

Original Research Article

ACUTE HYPONATREMIA AND HYPERNATREMIA RELATED TO INTRAVENOUS FLUID ADMINISTRATION IN HOSPITALIZED CHILDREN: A RANDOMIZED OBSERVATIONAL STUDY

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ABSTRACT

Background: Intravenous fluid and electrolyte therapy in most of the acutely ill hospitalized children has been the cornerstone of medical practice for a well over 50 years.

Objective: To determine optimal maintenance fluid therapy by comparing the incidence of hyponatremia or hypernatremia in hospitalised children.

Methods: A prospective Randomized study done in PICU in patients admitted to paediatric emergency. The study was conducted between September 2007 to May 2008. Children of age group 1 month to 16 years were included. The fluid groups were divided into four groups. SPSS version 18 was used for analysis.

Results: The mean age in group I is 4.42, in group 2 is 3.84, in group 3 is 3.67 and in group 4 is 4.45. The mean serum sodium levels in fluid group I is 137.4 mmol/L, in fluid group II 138.2 mmol/L, in fluid group III is 138.9 mmol/L and fluid group IV is 137.8 mmol/L. After initiating maintenance fluid therapy serum sodium levels changed in each group. As we can see in group 1 mean serum sodium level at the start of the therapy is 137.43 mmol/L and after 24 hours of hypotonic fluid infusion it reduced to 135.4 mmol. 69 patients had hyponatremia and 44 had hypernatremia.

Conclusion: Amount of free fluid in the IV maintenance fluid can be factor in causing hypernatremia. Caution is warranted to guard off a rapid fall of serum sodium level.

KEY WORDS: Hyponatremia, Hypernatremia, electrolytes, PICU.

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BACKGROUND

The most appropriate maintenance solution for children continues to be a furiously debated topic in the paediatric literature. Intravenous fluid and electrolyte therapy in most of the acutely ill hospitalized children has been the cornerstone of medical practice for a well over- 50 years. The scientific methodology behind fluid regimens generated much debate in the early 1950s following the pioneer work of Darrow, Talbot,

Gamble and others recognized the important relationship between caloric expenditure and requirements for water [1]. SIADH is a disorder that can lead to hyponatremia as a result of the non-physiologic secretion of ADH, which leads to free water retention followed by a natriuresis that maintains fluid balance at the expense of serum osmolality [2]. SIADH is one of the most common causes of hyponatremia in both children and adults in a hospital setting. There have

been > 50 reported cases of neurologic morbidity and mortality, including 26 deaths, resulting from hospital acquired hyponatremia in children who were receiving hypotonic fluids [3-6]. Since there is a lacunae in literature regarding the optimal maintenance fluid for hospitalized children, there is an immediate need to find out the best maintenance fluid so this study was conducted. There are on randomized controlled trials to evaluate the effects of various types of intravenous fluids to maintain normonatremia in sick hospitalized children.

MATERIALS AND METHODS

Study Design: Prospective Randomized Observational Study.

Study Settings: Patients admitted in paediatric emergency unit to the trauma centre, paediatric wards and the PICU of the Department of paediatrics, Gandhi Memorial and Associated hospitals, CSMMU(now KGMU Lucknow) .

Study Duration: 10 months.

Sampling Technique: Simple random sampling using random number table

Inclusion Criteria: Children of age group 1 months to 16 years admitted to emergency ward, paediatric ward and the PICU of the department of paediatrics, CSMMU (now KGMU, Lko), were included in the study which require exclusive intravenous maintenance fluid therapy for at least 24 hours.

Exclusion Criteria-

- Those children whose Baseline serum sodium was less than 130 mmol/L.
- Baseline serum sodium was more than 150 mmol/L.
- Shock, Diarrhea and dehydration, Fluid overload, Hyperglycemia were excluded from the study.

Sample Size: Based on literature review [6], the incidence of hyponatremia with standard intravenous therapy was found 30% A sample of at least 75 patients were chooses in each group to demonstrate the incidence of hyponatremia 10%, with a beta of 0.2 (power 80%) and alpha error of 0.05. So, the estimated sample size was 300.

METHODOLOGY: Total 300 patients were divided in four groups with pre allotted random

numbers:

Group 1: were put on paediatric maintenance solution with 5% dextrose at normal maintenance rate.

Group 2: were put on paediatric maintenance solution with 5% dextrose at 75% maintenance rate.

Group 3: were put on 0.9% saline+5% Dextrose at normal maintenance rate.

Group 4: were given- 20-40 ml/kg of 0.9% saline + 5% dextrose first at maintenance rate followed by paediatric maintenance solution with 5% dextrose.

The demographic details, admission diagnosis, indication for hospitalization were recorded for all subjects at the time of inclusion in the study. A baseline clinical history was taken, and examination done for purpose of inclusion and exclusion in the study. Venous blood samples were taken at the time of enrolment for estimation of haemoglobin levels, serum sodium serum potassium, serum bicarbonate, random blood sugar blood urea and serum Creatinine, and transported immediately to laboratory or kept in refrigerator. Urine sample were taken for urine sodium and urine potassium collected either from uro-bags or form a collected sample of last 24 hours and sent to laboratory. Serum sodium and serum potassium were estimated at least once a day and preferably twice daily till the patient was on maintenance fluid and 12 hours after stopping maintenance fluid. Urinary electrolytes were estimated daily obtained from an aliquot from total collection.

Statistical Analysis: The questionnaire responses were entered in Epi data software and the collected data were consolidated on Microsoft Excel sheets and further analysed in Epi-info 7.1.3.0 version. The results were expressed as proportions and percentages. The outcomes in the four groups were compared by ANOVA test and independent t-test and P value <0.05 was considered statistically significant.

RESULTS

As per table 1 the mean age in group I is 4.42, in group 2 is 3.84, in group 3 is 3.67 and in group 4 is 4.45. as seen Mean age is more or less similar in four groups and it shows that the age

Table 1: Age and Weight Distribution of the Study Group.

| FLUID | N | MEAN \pm SD | MEAN \pm SD |
|---|----|-----------------|------------------|
| | | Age (years) | Weight (kg) |
| 0.15% N + 5% D (normal maintenance) | 75 | 4.42 \pm 3.54 | 13 \pm 7.16 |
| 0.15% N + 5% D (75% maintenance) | 75 | 3.84 \pm 3.6 | 11.25 \pm 6.58 |
| 0.9% N + 5% D (normal maintenance) | 75 | 3.67 \pm 3.67 | 11.18 \pm 7.57 |
| 0.9% N + 5% D followed by 0.15%N + 5% D | 75 | 4.45 \pm 3.89 | 12 \pm 7.72 |

Table 2: Sodium Levels at the beginning and after 24 hours in the study groups.

| FLUID | N | MEAN (SD) mEq/L | S. SODIUM D2 (MEAN) |
|-------------------------------------|----|-------------------|---------------------|
| 0.15% N + 5% D (normal maintenance) | 75 | 137.4 \pm 4.017 | 135.4 \pm 3.56 |
| 0.15% N + 5% D (75% maintenance) | 75 | 138.2 \pm 5.014 | 138.4 \pm 5.13 |
| 0.9% N + 5% D (normal maintenance) | 75 | 138.9 \pm 5.041 | 140.5 \pm 8.48 |
| 0.9% N + 5% D F/B | 75 | 137.8 \pm 3.972 | 135.8 \pm 5.597 |
| 0.15% N + 5% D | | | |

Table 3: Hyponatremia in fluid groups during overall study.

| FLUID | N | HYPONATREMIA | HYPONATRAMIA (%) |
|--|----|--------------|------------------|
| 0.15% N + 5% D (normal maintenance) | 75 | 20 | 26.7 |
| 0.15% N + 5% D (75% maintenance) | 75 | 20 | 26.7 |
| 0.9% N + 5% D (normal maintenance) | 75 | 17 | 22.7 |
| 0.9% N + 5% D followed by 0.15% N + 5% D | 75 | 12 | 16 |

Table 4: Comparison of Hyponatremia after fluid infusion between Group I and Group II, III & IV.

| Hyponatremia | Group I | Group II | Group III | Group IV | Total |
|--------------|---------|----------|-----------|----------|-------|
| Present | 20 | 20 | 17 | 12 | 69 |
| Absent | 55 | 55 | 58 | 63 | 231 |
| Total | 75 | 75 | 75 | 75 | 300 |
| p-value | 0.49 | | 0.555 | 0.295 | |

Table 5: Incidence of Hyponatremia at various days of maintenance fluid infusion.

| FLUID | Incidence Overall | Incidence at 24 hours | Incidence at 48 hours | Incidence at 72 hours | Incidence at 96 hours or onwards |
|---|-------------------|-----------------------|-----------------------|-----------------------|----------------------------------|
| 0.15% N + 5% D (normal maintenance) | 20/75 (26.70%) | 12/75 (16%) | 8/23 (34.8%) | 0/7 (0%) | 0/4 (0%) |
| 0.15% N + 5% D (75% maintenance) | 20/75 (26.7%) | 6/75 (8%) | 9/37 (24.3%) | 4/14 (21.4%) | 2/4 (50%) |
| 0.9% N + 5% D (normal maintenance) | 17/75 (22.7%) | 4/75 (5.3%) | 10/32 (31.3%) | 02/10 (22.2%) | 1/2 (50%) |
| 0.9% N + 5% D followed by 0.15%N + 5% D | 12/75 (16%) | 4/75 (5.3%) | 8/18 (44.4%) | 0/3 (0%) | 0/2 (0%) |
| TOTAL | 69/300 (23%) | 26/300 (8.6%) | 35/10 (31.8%) | 5/33 (15.2%) | 3/12 (25%) |

Table 6: Overview of hypernatremia in four fluid groups.

| FLUID | N | Hypernatremia | Hypernatremia (%) |
|---|-----|---------------|-------------------|
| 0.15% N + 5% D (normal maintenance) | 75 | 0 | 0 |
| 0.15% N + 5% D (75% maintenance) | 75 | 16 | 21.3 |
| 0.9% N + 5% D (normal maintenance) | 75 | 26 | 34.7 |
| 0.9% N + 5% D followed by 0.15%N + 5% D | 75 | 2 | 2.7 |
| TOTAL | 300 | 44 | |

Table 7: Incidence of Hypernatremia on various days of maintenance fluid infusion.

| FLUID | Incidence Overall | Incidence at 24 hours | Incidence at 48 hours | Incidence at 72 hours | Incidence at 96 hours or onwards |
|---|-------------------|-----------------------|-----------------------|-----------------------|----------------------------------|
| 0.15% N + 5% D (normal maintenance) | 0/75 (0%) | 0/75 (0%) | 0/23 (0%) | 0/7 (0%) | 0/4 (0%) |
| 0.15% N + 5% D (75% maintenance) | 16/75 (21.3%) | 3/75 (4%) | 10/37 (27%) | 3/14 (21.4%) | 0/4 (0%) |
| 0.9% N + 5% D (normal maintenance) | 26/75 (34.7%) | 13/75 (17.3%) | 10/32 (34.4%) | 2/9 (22.2%) | 0/2 (0%) |
| 0.9% N + 5% D followed by 0.15%N + 5% D | 2/75 (2.7%) | 2/75 (2.7%) | 0/18 (0%) | 0/3 (0%) | 0/2 (0%) |
| TOTAL | 44/300 (14.7%) | 18/300 (6%) | 21/110 (19.1%) | 5/33 (15.2%) | 0/12 (0%) |

difference is not significant in fluid group and they are comparable. The mean weight in group 1 is 13 kilograms, in group 2 is 11.25 kilograms, in group 3 is 11.18 kilograms and in group 4 is 12 kilograms We can see that there is no marked difference in children of four groups based on their weight. So, they are comparable in this respect too.

Serum sodium levels at the enrolment of the patients in the study were recorded. The mean serum sodium levels in fluid group 1 is 137.4 mmol/L, in fluid group II 138.2 mmol/L, in fluid group III is 138.9 mmol/L and fluid group IV is 137.8 mmol/L. After initiating maintenance fluid therapy serum sodium levels changed in each group. As we can see in group 1 mean serum sodium level at the start of the therapy is 137.43 mmol/L and after 24 hours of hypotonic fluid infusion it reduced to 135.4 mmol/L. reduction in sodium levels were seen in Group I and Group IV.

As per table 3 at the start of the study all the patients included had normal serum sodium levels. During overall study, in fluid group 1, 20 out of 75 patients (26.7% patients) developed hyponatremia. In fluid group II, also 20 out of 75 patients (26.7%) developed hyponatremia.

In fluid group III 17 out of 75 patients (22.7% patients) developed hyponatremia. In fluid group IV 12 out of 75 patients (16% patients) developed hyponatremia. In fluid group III 17 out of 75 patients (22.7% patients) developed hyponatremia. In fluid group IV 12 out of 75 patients (16% patients) developed hyponatremia.

As per table 4 incidence in hyponatremia was equal in group I and II i.e. 20 cases out of 75 cases. Statistically this result was not significant (p value > 0.05). On comparing the incidence of hyponatremia between group 1 and group III we found that of hyponatremia in fluid group 1 was 20 cases and in group III was 17. Statistically this result was not significant. (p value > 0.05). On comparing the group 1 and group IV we found that in group 1 hyponatremia cases were 20 and in group IV were 12. This result was also found insignificant (p value > 0.05).

As shown in the table 5 in fluid group 1 after 24 hour of infusion 12 patients (16%) developed hyponatremia, and after 48 hours in rest of the patient's incidence of hyponatremia shot up to 34.8% (8 out of 23 patients). In fluid group II after 24 hours 6 out of 75 patients (8%) developed hyponatremia, after 48 hours 9 out of 37 (24.3%) patients developed hyponatremia, after 72 hours 3 out of 14 (21.4%) patients developed hyponatremia and after 96 hours 2 out of 4 patients (50%) developed hyponatremia. Overall it can be said that in each group tendency to develop hyponatremia was more after 48 hours.

As per table 6 Fluid group I had no case of hyponatremia. Fluid group II total 16 cases of hyponatremia during study i.e. 21.3% of the total 75 cases. Fluid group III had maximum 26 cases of hyponatremia in the study i.e. 34.7% of the total 75 cases. Fluid group IV had only 2 cases of hyponatremia in the study i.e. 2.7% of the total 75 cases.

Table 7 In fluid group II out of total 16 hypernatremic patients 3 out of 75 (4%) developed hypernatremia after 24 hours of infusion, 10 out of 37 developed hypernatremia (27%) after 48 hours, 3 out of 14 (21.4%) patients developed hypernatremia after 72 hours and none developed hypernatremia thereafter. In fluid group III total 26 patients developed hyper-

natremia out of which 13 developed (17.3%) hypernatremia after 24 hours, 11 out of 32 patients (34.4%) developed hypernatremia after 48 hours, 2 out of 9 (22.2%) developed hypernatremia after 72 hours and none thereafter.

DISCUSSION

After long duration of controversy, it seemed that Holliday and Segar's approach had settled everything through their landmark article published in 1957 regarding their recommendation of 0.18% normal saline with 5% dextrose using as maintenance fluid of choice in children. Since then administration of hypotonic maintenance fluid has become a common practice in hospitalized children without giving any second thought. 23% (69 patients out of 300 total patients) incidence of hyponatremia in our study seems somewhat higher than many other studies eg. Hoorn et al. [7] (10%). However, many other authors have also described very high incidence of hyponatremia in children receiving hypotonic fluid, 20-45% incidence of hyponatremia [8]. Hypernatremia was found in overall 14.7% patients. None of the patients developed severe hypernatremia and none had neurologic sequelae that could be attributed to hypernatremia to the degree of causal relationship. In our second group which received 75% of the usual requirement of the paediatric maintenance fluid, the incidence of hyponatremia was 26.7% this is in agreement with Moritz and Ayus [9] that the strategy to combat hyponatremia developing after intravenous maintenance fluid by restricting the amount of maintenance fluid is not correct [10] and is in contrast to what Halperin et al [11] had opined that hypotonic fluid were source of electrolyte free fluids so causing expansion of the plasma resulting finally in hyponatremia.

CONCLUSION

IV maintenance Solutions may not be generalized, and individual clinical needs should be considered. In our study, it appears that all the fluid groups were comparable in their possibility of causing and trials specially designed for this question warrant more studies regarding relationship between the maintenance intravenous fluid and hyponatremia during or due to

its infusion. Amount of free fluid in the IV maintenance fluid can be a factor in causing hyponatremia. Caution is warranted to guard off a rapid fall of serum sodium level.

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