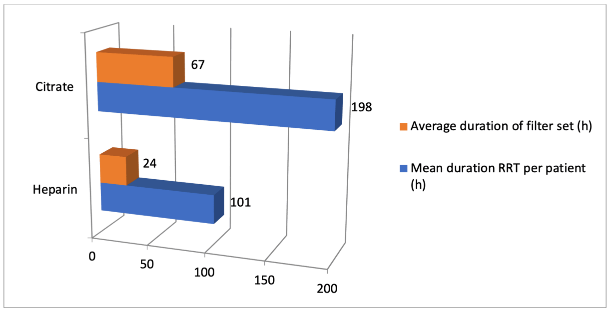

Figure 1. Comparison of Heparin vs Citrate Anticoagulation. X-axis: Anticoagulation method. Y-axis: Duration in hours. Blue bars represent Average duration of filter set. Orange bars represent Mean RRT duration per patient.

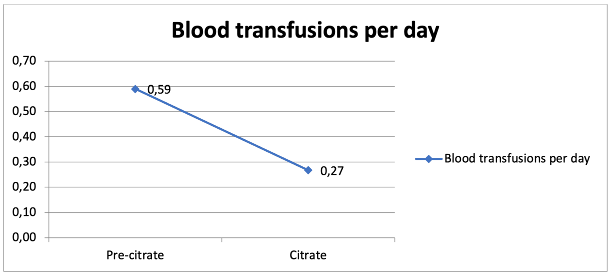

Figure 2. Blood transfusions per day comparing Heparin vs Citrate Anticoagulation.

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Metric	Heparin anticoagulation	Citrate anticoagulation	P-value
Number of patients	39	53	-
Mean RRT Duration per Patient (hours)	101.00	198.00	0.037*
Average Filter Cost per Patient (£)	412.82	473.89	0.573
Filter Cost per Renal Day (£)	98.05	57.48	0.04*
Total Filter Cost per Annum (£)	16,100.00	25,187.76	-
Average Duration of Filter Set (hours)	24.00	67.00	<0.001*
Blood Transfusions per Renal Day	0.59	0.27	-
Blood Transfusion Cost per Day (£)	84.96	39.58	-

Table 1. Summary of Key Outcomes

* *indicates statistically significant difference (p < 0.05)*

List of abbreviations

- CRRT: Continuous renal replacement therapy
- RCA: Regional citrate anticoagulation
- ICU: Intensive Care Unit
- KDIGO: Kidney Disease: Improving Global Outcomes

References

1. ^*Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group (2012). KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2:1-138.*
2. ^*Oudemans-van Straaten HM, Kellum JA, Bellomo R (2010). Clinical review: anticoagulation for continuous renal replacement therapy – heparin or citrate? Crit Care. 15:202.*
3. ^*Doidge J, Gould DW, Sadique Z, et al. (2022). Regional citrate anticoagulation versus systemic heparin anticoagulation for continuous kidney replacement therapy in intensive care. J Crit Care. 74. doi: 10.1016/j.jcrc.2022.154218.*

Declarations

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Potential competing interests: No potential competing interests to declare.