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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/16759
DOI URL: http://dx.doi.org/10.21474/IJAR01/16759

RESEARCH ARTICLE

SHORT TERM EFFECT OF INTRAVENOUS FLUID THERAPY IN PAEDIATRIC INTENSIVE CARE UNIT ON SERUM ELECTROLYTES AND RENAL FUNCTION TESTS OF CHILDREN

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Manuscript Info

Manuscript History
Received: 28 February 2023
Final Accepted: 31 March 2023
Published: April 2023

Key words:-
Paediatric Intensive Care Unit, Intravenous Fluid Therapy, Hyponatremia, Isotonic Fluids, Hypotonic Fluids

Abstract

Background: Studies have shown that using hypotonic fluids may result in hyponatremia and the use of isotonic fluids is associated with lower incidence of electrolyte disturbances. Renal functions usually based on measurements of serum urea and creatinine are dependent on the maintenance of appropriate intravascular volume in order to maintain adequate organ perfusion and functioning.
Aims and Objectives: To analyze the short term effect of IV Fluids in PICU on serum electrolytes and renal function tests.
Methods: This observational descriptive study was conducted in 125 children admitted PICU from April 2022 to September 2022 receiving IV fluids and kept nil by mouth. The levels of serum sodium, potassium, urea and creatinine done at day1 of admission were compared to the investigations done after 72hrs.The data was categorized based on the type of fluid received by the child. Hypotonic fluids (0.45% DNS, D10) and isotonic fluids (0.9% DNS).
Results: Out of 125 children, 61(48.8%) received hypotonic fluids whereas 64(51.2%) received isotonic fluids. The average volume of hypotonic fluid given was 3.2±1.7 ml/kg/hr whereas of isotonic fluid given was 2.7±1.3 ml/kg/hr (p=0.11). Hyponatremia developed in 16 out of 42 baseline normal sodium patients in hypotonic group and 6 out of 46 in isotonic group(p=0.03). Serum creatinine was raised in 6(12%) patients out of 50 baseline normal patients in hypotonic group. Serum urea from baseline normal was raised in 7(21.9%) in hypotonic and in 5(17.9%) in isotonic group (p=0.4). Mortality was significantly higher in hypotonic group (13.1%) compared to isotonic group (3.1%) (p=0.04).
Conclusions: For preventing positive fluid balance and also development of hyponatremia, isotonic fluids should be considered as routine maintenance fluids.

Introduction:-

Intravenous fluid therapy is one of the fundamental aspects of paediatric critical care. Electrolyte imbalances are observed frequently and therefore require monitoring and appropriate management. The composition, volume and duration of intravenous fluids vary according to different situations. Fluidsrequired for fluid resuscitation, routine maintenance and replacement can be either colloids, crystalloids or other combinations of fluids. The use of

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hypotonic intravenous maintenance fluids in hospitalized children has been considered the standard of care since 1957, when Holliday and Segar published their landmark paper. Hyponatremia is the most common electrolyte disturbance observed with fluid therapy and studies reporting that the administration of hypotonic solutions in children increases the risk of hyponatremia in contrast to that for isotonic solutions have been increasing.[1,2]Hence the approach of using hypotonic solutions being for over four decades is now being reconsidered.

Kidney functions rely upon appropriate intravascular volume in order to maintain adequate organ perfusion. Urea is the primary waste product excreted by the kidney andalso plays a role in urine concentration, particularly in the inner medulla. Definition of acute kidney injury as per the KDIGO criteria considers both serum creatinine and urine output. urine output is a problematic element of these criteria, as it is recorded inconsistently especially in a non critical-care setting.[3]Accuracy of serum creatinine and urea are also imperfect as it is affected by ethnicity, body-mass, age, sex, diet, and medications.[4] The fluid balance concept is based on the principal physiologic function of maintenance of stable volume of the body cells and has been observed to be protective of kidney functions.[5,6]Kidney functions therefore need consideration of multiple factors for correlation with the clinical outcomes.[7]

The tonicity of fluids needs to be considered while maintaining the fluid balance. Hence consideration of both the parameters are essential for improvement of clinical outcomes.[8]

The objective of the present study was to analyze the short term effect of intravenous fluids in paediatric intensive care unit on serum electrolytes and renal function tests. The secondary objective included the comparison of the incidence of mortality in the groups.

Methods:-

This hospital-based observational descriptive study was conducted in 125 children admitted Paediatric intensive care unit (PICU) of a tertiary care centre from April 2022 to September 2022.The data was collected retrospectively and approved by Institutional ethical; committee. The study included children between the age group of >1month and <12 years. The children admitted in PICU and started on intravenous fluid therapy which were nil by mouth forat least 72 hrs after admission were included in the study. The children who received oral fluids, in acute or chronic renal failure or referred from other paediatric intensive care units were excluded from the study.The Serum electrolytes and renal function tests done at day 1 of admission were compared to the investigations done after 72hrs of admission. Data was analyzed by categorizing the children as per the type of fluids received. Hypotonic fluids included Dextrose 10% (D10) and 0.45% w/v Sodium chloride and 5% w/v dextrose (0.45% DNS), while isotonic fluid included 0.9 % w/v Sodium chloride and 5% w/v dextrose(0.9% DNS).The parameters analyzed in the study were: Evidence of hyponatremia or hypernatremia and evidence of hypokalemia or hyperkalemia after administration of fluids. Changes in the levels of serum urea, serum creatinine and observed urine output and fluid balance states.Data was analyzed using IBM SPSS version 20. Categorical data was compared using Chi square T test. Averages were compared using independent sample T test and Mann-Whitney μ test**.**

The definitions used are as follows:

1.Hyponatremia is serum sodium level <135 mEq/L.[9]

2.Hypernatremia is serum sodium level >145 mEq/L, although sometimes it is defined as >150 mEq/L.[11]

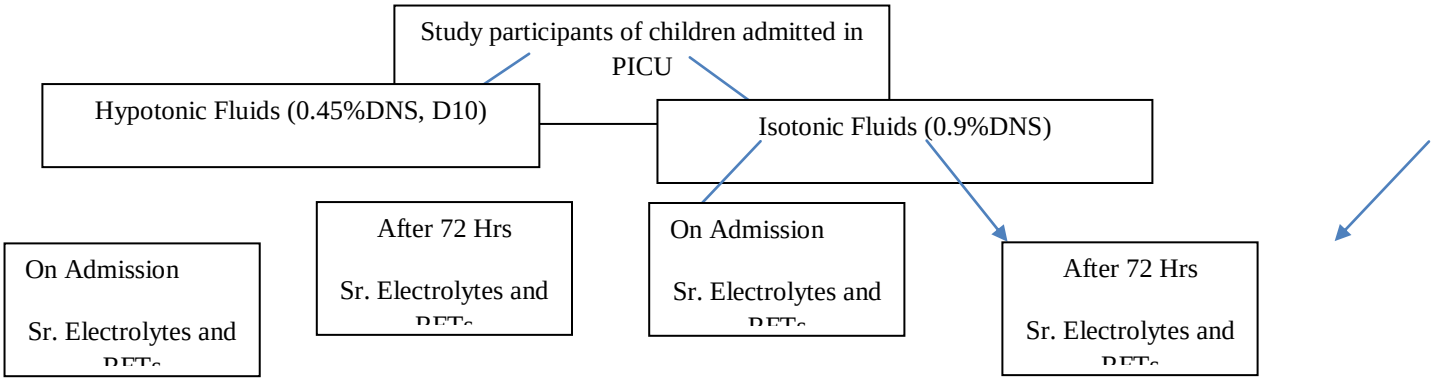
3.Hypokalaemia is serum potassium level <3.5mEq/L.

4.Hyperkalaemia is serum potassium level >5.5mEq/L.[10]

5.Normal serum creatinine values taken as 0.4 to 0.9 mg/dl. Normal values of serum urea taken as less than 40 mg/dl.

6.The daily fluid balance (FB) was calculated using the formula: FB = Total Daily Intake (all fluids received by the patient) - Total Daily Output (all fluids eliminated by the patient).[6]

Study Design:



Results:-

This is a hospital- based observational descriptive study was conducted in 125 children admitted Paediatric intensive care unit (PICU) as per the inclusion criteria. The electrolytes and renal function tests of the study participants receiving hypotonic fluids and isotonic fluids has been compared. The observations and results are as follows:

Table 1:- Distribution of study participants as per the gender of the child:

Gender	Hypotonic Fluids n(%)	Isotonic Fluids n(%)	Total n(%)	p value
Female N=55	26(42.6)	29 (45.3)	55 (44)	0.857
Male N=35	35 (57.4)	35 (54.7)	35 (54.7)	

There was no significant difference observed in gender distribution in the groups receiving hypotonic or isotonic fluids however females outnumbered male during study duration. (Table 1)

Table 2:- Distribution of study participants as per the age of the child:

Age(years)	**Hypotonic Fluids (n=61)**	**Isotonic Fluids (n=64)**	**p value**
Mean (±SD)	7.7(±7.13)	16.5172(±7.89)	<0.001
Median	5.5	0.92	

As depicted in table 2, the median age of the children who received isotonic fluids (0.9%DNS) was significantly higher than children who received hypotonic fluids. (9 months vs 5.5 years)<0.01). This difference was observed might be because of age wise fluid therapy policy of treating unit.

Table 3:- Distribution of cases included in the study as per their primary diagnosis.

Diagnosis	**Number**	**Percentage**
Acute gastroenteritis	39	31.2
Acute hepatitis	10	8
Acute Febrile Illness	5	4
Acute Lymphoblastic Leukemia	3	2.4
Febrile Neutropenia	2	1.6
Severe anemia	8	6.4
Aspiration pneumonia	3	2.4
Bronchopneumonia	16	12.8
Convulsions	14	11.2
Meningitis	2	1.6
Guillian Barre Syndrome	1	0.8

Dengue	3	2.4
Drug reaction/Poisoning	3	2.4
Epidermolysis bullosa	1	0.8
Ichthyosis vulgaris	1	0.8
HLH syndrome	1	0.8
Hyper IgE syndrome	1	0.8
Idiopathic thrombocytopenic purpura	1	0.8
Late onset sepsis	1	0.8
Multisystem Inflammatory syndrome in children	1	0.8
Pancreatitis	1	0.8
Systemic Lupus Erythematosus	1	0.8
Tetanus	2	1.6
Congenital Heart Disease	5	4
Total	125	100.0

Table 4:- Distribution of serum sodium and renal function test values on admission:

Sr. No.	**Parameter**	**Values on Admission**	**Hypotonic fluids (N=61) n(%)**	**Isotonic fluids (N=64) N(%)**
1.	Sodium	Normal	42(68.85)	46(71.87)
		Abnormal	19(31.14)	18(28.12)
2.	Urea	Normal	32(52.45)	28(43.75)
		Abnormal	29(47.54)	36(56.25)
3.	Creatinine	Normal	50(81.96)	54(84.37)
		Abnormal	11(18.03)	10(15.62)

In Table 4, baseline normal sodium values were observed in 42 out of 61 children receiving hypotonic fluids and 46 out of 64 children receiving isotonic fluids. Baseline normal urea values were observed in 32(52.45%) and 28(43.75%) children receiving hypotonic and isotonic fluids respectively. Baseline normal creatinine were observed in 50(81.96%) and 54(84.37%) children receiving hypotonic and isotonic fluids respectively.

Table 5:- Distribution of changes after 72hrs of fluid therapy in baseline normal serum sodium and renal function tests:

Sr. No.	Parameter	Values after 72hrs of admission	Hypotonic fluids n(%)	Isotonic fluids n(%)	p-value
1.	Sodium	Hyponatremia	16(38.09)	6(13.04)	0.03
		Normal	26(61.90)	40(86.96)	
2.	Urea	Abnormal	7(21.9)	5(17.9)	0.4
		Normal	25(78.1)	26(86.7)	
3.	Creatinine	Abnormal	6(12.0)	5(9.3)	0.656
		Normal	44(88.0)	49(90.7)	

In Table 5, hyponatremia developed in 16 out of 42 baseline normal sodium patients in children receiving hypotonic fluids and 6 out of 46 in those receiving isotonic fluids. The p-value is significant for the development of hyponatremia in study participants receiving hypotonic fluids (p=0.03). There is no significant derangement observed in the values of serum urea and creatinine after 72hrs of admission.

Table 6:- Development of hyponatremia after 72hrs of fluid therapy in relation to the on admission values of serum sodium and the type of fluids administered:

Sr. No.	Hyponatremia	Hypotonic fluids	Isotonic fluids
1.	No Hyponatremia		
	Baseline sodium ≥135	26(61.90)	40(86.96)
	Baseline sodium <135	12(63.15)	14(77.77)
2.	Hyponatremia present		
	Baseline sodium ≥135	16(26.22)	6(9.37)
	Baseline sodium <135	7(36.84%)	4(28.5%)

	Total	61	64

In Table6, the development of hyponatremia in baseline normal serum sodium values is compared with the children with baseline hyponatremia on admission. Hyponatremia was present in 7 (36.84%) out of 19 and 4 (28.57%) out of 18 in children with baseline hyponatremia in children receiving hypotonic fluids and isotonic fluids respectively.

Table 7:- The total input volume of intravenous fluids (ml/kg/hr):

Input Volume (ml/kg/Hr)	Hypotonic Fluids (N=61)	Isotonic Fluids (N=64)	p
Mean	3.2000	2.7000	0.11
Std. Deviation	1.70000	1.30000	

In Table 7, the average volumes of fluids transfused were similar in both the groups. The volume of hypotonic fluid given was 3.2±1.7 ml/kg/hr whereas of isotonic fluid given was 2.7±1.3 ml/kg/hr (p=0.11).

Table 8:- The distribution of fluid balance in both the groups:

Fluid Balance (ml/kg/Hr)	Hypotonic Fluids N=61 n(%)	Isotonic Fluids N=64 n(%)	Total N=125	p
≤1.5	1(1.6)	3(4.7)	4(3.2)	0.54
0 to -1.5	7(11.5)	6(9.4)	13(10.4)	
0-1.5	30(49.2)	37(57.8)	67(53.6)	
>1.5	23(37.7)	18(28.1)	41(32.8)	

In Table8, positive fluid balance (> 1.5 ml/kg/hr) developed in 37.7 % in patients receiving hypotonic fluids and in 28.1% in patients receiving isotonic fluids. There was no significant change in the development of positive fluid balance.

Table 9:- Incidence of Mortality.

Outcome	Hypotonic Fluids N=61 n(%)	Isotonic Fluids N=64 n(%)	Total N=125 n(%)	p
Mortality	8(13.1)	2(3.1)	10(8.0)	0.04
Survival	53(86.9)	62(96.9)	115(92.0)	

In Table 9, mortality was significantly higher in hypotonic group (13.1%) compared to isotonic group (3.1%) (p=0.04)

Discussion:-

In this study, the use of isotonic solutions reduces the development of hyponatremia as compared to the ones receiving hypotonic solutions in children admitted in PICU. There have been fewer studies observing the electrolyte derangements in children receiving intravenous fluids for >24 Hrs. In this study significant hyponatremia has been observed after 72hrs of exclusive intravenous therapy and it thus strengthens the association of hyponatremia with hypotonic maintenance fluids.The observation of the present study has been compared with other published studies in India and other countries with reference to the use of fluid therapy in paediatric intensive care units.

Table 10:- Comparison with the other published studies:

Study	Present Study	Francis Carandang et al[11]	Helena Isabel Almeida et al[12]	Pilar Velasco et al[5]	Spyridon A. Karageorgos et al[4]	Silvio Fabio Torres et al[13]	Manish Kumar et al[14]
Year	2022	2013	2014	2017	2018	2019	2019
Place	India	United States	Portugal	Madrid	Philadelphia	Argentina	India
Sample size	125	1048	233	111	472	299	168
Age	1month to 12yrs	1month to 18yrs	1 day to 18yrs	1week to 15yrs	2month to 18yrs	29days to 15 yrs	3 months to 5yrs

Study Type	Observational descriptive study	Retrospective Cohort study	Randomized Controlled study	Retrospective Cohort study	Retrospective Cohort study	Randomized controlled trial	Randomized Controlled trial
Follow up Duration	72Hrs	24Hrs	24Hrs	24Hrs	12Hrs	12Hrs	24Hrs

In the present study children in the age group of 1month to 12yrs were included and infants less than 28 days of age have been excluded. Majority of studies have included children within the age range of 1month to 18yrs of age. [11,4,13,14]The study conducted by Helena Isabel Almeida et al[12] and Pilar Velasco et al[5] have also included neonates in the study less than 1 month of age. The guidelines published by American academy of Pediatrics [1] recommend the use of isotonic solutions in the age group patients from 28 days to 18 years of age.

The other studies compared with the present study have a shorter follow up time of 12 Hrs to 24 Hrs. The follow up time of present study has a follow up time of 72 Hrs. In the present study the children on exclusive intravenous fluids for 72Hrs have been included and thus changes due to free water from enteral route are avoided.

Significant hyponatremia developed in the study conducted by Francis Carandang et al[11], Helena Isabel Almeida et al[12], Spyridon A. Karageorgos et al[4]and Pilar Velasco et al[5]. Significant hyponatremia was observedin study participants receiving hypotonic fluids which is comparable with other published studies.In study conducted by Pilar Velasco et al[5], ,hyponatremia in 14(63.6%) children out of 22 children with baselinehyponatremia was not corrected after administration of hypotonic fluids. The result was significant with a p-value of 0.027 as compared to the children receiving isotonic fluids. The results in the present study were comparable, with hyponatremia being persistent in children with baseline hyponatremia on admission.

In the present study there is no significant derangement in the values of urea and creatinine which is comparable with other published studies.[1,5]. Positive fluid balance though observed to be more in patients receiving hypotonic fluids (37.7 %) was not statistically significant. Positive fluid balance has been considered as an early biomarker of acute kidney injury in critically ill patients and thus has been compared in the present study.[6]

In the study conducted by Pilar Velasco et al[5], there were 2 deaths (2.9%) in the participants receiving hypotonic fluids but the values were not significant.In the present study mortality was significantly higher in hypotonic group as compared to isotonic group. (p=0.04).

Unique About The Study

1. In this study results have been observed after 72 hrs as compared to shorter duration of most studies.
2. Results have been compared with fluid balance.
3. As the study population is NBM for 72hrs and there is no source of free water from enteral route and thus hyponatremia associated has been avoided in the study results.

Limitations

1. The primary outcome prior to 72 hrs of therapy was not examined.
2. Hyponatremia developing acutely in fewer hours have not been included in the study.
3. As this is a single-centre trial and hence the sample size was relatively small so there may be deviations in the results and generalizability of the results.

Conclusion:-

For preventing positive fluid balance and also development of hyponatremia, isotonic fluids should be considered as routine maintenance fluids.

Declaration
Funding:
None.

Conflict of interest:
None.

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