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〔Original Article〕

Risks attending the use of hypotonic solution in the pediatric intensive care unit

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Abstract

***Background*: Hypotonic solutions are traditionally used as maintenance fluid in pediatric practice. Recently, several questions were raised regarding the safety of this practice particularly for critically ill or injured children. The aim of this research is to evaluate the risk of this widespread practice.**

***Methods*: We compared the change in serum sodium levels during the use of different kinds of maintenance fluid, i.e., a hypotonic solution（HYPO group, n＝48）and isotonic solution（ISO group, n＝31）, for postoperative children in the pediatric intensive care unit. The student T–test was used for statistical analysis.**

***Results*: No statistical significance was found between these two groups with regard to age, sex, sampling period, or initial laboratory findings（HYPO 137±3 mEq/l vs. ISO 137±5 mEq/l）. Over time, the difference in serum sodium levels became statistically significant between the groups（HYPO 131±4 mEq/l vs. ISO 135±3 mEq/l, $p<0.05$）.**

***Conclusions*: There is a significant risk of decreasing serum sodium levels during hypotonic solution use with postoperative children even if they are healthy. Using an isotonic solution instead can prevent the silent progression of hyponatremia in postoperative children.**

***Key words*: Hyponatremia, Iatrogenic, Postoperative, Antidiuretic hormone, Holliday and Segar**

Ⅰ. Introduction

The basic principles of pediatric fluid therapy were published by Holliday and Segar in 1957[1]. This milestone article described a simple formula for determining the maintenance requirements for water, glucose, and several kinds of electrolytes in children. Based on their theory, a hypotonic saline solution, such as 0.2% sodium chloride and 5% dextrose, is recommended to this day as pediatric maintenance fluid [2].

Currently, increasing evidence is showing that hypotonic maintenance fluids may lead to fatal hyponatremia in cases of excess antidiuretic hormone（ADH）production[3-6]. However, despite the general acceptance of isotonic saline use for fluid resuscitation in children[7], using isotonic saline as maintenance fluid it is not common practice. Since pediatric intensive care medicine has progressed greatly in the past 50 years and the severity of patients' condition has been changed significantly, it is time to reconsider whether Holliday

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and Segar's formula is still good practice for the current pediatric in-patients[8].

In this study we compared the change in serum sodium levels during different kinds of maintenance fluid use, e.g., hypotonic and isotonic solutions, in postoperative children at our pediatric intensive care unit (PICU) to evaluate the risks attendant on hypotonic solution use.

Ⅱ. Patients and methods

One hundred fifty-nine consecutive children (1 month to 17 years old) admitted to the pediatric intensive care unit (PICU) at the National Center for Child Health and Development (NCCHD) between June 2002 and February 2007 after elective plastic surgery were initially included. Children with an organ dysfunction and/or somatic diseases, developmental anomalies of the central nervous system, hereditary enzyme diseases, or incomplete data were excluded. Data from 79 children were included in the final analysis.

From June 2002 to June 2005, we used a hypotonic solution as a post-operative maintenance fluid based on the customary practice (HYPO group). After July 2005, we changed our practice and began using an isotonic solution (ISO group). Veen 3G™ was used as the hypotonic solution and Veen D™ was used as the isotonic solution (Table 1).

After admission to the PICU, all the children remained intubated and ventilated overnight and were extubated on the following day. PICU care was standardized, including adequate oxygenation and ventilation, analgesia, and sedation. The daily amount of maintenance fluid was calculated based on the children's total body water estimate of 80%. An arterial line was inserted in the theater as routine practice to monitor the arterial pressure continuously during plastic surgery and was kept in place until extubation in the PICU.

Arterial blood gas analysis including electrolytes was performed at the time of admission to the PICU (day 1) and on the following morning (day 2). Blood samples were taken through the arterial line. Serum sodium levels were measured using BM-1650 (Nihon Denshi Co., Ltd.).

The change in serum sodium levels was compared between the HYPO and ISO groups. The student T-test was used for statistical analysis and $p < 0.05$ was considered significant. This study was approved by the ethics section of institution's Medical Research Committee of NCCHD. Publication of the study was approved by the Institutional Review Board of NCCHD and Tokyo Metropolitan Children's Medical Center.

Ⅲ. Results

The HYPO group consisted of 48 children, and the ISO group consisted of 31 children. Between these groups, no statistical significance was found with regard to age, sex, sampling period, or initial laboratory findings (HYPO 137 ± 3 mEq/l vs. ISO 137 ± 5 mEq/l) (Table 2).

Table 1 Maintenance fluid

Solution	Contents (mEq/l)					
	Na^+	K^+	Mg^{2+}	Cl^-	H_2PO_4	CH_3COO^-
Veen 3G™	45	17	5	37	10	20
Veen D™	130	4	3	109	−	28

Table 2 Initial data and findings

Groups (n)	Age (months)	Sex (%)		Sampling period (hrs)
		Female	Male	
HYPO (n = 48)	84 ± 42	49	51	14.6 ± 3.0
ISO (n = 31)	82 ± 37	48	52	12.5 ± 4.6
p-value	NS	NS	NS	NS

Table 3 Change in serum Na (mEq/L) levels

Groups	Na (day 1)	Na (day 2)	p-value
HYPO	137 ± 3	130 ± 4	＜0.05
ISO	137 ± 5	135 ± 3	＜0.05

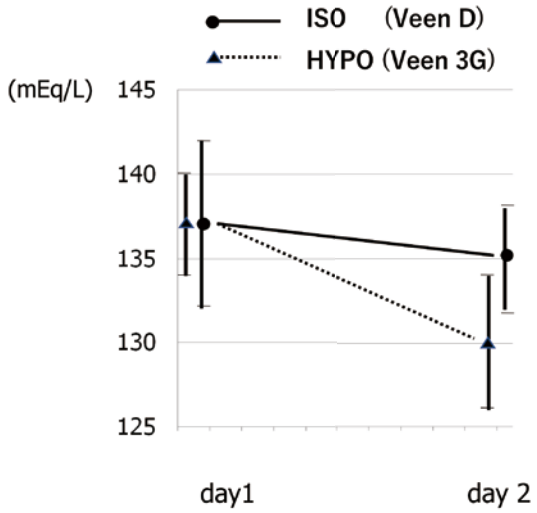

Fig. 1 Serum sodium levels of the HYPO and ISO groups on days 1 and 2

Over time, our results showed that the serum sodium levels dropped in both the HYPO and ISO groups (Table 3). Moreover, this change became more obvious and statistically greater in the HYPO group than in the ISO group (HYPO 130 ± 4 mEq/l vs. ISO 135 ± 3 mEq/l, $p < 0.05$) (Fig. 1).

Ⅳ. Discussion

More than 50 cases of neurological morbidity and mortality including 26 deaths resulting from hospital-acquired hyponatremia in children who were receiving hypotonic fluids have been reported. More than half of these cases occurred in the postoperative setting in previously healthy children who underwent minor surgery[8-10].

Arieff et al. reported 16 previously healthy children who died or experienced permanent neurological damage as a result of hyponatremic encephalopathy soon after receiving hypotonic fluids following minor surgical procedures or for the treatment of common childhood infections[3]. Halberthal et al. reported 23 children with no underlying diseases impairing hydration status, in whom acute symptomatic hyponatremia developed after the administration of hypotonic fluids[4].

Children are at high risk for symptomatic hyponatremia, i.e., hyponatremic encephalopathy or cerebral edema precipitated by an acute fall in serum osmolality. This seems to be attributable to the higher brain-to-skull size ratio in children, which leaves less space for brain expansion. Children achieve adult brain size by 6 years of age, whereas full skull size is not achieved until 16 years of age[11].

Postoperative children are at particularly high risk of developing hyponatremia, and many associated complications have been reported[12-17]. Postoperative nonosmotic stimuli for ADH release typically resolves by the third postoperative day but can last until the fifth postoperative day[18]. The most important factors that lead to postoperative hyponatremia are the failure to recognize the compromised ability of the patient to maintain fluid balance and the administration of hypotonic fluids. The same pathophysiology is apparent in severely ill or injured children who are given hypotonic fluids.

Traditionally used intravenous fluids contain a significant amount of free water that may contribute to hyponatremia. However, using an isotonic solution as maintenance fluid can help prevent the silent progression of hyponatremia in postoperative or severely ill / injured children[19]. In previously healthy children, after even minor surgery we observed a significant drop in the serum sodium levels due to hypotonic solution use. This risk was eliminated by using an isotonic solution.

Hospitalized sick children receiving parenteral fluid therapy should be considered at risk of hyponatremia and their body weight, fluid balance, blood pressure, any signs of edema, and serum and urine sodium levels should be monitored daily. An isotonic solution is a good option for hospitalized children who have a high risk of hyponatremia[20-22].

Recent practice has been changed and maintenance fluid is mostly administered as isotonic solutions in PICUs in overseas[23-26]. However, the use of hypotonic fluid in perioperative care in pediatric population or sick children in PICU is still being

practiced despite the current guidelines in some countries including Japan. This fact pints to a considerable gap between the available evidence and practice[27].

Compared to many drugs in our therapeutic armamentarium, salt and water are cheap and relatively easy to use. However, iatrogenic incidents resulting from the improper use of these substances are disturbingly common. To avoid errors in fluid management, clinicians should pay close attention to the risks inherent in the customary use of hypotonic solutions.

Contributors

NS conceived and designed the study. BZ and NN are involved in data collection. NS and BZ analyzed and interpreted the data. NS, BZ, and NN were involved in writing and reviewing the manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest with regard to the content of this article.

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