Section: Pediatrics

Original Research Article

COMPARISON OF OUTCOME OF PATIENTS ADMINISTERED HYPOTONIC SALINE TO THOSE ADMINISTERED ISOTONIC SALINE

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Abstract

Background: The objective is to compare the outcome of patients administered hypotonic saline to those administered isotonic saline. **Materials and Methods:** This study was a prospective, randomized controlled trial conducted between october 2010 and september 2012 in patients aged between 1 month and 18 years who were admitted to the pediatric intensive care unit of Vani Vilas hospital, which is attached to Banglore Medical College and Research Institute. **Result:** 3 patients in group A developed hypernatremia (S.Na>145meq/L) whereas none in group B developed hypernatremia. The difference is not statistically significant. None in either group developed severe hyperntremia (S.Na>150meq/L) Duration of ICU stay was significantly more in hypotonic group (group B) compared to isotonic group (group A) with P value of 0.001. But total duration of stay remains the same in both the groups, which was the duration of stay required for the completion of IV antibiotics. Other outcome measures like number of deaths, dehydration were similar in 2 groups. **Conclusion:** There was no significant increase in the risk of hypernatremia in isotonic fluid group. Duration of ICU stay was significantly more in group B (hypotonic fluid group) compared to group A (isotonic fluid group) which is significant (P value 0.001). Duration of ICU stay was more in patients presenting with CNS symptoms and receiving hypotonic fluids, as it took longer time for them to regain consciousness.

INTRODUCTION

The administration of IV maintenance fluid is an essential part of management of sick children. In pediatric patients, at present, standard practice is to give isolyte p as maintenance fluid as it contains electrolyte composition as proposed by Holiday and Segar formula.[1] In our hospital, in sick children, use of 2/3 maintenance volume of isolyte p is used as a routine practice, to prevent hyponatremia due to SIADH. Hyponatremia, a very commom electrolyte abnormality in hospitalized patients, is a serum sodium concentration less than 135 mEq/L.[2] In recent years there has been concern regarding hospital acquired hyponatremia in sick children. Hyponatremia among children has been reported to range from as low of 8% to as high of 100% in those children receiving hypotonic intravenous fluid.[3]

A systematic review of maintenance intravenous fluids for hospitalized children revealed that the use of hypotonic fluids increases the odds of hyponatremia by 17 folds, when compared to isotonic fluid.[4] The administration of hypotonic fluids is based on the guidelines developed by studying healthy children, and the authors of the guidelines cautioned that appropriate changes should be made when using the same data in sick children. Recent prospective studies have demonstrated that administration of 0.9% NaCl as maintenance fluids can prevent the development of hyponatremia.

In 2003 Moritz and Ayus introduced the concept of using 0.9% NaCl as a maintenance parenteral fluid for the prevention of hospital acquired hyponatremia.[5] Most of the studies conducted following this have confirmed that hypotonic fluids produce hyponatremia and the administration of 0.9% NaCl does not result in either hypernatremia or fluid overload.[6] Considering the incidence of hyponatremia, complications involved, and the fact that it is preventable, it is valuable to compare the effectiveness of isotonic versus hypotonic fluids in preventing hyponatremia and improving the patient outcome.

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Hence this study was conducted to compare the outcome of patients administered hypotonic saline to those administered isotonic saline.

MATERIALS AND METHODS

This study was a prospective, randomized controlled trial conducted between october 2010 and september 2012 in patients aged between 1 month and 18 years who were admitted to the pediatric intensive care unit of Vani Vilas hospital, which is attached to Banglore Medical College and Research Institute. Written informed consent was obtained from the parent or guardian of all patients before enrollment. The study protocol was approved by the Institute Ethics Committee.

240 children were enrolled, out of which 2 groups were made depending on the day of admission. Those admitted on even days (eg.2, 4, 6) were considered in group A for whom DNS with potassium supplementation, full maintenance volume was used. Those admitted on odd days (eg.1, 3, 5) were considered in group B for whom isolyte-p 2/3rd maintenance volume was used as maintenance fluid.

Inclusion Criteria

All children admitted to PICU aged 1 month to 18 years who need intravenous fluids for a minimum period of 24 hour

Exclusion Criteria

Children having following associated factors at admission

- Hyponatremia
- Hypernatremia
- Dehydration
- Hyperglycemia
- Shock
- Severe malnutrition
- Cirrhosis
- Congestive heart failure
- Acute or chronic renal failure
- Nephrotic syndrome
- Diabeticketoacidosis
- Drugs- furesemide, thiazide, vasopressin, desmopressin

Method: Patients who were judged by the treating doctor to require i.v. maintenance fluid administration for at least the following 24 h of their hospital stay were eligible for inclusion in the study. Children with hyponatraemia (plasma sodium<135 mEq/L), hypernatraemia (plasma sodium >145 mEq/L) or hyperglycemia (blood glucose>180 mg/dL), dehydration, shock, severe malnutrition, cirrhosis of liver, congestive heart failure, acute or chronic renal failure and nephrotic syndrome were excluded. Children who were receiving drugs that alter plasma sodium levels, such as frusemide, hydrochlorothiazide, vasopressin or desmopressin and mannitol, were also excluded.

The study subjects were randomized to receive any one of the two study interventions (Group A, 0.9% saline in 5% dextrose at the standard maintenance rate (DNS); Group B, 0.18% saline in 5% dextrose (isolyte-P) at two-thirds of the standard maintenance rate). The patient's weight was measured, and the standard maintenance volume was calculated according to the Holliday and Segar formula1. The standard maintenance volume of fluid was administered to patients in Group A, while two-thirds of the standard maintenance volume was administered to patients in Group B. The amount of fluid infused was documented. Maintenance potassium was added to the DNS as 20 mEq/L of fluid. The patients continued to receive therapy for their primary disease, as decided upon by the treating physician.

The primary outcome of the study was the incidence of hyponatraemia (defined as plasma sodium <135 mEq/L). Serum sodium values between 130-135meq/L was considered mild hyponatremia, between 125-130meq/L was considered moderate hyponatremia and that below 125meq/L was considered severe hyponatremia. The incidences of hypernatraemia (defined as plasma sodium >145 mEq/L), symptomatic hyponatraemia or hypernatraemia (defined as the presence of hyponatraemia or hypernatraemia, respectively and features of encephalopathy which did not have any other obvious explanation), duration of ICU stay and total hospital stay, outcome (improvement/death) were secondary outcome measures.

Baseline demographic and clinical parameters were noted at enrolment. The Pediatric Risk of Mortality III (PRISM III; 24 h) score36 was calculated to compare the severity of illness among the study subjects. All patients were monitored clinically for symptoms and signs of encephalopathy and signs of fluid overload or dehydration throughout the study period.

At enrolment, 2 mL of venous blood was taken for estimation of plasma sodium, potassium, chloride, blood sugar, urea and creatinine. Plasma sodium, potassium, chloride, blood sugar, blood urea and serum creatinine levels were estimated after 24 h. We measured the urine specific gravity at 0, 24h after the initiation of i.v. fluid administration.

The study measurements were carried out until 24-h time-point following the initiation of the i.v. fluid therapy. The fluid regimen was modified appropriately if a child developed hyponatraemia or hypernatraemia.

Statisticl Analysis: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean □ SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of

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the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Total of 240 children were enrolled after considering inclusion and exclusion criteria. They were randomized into 2 groups of 120 each (both groups were comparable in age, sex, ICU diagnosis.

Table 1: Age distribution of patients studied

Age	Group A		Group B	
	No	%	No	%
<6 months	16	13.3	15	12.5
7-12 months	12	10.0	13	10.8
1-2 years	40	33.3	27	22.5
>2 years	52	43.3	65	54.2
Total	120	100.0	120	100.0

Samples are age matched with P=0.257

Table 2: Distribution of step down stay in days in two groups of patients studied

Step down in days	Group A		Group B	
	No	%	No	%
Nil	2	1.7	3	2.5
<5 days	114	95.0	113	94.1
>5 days	4	3.3	4	3.3
Total	120	100.0	120	100.0
Mean ±SD	2.64±0.96		2.44±1.18	

Distribution of S/D is statistically similar in two groups with P=0.903

Table 3: Distribution of Total hospital stay in days in two groups of patients studied

Total hospital stay in days	Group A		Group B	
	No	%	No	%
Up to 1 week	56	46.7	61	50.8
1 week-2 weeks	64	53.3	56	46.7
> 2 weeks	0	0.0	3	2.5
Total	120	100.0	120	100.0
Mean ±SD	7.48±1.75		7.56±2.46	

Total duration of hospital stay in days is statistically similar in two groups with p=0.788

Table 4: Distribution of outcome in two groups of patients studied

Outcome	Group A		Group B	
	No	%	No	%
Improved	116	96.7	116	96.7
Death	3	2.5	4	3.3
DAMA	1	0.8	0	0.0
Total	120	100.0	120	100.0

Outcome is statistically similar in two groups with p=0.565

Table 5: Distribution of Cause of death (COD) in two groups of patients studied

Cause of death	Group A(n=120)		Group B(n=120)	
	No	%	No	%
Nil	117	97.5	117	97.5
Present	3	2.5	3	2.5
ARDS	0	0.0	1	0.8
ICH	1	0.8	0	0.0
MODS	1	0.8	1	0.8
Shock	1	0.8	1	0.8

COD is statistically similar in two groups with P=0.565

Table 6: Distribution of Symptomatic hyponatremia in two groups of patients studied

Symptomatic hyponatremia	Group A(n=120)		Group B(n=120)	
	No	%	No	%
No	118	98.3	117	97.5
Yes	2	1.7	3	2.5

Symptomatic Hyponatremia is statistically similar with P=0.651

Table 7: Distribution of features of dehydration in two groups of patients studied

Features of dehydration	Group A(n=120)	Group B(n=120)

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	No	%	No	%
No	117	97.5	117	97.5
Yes	3	2.5	3	2.5

Features are dehydration are statistically similar in two groups with P=1.000

Symptomatic hyponatremia was seen in 2 patients in group A (isotonic group) and 3 in group B (hypotonic fluid group) with P value of 0.065. 2 patients presented with seizures and 3 patients with head ache, altered sensorium. All were treated with 3% NS, 5ml/kg and improved. No deaths occurred.

DISCUSSION

From present study it is evident that use of hypotonic fluids increases the incidence of hyponatremia compared to isotonic fluids. Use of hypotonic fluids in full maintenance volume leads to more incidence of hyponatremia compared to the use of hypotonic fluids in 2/3rdvolume, signifying the fact that free water excess is the major cause of hyponatremia in a sick child where other factors like ADH excess play an additional role.

Severe hypontremia (S.Na<125meq/L) was seen in 1 patient in group B (hypotonic fluid group) whereas in group A (isotonic fluid group) none had severe hyponatremia. This emphasizes that even though patients in isotonic fluid group developed hyponatremia, none of them developed severe hyponatremia.

Results of Alvarez Montanana et al,[7] are similar to our study. No one developed severe hyponatremia, 3 in hypotonic group developed moderate hyponatremia. 10 in hypotonic group and 3 in isotonic group developed mild hyponatremia.

Symptomatic hyponatremia was seen in 2 patients in group A (isotonic group) and 3 in group B (hypotonic fluid group). Difference was not statistically significant (P value 0.065). 2 patients presented with seizures and 3 patients with head ache, altered sensorium. All were treated with 3% NS, 5ml/kg and improved. No deaths occurred.

In a study by Lakshminarayanan Kannan et al,[8] only one patient developed symptomatic hyponatremia in full volume hypotonic fluid group and improved with treatment with 3% NaCl.

Results of present study emphasizes that even patients on isotonic maintenance fluid can develop symptomatic hyponatremia and hence frequent monitoring of electrolytes, early detection of symptoms and treatment is important.

In present study hyponatremic encephalopathy was seen in 2 patients in group A (isotonic group) and 3 in group B (hypotonic fluid group). Difference was not statistically significant (P value 0.065). 2 patients presented with seizures and 3 patients with head ache, altered sensorium. All were treated with 3% NS, 5ml/kg and improved. Other studies show similar results with respect to incidence of hyponatremic encephalopathy and response to treatment.

Hyponatremic encephalopathy can occur with a mild fall in S.Na in few cases (<130meq/L in present study/138 to 124 meq/L Duke et al,[9] 2005) and in few cases large fall in SNa (Osier et al,[10] 2006 138 to 96 meq/L) is required to cause encephalopathy. This depends on the factors like type of disease, time taken for the fall in serum sodium to that level (acute/chronic hyponatremia). The symptoms of hyponatremia are mostly due to the decrease in extracellular osmolality and the resulting movement of water down its osmotic gradient into the intracellular space. Brain swelling can be significantly obviated if the hyponatremia develops gradually because the brain adapts to the decreased extracellular osmolality by decreasing its internal osmolality. Higher incidence of symptomatic hyponatremia in our study was secondary to disease population involved. 25% of our study population had CNS involvement, and all of them who developed hyponatremia had an acute illness with sudden decrease in SNa levels.

It is evident that hyponatremic encephalopathy when treated with 3% NaCl shows good improvement, with no deaths occurring in any studies who used 3% NaCl. Deaths occurred when no treatment was given or when seizures were treated with anticonvulsants. Hence it is important to have high index of suspicion, monitor electrolytes regularly in a sick child and recognize hyponatremic encephalopathy at an early stage and treat with 5-10ml/kg of 3% NaCl depending on response.

3 patients in group A (isotonic fluid group) developed hypernatremia (S.Na>145meq/L) whereas none in group B (hypotonic fluid group) developed hypernatremia. The difference is not statistically significant. None in either group developed severe hyperntremia (S.Na>150meq/L). In the other 2 studies, incidence of hypernatremia was similar in both isotonic and hypotonic fluid groups.

Results of present study emphasizes that administration of isotonic fluids doesn't increase the risk of hypernatremia which is a theoretical concern. In our study though 3 patients in isotonic fluid developed hypernatremia, none of them had severe hypernatremia (SNa>150meq/L) or symptomatic hypernatremia.

Duration of ICU stay was significantly more in group B (hypotonic fluid group) compared to group A (isotonic fluid group) which was significant (P value 0.001). 35% of in group B stayed in ICU for 3-5 days compared to 15% in group A. The study population consisted of heterogenous group of diseases, 65% of them being diagnosed with pneumonia.25% with CNS disease. Duration of stay in ICU was increased in patients presenting with CNS symptoms and who were treated with

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hypotonic fluids as they took longer time for the improvement of their sensorium and as they had more incidence of hyponatremia they were kept in ICU for longer time for monitoring. Even though CNS cases accounted for 25% of admissions, they accounted for 40% of patients who stayed in ICU for 3-5 days. Total duration of hospital stay remains same in both the groups which correlates with the duration of IV antibiotic administration. There was no significant difference in other electrolyte levels (K, Cl) between 2 groups at 0 and 24 hours.

Other outcome measures like number of deaths, dehydration was similar in 2 groups.

CONCLUSION

There was no significant increase in the risk of hypernatremia in isotonic fluid group. Duration of ICU stay was significantly more in group B (hypotonic fluid group) compared to group A (isotonic fluid group) which is significant (P value 0.001). Duration of ICU stay was more in patients presenting with CNS symptoms and receiving hypotonic fluids, as it took longer time for them to regain consciousness. They also had more incidence of hyponatremia and had to be kept in ICU for monitoring.Total duration of hospital stay remains same in both the groups. There was no difference in total duration of hospital stay, death, dehydration, other electrolyte levels (K, Cl).

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