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Original Article

Effect of Red Cell Concentrate Storage on Electrolyte Levels and Hematological Parameters

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ABSTRACT

Objective: To observe the changes in Electrolyte levels and Hematological Parameters in Stored Red Cell Concentrate (RCC).
Study Design: Analytical Cross-Sectional Study.
Place and Duration of Study: Blood Bank and Department of Pathology, Combined Military Hospital, Multan, Pakistan, from Jan to Aug 2025.
Methodology: Stored RCC units prepared from healthy voluntary blood donors and stored under standard blood bank conditions (2–6°C) in CPDA-1 triple bags were selected for study. One hundred and fifty RCC units were sampled, and a 5 mL sample was aseptically withdrawn from each RCC unit on the donation day, 20th and 35th days. Electrolyte parameters, including potassium, sodium, calcium, and chloride, along with pH and Hematological parameters such as mean corpuscular volume (MCV) and red cell count, were measured, and the trend of change was compared between all three samples from designated bags.
Results: RBC count demonstrated 11.4% decline with median RBC 4.88(0.66)×10^9/L on Day-1 to 4.32(1.15)×10^9/L by Day-35 (p<0.001). In contrast, MCV increased 8.8%, from median 84.50(14.00) fL on Day-1 to 92.00(10.00) fL on Day-35 (p<0.001). Sodium decreased 3.8% from 142.00(2.85) mmol/L on Day-1 to 136.52(1.46) mmol/L on Day-35 and Potassium increased markedly 248.1% from median 4.03(0.85) mmol/L on Day-1, to 14.03(0.94) mmol/L on Day-35 (p<0.001). Calcium and Chloride levels showed 7.5% and 18.3% decrease respectively, whereas pH decreased 6% from 7.43(0.67) on Day-1 to 6.98(0.60) on Day-35 (p<0.001).
Conclusion: There were significant hematological and biochemical alterations in RCC during storage, proportional to the duration of the stored RCC bag.

Keywords: Blood transfusion, Citrate-Phosphate-Dextrose-Adenine triple bag, Electrolytes, Mean corpuscular volume (MCV), Red cell concentrate (RCC).

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INTRODUCTION

Blood transfusion remains a cornerstone of modern clinical practice, especially in critical care, trauma, surgery, and hematologic disorders.[1] In Pakistan, most blood banks follow standard practices that involve the collection and storage of whole blood using CPDA-1 (Citrate-Phosphate-Dextrose-Adenine) triple-bag systems.[2] These systems are widely used due to their cost-effectiveness and the ability to separate whole blood into red cell concentrate (RCC), plasma, and platelets for targeted therapy.[3] The CPDA-1 solution performs multiple roles: citrate acts as an anticoagulant by chelating calcium, phosphate serves as a buffer and supports red cell metabolism, dextrose provides an energy source, and adenine helps maintain ATP levels in red cells during storage. RCC derived from these systems can be stored up to 35 days at 2–6°C.[4] However, over time, stored red cells undergo various biochemical and structural changes—collectively referred to as "storage lesions"—that may impact the safety and efficacy of transfusions.[5]

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One significant concern is the alteration in the electrolyte composition of stored RCC. Due to leakage through damaged cell membranes, potassium levels increase steadily during storage, posing risks especially in neonates, patients with renal insufficiency, or those requiring massive transfusions.[6] Concurrently, sodium levels tend to decrease. The citrate in CPDA-1 binds ionized calcium, potentially leading to hypocalcemia when large volumes are transfused, with clinical manifestations like hypotension, arrhythmias, and tetany.[7] Additionally, phosphate levels rise due to the breakdown of intracellular components, while pH declines progressively due to lactate accumulation and ATP degradation, further compromising red cell viability and function.[8]

Hematological parameters are also affected; mean corpuscular volume (MCV) may change due to osmotic shifts, and red cell deformability is reduced. Leucocytes and Platelets are decreased, on the other hand.[9] These changes can affect oxygen delivery capacity and microcirculatory flow.

In resource-limited settings like Pakistan, where cold chain maintenance and inventory rotation are challenging, older RCC units are more likely to be transfused, increasing the likelihood of adverse outcomes.[10]

Despite these risks, there is a paucity of local data assessing the impact of RCC storage duration on biochemical and hematological parameters. Understanding these changes is essential for guiding transfusion practices, especially for high-risk patients, and could reform the national blood banking policies. The objective of this study was to evaluate the effect of red cell concentrate storage duration on electrolyte levels and hematological parameters in a tertiary care setting in Pakistan.

METHODOLOGY

This was a laboratory-based analytical cross-sectional study conducted in the Blood Bank and Department of Pathology, Combined Military Hospital, Multan, Pakistan, from Jan to Aug 2025. Permission was obtained from the Institutional Ethical Review Committee before data collection (ERC no 129 dated 23-12-2024). Anonymity of patient data was ensured at every point in the study. The sample size was calculated using the WHO online sample size calculator, taking a confidence level 95%%, a margin of error of 5%, and a reported mean difference of 1.02±0.27 in mean corpuscular volume (MCV) of RBCs at days 1 and 35 of storage reported by Zhong *et al*.[11] The estimated sample size came out to be 430. A total of 450 red cell concentrates (RCC) units stored in CPDA-1 triple bags were included in the study. Non-probability purposive sampling was used based on the availability of RCC units of varying storage durations.

Inclusion Criteria: The RCC units that are ready for transfusion and being issued for clinical use. RCC units selected were those prepared from healthy voluntary blood donors and stored under standard blood bank conditions (2–6°C) in CPDA-1 triple bags.

Exclusion Criteria: Blood units subjected to special modifications (e.g., leukoreduction, irradiation) were not included. Units showing evidence of contamination, hemolysis, leakage, or improper storage were also excluded.

One hundred and fifty RCC units were sampled at each of 3 predefined storage durations: Day 1, Day 20, and Day 35. For data collection, a 5 mL sample was aseptically withdrawn from each RCC unit on the donation day, 20th and 35th days. This procedure was performed in coordination with blood bank staff to avoid any delay or compromise in patient care. Electrolyte parameters, including potassium, sodium, calcium, and chloride, along with pH, were measured using a fully automated biochemistry analyzer. Hematological parameters such as mean corpuscular volume (MCV) and red cell count were analyzed using an automated hematology analyzer. All equipment was calibrated daily, and internal quality control measures were strictly observed.

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS v25.0). Normality of the data was checked using the Kolmogorov-Smirnov test. Continuous variables, including RBC count, MCV, Na, K, Ca, Cl, and pH, were all expressed as median (interquartile range). Friedman test was used to compare biochemical parameters across different storage durations. Correlation and variations between potassium levels and pH were assessed using the Spearman coefficient of determination (R2) using mean changes in respective values. A p-value ≤0.05 was considered statistically significant.

RESULTS

Four hundred and fifty RCC units stored under standard conditions (2–6°C) and meeting inclusion criteria were analyzed; 150 (33.33%) were sampled on Day 1, Day 20, and Day 35, respectively. RBC count demonstrated a statistically significant decline with storage duration. The median RBC count was 4.88(0.66) $\times 10^9$/L on Day 1, decreasing to 4.32(1.15) $\times 10^9$/L by Day 35, reflecting an 11.4% decrease (p<0.001). In contrast, mean corpuscular volume (MCV) increased over time, from a median of 84.50(14.00) fL on Day 1 to 92.00(10.00) fL on Day 35, showing an 8.8% increase (p<0.001), likely due to osmotic swelling of stored erythrocytes. (Table)

Sodium levels demonstrated a consistent decreasing trend over time. The median sodium level was 142.00(2.85) mmol/L on Day 1, 139.02 mmol/L on Day 20 (IQR not specified), and 136.52(1.46) mmol/L on Day 35 (p<0.001), reflecting a 3.8% decrease from baseline. Potassium levels increased markedly with storage duration. The median potassium level was 4.03(0.85) mmol/L on Day 1, 12.24(4.24) mmol/L on

Day 20, and 14.03(0.94) mmol/L on Day 35 (p<0.001), representing a 248.1% increase. Calcium levels, measured as total calcium, showed a downward trend. The median calcium value was 1.32(1.09) mg/dL on Day 1, 1.34(0.22) mg/dL on Day 20, and 1.22(0.24) mg/dL on Day 35 (p<0.001), indicating a 7.5% decrease. Chloride levels also declined over time. The median chloride value was 85.03(11.55) mmol/L on Day 1, 74.50(4.00) mmol/L on Day 20, and 69.45(2.21) mmol/L on Day 35 (p<0.001), with an 18.3% decrease across the storage period.

The pH of RCC units declined significantly during storage. The median pH was 7.43(0.67) on Day 1, 7.03(1.22) on Day 20, and 6.98(0.60) on Day 35 (p<0.001), representing a 6% decrease. This decline was found to be significantly and negatively correlated with potassium levels (r = –0.490, p<0.001). The average daily increase in potassium was approximately 0.286 mmol/L/day, while pH dropped by around 0.013 units/day over the 35-day storage period.

Table: Comparison of Hematological and Electrolyte Parameters across Storage Durations (n=450)

Parameter	Day 1 (n = 150)	Day 20 (n = 150)	Day 35 (n = 150)	% Change Days 1 to 35	p-value
RBC Count x 109/L	4.88(0.66)	4.67(0.87)	4.32(1.15)	11.4% decrease	<0.001
MCV (fL)	84.50(14.00)	85.00(10.00)	92.00(10.00)	8.8% increase	<0.001
Sodium (mmol/L)	142.00(2.85)	139.02()	136.52(1.46)	3.8% decrease	<0.001
Potassium (mmol/L)	4.03(0.85)	12.24(4.24)	14.03(0.94)	148.1% increase	<0.001
Calcium (mg/dL)	1.32(1.09)	1.34(0.22)	1.22(0.24)	7.5% decrease	<0.001
Chloride (mmol/L)	85.03(11.55)	74.50(4.00)	69.45(2.21)	18.3% decrease	<0.001
pH	7.43(0.67)	7.03(1.22)	6.98(0.60)	6 % decrease	<0.001

**RBC – Red Blood Cells, MCV – Mean Cell Volume*

A statistically significant moderate negative correlation was observed between potassium and pH levels in stored red cell concentrate units (Spearman's ρ=–0.490, p<0.001). As pH levels decreased, potassium concentrations showed a marked increase, consistent with red cell membrane leakage and storage-related metabolic changes. The coefficient of determination (R^2=0.259) indicates that approximately 25.9% of the variation in potassium levels can be explained by the changes in pH. (Figure)

DISCUSSION

This study provided a comprehensive evaluation of the measured biochemical and hematological alterations occurring in red cell concentrate (RCC). Among the most prominent changes observed was the substantial rise in extracellular potassium levels, accompanied by a parallel decline in pH. This inverse relationship (ρ=–0.490, p<0.001) supports the well-established mechanism of potassium leakage from erythrocytes into the storage medium due to impaired sodium-potassium ATPase activity and loss of membrane integrity. Concurrently, the gradual fall in pH is attributable to ongoing anaerobic glycolysis and lactate accumulation. Tran *et al*., also explained the same results that stored RCC had significantly higher levels of potassium, as well as lactate, with reduced pH. Although these changes had a minimal effect on the final transfusion product.[12] Khandrashina *et al*., concluded similar findings showing mean K levels of 4.373±0.417 mmol/L on day 0 of freshly stored blood, with a significant change in potassium levels in a 1-week stored blood bag, 8.290±0.275 mmol/L (p<0.001).[13]

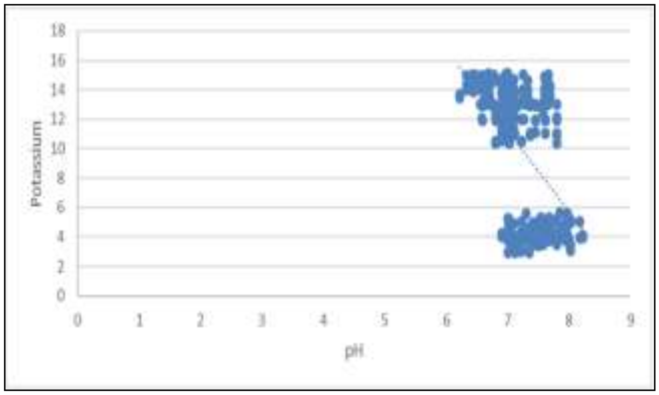

Figure: Scatter Plot Showing the Relationship between Potassium and pH in Stored Red Cell Concentrates

Equally notable were the reductions in sodium, calcium, and chloride levels, all of which exhibited statistically significant downward trends. While less dramatic than potassium, these changes point toward a broader spectrum of membrane and metabolic dysfunction in stored red cells. As observed, sodium levels demonstrated a consistent decreasing trend with a 3.8% decrease from baseline on day 35, as the median sodium level was 142.00 (2.85) mmol/L on day 1 and 136.52(1.46) mmol/L on day 35 (p<0.001). Bakaloudis *et al*., studied the change of electrolyte in stored RCC and noted that the mean potassium had a sharp rise to 14.60 mmol/L on day 21 from a baseline of 3.45 mmol/L on day 1. Contrarily, sodium had a higher value on day 1 (148 mmol/L) and then a gradual decline to 135.6 mmol/L on day 21.[14]

Sahoo *et al*., concluded that the trend of change in electrolytes, as mean potassium, showed a rising trend over the storage period, from 7.31 mmol/L on day 1 to

20.14 mmol/L at week 5 (p<0.001). Meanwhile, sodium significantly decreased from 150.72 mmol/L to 121.56 mmol/L at week 5 (p<0.001), and pH also had a significant change from 7.48 to 6.15 at week 5.[15] Lee *et al*., reported similar findings that sodium (152.9±3.8 mEq/l to 139.5±4.8 mEq/l on day 21) and chloride (71.9±6.6 mEq/l to 67±5.9 mEq/l) Levels showed a declining trend over storage time, whereas potassium levels showed a significant spike (4.2±0.4 mEq/l to 15.2±0.7 mEq/l) from day 1 to day 21.[16] Literature has abundantly reported that Na and Cl showed a declining trend during RCC storage, whereas K showed a rapid spike followed by a gradual rising trend in the stored RCC bag.3

A 6% decrease in pH was observed over the course of storage through day 35, as the median pH decreased from 7.43(0.67) on Day 1 to 6.98(0.60) on Day 35 (p<0.001). These findings were consistent with those of Kandrashina *et al*., who also observed similar pH changes in stored RCC, with storage duration having a significant effect on pH.[13] Similarly, RBC count declined from 4.44±0.11 g/L on Day 1 to 4.36±0.14 g/L on Day 14. However, osmotic fragility didn't change significantly with storage time.

In the current study, the decline in total calcium, though subtle, may influence clotting and transfusion efficacy, while the fall in chloride contributes to the overall acid-base disturbance. Calcium and chloride levels showed a downward trend. Calcium showed a 7.5% decrease with a median calcium of 1.32(1.09) mg/dL on Day 1 and 1.22(0.24) mg/dL on Day 35. Chloride levels declined 18.3% across the storage period, with median chloride 85.03(11.55) mmol/L on Day 1 and 69.45(2.21) mmol/L on Day 35. Balakoudis et al., also observed a decreasing trend in calcium and chloride alongside other electrolytes in stored blood over weeks, as Ca decreased from 2.46±0.12 to 1.06±0.17, and Cl also declined from a mean of 97.4±1.7 to 88.8±2.8 at day 30.14

The observed hematological trends, including the reduction in RBC count and increase in MCV, also show the cumulative cellular damage and osmotic shifts during storage. Our study showed a statistically significant 11.4% decline with storage duration in RBC count, with a median RBC count of 4.88(0.66) × 10^9/L on Day 1 and 4.32(1.15) × 10^9/L on Day 35. In contrast, mean corpuscular volume (MCV) showed an 8.8% increase from the baseline median of 84.50 (14.00) fL to 92.00(10.00) fL on Day 35. Saho0 *et al*., observed change in RBC parameters as RBC count decreased from 6.31±0.28 on day 1 to 6.33±0.72 on day 35 whereas mean MCV gradually increased from base line 88.17±2.37 to 93.9±3.42 on day 35 whereas MCH showed gradual decrease from 30.3±1.45 on day 1 to 28.99±1.28 on day 35.[15] In another study, Burke *et al*., observed a weekly 2.31 fL change as an increasing trend was observed in the mean MCV of stored blood.[17] Additionally, literature has also specified how red blood cells (erythrocytes) lose most of their complex regulated cell death (RCD) machinery during maturation. This RBC storage concentrate undergoes biochemical and structural changes that cause a storage lesion, which aggravates the erythrocyte death.[18]

Our findings reveal marked and statistically significant shifts in several key parameters, reflecting the classic storage lesions that compromise the quality of blood components over time. These biochemical changes are not merely academic but carry clinical implications, particularly for vulnerable patient populations such as neonates and those requiring massive transfusion, where electrolyte imbalances can have serious consequences.

Together, these results underscore the biochemical instability of RCCs with prolonged storage and provide critical insights into optimizing transfusion safety and practices.

LIMITATIONS OF STUDY

The authors are well aware of the limitations of this study, foremost being the limited sample size with a single-center study. The change in hematological parameters and electrolytes was only checked in RCC bags, and not checked or compared with washed RBC and whole blood, nor was the effect of leukoreduction studied. In addition, trends of change and the effect of storage temperature and material were not studied or compared with different storage materials or temperatures. Hence, further studies with a large sample size and a multicenter approach are needed before implementing these results on a national level.

CONCLUSION

The results of our study showed that with prolonged storage, there was an imbalance in hematological parameters as well as electrolytes proportional to the duration of the stored RCC bag. These findings highlighted the significant biochemical alterations in RCC during storage, suggesting that prolonged storage may compromise cellular and electrolyte integrity, potentially affecting transfusion outcomes.

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Discolure:

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Authors' Contribution

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

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

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

MH: 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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