ORIGINAL ARTICLE

Comparison of the effect of isotonic and hypotonic saline solutions for children with mild dehydration at Lampang Hospital

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ABSTRACT

Administering the appropriate type and rate of fluids is crucial for pediatric patients. Young patients should be given isotonic solutions, as they are safer than hypotonic solutions for fluid maintenance. However, limited studies exist on the efficacy and complications of isotonic solutions for treating acutely ill pediatric patients with mild dehydration. This study aimed to compare isotonic and hypotonic solutions in such cases. A stratified randomized controlled trial was conducted on patients aged 6 months to 15 years with acute illness and mild dehydration in two disease groups: acute gastroenteritis and other diseases. The trial involved administering intravenous fluids, either isotonic or hypotonic solution, for at least 24 hours. Pre and post-treatment serum sodium levels and treatment complications were assessed and compared between patients who received isotonic and hypotonic solutions. A total of 144 patients were randomly assigned to receive either isotonic solution or hypotonic solution. Of the 144 patients, 72 received isotonic and 72 received hypotonic solutions. The isotonic group comprised 51.4% males with a median age of 27.5 months. On the other hand, the hypotonic group comprised 56.9% males with a median age of 38 months. At baseline, both groups' sodium levels were similar at 136.2±2.5 and 136.8±2.5 mmol/L, respectively. After 24 hours, the isotonic group had a statistically significant increase in sodium levels (138.8±2.2 mmol/L; increased median 2.3) compared to the hypotonic group (138.1±2.0 mmol/L; increased median 1.5). In conclusion, no cases of hypernatremia, drowsiness, or seizures were observed, suggesting isotonic solutions can be safely used in these selected groups of acutely ill pediatric patients with mild dehydration.

Key words:
isotonic solution, hypotonic solution, pediatric patients, mild dehydration, serum sodium levels

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INTRODUCTION

Dehydration is a common and potentially serious condition among pediatric patients, often requiring prompt intervention with intravenous fluids. Selecting the appropriate type and rate of fluid administration is crucial for patient safety and optimal recovery.[1] Historically, administering intravenous fluids in children followed Holiday Segar's guidelines, which recommended a maintenance sodium level of 3 mEq per 100 kilocalories of energy required. Therefore, hypotonic solution is often used as an intravenous fluid in children.[2] However, this practice of administering hypotonic parenteral fluids was established over 50 years ago, before it was recognized that there are numerous potential stimuli for antidiuretic hormone (arginine vasopressin; AVP) production in most hospitalized patients. Dehydration in children prompts the secretion of AVP, leading to water retention.[3] In such cases, if a hypotonic solution is administered to a child, it could increase the risk of hyponatremia (low sodium levels) due to the patient's retention of excess AVP, which impairs their excretion of free water.[4,5] Recent studies have shown that administering hypotonic solutions to children may have potential risks and lead to hyponatremia.[4-7]

The American Academy of Pediatrics (AAP) conducted a systematic review in 2018 and found that intravenous administration of hypotonic solutions to pediatric patients can cause significant hyponatremia, albeit with most patients being asymptomatic.[7] Consequently, the AAP issued guidelines recommending the use of isotonic solutions containing dextrose and appropriate doses of potassium chloride for intravenous maintenance fluids in children aged 28 days to 18 years to mitigate the risk of hyponatremia.[7] Nonetheless, isotonic solutions have also been associated with potential adverse effects, such as hypernatremia (high sodium levels) or acidosis.[3]

Amidst these conflicting guidelines and inconsistent findings, further research is warranted to address the optimal fluid management approach, particularly in mild and moderate dehydration cases. Several studies have investigated the effects of hypotonic and isotonic solutions in pediatric patients with acute gastroenteritis and mild to moderate dehydration, yielding mixed results. A retrospective descriptive study by Hanna and Saberi [8] (2010) found that hypotonic solutions had a higher risk of causing hyponatremia compared to isotonic solutions. In addition, a randomized trial by Neville et al. in 2006 showed that normal saline was better than hypotonic solutions as it prevented hyponatremia without causing hypernatremia.[9] However, a clinical study by Sanchez-Bayle et al. (2014) did not find an increased risk of hyponatremia when administering hypotonic fluids.[10] Additionally, a randomized study by Golshekan et al. in 2016 did not observe a difference in sodium levels between the isotonic and hypotonic solution groups.[11]

Notably, most previous studies have been conducted in the Americas and Europe, and there is a lack of established guidelines for treating acute illness patients with mild dehydration in Thailand. To address the knowledge gap, our study aims to compare the effectiveness and safety of isotonic and hypotonic solutions for mildly dehydrated pediatric patients in Thailand. By contributing to the growing body of evidence, we hope to provide valuable insights and inform clinical practice guidelines for optimal fluid management in this vulnerable population.

METHOD

Study Design and Participant

This study was a stratified, parallel-group, randomized controlled trial conducted in the Pediatric unit at Lampang Hospital. The institutional review board approved the study protocol, and written informed consent was obtained from parents/guardians before enrollment. Children aged 6 months to 15 years with acute illness and mild dehydration, admitted as inpatients to the Pediatric ward, were eligible for inclusion. Exclusion criteria included lack of consent, abnormally high serum sodium levels (>145 mmol/L/) before enrollment, missing follow-up laboratory results, underlying conditions (heart failure, acute/chronic kidney disease, nephritis, nephrotic syndrome), and prior/concomitant diuretic use.

Randomization and Blinding

Eligible participants were stratified by diagnosis (acute gastroenteritis or other diseases) and randomly assigned in a 1:1 ratio to receive either isotonic or hypotonic intravenous fluids. A block randomization sequence with a block size of four was computer-generated and concealed in opaque, sealed envelopes. Treatment allocation was blinded to investigators and participants until after enrollment (Fig 1).

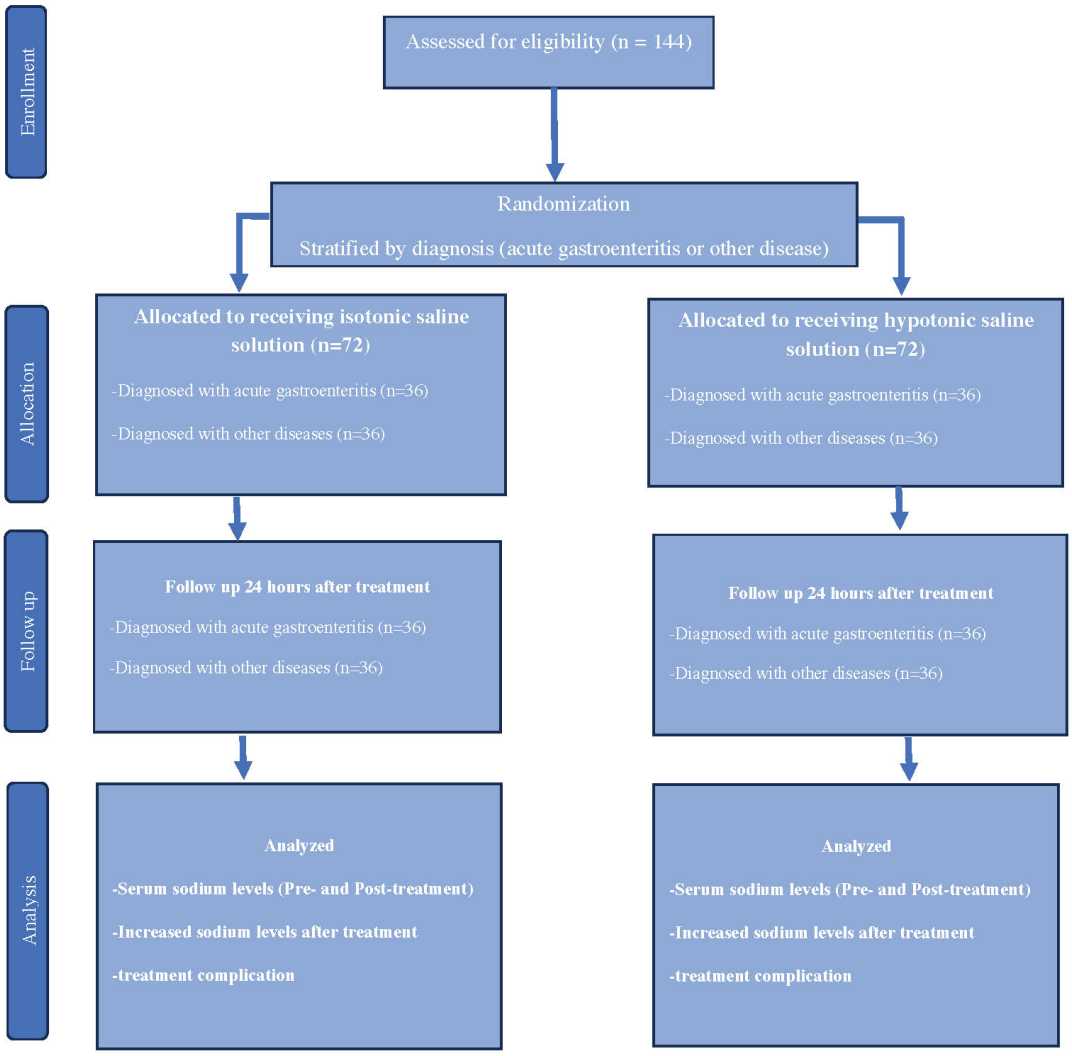

Figure 1. Consort diagram

Interventions

According to their randomized groups, participants received the assigned intravenous fluid (isotonic or hypotonic solution). The total fluid volume was calculated as maintenance plus a 5% deficit for children aged 6 months to 1 year and maintenance plus a 3% deficit for children older than 1 year. Serum sodium levels were measured before fluid administration and 24 hours after fluid replacement was initiated**.**

Study Outcomes

The primary outcome was the change in serum sodium levels before and after administering isotonic or hypotonic solutions. Secondary outcomes included treatment complications, such as drowsiness (defined as a Glasgow Coma Scale score <13) and seizures.

Data Collection and Safety Monitoring

Demographic data, diagnosis, fluid type, and serum sodium levels were recorded. Clinical monitoring for adverse events, such as drowsiness or seizures, was performed during fluid administration. If any concerning symptoms developed, fluid administration would be stopped, and serum electrolytes would be rechecked.

Statistical Analysis

Data were analyzed according to the intention-to-treat principle using appropriate statistical tests (e.g., t-test, Wilcoxon rank-sum test, chi-square, or Fisher's exact test) for continuous and categorical variables. Box plots were used to illustrate the comparison of sodium levels between groups. All statistical tests were two-tailed, with a p-value <0.05 and a standardized difference <1 considered statistically significant.

Ethical Considerations

The study was approved by the Lampang Hospital Human Research Ethics Committee (certification number EC 180/66, dated October 30, 2023) and registered before patient enrollment at the Thai Clinical Trials Registry (TCTR20240316002). Informed consent was obtained from parents/guardians, and participants' rights were protected throughout the study.

RESULTS

A total of 144 patients aged 6 months to 15 years with acute illness and mild dehydration admitted to the pediatric ward at Lampang Hospital met the inclusion criteria. They were randomized to receive either isotonic solution (5%Dextrose + 0.9%NaCl, n=72) or hypotonic solution (5%Dextrose + 0.45%NaCl, n=72), with 36 cases of acute gastroenteritis and 36 cases of other diseases in each group. In the isotonic solution group, there were 37 males (51.4%), with a median age of 27.5 months (IQR: 15-54). The hypotonic solution group comprised 41 males (56.9%) with a median age of 38 months (IQR: 24-74). The mean baseline sodium level was 136.2±2.5 mmol/L in the isotonic group and 136.8±2.5 mmol/L in the hypotonic group. After 24 hours of treatment, the mean sodium levels were 138.8±2.2 mmol/L and 138.1±2.0 mmol/L in the isotonic and hypotonic groups, respectively, showing a statistically significant difference (Table 1). Figure 2 presents a box plot comparison of serum sodium levels before and after 24 hours of receiving intravenous fluid therapy with either hypotonic or isotonic saline solution.

Table 1. Demographic characteristics of participants

Demographic characteristics	Isotonic saline solution (5%Dextrose + 0.9%NaCl) (N=72)	Hypotonic saline solution (5%Dextrose + 0.45%NaCl) (N=72)	Standard difference
Gender, male	37 (51.4)	41 (56.9)	-0.11
Age (month)[a]	27.5 (15-54)	38 (24-74)	-0.27
Acute illness			0
Acute gastroenteritis	36 (50.0)	36 (50.0)	
Other diseases	36 (50.0)	36 (50.0)	
Serum sodium level before treatment (mmol/L)[b]	136.2±2. 5	136.8±2.5	-0.25
Serum sodium level after 24 hours of treatment (mmol/L)[b]	138.8±2.2	138.1±2.0	0.32

Data presented as number (percentage), [a]Data presented as median (IQR), [b]Data presented as mean ± S.D.

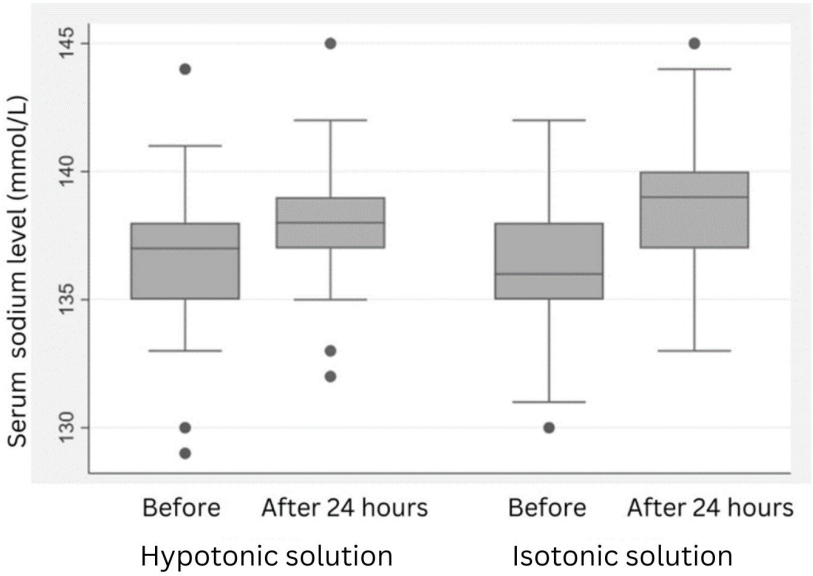

Figure 2. Box plot comparing sodium levels before and after 24 hours of treatment with isotonic (5%Dextrose + 0.9% NaCl; 5DNSS) and hypotonic (5%Dextrose + 0.45% NaCl; 5DNS2) solutions

In the subgroup analysis by diagnosis, for patients with acute gastroenteritis receiving isotonic solution, the mean baseline sodium was 136.1±2.8 mmol/L, and after 24 hours, it increased to 138.9±2.2 mmol/L. For those with other diseases in the isotonic group, the baseline sodium was 136.3±2.1 mmol/L, increasing to 138.7±2.3 mmol/L after treatment. In the hypotonic solution group, patients with acute gastroenteritis had a mean baseline sodium of 136.9±2.1 mmol/L, which increased to 138.0±1.9 mmol/L after 24 hours. For those with other diseases receiving hypotonic solution, the baseline sodium was 136.8±2.9 mmol/L, increasing to 138.2±2.2 mmol/L after treatment (Table 2). Figure 3 illustrates the changes in serum sodium levels for each individual patient from before treatment to 24 hours after receiving intravenous fluid therapy with either hypotonic or isotonic saline solution. Figure 3A displays the changes observed in patients with acute gastroenteritis, while Figure 3B shows the changes for patients in the other disease group. The figure allows

for visualizing individual trajectories of sodium level changes within 24 hours of treatment, comparing the two fluid types across different disease conditions.

Table 2. Comparison of serum sodium levels before and after treatment classified by disease group

Serum sodium level	Isotonic saline solution (5%Dextrose + 0.9%NaCl) (N=72)		Hypotonic saline solution (5%Dextrose + 0.45%NaCl) (N=72)	
	AGE (N=36)	Other disease (N=36)	AGE (N=36)	Other disease (N=36)
Before treatment (mmol/L)	136.1±2.8	136.3±2.1	136.9 ±2.1	136.8 ±2.9
After 24 hours of treatment (mmol/L)	138.9±2. 2	138.7±2.3	138.0±1.9	138.2±2.2

Data presented as mean ± S.D.
Abbreviation: AGE = acute gastroenteritis

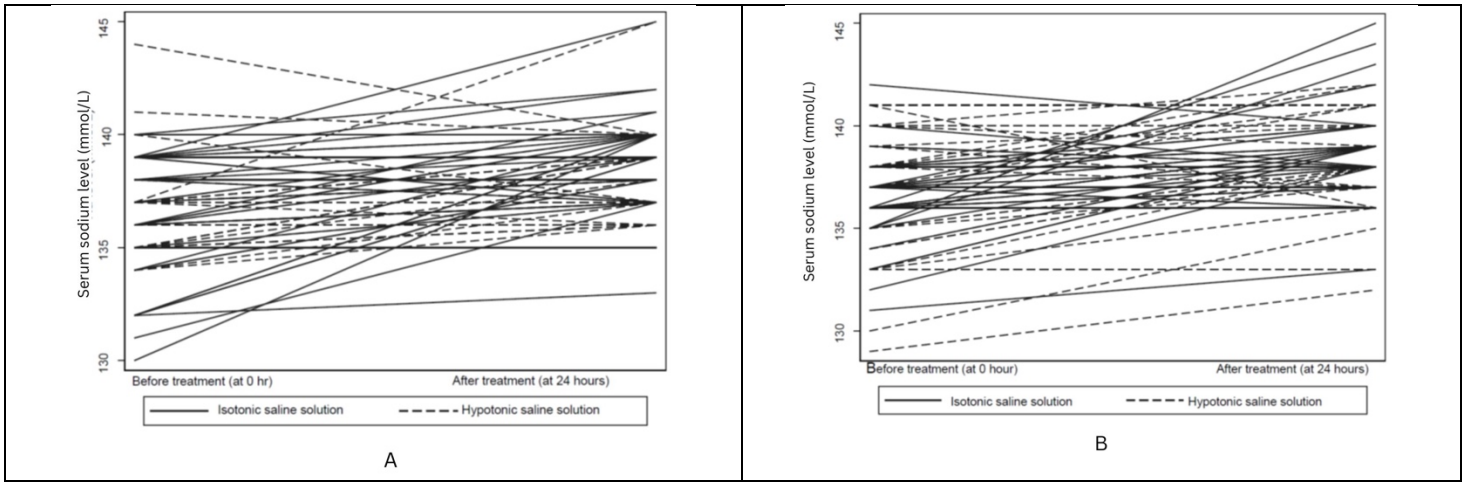

Figure 3. Individual trajectories of serum sodium level changes from before treatment to 24 hours after intravenous fluid therapy with isotonic (5%Dextrose + 0.9% NaCl; 5DNSS) or hypotonic (5%Dextrose + 0.45% NaCl; 5DNS2) solutions, separated by acute gastroenteritis group (A) and other diseases group (B)

Due to an imbalance in prognostic factors between the groups, adjustments were made to evaluate the difference in sodium levels. After adjustment, the mean difference in sodium levels was 2.3 mmol/L (IQR: 1.9-2.8) in the isotonic solution group and 1.5 mmol/L (IQR: 1.1-2.0) in the hypotonic solution group, which was a statistically significant difference (p=0.009) (Table 3).

Table 3. Difference in serum sodium levels after adjusting for imbalanced prognostic factors

Serum sodium level	Isotonic saline solution (5%Dextrose + 0.9%NaCl) (N=72)	Hypotonic saline solution (5%Dextrose + 0.45%NaCl) (N=72)	Standard difference (95%CI)	*p*-value
Before treatment (mmol/L)	136.2±2.5	136.8±2.5	-	-
After 24 hours of treatment (mmol/L)	138.8±2.2	138.1±2.0	-	-
Difference between before and after 24 hours of treatment (mmol/L)[a]	2.3 (1.9, 2.8)	1.5 (1.1, 2.0)	0.9 (0.2, 1.5)	0.009*

Data presented as mean ± S.D., [a]Data presented as median (IQR)
*p-value < 0.05

In the subgroup with baseline sodium levels below 135 mmol/L, the mean difference in sodium levels was 5.9 mmol/L (IQR: 4.9-6.9) in the isotonic group and 3.1 mmol/L (IQR: 1.8-4.3) in the hypotonic group, which was also a statistically significant difference (p<0.001) (Table 4). Additionally, two participants (one from the acute gastroenteritis group and the other from the other diseases group) who received isotonic saline solution had sodium levels increase from baseline to 10 mmol/L. However, both patients had serum sodium levels of not more than 145 mmol/L after 24 hours of administering intravenous fluids, and no side effects were associated with a rapid increase in serum sodium levels.

Table 4. Difference in increased serum sodium levels for patients with baseline hyponatremia (serum sodium level < 135 mmol/L)

Serum sodium level	Isotonic saline solution (5%Dextrose + 0.9%NaCl) (N=13)	Hypotonic saline solution (5%Dextrose + 0.45%NaCl) (N=12)	Standard difference (95%CI)	*p*-value
Before treatment (mmol/L)	132.4 ± 1.2	132.8 ± 1.8	-	-
After 24 hours of treatment (mmol/L)	138.1 ± 2.3	136.2 ± 2.3	-	-
Difference between before and after 24 hours of treatment (mmol/L)[a]	5.9 (4.9, 6.9)	3. 1 (1.8,4.3)	2.9 (1.2,4.6)	< 0.001*

Data presented as mean ± S.D., [a]Data presented as median (IQR)
*p-value < 0.05

DISCUSSION

The present study compared the effects of administering isotonic (0.9% NaCl + 5% Dextrose) and hypotonic (0.45% NaCl + 5% Dextrose) intravenous solutions in pediatric patients aged 6 months to 15 years with acute illness and mild dehydration. The findings align with current American Academy of Pediatrics guidelines recommending the use of isotonic saline solution to reduce the risk of iatrogenic hyponatremia in acutely ill children.[7]

Consistent with previous research,[9,12] no cases of hypernatremia were observed in the isotonic saline group. Similarly, hypotonic solution administration did not cause hyponatremia, corroborating the results of Sánchez-Bayle et al.'s study[10]. However, the subgroup analysis revealed a statistically significant 5.9 mmol/L increase in sodium levels among patients receiving isotonic solution compared to a 2.5 mmol/L increase in the hypotonic group across acute gastroenteritis and other disease subgroups. This result contrasts with Golshekan et al.'s study[11], which found no difference in sodium levels between isotonic and hypotonic groups.

The observed increase in sodium levels, particularly among patients with baseline hyponatremia (<135 mmol/L) in this study, may be attributable to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). SIADH is a potential complication in acute illnesses, leading to lower-than-normal sodium levels before treatment.[3] For this reason, the administration of intravenous hypotonic solutions to patients with acute illness and mild dehydration results in a low rate of serum sodium increase and may worsen hyponatremia, which is consistent with previous studies[13-18] that found a significantly different decrease in sodium levels in these patients receiving hypotonic solutions compared to isotonic solutions.

However, two participants' sodium levels increased by up to 10 mmol/L after receiving intravenous fluids within 24 hours. Both patients received isotonic solutions, one from the acute gastroenteritis group and the other from the other diseases group. In both cases, the patients initially had sodium levels below 135 mmol/L, which did not exceed 145 mmol/L after treatment. This occurrence can be explained by the fact that ADH levels return to normal after their condition improves.[19] Hence, patients who receive intravenous isotonic solutions should also be monitored for hypernatremia, even after demonstrating an improvement in acute illness.

Ultimately, no treatment complications, such as drowsiness or seizures, were observed in either group, supporting the safe administration of isotonic solutions in pediatric patients with acute illness and mild dehydration. The study's findings, particularly the inclusion of patients with acute illnesses beyond gastroenteritis (e.g., hand-foot-mouth disease, pneumonia, bronchitis), suggest that isotonic solutions can be safely used in these diverse populations.

However, it is crucial to interpret these results within the study's limitations, including the single-center design, small sample size, and follow-up limited to 24 hours. More extended follow-up periods of 48-72 hours would provide more clarity on the sustained effects of the interventions. Additionally, this study did not exclude patients with baseline hyponatremia (serum sodium 135 mmol/L) as they may require different standard treatments, potentially affecting result interpretation. Future studies should stratify participants based on the underlying cause of acute illness, such as respiratory tract infections or central nervous system infections, as these conditions may influence sodium levels differently. Furthermore, this study only focused on patients with mild dehydration. As a result, it is essential to extend the research to examine the safety of isotonic saline solutions in patients with moderate to severe dehydration to establish evidence-based guidelines for fluid management in pediatric acute illnesses.

CONCLUSION

This study supports the administration of isotonic saline solution in Thai pediatric patients aged 6 months to 15

years with acute illness and mild dehydration. While no significant complications were observed, carefully monitoring sodium levels and hydration status is recommended, particularly in patients with potential SIADH or underlying fluid and electrolyte imbalance conditions.

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