Artículos Originales

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Crystalloid fluid choices and their impact on acute kidney injury and other outcomes in pediatric sepsis: a prospective study in Ecuador

Elección de cristaloide y su impacto en la lesión renal aguda y otros resultados en la sepsis pediátrica: un estudio prospectivo en Ecuador

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Abstract

Introduction: Sepsis and septic shock are significant causes of morbidity and mortality in pediatric patients, with fluid resuscitation being a critical intervention. This study compares the effects of 0.9% saline solution and Ringer Lactate on acute kidney injury (AKI), metabolic acidosis, and overall outcomes in pediatric sepsis. **Objective:** To evaluate the association between fluid type and the incidence of AKI, metabolic acidosis, and mortality in pediatric patients with sepsis or septic shock. **Methods:** A prospective observational study was conducted from January to November 2023 at Hospital Padre Carollo "Un Canto a la Vida" in Quito, Ecuador. Thirty-five children aged 1 month to 179 months with sepsis or septic shock were included. Patients received either 0.9% saline or Ringer Lactate based on clinician judgment. Primary outcomes were the incidence of AKI and metabolic acidosis. Secondary outcomes included mortality and length of stay. Logistic regressions were performed to assess outcomes. **Results:** The incidence of AKI was significantly higher in the saline group (30%) compared to the Ringer Lactate group (13.3%) (p=0.045). Metabolic acidosis was also more common in the saline group (25% vs. 6.7%; p=0.037). Mortality did not differ significantly between groups (5% in saline vs. 0% in Ringer Lactate; p=0.325). The median ICU length of stay was 12 days for saline and 10 days for Ringer Lactate (p=0.356). **Conclusions:** Ringer Lactate is associated with a lower incidence of AKI and metabolic acidosis compared to 0.9% saline in pediatric sepsis patients. These findings suggest that balanced crystalloids may offer safer outcomes for fluid resuscitation in this population.

Keywords: sepsis, fluid therapy, acute kidney injury, metabolic acidosis.

Resumen

Introducción: La sepsis y el shock séptico son causas significativas de morbilidad y mortalidad en pacientes pediátricos, siendo la reanimación con líquidos una intervención crítica. Este estudio compara los efectos de la solución salina al 0,9% y el lactato de Ringer sobre la lesión renal aguda (LRA), la acidosis metabólica y los resultados generales de la sepsis pediátrica. **Objetivo:** Evaluar la asociación entre el tipo de líquido y la incidencia de LRA, acidosis metabólica y mortalidad en pacientes pediátricos con sepsis o shock séptico.

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Métodos: Se realizó un estudio observacional prospectivo de enero a noviembre de 2023 en el Hospital Padre Carollo "Un Canto a la Vida" de Quito, Ecuador. Se incluyeron 35 niños de 1 mes a 179 meses con sepsis o shock séptico. Los pacientes recibieron solución salina al 0,9% o lactato de Ringer según el criterio clínico. Los resultados primarios fueron la incidencia de LRA y acidosis metabólica. Los resultados secundarios incluyeron la mortalidad y la duración del hospital. Se realizaron regresiones logísticas para evaluar los resultados. **Resultados:** La incidencia de LRA fue significativamente mayor en el grupo de solución salina (30%) en comparación con el grupo de lactato de Ringer (13,3%) (p=0,045). La acidosis metabólica también fue más frecuente en el grupo salino (25% vs. 6,7%; p=0,037). La mortalidad no difirió significativamente entre los grupos (5% en solución salina vs. 0% en lactato de Ringer; p=0,325). La mediana de estancia en UCI fue de 12 días para suero fisiológico y de 10 días para lactato de Ringer (p=0,356). **Conclusiones:** El lactato de Ringer se asocia con una menor incidencia de LRA y acidosis metabólica en comparación con la solución salina al 0,9% en pacientes pediátricos con sepsis. Estos hallazgos sugieren que los cristaloides equilibrados pueden ofrecer resultados más seguros para la reanimación con líquidos en esta población.

Palabras clave: sepsis, fluidoterapia, lesión renal aguda, acidosis metabólica.

Introduction

Sepsis and septic shock remain leading causes of morbidity and mortality among pediatric patients worldwide[1,2]. Despite advances in critical care medicine, the effective management of sepsis in children continues to pose significant challenges, particularly in the context of fluid resuscitation strategies[3]. Crystalloid fluids, such as normal saline and Ringer Lactate, are cornerstone interventions in the initial resuscitation phase for septic patients. However, the choice between these fluids can have crucial implications for patient outcomes, including acute kidney injury (AKI), metabolic acidosis, and overall mortality[4]. Understanding these implications is essential for optimizing treatment protocols and improving survival rates in pediatric intensive care units (PICUs).

Background and Rationale

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock, a subset of sepsis, is characterized by profound circulatory, cellular, and metabolic abnormalities, which substantially increase mortality risk. In pediatric populations, the pathophysiology of sepsis is influenced by factors such as age, immune response, and developmental stage, making its management particularly complex[1,5,6].

Fluid resuscitation is a critical component of sepsis management, aimed at restoring intravascular volume, improving tissue perfusion, and preventing organ failure. The Surviving Sepsis Campaign guidelines recommend the rapid administration of isotonic crystalloids as the first-line fluid therapy in sepsis[5] 0.9% saline solution (SS) and balanced solutions like Ringer Lactate (RL) are the most used crystalloids. However, their differing electrolyte compositions and effects on acid-base balance have led to ongoing debates regarding their optimal use in sepsis management.

0,9 % saline solution, composed primarily of sodium and chloride, is widely available and commonly used due to its simplicity and cost-effectiveness. Nevertheless, it has been associated with the development of hyperchloremic metabolic acidosis and subsequent adverse renal outcomes. Excessive chloride load from normal saline can lead to renal vasoconstriction and decreased glomerular filtration rate, exacerbating AKI[7].

Ringer Lactate, a balanced electrolyte solution, includes additional ions such as potassium, calcium, and lactate, which can mitigate the risk of metabolic acidosis. The lactate component is metabolized in the liver to bicarbonate, potentially counteracting acidosis and offering a more physiologically appropriate fluid composition for maintaining acid-base homeostasis[7].

Several studies have explored the clinical outcomes associated with these fluids

in adult and pediatric populations[8-12]. For instance, balanced crystalloids have been shown to reduce the incidence of AKI and metabolic complications compared to SS in adult sepsis patients. However, evidence in the pediatric context remains limited, and existing studies often yield conflicting results. The choice of crystalloid fluid in pediatric sepsis resuscitation thus requires further investigation to determine its impact on critical outcomes such as AKI, metabolic acidosis, and mortality.

Given the high stakes involved in pediatric sepsis management, understanding the implications of fluid choice is critical for guiding clinical practice and improving patient outcomes. Fluid resuscitation not only addresses immediate hemodynamic stabilization but also influences longer-term renal and metabolic health. Identifying the optimal fluid for resuscitation could lead to improved clinical guidelines, enhance patient safety, and reduce healthcare costs by minimizing complications associated with fluid therapy[7].

This study, conducted at Hospital Padre Carollo "Un Canto a la Vida" in Quito, Ecuador, contributes to the growing body of evidence needed to inform evidence-based practices in pediatric sepsis care. By focusing on the comparative effects of SS and RL, we aim to provide actionable insights for clinicians and ultimately enhance the quality of care for pediatric patients facing the critical challenges of sepsis and septic shock.

Methods

Study Design

This prospective observational study was conducted from January to November 2023 in the pediatric critical care unit at Hospital Padre Carollo "Un Canto a la Vida" in Quito, Ecuador. The study aimed to compare the effects of 0.9% saline solution versus Ringer Lactate on the incidence of AKI, metabolic acidosis, and other clinical outcomes in pediatric patients with sepsis or septic shock.

Patient Selection

Inclusion Criteria:

- Children aged 1 month to 179 months.
- Diagnosed with sepsis or septic shock based on the Latin American Consensus on the Management of Sepsis in Children 1 and the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children 5
- Admitted to the PICU and requiring fluid resuscitation as part of initial management.

Exclusion Criteria:

- Pre-existing chronic kidney disease or any known renal impairment.
- Underlying metabolic disorders affecting acid-base balance.
- Known allergies or contraindications to SS or RL.
- Admission due to non-infectious causes or without a primary diagnosis of sepsis or septic shock.
- Out of an initial cohort of 40 children admitted for sepsis or septic shock during the study period, 5 children were excluded due to failure to meet the inclusion criteria, resulting in a final sample size of 35 patients.

Fluid Administration

Fluid resuscitation was administered according to clinical judgment and existing hospital protocols. Patients received either SS or RL based on the discretion of the attending clinician. The choice of fluid was not randomized but was guided by the clinician's assessment of the patient's condition and clinical experience. Fluid bolus therapy was defined as a minimum of 10mL/kg and a maximum of 20 ml/kg for one fluid administration event to be registered for this research based on clinical response and he-

modynamic parameters. Additionally, the total volume of fluids administered during the initial resuscitation phase was measured in liters.

Data Collection

Data were collected prospectively for each patient, including demographic details, clinical characteristics, and outcomes.

Outcomes

- Incidence of AKI, defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria[13,14].
- Incidence of metabolic acidosis, defined as arterial pH < 7.35 and bicarbonate < 22 mEq/L.
- Length of stay (LOS) in the PICU and total hospital stay.

Mortality during hospital stay

In addition to the previously mentioned variables, the Pediatric Risk of Mortality (PRISM) III score and the Pediatric Logistic Organ Dysfunction (PELOD) 2 score were collected to assess the severity of illness and organ dysfunction. These scores were included to ensure comparability in severity and treatment approach between the two groups.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 28.0 v. 2021, Armonk, NY: IBM Corp and R Core Team (2023) v.4.3.1, Vienna, Austria. Continuous variables were summarized using medians and interquartile ranges (IQR), and categorical variables were presented as frequencies and percentages. The following statistical tests were used: Comparison of Baseline Characteristics: Mann-Whitney U test for non-normally distributed continuous variables. Chi-square or Fisher's exact test for categorical variables.

Multivariable Analysis

Logistic regression was performed to identify independent predictors of AKI and metabolic acidosis, adjusting for potential confounders such as age, weight, and underlying conditions.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Board of Hospital Padre Carollo. The study was conducted in accordance with the Declaration of Helsinki[15].

Results

Demographics and Clinical Characteristics

A total of 35 pediatric patients diagnosed with sepsis or septic shock were included in this study. The median age was 3.1 years (range: 1 month to 179 months) with a balanced distribution between males and females. The primary sources of sepsis were pneumonia, CNS infections, sinusitis, and complicated thoracic post-operative infections. The demographic and clinical characteristics, including weight, height, and biochemical parameters such as CRP and procalcitonin levels, were similar across the two groups, ensuring comparability between the SS and RL cohorts.

The PRISM III and PELOD 2 scores, used to assess severity of illness and organ dysfunction, showed no significant differences between the groups. The median PRISM III score was 12 in the saline group and 11 in the Ringer Lactate group ($p = 0.689$), while the median PELOD 2 score was 5 and 4, respectively ($p = 0.754$). Additionally, the total volume of fluids administered during resuscitation was similar between the two groups, with a median of 0.4 liters in both groups ($p = 0.827$), indicating comparable resuscitation efforts. These findings confirm that both groups had equivalent baseline severity and fluid management.

Clinical Outcomes

AKI: The incidence of AKI was significantly higher in the SS group compared to the RL group. Specifically, 30% of patients in the SS developed AKI, whereas only 13.3% of patients in the RL group experienced this outcome (p = 0.045). This indicates that resuscitation with Ringer Lactate is associated with a lower risk of AKI.

Metabolic Acidosis: Similarly, metabolic acidosis was more prevalent in the SS group, with an incidence of 25%, compared to 6.7% in the RL group (p = 0.037). The higher bicarbonate levels observed in the RL group (22.5 ± 2.8 mEq/L vs. 19.2 ± 3.1 mEq/L, p = 0.001) further support the superior acid-base balance achieved with RL.

Mortality: Mortality rates were low and did not differ significantly between the two groups. One patient (5%) in the SS group succumbed to their illness, whereas no deaths were recorded in the RL group (p = 0.325).

Length of Stay: The median duration of ICU and hospital stay did not show statistically significant differences between the two groups. The SS group had a median ICU stay of 12 days and a hospital stay of 13.4 ± 5.2 days, while the RL group had a median ICU stay of 10 days and a hospital stay of 11.7 ± 4.8 days (ICU stay p = 0.153; hospital stay p = 0.308).

Renal Function: The eGFR was significantly higher in the RL group compared to the saline group (85.6 ± 16.3 mL/min/1.73 m^2 vs. 75.2 ± 18.5 mL/min/1.73 m^2, p = 0.049), indicating better preservation of renal function with RL.

Table 1. Demographics and Clinical Characteristics by Fluid Type.

Variable	Saline Group (n=20)	Ringer Lactate Group (n=15)	Total (n=35)	p-value
Age (months)	36 ± 30.5 (3–113)	34 ± 31 (3–90)	36 ± 30 (3–113)	0.897
Weight (kg)	13.4 ± 6.5 (4.0–40.0)	12.8 ± 6.7 (4.0–27.0)	13.2 ± 6.6 (4.0–40.0)	0.724
Height (cm)	94 ± 33.0 (47.0–140.0)	93 ± 33.5 (52.0–127.0)	93.5 ± 32.8 (47.0–140.0)	0.857
BMI (kg/m^2)	16.5 ± 3.2 (11.3–24.6)	16.3 ± 3.1 (12.1–24.3)	16.4 ± 3.1 (11.3–24.6)	0.823
BSA (m^2)	0.590 ± 0.28 (0.229–1.247)	0.573 ± 0.25 (0.264–0.981)	0.573 ± 0.27 (0.229–1.247)	0.790
CRP (mg/L)	96 ± 52.4 (10–288)	82 ± 55.2 (8–245)	89 ± 53.6 (8–288)	0.723
Procalcitonin (ng/mL)	15.4 ± 10.4 (0.5–85.0)	15.5 ± 9.8 (0.5–80.0)	15.5 ± 10.1 (0.5–85.0)	0.912
Albumin (g/dL)	3.4 ± 0.5 (1.8–4.5)	3.3 ± 0.6 (1.8–4.4)	3.4 ± 0.5 (1.8–4.5)	0.712
ICU LOS (days)	12 ± 6.2 (5–20)	10 ± 5.8 (4–18)	11 ± 6.0 (4–20)	0.356
Hospital Stay (days)	14 ± 5.1 (7–25)	12 ± 4.8 (6–21)	13 ± 5.0 (6–25)	0.231
Female (%)	11 (55%)	8 (53.3%)	19 (54.3%)	0.912
Male (%)	9 (45%)	7 (46.7%)	16 (45.7%)	0.912
Sepsis Origin (%)				
Pneumonia	15 (75%)	10 (66.7%)	25 (71.4%)	0.599
CNS Infection	1 (5%)	1 (6.7%)	2 (5.7%)	0.847
Sinusitis	0 (0%)	1 (6.7%)	1 (2.9%)	0.409
Complicated Thoracic Post Op	4 (20%)	3 (20%)	7 (20%)	1.000
AKI (%)	6 (30%)	2 (13.3%)	8 (22.9%)	0.045
Metabolic Acidosis (%)	5 (25%)	1 (6.7%)	6 (17.1%)	0.037
PELOD 2 score, median (IQR)	5 (1-12)	4 (1-13)	5(1-13)	0.754
PRISM III Score, median (IQR)	12 (5-22)	11(4-21)	12 (4-22)	0.689
Total Administered Fluid for resuscitation (L), median (IQR)	0.4 (0.3-0.8)	0.4 (0.3-0.9)	0.4 (0.3-0.9)	0.827

Source: statistical analysis. p < 0,05. Table 1 presents the demographics and clinical characteristics of pediatric sepsis patients treated with either SS or RL. The table provides a comprehensive overview of the patient populations in each group, highlighting any differences in baseline characteristics and clinical parameters that may influence the outcomes of interest.

Table 2. Comparison of Clinical Outcomes and Biochemical Parameters by Fluid Type.

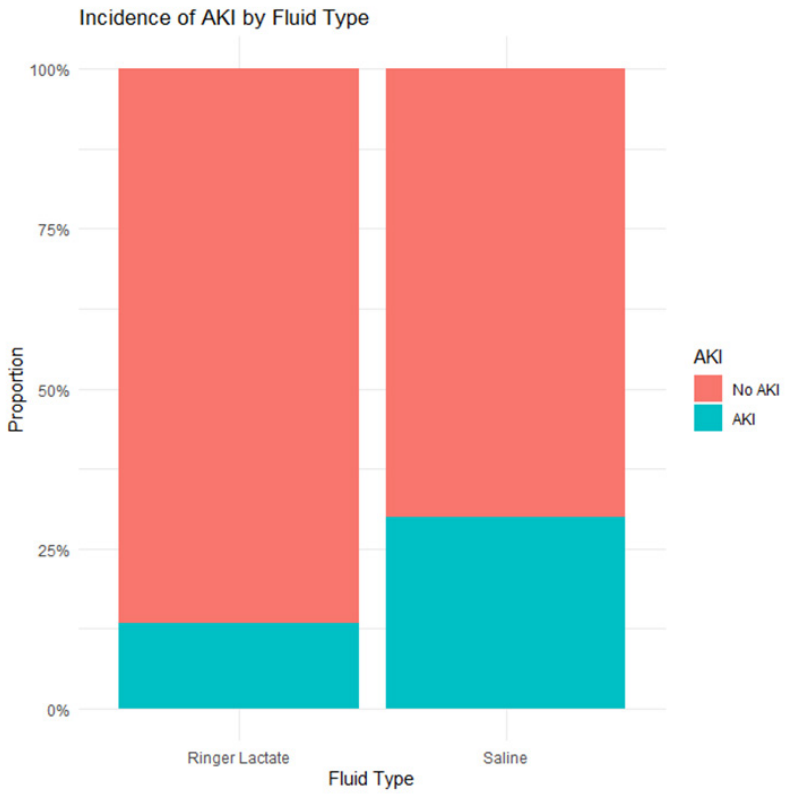
Variable	Saline Group (n=20)	Ringer Lactate Group (n=15)	Test Statistic	p-value
eGFR (mL/min/1.73 m^2)	75.2 ± 18.5	85.6 ± 16.3	t = -2.032	0.049
Bicarbonate (mEq/L)	19.2 ± 3.1	22.5 ± 2.8	t = -3.662	0.001
Hospital LOS (days)	13.4 ± 5.2	11.7 ± 4.8	U = 127.5	0.308
Mortality	1 (5%)	0 (0%)	χ^2 = 0.969	0.325
Acute Kidney Injury	6 (30%)	2 (13.3%)	χ^2 = 4.025	0.045
Metabolic Acidosis	5 (25%)	1 (6.7%)	χ^2 = 4.345	0.037

Source: statistical analysis. p < 0,05. Table 2 presents a comparative analysis of clinical outcomes and biochemical parameters between pediatric sepsis patients treated with SS and those treated with RL. The eGFR was found to be significantly higher in the RL group, with a mean of 85.6 ± 16.3 mL/min/1.73 m^2, compared to 75.2 ± 18.5 mL/min/1.73 m^2 in the SS group. This difference, indicated by a t-value of -2.032 and a p-value of 0.049, suggests improved renal function in the RL group. Bicarbonate levels were also notably higher in the RL group (22.5 ± 2.8 mEq/L) than in the SS group (19.2 ± 3.1 mEq/L), with a t-value of -3.662 and a p-value of 0.001. This significant difference highlights the better acid-base balance maintained with RL.

The median duration of hospital stay did not show a statistically significant difference between the groups. Patients in the RL group had a median hospital stay of 11.7 ± 4.8 days, compared to 13.4 ± 5.2 days in the SS, with a Mann-Whitney U value of 127.5 and a p-value of 0.308, indicating similar lengths of hospitalization regardless of fluid type.

Mortality rates were low and comparable between the two groups, with one death (5%) occurring in the SS and none in the RL group. The chi-square value for mortality was 0.969 with a p-value of 0.325, suggesting no significant difference in mortality outcomes.

The incidence of AKI and metabolic acidosis was significantly lower in the RL group. Specifically, 30% of patients in the SS group developed AKI compared to 13.3% in the RL group (chi-square value of 4.025, p-value of 0.045). Similarly, metabolic acidosis occurred in 25% of the SS group versus 6.7% of the RL group (chi-square value of 4.345, p-value of 0.037).



Graphic 1. Incidence of AKI by Fluid Type.

Source: statistical analysis. This bar chart illustrates the proportion of pediatric sepsis patients who developed AKI in the RL group versus the SS group. The chart shows a significantly lower incidence of AKI in patients treated with RL compared to those treated with SS, highlighting the potential renal protective effects of RL in fluid resuscitation.

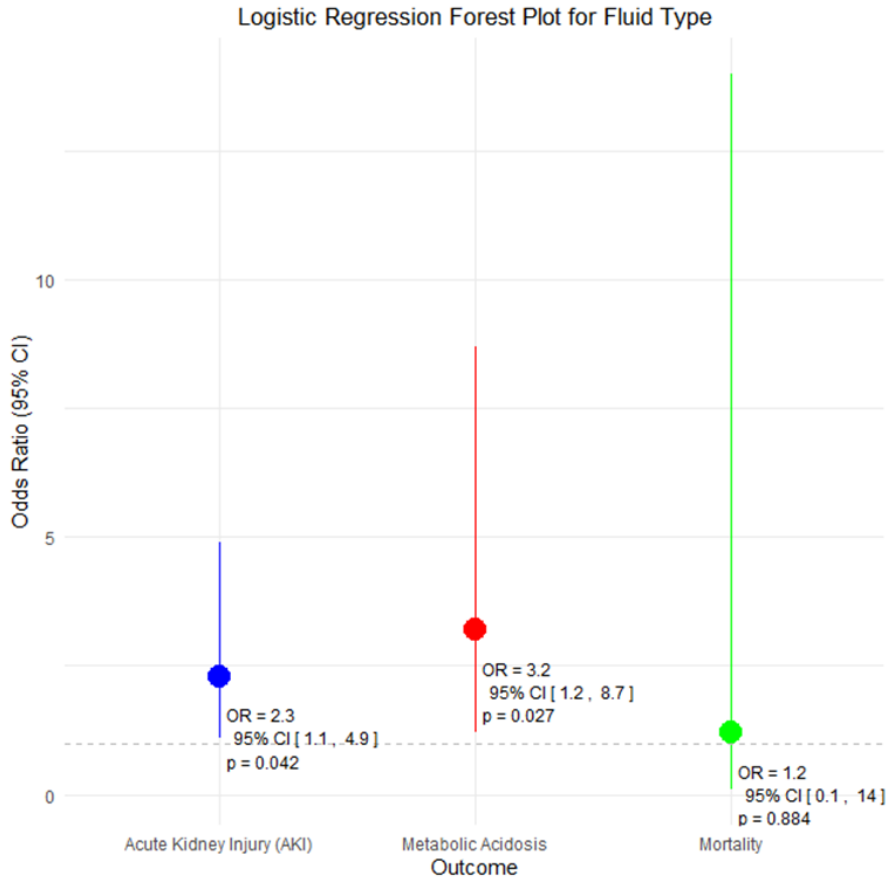
Table 3. Logistic Regression Analysis for Outcomes and Length of Stay by Fluid Type (Saline vs. Ringer Lactate).

Outcome	Variable	Adjusted Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Acute Kidney Injury (AKI)	Saline vs. Ringer Lactate	2.3	1.1–4.9	0.042
Metabolic Acidosis	Saline vs. Ringer Lactate	3.2	1.2–8.7	0.027
Mortality	Saline vs. Ringer Lactate	1.2	0.1–14.0	0.884
ICU Length of Stay > Median (11 days)	Saline vs. Ringer Lactate	1.8	0.8–4.1	0.153
Hospital Length of Stay > Median (13 days)	Saline vs. Ringer Lactate	1.6	0.7–3.8	0.258

Source: statistical analysis. $p < 0,05$. Table 3 presents the results of logistic regression analyses comparing the outcomes of pediatric sepsis patients treated with either SS or RL. For AKI, the adjusted odds ratio (OR) is 2.3 with a 95% confidence interval (CI) of 1.1 to 4.9 and a p-value of 0.042, indicating that the use of SS is associated with a significantly higher risk of AKI compared to RL. Similarly, the odds of developing metabolic acidosis are significantly higher in the SS, with an OR of 3.2 (95% CI: 1.2 to 8.7, p =

0.027). These findings suggest that RL is more effective in preventing these adverse renal and metabolic outcomes.

The analysis for mortality showed an OR of 1.2 (95% CI: 0.1 to 14.0, p = 0.884), indicating no significant difference between the groups. Additionally, the logistic regression for ICU length of stay greater than the median of 11 days resulted in an OR of 1.8 (95% CI: 0.8 to 4.1, p = 0.153), and for hospital length of stay greater than the median of 13 days, the OR was 1.6 (95% CI: 0.7 to 3.8, p = 0.258). These results suggest that the type of fluid used for resuscitation does not significantly impact mortality or the length of stay in the ICU and hospital, though there is a non-significant trend towards longer stays in SS group.



Graphic 2. Logistic Regression Forest Plot for Fluid Type.

Source: statistical analysis. This forest plot displays the odds ratios and 95% confidence intervals for acute AKI, metabolic acidosis, and mortality, comparing pediatric sepsis patients treated with SS versus RR.

This forest plot visualizes the ORs and 95% CIs for three clinical outcomes, AKI, metabolic acidosis, and mortality comparing pediatric sepsis patients treated with SS versus RL. The plot shows that the odds of developing AKI are significantly higher in the SS group compared to the RL group, with an OR of 2.3 (95% CI: 1.1–4.9, p = 0.042). Similarly, the odds of developing metabolic acidosis are also higher in the SS group, with an OR of 3.2 (95% CI: 1.2–8.7, p = 0.027). This suggests that RL is associated with a lower risk of these adverse outcomes compared to saline.

In contrast, the OR for mortality is 1.2 (95% CI: 0.1–14, p = 0.884), indicating no significant difference between the two groups. The wide confidence interval and the p-value above 0.05 suggest that the type of fluid does not significantly impact mortality in this study cohort. These findings highlight the renal and metabolic benefits of using RL in the resuscitation of pediatric sepsis patients while indicating no difference in overall survival between the fluid types.

Discussion

Key Findings

The results of this study highlight significant differences in the clinical outcomes associated with the use of SS versus RL for fluid resuscitation in pediatric patients with sepsis or septic shock. Notably, the use of RL was associated with a reduced incidence of AKI and metabolic acidosis compared to 0.9% saline. These findings suggest that RL, with its balanced electrolyte composition, may provide a more physiologically appropriate fluid for initial resuscitation, reducing the risk of renal and metabolic complications.

Mechanisms

The pathophysiological differences between SS and RL likely underpin the observed clinical outcomes. 0,9 % saline solution, with its high chloride content, can induce hyperchloremic metabolic acidosis and renal vasoconstriction, leading to reduced GFR and subsequent AKI. In contrast, Ringer Lactate's balanced composition, including lactate, which is metabolized to bicarbonate, helps maintain acid-base equilibrium and supports renal function by preventing chloride overload and its adverse effects[7].

Limitations

Several limitations should be considered when interpreting the results of this study:

Non-Randomized Design: The fluid type was chosen based on clinician discretion rather than random assignment, which could introduce selection bias and confound the results.

Sample Size: The relatively small sample size (n=35) limits the generalizability of the findings and may affect the statistical power to detect differences in outcomes, particularly for mortality.

Single-Center Study: Conducted at a single hospital in Quito, Ecuador, the findings may not be applicable to different healthcare settings or populations with varying disease severity and treatment protocols.

Short Follow-Up: The study's follow-up was limited to the duration of the hospital stay, precluding long-term assessment of renal function and other late-onset complications.

Strengths

Despite these limitations, the study has several strengths:

Prospective Data Collection: The prospective nature of the study allowed for systematic data collection and minimized recall bias.

Focused Pediatric Population: The study specifically targeted a pediatric sepsis cohort, providing valuable insights into a demographic often underrepresented in critical care research.

Comprehensive Outcome Assessment: The study evaluated multiple relevant outcomes, including AKI, metabolic acidosis, and mortality, offering a holistic view of the effects of fluid choice on pediatric sepsis management.

Real-World Clinical Setting: Conducted in a real-world clinical setting, the study's findings are directly applicable to everyday practice, highlighting practical implications for fluid resuscitation strategies.

Future Research

Further research is warranted to validate these findings in larger, multi-center stu-

dies with randomized designs to control for potential biases and confounders. Long-term follow-up studies are also needed to assess the sustained impact of fluid choice on renal function and overall outcomes in pediatric sepsis. Additionally, exploring the underlying mechanisms through which balanced fluids confer their benefits could inform more targeted interventions and optimize fluid management strategies in sepsis.

The results of our study align closely with the findings of a recent comprehensive meta-analysis[11] comparing the effects of balanced crystalloids (BC) and isotonic saline (IS) in pediatric sepsis. This meta-analysis, which included six studies with a total of 8753 children, demonstrated significant reductions in mortality and AKI when using balanced crystalloids compared to isotonic saline. Specifically, the meta-analysis reported an OR of 0.84 for mortality and 0.74 for AKI, indicating a notable protective effect of balanced fluids. Our study similarly found that RL was associated with a significantly lower incidence of AKI (13.3% vs. 30%) and metabolic acidosis (6.7% vs. 25%) compared to 0.9% saline, though mortality rates did not differ significantly between the groups.

In terms of hospital and PICU LOS, the meta-analysis concluded that there were no significant differences between balanced crystalloids and isotonic saline, although a subgroup analysis of randomized controlled trials suggested a shorter hospital LOS with balanced fluids[11]. Our findings are consistent with these results, as we observed no significant differences in ICU or total hospital LOS between the groups, with median ICU stays of 12 days for the saline group and 10 days for the Ringer Lactate group. This concordance with the broader literature underscores the potential advantages of using balanced crystalloids like Ringer Lactate in pediatric sepsis management, particularly in reducing renal and metabolic complications.

Our study's findings provide a nuanced addition to the ongoing debate about the efficacy of balanced crystalloids versus normal saline for fluid resuscitation in pediatric sepsis. The meta-analysis by Liu et al.[16] comparing balanced crystalloids and normal saline in critically ill patients, including nine randomized controlled trials (RCTs), found no significant differences in mortality, incidence of AKI, or the need for renal replacement therapy (RRT). Specifically, their analysis reported a relative risk (RR) of 0.93 for mortality ($p = 0.08$), 0.94 for AKI ($p = 0.06$), and 0.94 for RRT use ($p = 0.67$). These findings suggest that balanced crystalloids may not offer a clear advantage over normal saline in these broad outcomes.

In contrast, our study specifically in pediatric sepsis patients found significant benefits of Ringer Lactate over 0.9% saline in terms of reducing the incidence of AKI (13.3% vs. 30%, $p = 0.045$) and metabolic acidosis (6.7% vs. 25%, $p = 0.037$). These differences may be attributed to the specific patient population (pediatric sepsis), the nature of the study (observational versus RCTs), and the focused outcomes (renal and metabolic parameters). While Liu et al.[16] did not find conclusive evidence for the superiority of balanced fluids in overall mortality and severe renal outcomes, our findings suggest that, at least in pediatric sepsis, balanced crystalloids like Ringer Lactate may provide renal and metabolic benefits. This underscores the importance of further large-scale, pediatric-specific randomized trials to explore these potential advantages and inform clinical practice more definitively.

Our study's findings are also consistent with the systematic review by Lehr et al 12 that compared balanced versus unbalanced fluid bolus therapy in critically ill children, which found that balanced fluids, such as Ringer Lactate, were associated with improvements in serum bicarbonate and blood pH levels within 24 hours of rehydration. This systematic review, which included three RCTs with a total of 162 patients, reported a

greater mean change in serum bicarbonate (pooled estimate 1.60 mmol/L; p = 0.04) and pH (pooled mean difference 0.03; p = 0.03) with balanced fluids. Similarly, our study observed a significantly lower incidence of metabolic acidosis in the Ringer Lactate group compared to the saline group (6.7% vs. 25%, p = 0.037), highlighting the acid-base benefits of balanced fluids in pediatric sepsis.

However, the systematic review did not find significant differences in chloride serum levels, AKI, renal replacement therapy (RRT), or mortality between balanced and unbalanced fluids. In contrast, our study found a significant reduction in AKI incidence with Ringer Lactate (13.3% vs. 30%, p = 0.045), suggesting that the benefits of balanced fluids might extend beyond acid-base balance to renal protection in a broader pediatric sepsis population. This discrepancy might be attributed to differences in study populations, sample sizes, and methodologies. Despite these differences, both studies underscore the potential advantages of balanced fluids, emphasizing the need for larger RCTs to confirm these findings and guide clinical practice in pediatric fluid resuscitation.

Our study's findings are in line with the results of the multicenter randomized clinical trial conducted by Sankar et al.[17], which compared the use of multiple electrolytes solution (MES) versus 0.9% saline for fluid resuscitation in pediatric septic shock. Sankar et al. found that the use of MES significantly reduced the incidence of new and/or progressive AKI compared to saline (21% vs. 33%, RR 0.62, p < 0.001). Similarly, our study observed a lower incidence of AKI in patients resuscitated with Ringer Lactate (13.3%) compared to those receiving 0.9% saline (30%, p = 0.045). These consistent findings across different balanced crystalloids (MES and Ringer Lactate) highlight the potential renal protective effects of balanced fluids in pediatric sepsis.

Moreover, Sankar et al. reported lower rates of hyperchloremia in the MES group compared to the saline group, which aligns with our observation of a significantly lower incidence of metabolic acidosis in the Ringer Lactate group (6.7%) versus the saline group (25%, p = 0.037)[17]. Both studies did not find significant differences in ICU mortality between the balanced crystalloid and saline groups, underscoring that the primary benefits of balanced fluids may lie in reducing renal and metabolic complications rather than impacting overall survival rates. These results support the consideration of balanced crystalloids over 0.9% saline in the initial resuscitation of pediatric septic shock, given their favorable effects on renal function and acid-base balance.

Our study's findings complement the results of the randomized controlled trial by Trepatchayakorn et al.[18], which compared the outcomes of pediatric sepsis resuscitation with different types of crystalloid fluids, including normal saline solution, Ringer lactate solution, and Sterofundin. Trepatchayakorn et al. found no significant differences in clinical complications among the fluid groups. However, the RL group demonstrated a significant reduction in urinary neutrophil gelatinase-associated lipocalin (uNGAL) levels, a marker for AKI, when larger doses of fluid were administered. This suggests a potential renal protective effect of Ringer lactate, aligning with our findings of a lower incidence of AKI in the Ringer Lactate group (13.3%) compared to the saline group (30%, p = 0.045).

While Trepatchayakorn et al.'s study did not find differences in broader clinical outcomes, the observed reduction in uNGAL levels in the RL group highlights the importance of fluid choice in pediatric sepsis resuscitation. Similarly, our study found significant reductions in AKI and metabolic acidosis with the use of RL, suggesting that balanced crystalloids may offer advantages in maintaining renal function and acid-base balance in critically ill pediatric patients. By

refining fluid resuscitation strategies, we can improve outcomes and reduce complications in this vulnerable patient population.

Our study's results align with those of the double-blind randomized controlled trial conducted by Anantasit et al.[19] which investigated the impact of balanced salt solution (BS) versus normal saline (NS) on pediatric septic shock. They found that while the clinical outcomes, including hospital mortality and the prevalence of AKI, were similar between the two groups, there was a trend towards a higher incidence of hyperchloremic metabolic acidosis in the NS group (54.8% vs. 33.3%, p = 0.091). This observation underscores the potential metabolic benefits of using balanced salt solutions over normal saline in fluid resuscitation for pediatric septic shock.

Similarly, our study found that the use of RL significantly reduced the incidence of metabolic acidosis compared to 0.9% saline (6.7% vs. 25%, p = 0.037). Furthermore, we observed a lower incidence of AKI in the RL group (13.3%) compared to the SS group (30%, p = 0.045). These findings support the trend noted by Anantasit et al 19. that balanced salt solutions may offer metabolic advantages without compromising other clinical outcomes. Both studies highlight the need for further research to establish whether balanced crystalloids should be preferred in initial fluid resuscitation protocols for pediatric septic shock, particularly in reducing metabolic complications such as hyperchloremia.

Our study findings are consistent with those of Emrath et al.[20], who conducted an observational cohort review evaluating the impact of balanced fluids versus unbalanced fluids on pediatric severe sepsis outcomes. Emrath et al. analyzed data from 36,908 pediatric patients across 43 children's hospitals and found that those receiving balanced fluids exclusively within the first 72 hours of treatment had significantly lower mortality (12.5% vs. 15.9%; p = 0.007), reduced prevalence of acute kidney injury (AKI) (16.0% vs. 19.2%; p = 0.028), and fewer days requiring vasoactive infusions (3.0 vs. 3.3 days; p < 0.001) compared to those receiving unbalanced fluids.

Similarly, our study observed a significantly lower incidence of AKI in the RL group (13.3%) compared to the 0.9% saline group (30%, p = 0.045), as well as a lower incidence of metabolic acidosis (6.7% vs. 25%, p = 0.037). While our study did not specifically evaluate mortality differences, the alignment with Emrath et al.[20] findings regarding AKI underscores the renal protective effects of balanced fluids in pediatric sepsis. Both studies emphasize the importance of considering fluid composition in the initial resuscitation of pediatric sepsis patients. The consistent reduction in AKI incidence across these studies supports the preferential use of balanced fluids like RL to potentially improve renal outcomes and overall survival in this vulnerable population.

Conclusions

This study demonstrates that the use of Ringer Lactate for fluid resuscitation in pediatric patients with sepsis or septic shock is associated with a significantly lower incidence of AKI and metabolic acidosis compared to 0.9% saline. The findings suggest that Ringer Lactate, as a balanced crystalloid, provides a safer alternative by better maintaining physiological electrolyte balance and reducing renal and metabolic complications. While mortality did not differ significantly between the groups, the improved renal and metabolic outcomes with Ringer Lactate indicate its potential for enhancing overall patient care and reducing complications in pediatric sepsis management. These results support the consideration of Ringer Lactate over 0.9% saline in the initial resuscitation of pediatric sepsis patients, emphasizing the need for further research and potential updates to clinical guidelines.

Conflicts of interest

The authors reported no personal, financial, intellectual, economic, or corporate conflicts of interest in conducting this research.

Authors' contribution

AR: conception and design of the research; collection and obtaining of results; data analysis and interpretation; writing of the manuscript.

AC: data analysis and interpretation; writing of the manuscript.

IJ: collection and obtaining of results; data analysis and interpretation.

MV: collection and obtaining of results; data analysis and interpretation.

RG: collection and obtaining of results; data analysis and interpretation.

RY: Data analysis and interpretation, manuscript review and writing.

SC: Data analysis and interpretation, manuscript review and writing

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