

# COMPARISON OF SODIUM ABNORMALITIES ASSOCIATED WITH HYPOTONIC VERSUS ISOTONIC MAINTENANCE INFUSIONS IN HOSPITALIZED CHILDREN

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## ABSTRACT

**OBJECTIVE:** To compare Sodium abnormalities associated with Maintenance Infusions, Hypotonic versus isotonic in hospitalized children: A Randomized Controlled Trial

**Material and Methods:** This study was a randomized control trial conducted in the Department of Pediatrics A Hayat Abad Medical Complex Peshawar from 28 October 2020 to 28 April 2021. All the admitted patients aged 1 year to 12 years requiring maintenance infusion and were nothing by mouth (NBM) for at least 48 hours and serum sodium between 135-145 mmol/l were included in the study. Patients with renal disease diabetic ketoacidosis and on drugs affecting sodium level were excluded from the study. Two hundred and four patients who fulfilled the inclusion criteria, were randomly classified into groups A and B 102 each by lottery method. Group A was given Isotonic fluids (0.9% Sodium Chloride and 5% Dextrose water with Potassium 20 mmol/L) and Group B was given hypotonic fluids (0.45% Sodium Chloride and 5% Dextrose water with Potassium 20 mmol/L). The baseline tests and targeted tests, such as CBC, Blood sugar, urea, creatinine, electrolytes (sodium, potassium, and chloride), osmolality, and arterial blood gases, were performed. Data was analyzed using SPSS version 21.0. The post-stratification chi-square test was utilized to examine potential effect modifiers, and results were presented in tables.

**Results:** For a total of 204, there were 43 (42.3%) female patients and 59 (57.8%) male patients in Group A. Eighty (78.4%) male patients and twenty-two (21.6%) female patients were documented in Group B. In Group A, 61 (59.8%) patients had ages of 1-6 years while 41 patients (40.2%) were 7-12 years old. Eighteen patients in this group developed hyponatremia after receiving isotonic fluids. Fifty-two (51.0%) patients in Group B were 1-6-year-old and 50 (49.0%) patients were 7-12 years old. while 49 patients in this group developed, hyponatremia receiving hypotonic fluids. Patients given isotonic fluids didn't develop any complications (Hypernatremia and hyperchloremic metabolic acidosis).

**Conclusion:** On the basis of the results of this study, Isotonic intravenous maintenance fluids are a safe option in the pediatric population.

**Keywords:** Children, Intravenous fluids, Hypotonic, Isotonic Maintenance Infusions

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## INTRODUCTION

Since 1957, Holliday and Segar have advocated for the use of the hypotonic solution as a maintenance intravenous fluid (IVF) in children. Their suggestion was

supported by data on the caloric intake of healthy youngsters and the electrolyte content of human and cow's milk. When compared to plasma tonicity, it is equivalent to 0.2% sodium chloride in a 5% dextrose solution, which is hypotonic. <sup>1</sup> Moritz and Ayus suggested that an isotonic solution would be a better choice as maintenance IVF in children after reporting over 50 deaths and major unfavorable neurological sequelae associated with hypotonic fluids in 2003. <sup>2</sup>

The movement of water from the extracellular fluid (ECF) compartment into the intracellular fluid (ICF) com-

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partment is constrained by the osmolality of an isotonic solution, which is close to that of plasma (275-295 mOsm/kg). This is important for preventing cerebral edema as a result of hyponatremia, which can cause significant neurological morbidity.<sup>3</sup>

In 2018, the American Academy of Pediatrics (AAP) released guidelines recommending isotonic solutions as an intravenous maintenance fluid therapy for children between the ages of 28 days and 18 years.<sup>4</sup> In 2020, the National Institute for Health and Care Excellence (NICE) modified its recommendations and suggested that term newborns older than eight days be provided isotonic fluids<sup>5</sup>. Compared to prior years, pediatricians have recommended isotonic solutions.<sup>6-9</sup>

Isotonic fluid's safety is questioned since it can cause fluid overload and hypernatremia, cardiac dysfunction, hyperperfusion, and hypertension, as well as fluid overload and metabolic acidosis.<sup>10,11</sup>

In order to compare the effectiveness and safety of isotonic versus hypotonic solutions for the maintenance of IVF in hospitalized children, the current study was carried out.

The aim of this study was to compare the complications of sodium abnormalities associated with hypotonic and isotonic maintenance infusions in hospitalized children.

## MATERIAL AND METHODS

This study was a randomized control trial conducted in the Department of Pediatrics A MTI-HMC Peshawar from 28 October 2020 to 28 April 2021 after approval from an ethical committee. All the admitted patients aged 1 year to 12 years requiring maintenance infusion and were nothing by mouth (NBM) for at least 48 hours and serum sodium between 135-145 mmol/l were included in the study. Patients with renal disease diabetic ketoacidosis and on drugs affecting sodium levels were excluded from the study.

Two hundred and four patients who fulfilled the inclusion criteria, were randomly classified into two groups A and B (102 each) by lottery method. Group A was given Isotonic fluids (0.9% Sodium Chloride and 5% Dextrose water with Potassium 20 mmol/L) and Group B was given hypotonic fluids (0.45% Sodium Chloride and 5% Dextrose water with Potassium 20 mmol/L).

The purpose of the study was explained to guardians and informed written consent was obtained. Pre-designed proforma was used for documentation of each individual record including name, age, sex, address, history, clinical examination, investigations, response to management, and complications. The baseline tests and targeted tests, such as CBC, Blood sugar, urea, creatinine, electrolytes (sodium, potassium, and chloride), osmolality, and arterial blood gases, were performed. The hospital offered investigations to all patients. Patients whose follow-up was not maintained were removed from the study.

The sample size was 204 (102 patients in each group) keeping isotonic fluid had a substantially lower risk of hyponatremia (17% versus 34%) as compared to hypotonic fluid with 80% power of the test, 5% level of significance and 5% margin of error calculated on WHO formula for sample size determination. The sampling technique was random Sampling using lottery method.

Data was analyzed using SPSS version 21.0. Means and standard deviations were calculated for name, age, and disease duration, while frequencies and percentages were determined for categorical factors. The post-stratification chi-square test was utilized to examine potential effect modifiers, and results were presented in tables.

## RESULTS

This study was conducted on 204 patients (102 in each group). Group A received isotonic maintenance fluids and group B received hypotonic maintenance fluids.

The mean age and SDs in Group A were 6.29 +/- 2.013 years while 6.74 +/- 2.602 years in Group B. In Group A, 61 (59.8%) patients had ages of 1-6 years while 41 patients (40.2%) were 7-12 years old. Fifty-two (51.0%) patients in Group B were 1-6-year-old and 50 (49.0%) patients were 7-12 years old.

There were 43 (42.3%) female patients and 59 (57.8%) male patients in Group A. Eighty (78.4%) male patients and twenty-two (21.6%) female patients were documented in Group B. According to frequencies and percentages, 18 (17.6 percent) patients in Group A, while 49 (48.0 percent) patients in Group B experienced hyponatremia. Age, gender, and disease duration were used to stratify hyponatremia. None of our patients on isotonic maintenance (IVF) developed hypernatremia and metabolic acidosis.

## DISCUSSION

When oral intake is insufficient to maintain the extracellular volume, maintenance IVF is used to maintain a

**Table 1: Frequencies and Percentages for Hyponatremias (n=204)**

Treatment Groups	Hyponatremia	Frequency	Percent	P Value
Group A (n=102)	Yes	18	17.6%	0.00001
	No	84	82.4%	
	Total	102	100.0%	
Group B (n=102)	Yes	49	48.0%	0.00001
	No	53	52.0%	
	Total	102	100.0%	

**Table 2: Stratification of Hyponatremia with Age Groups**

Age Groups			Hyponatremia		Total	P Value
			Yes	No		
1-6 Years	Treatment Groups	Group A	13(11.50%)	48(42.47%)	61(53.98%)	0.005
		Group B	24(21.23%)	28(24.77%)	52(46.01%)	
	Total		37(32.7%)	76(67.3%)	113(100%)	
7-12 Years	Treatment Groups	Group A	5(5.49%)	36(39.56%)	41(45.05%)	0.000
		Group B	25(27.47%)	25(27.47%)	50(54.94%)	
	Total		30(32.96%)	61(67.03%)	91(100%)	

**Table 3: Stratification of Hyponatremia with Gender Groups**

Gender			Hyponatremia		Total	P Value
			Yes	No		
Male	Treatment Groups	Group A	10(7.19%)	49(35.25%)	59(42.44%)	0.000
		Group B	39(28.05%)	41(29.49%)	80(57.55%)	
	Total		49(35.25%)	90(64.74%)	139(100%)	
Female	Treatment Groups	Group A	8(12.30%)	35(53.84%)	43(66.15%)	0.022
		Group B	10(15.38%)	12(18.46%)	22(33.84%)	
	Total		18(27.69%)	47(72.30%)	65(100%)	

**Table 4: Stratification of Hyponatremia with Duration of Treatment (n=204)**

Duration of Treatment			Hyponatremia		Total	P Value
			Yes	No		
>24 Hours	Treatment Groups	Group A	14(13.72 %)	88(86.27%)	102(100%)	0.000
		Group B	34 (33.33%)	68(66.66%)	102(100%)	
<24 Hours	Treatment Groups	Group A	4 (3.92%)	98(96.07%)	102(100%)	0.003
		Group B	15 (14.70%)	87 (85.3%)	102(100%)	

normal electrolyte balance<sup>12,13</sup>. Children getting hypotonic intravenous fluid in hospitals frequently develop hyponatremia<sup>14</sup>. The choice of the best treatment option for the pediatric population is still up for debate. The purpose of this study was to compare the safety and effectiveness of giving hospitalized children isotonic versus hypotonic intravenous maintenance fluid.

According to our study, 49 out of 102 individuals who used hypotonic fluid experienced hyponatremia. Comparable to other studies<sup>14</sup>. Non-osmotic ADH secretion triggers such pain, stress, dehydration, and post-operative consequences can produce hyponatremia in hospitalized children, in line with our research, hyponatremia does not directly contribute to morbidity or mortality<sup>14</sup>. While it was linked to a higher risk of death and other side effects<sup>15</sup>.

Our study findings are analogous to those of Hasim N, who found that children who received isotonic fluid for intravenous maintenance were guarded against hyponatremia<sup>14</sup>. The structure and integrity of cells are preserved by isotonic fluid. Children are more susceptible to cerebral edema if hypotonic IVF is used because they have a greater brain-to-intracranial volume ratio. In order to prevent unforeseen problems, doctors must use extraordinary caution while administering IVF to youngsters.<sup>3</sup>

It was found that throughout the course of more than 24 hours, isotonic fluid consistently protects against hyponatremia. As a result, isotonic fluid is a better option for at least 72 hours after starting treatment<sup>14</sup>. More research is necessary to determine how IVF intake advised for a longer period of time affects children's sodium balance.

With extended usage of isotonic solution, Holliday et al.<sup>16</sup> have found evidence of hypernatremia. Isotonic IVF did not cause hypernatremia in any of our patients. This is consistent with earlier research.<sup>17,18,19,20</sup>

It has been claimed that isotonic solutions cause metabolic acidosis due to an excess of chloride, the reason may be rapid infusion.<sup>21</sup> Similar to our results, Torres et al. found no changes in the frequency of metabolic acidosis between the two management arms.<sup>22</sup> In their retrospective study, Bulfon et al. discovered that the use of 0.9% sodium chloride as a bolus and maintenance fluid increases the incidence of hyperchloremic metabolic acidosis (HCMA). Although its use was restricted to maintenance purposes, it wasn't a standalone risk factor for the development of HCMA<sup>23</sup>. To determine the impact of isotonic solution as maintenance therapy on the emergence of metabolic acidosis, particularly in youngsters, more research is necessary.

## CONCLUSION

When compared to hypotonic intravenous fluids, isotonic intravenous maintenance fluids have a lower risk of hyponatremia and were not associated with complications like hypernatremia and hyperchloremic metabolic acidosis. Therefore, isotonic fluids should be prescribed as maintenance intravenous fluids in the pediatric population.

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**AUTHOR'S CONTRIBUTION**

Following authors have made substantial contributions to the manuscript as under

**Karim R:** Concept, Critical appraisal, and Discussion Writing

**Afridi JK:** Data collection, compilation of results, formatting of the article

**Afaq S:** Data Collection,

**Zaman MB:** Manuscript Writing, Bibliography

**Naeem S:** Overall compilation of the article

**Zaman MA:** Manuscript writing, Bibliography

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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