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Original Research Article

# Maintenance IV Fluid in Children: Beyond Dysnatremia after Isotonic and Hypotonic Infusion

**Arvind Kumar[1], Neeraj Anand[2], Yogesh Chandr Govil, Prabhakar Mishra[4], Sciddhartha Koonwar[5]**

[1]Consultant Paediatrics, RML Hospital, Lucknow
[2]Assistant Professor, Department of Paediatrics, KGMU Lucknow
[3]Former Professor & in-charge of PICU, Department of Paediatrics, KGMU Lucknow
[4]Professor, Department of Biostatistics, KGMU, Lucknow
[5]Paediatric Intensivist, Apollomedics Hospital, Lucknow

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**Corresponding Author: Dr. Sciddhartha Koonwar**
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**Abstract:**

**Background:** Holiday and Malcolm while explaining the phenomenon of hyponatremia in hospitalised children after IV fluid maintenance therapy, called the proposition of isotonic saline instead of hypotonic saline for maintenance purposes as inappropriate. This strategy poses risks of hypernatraemia and other consequences of sodium overload.

**Aim and Objective:** The aim of this study was to compare the effect of four different intravenous (I.V.) fluid regimes on the incidence of dysnatremia in hospitalized children ranging in age from 1 month to 15 years.

**Material and Methods:** The children were randomized to four I.V. fluid groups: Group I, Prepared by mixing Sodium and Potassium, calorie and free water calculated on daily requirement per kg body weight basis infused at the standard maintenance rate, Group II, Isolyte-P, infused at the standard maintenance rate, Group III, Normal Saline with potassium and 5% dextrose, infused at the standard maintenance rate, Group IV, 20 to 40 ml per kg of normal saline infused over two to four hours followed by Isolyte-P at the standard maintenance rate.

**Results:** Our results showed the dysnatremia from highest to lowest incidence in the following order: Hypotonic fluid > Isotonic fluid > Holiday and Malcolm protocol > Precalculated IV maintenance fluids. i.e. dysnatremia in decreasing order. Although Isotonic IV maintenance fluid did not cause any hyponatremia but it caused significant number of hypernatremia, though mild in this RCT.

**Summary & Conclusion:** Hypotonic fluid > Isotonic fluid > Holiday and Malcolm protocol > Precalculated IV maintenance fluids cause dysnatremia in decreasing order.

**Keywords:** IV fluid Maintenance Therapy, Dysnatremia, Hyponatrtemia, Hypernatremia.



## Introduction

Hyponatremia is a frequently found metabolic abnormality in children [1]. In 1957 Malcolm A. Holliday and William E. Segar proposed the use of 18% NS +5% dextrose (lsolyte-P) as a maintenance intravenous fluid for hospitalized paediatric patients based on studies of water requirements and energy expenditure done on normal children their recommendation of using lsolyte-P was being followed religiously by the world for the next 50 years.[2,3].

Since then many more cases have been reported as hospital–induced hyponatremia causing neurological morbidity including 26 deaths as reported by Hatherill et al [4]. In recent years, there has been a sharp increase in momentum to call for increasing the tonicity of the parenteral maintenance solution for children. However many authors disagree with this view [5]. The main objective of giving maintenance fluids to hospitalised children is to make up for the loss of water through renal, dermal and respiratory routes. The calculation for this maintenance fluid in the body traditionally used to be calculated based on the calorie expenditure of these children as per the 50-year-old traditional formula of holiday and segar [2].

There are various explanations given for the occurrence of hyponatremia in children on maintenance therapy. The phenomenon of excretion of extra sodium in the urine in response to increased central venous pressure is caused by rapid saline infusion, the phenomenon of desalination. some authors have therefore proposed that simple restriction of fluid rather than isotonic

saline would tackle the problem better by improving the secondary desalination that results from the overexpansion of the intravenous space. There seems to be a tendency to overestimate the need for fluids in stressed children because, in stress due to sickness, the metabolism and calorie expenditure may be reduced [6]. So the free water accumulation may cause some dilutional hyponatremia.

Some non-hemodynamic factors stimulate the arginine-vasopressin system (ADH) to operate and thus cause more stasis of free water, warranting curtailing the amount of intravenous maintenance from the calculated volume by the Holiday and Segar method of pure calorie expenditure [7].

Thus we see that the free water accumulation and lesser need for free water coupled with many other mechanisms may lead to hyponatremia in children on maintenance intravenous fluid therapy [6].[8]

Although isotonic IV-maintenance fluid therapy (IV-MFT) was superior to the hypotonic one in reducing the risk of iatrogenic hyponatremia in hospitalized children, however, the risk of hypernatremia cannot be ruled out. So can there be another fluid to ward off the possibility of renal dysfunction and other injuries? [9]

With this background, the principal objective of this prospective randomized controlled study was to find out the most suitable maintenance IV fluid to be given to the children, who due to any cause have to be kept on nil per oral orders and their need of free water calories and electrolytes especially sodium have to be fulfilled by intravenous route to maintain normonatremia

**Material and Methods:**

After obtaining ethical approval from the institutional Ethics committee, this Prospective Randomized Controlled Trial was conducted on children admitted to the paediatric emergency unit of a tertiary care teaching hospital for 12 months the first 10 months were utilised for the screening, randomisation (with the randomization table for the possible 250 patients) and inclusion/exclusion in the trial. The sample size calculation and later the data analysis were done in the biostatistics department of SGPGI Lucknow; The last two months were used for data tabulation, analysis and conclusion. 157 Children between the ages of 1 month to 15 years were enrolled in the study after informed consent from the parents/guardians using due process.

Children requiring I.V. maintenance fluid for at least 8 hours, having no symptoms and signs of dehydration/overhydration having serum sodium concentration between 135 and 145 mEq/L were included. The children having renal/cardiac disease/hypertension /SAM or those on diuretics were excluded. The demographic details and routine physical examination along with routine laboratory tests were done. The urine and plasma osmolality were intended to be done at the outset and at 24 hours of starting the maintenance IV fluid as per the group randomisation. Plasma sodium and urine sodium concentrations were recorded in all patients at three points of time: just before the start of the maintenance fluid, at 8-24 hours following initiation of maintenance fluid therapy and at or after 48 hours of the start of the maintenance fluids.

The patients in this RCT, after enrolment, were kept in any of the four groups randomised as per the randomisation table as they arrived for admission.

Group I- were given calculated electrolytes added to water (sodium at 3 meq. Per kilogram of the body weight per 24 hours + potassium at 2 meq per kilogram of the body weight added to the calculated amount of fluid 24 hours as per the caloric expenditure method.)

Group II- The Isolyte P group: were given 0.18% saline with 5% dextrose with 20meq of potassium per litre (i.e. commercially available isolyte P,) as their maintenance fluid.

Group III- were given normal saline as their maintenance fluid + potassium at the concentration of 20 meq per litre of the maintenance fluid.

Group IV- were given 20-40 ml/kg of normal saline first at the maintenance speed and then followed by 0.18% saline with 5% dextrose + potassium at the concentration of 20 meq per litre of the maintenance fluid (i.e. commercially available Isolyte P) as their maintenance fluid for the of the period. Holiday and Malcolm 2007) [10,11]

A detailed history including important negative history and complete general and systemic examination were done and recorded with the predecided proforma. The usual lab work including haemoglobin, CBC, KFT, LFT, osmolality, serum electrolytes were done before starting the maintenance fluid, electrolytes and osmolality between 8- 24 hours and after 48 hours of the maintenance therapy were duly recorded. Urine electrolytes and osmolality were recorded at the start and after 48 hours.

**Results:**

**Table 1: Overview of hyponatremia /hypernatremia after 8 to 24 hours of fluid administration**

| Serum sodium levels after 8-24 hrs. of the fluid administration | Fluid given | | | | Total | P value |
|---|---|---|---|---|---|---|
| | Calculated In % | ISO-P In % | NS In % | NS+ISOP In % | | |
| **Normal** | 31(91.18) | 31(68.89) | 26(76.47) | 39(88.64) | 127(80.89) | 0.03 |
| **Mild hypo (130- 134meq /lit)** | 3(8.82) | 11(24.44) | 0(0.00) | 4(9.09) | 18(11.46) | |
| **Moderate Hypo (121-129) meq/lit)** | 0(0.00) | 2(4.4) | 0(0.0) | 0(0.0) | 2(1.27) | |
| **Mild hyper (146-155meq /lit)** | 0(0.00) | 1(2.22) | 8(23.53) | 1(2.27) | 10(6.37) | |
| **Total** | **34(100.00)** | **45(100.00)** | **34(100.00)** | **44(100.00)** | **157(100.00)** | |

**Table 2: Overview of hyponatremia /hypernatremia at / after 48 hours of fluid administration**

| Serum sodium levels after 48 hrs. of the fluid administration | Fluid given | | | | Total | P value |
|---|---|---|---|---|---|---|
| | Calculated In % | ISO- P In % | NS In % | NS+ISOP In % | | |
| **Normal** | 31(91.18) | 25(55.56) | 23(67.65) | 38(86.36) | 117(74.52) | **<0.01** |
| **Mild hypo (130-134meq/lit)** | 3(8.82) | 19(42.22) | 0(0.00) | 6(13.64) | 28(17.83) | |
| **Moderate Hypo (121-129 meq/lit)** | 0(0.00) | 1(2.22) | 0(0.0) | 0(0.0) | 1(0.64) | |
| **Mild hyper (146-155meq /lit)** | 0(0.00) | 0(0.00) | 11(32.35) | 0(0.00) | 11(7.01) | |
| **Total** | **34(100.00)** | **45(100.00)** | **34(100.00)** | **44(100.00)** | **157(100.00)** | |

No case of hypernatremia was found in isolyte-p and NS + isolyte-p fluid after 48 hours of fluid administration.

Thus in nutshell, these results show that 1. the administration of Holiday and Malcolm suggested protocol for IV fluid maintenance by→ isotonic saline first at 20 to 40 ml per kg infused over two to four hours followed by the hypotonic saline with potassium with 5% dextrose in calorie expenditure method calculation of free fluid (caused mild hyponatremia average 13.6% at 48 hours and 0% hypernatremia at 48 hours) and 2. The IV maintenance fluid calculated on the basis of daily requirement of sodium and potassium per kg body weight mixed with free water and calories (5% dextrose) calculated on the basis of calorie expenditure method (caused Hyponatremia average 8.82% at 48 hours and 0% hypernatremia) are the two IV maintenance fluid arrangements, which are comparable and caused least incidence of dysnatremia, in hospitalised children.

The other two groups caused statistically significant dysnatremia namely 1. Isolyte-P caused hyponatremia average 44.4% at 48 hours and nil hypernatremia and 2. Normal saline group caused 0% hyponatremia at 48 hours but caused hypernatremia of average 32.35% at 48 hours.

Our results showed the dysnatremia from highest to lowest incidence in the following order: Hypotonic fluid > Isotonic fluid > Holiday and Malcolm protocol > Precalculated IV maintenance fluids. i.e. dysnatremia in decreasing order. Although Isotonic IV maintenance fluid did not cause any hyponatremia but it caused significant number of hypernatremia, though mild in this RCT.

## Discussion

The daily requirement of electrolytes is an undisputed quantitative entity fully established with narrow but flexible limits and allowances, For the last few years, few attempts have been made to find the most suitable maintenance fluid for the children needing total lV support for some time and these efforts have met with variable success without qualifying for a valid generalization.[12]

After a long controversy, it seemed for quite some time that Holiday and Segar's approach had settled everything regarding maintenance IV fluids through their article in 1957 in 'Paediatrics' and their recommendation of 0.18 N strength saline with 5% dextrose became the fluid of choice for IV Fluid maintenance in children. Since then the administration of hypotonic maintenance fluids has become a common practice in hospitalized children. [2]

Of late, more than many workers correlated and found a strong relation between iatrogenic dysnatremia and the type of fluid given to the children. Over the past decade, there has been increasing concern within the paediatric community that the commonplace practice of using hypotonic fluids for maintenance intravenous fluid (mIVF) therapy may contribute to or induce dangerous hyponatraemia in patients. [13,14]. Hyponatremia (serum sodium concentration <135 mEq/L) is the most common electrolyte abnormality in patients who are hospitalized, affecting approximately 15% to 30% of children and adults [15,16].

Although there were negligible incidences of hypernatremia in children on maintenance therapy,

sporadic incidences have been reported. So it looks prudent to look for incidences of hypernatremia too, in the children on maintenance therapy with isotonic saline. Recently, hypernatremia has been primarily a hospital-acquired disease, caused by failure to administer sufficient free water to patients unable to care for themselves. Although it has been established that isotonic fluids should be used for maintenance therapy, there are still a few questions to be answered. It has been of rare occurrence and heartening to note that Holiday who with Segar had proposed the so-called hypotonic fluid in 1957, in 2007 along with Malcolm after reports of hospital-acquired-hyponatremia had created a stir in the hospital care came out with the provision of an IV fluid plan of infusing isotonic IV fluid at 20 ml per kg in two to four hours (not as a bolus) to offset the possibility of secretion of extra ADH induced by multiple factors like stress, non-osmotic factors like cough, vomiting, nociceptive stimuli and respiratory and central nervous system diseases etc. induced volume contraction [10]. So Holiday and Malcolm in order to offset the probable subclinical or subtle and sometimes clinically apparent volume contraction, proposed a 20 -40 ml per kg isotonic saline infusion over 2 to 4 hours and then they advised the 18% saline with potassium chloride and 5% dextrose infusion till the need for maintenance.

There could be a fourth way also to cater to the maintenance needs. The daily requirement of electrolytes is an undisputed quantitative entity fully established with narrow but flexible limits and allowances, the maintenance need for sodium potassium and calories can be calculated and calculated requirements for the individual patient can be mixed with the amount of water required on the basis of mixing of daily required sodium and potassium by 3 and 2 mEq per kg per day to be mixed in the fluid calculated on the basis of calorie expenditure method. [17] and infused on a day-to-day basis in a separate group. Keeping these pertinent queries we designed a prospective randomised controlled study comparing four types of fluids namely: NS, NS initially at 20 – 40 ml/kg at maintenance rate followed by maintenance by 0.18%,) 0.18%NS with 5% dextrose and the fourth group of the calculated amount of sodium required added to the free water with 20 meq. /lit of potassium with 5% dextrose. So we did this prospective randomized controlled study comparing four types of IV maintenance fluids, namely:

Group I- were given IV fluid containing electrolytes and calories calculated on a daily requirement basis and added to water (sodium at 3 meq. Per kilogram of the body weight per 24 hours + potassium at 2 mEq per kilogram of the body weight and dextrose as 5% dextrose added to the calculated amount of fluid 24 hours as per the caloric expenditure method [17].

Our findings are consistent with most of the previous RCTs concluding that isotonic fluid is safer than hypotonic fluid in terms of hyponatremia as far as incidence of hyponatremia (mild to moderate) at 8 to 24 hours of running IV respective maintenance therapy as well as after 48 hours and also in the total incidence in 48 hours in these two maintenance groups. However when compared with the incidence of hyponatremia in all the four maintenance groups, the number of percentage-wise incidences in decreasing order were: 0.18% saline group with potassium with 5% dextrose group (28.8%, 44.4%)→ Calculated daily requirement group (8.82%, 8.82%) → Isotonic saline at 20 – 40 ml per kg followed by 0.18% saline + potassium + 5% dextrose group (i.e. Holiday and Malcolm group) (9.09%, 13.6%)→ finally the Isotonic saline with 5% dextrose with potassium group (5%,0%).

The second possibility in the incidence of dysnatremia to be estimated was that of hyper-natremia. We found that the incidence of hyper-natremia was of mild degree (serum Sodium 146 to 149 mEq /L) [18] though, was a definite entity in our study. The incidences across the groups were: Group I → (0%, 0%), Group II→ (2.2%, 0%), Group III → (23.53%, 32.35%), Group IV → (2.27%, 0%). So the Isotonic group (Saline with 5% dextrose and potassium) caused a significant number of mild hypernatremia both initially and when continued further to 28 hours. As understand-able, the Group II did not cause any episode of hy-pernatremia. Interestingly group II and group IV had minimal incidence of mild hypernatremia in 1st 8 to 24 hours which however disappeared on con-tinuation of the maintenance till 48 hours or more, though the percentage of hypernatremia in these 2 groups even in 1st 8 to 24 hours was minimal as per above.

So in our study, we used the physiologically sound principle of preparing IV maintenance fluid based on individual daily requirements as per weight.[19] in group I giving due weightage to the proponents of the hypotonic maintenance fluid, the famous holiday and segar [2] who came up with the solu-tion to offset the derangement in the physiology owing to stress, osmotic and non-osmotic stimuli proposed yet another option of infusing 20-40 ml/kg of isotonic saline to minimise effect of un-wanted ADH secretion followed by the same 0.18% normal saline with 5% dextrose and potassi-um for rest of the period. Of all other retrospec-tive/RCT's/ metanalyses the 2 groups seem to be least likely to cause dysnatremia and preserve the milieu interior better than hypotonic fluid and iso-tonic fluid as both hypo and hypernatremia are un-desirable.

So either individualised IV maintenance fluid prepared based on calculating daily requirements of sodium, potassium, calories and water or initial 20-40 ml/kg of isotonic fluid over 2-4 hours followed by 0.18% saline plus 5% dextrose plus calories plus water as calculated by holiday and segar formula of caloric expenditure method are the 2 IV maintenance fluid method seem to be the candidate for further trial and testing. A balanced fluid instead of normal saline for initial 20-40 ml/kg in the Holiday and Malcolm method may well be devised and tested.

## Conclusion

Hypotonic fluid > Isotonic fluid > Holiday and Malcolm protocol > Precalculated IV maintenance fluids cause dysnatremia in decreasing order.

Although Isotonic IV maintenance fluid did not cause any hyponatremia it caused a significant number of hypernatremia, though mild in this RCT.

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