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Comparison of the Incidence of Postoperative Hyponatremia after Infusion of Hypotonic Versus Isotonic Intravenous Solutions in Children

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Introduction: Hyponatremia is the most common electrolyte disorder in patients following surgical interventions (19-50%). Hospital acquired hyponatremia is often due to using hypotonic solution s and can be lethal.

Materials and Methods: Between January and December 2014, 190 children (1 month to 12 years) who were admitted in the urology department of Children's Hospital Medical Center for elective surgical procedures were enrolled in the study. The patients were randomly divided into two groups: group I received 50 mEq/L sodium and 20 mEq/L potassium in D/W 5% and group II received 154 mEq/l sodium and 20 mEq/L potassium in D/W 5% at the maintenance dose for a period of 6 hours following the operation. The patients did not have any oral fluid intake 6 hours postoperatively. The incidence of hyponatremia before and after maintenance IV fluid therapy was analyzed. Other characteristics of the patients such as age, gender, duration of hospitalization, other concomitant electrolyte disturbances, and symptoms of hypervolemia were also evaluated. The incidence of fluid-IV therapy-induced hyponatremia was investigated and analyzed in different categories of patients.

Results: One hundred and ninety patients were enrolled**.** The mean age was 3.75 years (ranging from 1 month to 12years). One hundred and thirty-three patients (70%) were boys. The incidence of hyponatremia before and after maintenance IV fluid therapy was 9.5% and 36%, respectively. After the therapy, the incidence of hyponatremia was 54% and 17% in hypotonic and isotonic groups, respectively. Final multivariate logistic analysis showed that hyponatremia was common in patients that received hypotonic solution after surgery.

Conclusions: Hyponatremia was markedly induced in patients receiving hypotonic solution after surgery. It seems isotonic fluid therapy after surgery protects the patients from hyponatremia.

Keywords: Hyponatremia; Isotonic solutions; Hypotonic solutions; Child.
Running Title: Incidence of Postoperative Hyponatremia

Introduction

The use of intravenous (IV) fluids in children was proposed by Holliday and Segar in 1957 for the first time. The choice of maintenance fluid therapy in children was hypotonic solution with 20 mEq/L potassium adding 5% glucose [1]. More recent studies have shown that the incidence of hyponatremia increases in hospitalized children following the use of this formula; the side effects include serious complications and even death [2].

In recent years, there have been reports of postoperative deaths or significant neurological damage due to hospital-acquired hyponatremia in previously healthy children receiving hypotonic maintenance solutions during and after elective surgery [3]. The use of hypotonic solutions in hospitalized children can increase the risk of hyponatremia by 30% [4]. During the preoperative period, calculating the appropriate volume of necessary IV fluid is challenging, particularly in small children, because they are prone to electrolyte disturbances [5].

The preoperative period is characterized by various factors affecting the physiology of a previously healthy child. The proposed mechanisms for hyponatremia include the following: nonosmotic antidiuretic hormone (ADH) secretion and impaired electrolyte-free water (EFW) clearance, cerebral salt wasting, "desalination" phenomenon, translocation hyponatremia, and the sick cell syndrome [6, 7].

An increase in ADH release results from both osmotic and a variety of non-osmotic stimuli such as pain, stress, nausea, hypovolemia, narcotics, and non-steroidal anti-inflammatory drugs [8]. The majority of these factors are commonly encountered in the preoperative period. These factors can override the osmotic control of ADH secretion. This situation prevents a surgical patient from eliminating electrolyte-free water even in the presence of water excess [5]. The aim of this study was to compare two fluid maintenance therapy regimens in healthy children undergoing elective surgery.

Materials and Methods

This study was done on 190 patients aged 1 month to 14 years that were admitted to the urology ward of Children's Medical Center Hospital, Tehran, Iran for elective surgery. After ethics approval by the university committee (code: 93-03-184-27280 date: 2014/10/02) and obtaining the parents' consent, the patients were randomly divided to two groups. Hyponatremia was defined as a serum sodium level below 135mEq/liter and hypernatremia was defined as a serum sodium level above 145mEq/Liter. All patients that had underlying diseases like renal failure, cardiac problems, liver failure, diabetes insipidus, and diabetes mellitus were excluded from study. Drug history, especially the use of diuretics and desmopressin, was carefully recorded. The patients were excluded from the study if they received any drug. The patients were randomly divided into two groups: group I received 50 mEq/L sodium and 20 mEq/L potassium in D/W 5% and group II received 154 mEq/l sodium and 20 mEq/L potassium in D/W 5% at the maintenance dose for a period of 6 hours following the operation.

The duration of general anesthesia and surgery was between 30 minutes to 2 hours. Serum sodium (Na), potassium (K), urea nitrogen (SUN or BUN), and creatinine (Cr) were measured before the surgery. The patients did not have any oral fluid intake 6 hours postoperatively. Following the surgery, we observed the patients to detect any sign of cerebral edema and dehydration. Six hours after the surgery, serum Na, k, BUN, and Cr were measured again and the urine output were calculated in all patients; if they had polyuria, Na, k, BUN, Cr, and urinary Na and K were measured and an adequate appropriate solution was infused to correct hyponatremia and natriuresis. The primary outcome was hyponatremia (a plasma sodium level of _135mmol/L) occurring during the intervention. Secondary outcomes were as follows: (1) severe hyponatremia (a plasma sodium level of 125 mmol/L or symptomatic hyponatremia), (2) hypernatremia (a plasma sodium level of 150 mmol/L), (3) seizure or altered level of consciousness.

The data were analyzed using the SPSS software. The McNemar's test was used to evaluate the occurrence of hyponatremia after surgery in two groups and Chi square test was used to assess the relationship between different parameters. The mean values were compared between the two groups with t-test and the quantitative relationship between the parameters was assessed using the Pearson's correlation coefficient.

Results

This study was done on 190 patients undergoing elective urologic surgery. The patients were 1 month to 14 years old**.** The mean age of the patients was 3.75 years and 133 (70%) of them were female. one hundred patients received hypotonic infusion at a maintenance dose (group 1) and 90 patient received isotonic infusion (group 2). The prevalence of postoperative hyponatremia was then compared in the two groups. Overall, the incidence of hyponatremia was 9.5% pre-operatively and 36.0% post-operatively. Post-operative hyponatremia was found in 54% of the children who received hypotonic infusions and 17% of the children who received isotonic

infusions. The prevalence of hyponatremia in hypotonic and isotonic group was 54 % and 17%, respectively. Final multivariable logistic analysis showed that hypotonic infusion increased the rate of hyponatremia by up to 8 times. However, the sodium level before operation was an independent predictor of post treatment hyponatremia. The recorded blood pressure of the patients during the study was in the normal range. The laboratory finding and results are shown in the following tables. The incidence of hyponatremia according to the patient's age was as follows:

Hyponatremia was seen in 1 patient before surgery (12.5%) and in 4 patients (50%) after surgery in the neonatal group (30 days or less).

No patients had hyponatremia before surgery and four patients (36%) developed hyponatremia following surgery in patients aged 1-3 months.

There were 11 (15%) hyponatremic patients before and 31 hyponatremic patients (42.5%) after the surgery in patients aged 3 months to 3 years.

Table1. The descriptive results of laboratory findings in all children

Label	Mean	Range
Pre-treatment serum Na (mEq/L)	139.10	129-148
Post-treatment serum Na (mEq/L)	135.57	129-145
K	4.49	3.6-5.5
Cr	0.55	0-1
BUN	12.42	3-87
Urine (CC/kg)	7	4-9
Urine Na	87.78	30-134
Pre-treatment serum Na (mEq/L)	140.66	134-145
Post-treatment serum Na (mEq/L)	136.06	131-140

Polyuric patients(N=16)

Hyponatremia was seen in 6 patients (7%) before and in 29 patients (34%) after the surgery in patients aged 3 to 10 year. In children over 10 years of age, no patient had hyponatremia before and 2 patients (16%) developed hyponatremia after the surgery.

In this study, 27 children had polyuria that was common in younger children with a mean age of 6 months±2.5 months. No patients in the two groups, even with hyponatremia, had seizure due to edema or other side effects.

Table 2. Prevalence of hyponatremia in two groups that received 1/3 2/3 infusion versus N/S infusion

Variable	Subgroup	Type of fluid therapy	
		1/3- 2/3 Infusion	Normal Saline infusion
Sex	Male	55%	10%
	Female	52%	31%
Age	Neonate	100%	0%
	1 – 3 months	66%	0%
	3 months up to 3 years	56%	28%
	3 years to 10 years	48%	15%
	Above 10 years	40%	0%
Concurrent electrolyte Abnormality (K)	Normokalemia	40%	7%
	Hyperkalemia	66%	50%
Sodium level before fluid therapy	Normal	92%	95%
	Low	8%	5%
Duration of hospital admission	Less than 5 days	53%	17.5%
	More than 5 days	50%	20%

Table 3. Mean Na level before and after surgery in two groups

Variables	Groups	Means+/- SD	P-value
Pretreatment serum Na (mEq/L)	Group 1	137 +/- 7.9	**0.991**
	Group 2	136 +/- 6.8	
Posttreatment serum Na (mEq/L)	Group 1	131 +/- 4.3	**0.82**
	Group 2	135 +/- 6.1	

Table 4. Independent variables

Independent Determinant	Odds Ratio	P. value
1/3 2/3 infusion v/s NS infusion	7.69	<0.001
Hyponatremia before therapy	7.94	0.001
Female v/s Male	1.63	0.07

Table 5. Different situations of parameters recorded to perform the McNemar's test, P value <0.001

McNemar table	Eunatremic patients after serum therapy	Hyponatremic patients after serum therapy
Eunatremic patients before serum therapy	114	**57**
Hyponatremic patients before serum therapy	5	**13**

Discussion

In our study, two types of IV fluid were used for maintenance fluid therapy in children undergoing elective urologic surgery. The fluid used in the first group was 1/3-2/3 and normal saline was used in the second group. According to the results, hyponatremia was more common in the first group that received hypotonic infusion versus the isotonic group (54% versus 17% respectively). It seems that hyponatremia was induced more commonly in the hypotonic group (McNemar, P. value < 0.001) rather than the isotonic group (McNemar, P. value was 0.11). None of the patients in the two groups, even hyponatremic patients, had seizure due to cerebral edema or other side effects maybe because the duration of surgery and NPO was very short in our patients. Elective operations are usually short and oral fluids are usually allowed after 6 hours followed by normal diet, so hyponatremia was mild and did not need any interventions. No patients in the second group developed hypernatremia.

Karen Choong et al evaluated surgical patients 6 months to 16 years of age with an expected postoperative stay of 24 hours. A fully blinded randomized controlled trial was performed. The primary outcome was acute hyponatremia. Secondary outcomes included severe hyponatremia, hypernatremia, adverse events attributable to acute plasma sodium level changes, and antidiuretic hormone levels. A total of 258 patients were enrolled and assigned randomly to receive hypotonic infusion (Nr= 130) or isotonic infusion (Nr= 128). Baseline characteristics were similar in both groups. In this study, hypotonic solutions increased the risk of hyponatremia significantly as compared with isotonic solutions (40.8% v/s 22.7%; relative risk: 1.82 confidence interval). Admission to the pediatric critical care unit was not an independent risk factor for the development of hyponatremia. Isotonic infusions did not increase the risk of hypernatremia (relative risk: 1.30 [95% confidence interval: 0.30 –5.59). Antidiuretic hormone levels and adverse events were not significantly different between these two groups [9]. This study is similar to our research. Isotonic solutions after surgery decrease hyponatremia side effect.

Sarah McNab et al compared 140 mmol/L sodium versus 77 mmol/L sodium for maintenance intravenous fluid therapy in hospitalized children in a randomized controlled double-blind trial. They randomly assigned 690 patients to receive either isotonic intravenous fluid containing 140 mmol/L sodium (Na140) or hypotonic fluid containing 77 mmol/L sodium (Na77) for 72 hours. The primary outcome was the occurrence of hyponatremia (serum sodium concentration <135 mmol/L with a decrease of at least 3 mmol/L from baseline) during the treatment period. Fewer patients given Na140 than those given Na77 developed hyponatremia (12 patients [4%] vs. 35 [11%]; odds ratio [OR] 0.31, 95% CI 0.16–0.61; p=0.001). No clinically apparent cerebral edema occurred in either group. Eight patients in the Na140 group (two potentially related to intravenous fluid) and four in the Na77 group (none related to intravenous fluid) developed serious adverse events during the treatment period. One patient in the Na140 had seizures during the treatment period compared with seven patients who received Na77.

Two other studies and our research showed the patients are prone to hyponatremia after surgery because of pain, stress, anesthesia, and other insults. The use of isotonic solutions at a maintenance dose is safe after surgery.

The latest guideline of fluid therapy in children published in August 2015 recommends that the best solution for maintenance therapy is isotonic fluids [10, 11].

Conclusions

Hyponatremia is the most common electrolyte disorder, especially in postoperative patients. To reduce this problem and its potential consequences, it is recommended to use isotonic infusions at the maintenance dose after surgery.

Compliance with Ethical Standards

Dr. Mastaneh Moghtaderi and all other authors declare that they have no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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