Original Article

Indian Journal of Maternal-Fetal & Neonatal Medicine
Volume 7 Number 1, January - June 2020
DOI: http://dx.doi.org/10.21088/ijmfnm.2347.999X.7120.2

A Prospective Explorative Study to Determine the Adequacy of Fluids Provided to Sick Preterm Neonates and Compliance with Prescribed Fluids

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Received on: 01.02.2020
Accepted on: 14.03.2020

Abstract

Objective: To determine the adequacy of fluids provided to sick appropriate and small for gestational age preterm neonates and compliance with prescribed fluids. *Design:* Prospective exploratory study. *Setting:* Level III neonatal intensive care unit, KBNIMS, Kalaburagi. *Participants:* Neonates between 28 to 34 weeks of gestation, on exclusive intravenous fluids at 12 hours of life were enrolled and followed up till day 7 of life. *Intervention:* Sick neonates 28–34 wks gestations were started on exclusive intravenous fluids. Babies < 1500 g received fluids at 80 ml/kg/day and ≥1500 g at 60 ml/kg/day on day 1. Fluids were then increased by 20 ml/kg/d till day 5 upto a maximum of 160 ml/kg/d by day 7, provided acceptable levels of weight loss, serum sodium, urine output and urine specific gravity were achieved. Feeds were introduced when baby was hemodynamically stable. Outcome measures: Total fluids prescribed and received, weight ,serum sodium, any discrepancy in prescribed and received fluids, the frequency of PDA, NEC, IVH, jaundice and polycythemia, were assessed. *Results:* 100 consecutive neonates with mean birth weight of 1302 g and gestational age of 31.4 wks were studied. Thirty neonates were small for gestational age (SGA). The cumulative median weight loss was 8.6% and AGA neonates lost more weight than SGA (9.3% vs 4%, $p = 0.006$). There was no significant difference between the fluids prescribed and received and serum sodium levels. SGA neonates received more fluids than AGA neonates. On 85 occasions out of 609 times there was discrepancy in the fluids prescribed and received. All morbidities were similar in AGA and SGA neonates. *Conclusions:* Our current fluid policy resulted in appropriate fluid and electrolyte balance with no significant increase in morbidities of sick preterm neonates.

Keywords: SGA: small for gestational age; LGA: Large for gestational age; PDA: Patent Ductus Arteriosus; NEC: Necrotising Enterocolitis; IVH: Intra Ventricular Haemorrhage

How to cite this article:

Preeti Amarkhed, Charanraj Honnalli, VG Majumdar, et al. A Prospective Explorative Study to Determine the Adequacy of Fluids Provided to Sick Preterm Neonates and Compliance with Prescribed Fluids. Indian J Matern Fetal Neonatal Med. 2020;7(1):15–21.

Introduction

The fluid management of the preterm neonates has long been a controversial topic, inspite of itbeing an integral aspect of management of sick neonates. The sickness, high insensible water loss,[1,2] variable post natal diuresis causing extra cellular volume contraction[3,4] and developmental limitations in renal homeostatic mechanisms,[5,6] complicate fluid therapy in preterm neonates. Maintaining fluid volume is important because both dehydration and over hydration can lead to serious complications. Though healthy term neonates are able to modify their water excretion according to their intake,[7] sometimes even extreme preterm neonates are able to cope up with a water intake upto 200 ml/kg/day.[8] Because of the varying insensible losses and ability to maintain an adequate water balance over a wide range of intake, different fluid regimens are used worldwide, with no definite recommendations available. In addition, in a busy neonatal intensive care unit (NICU), sometimes the compliance with fluids prescribed may not be adequate. Hence we conducted this study to assess whether our unit fluid policy resulted in appropriate fluid and electrolyte balance in sick preterm neonates and also to check compliance with the prescribed regimen.

Materials and Methods

We prospectively studied consecutive neonates between 28 and 34 weeks of gestation, admitted to the our NICU from June 2017 to November 2019. Only neonates who were on exclusive intravenous (IV) fluids at the time of admission to the NICU and within 12 hours of life were enrolled after written informed consent. Neonates were excluded if they died within 12 hours of life, had an obvious congenital heart disease (diagnosed antenatal or postnatal) or life threatening congenital malformation, refused consent or required surgical interventions. Gestation was assessed by last menstrual period and post natal New Ballard Score.[9] In case of discrepancy the 1st trimester ultrasound report if available was utilized for assigning gestational age.

Lubchenco's intrauterine growth chart[10] was used to classify appropriate for gestational age (AGA) and small for gestational age (SGA) infants. All enrolled neonates were weighed immediately at admission to the NICU using an electronic weighing g scale (Indosaw, Osaw) with an accuracy of ± 1 gm and this was considered as baseline weight. Subsequent weight measurements were made 12th hourly. After birth, the neonates were started on IV fluids as per our unit policy.

hus sick neonates or neonates of 28-34 wks gestation were started on IV fluids. Neonates > 1500 g received fluid at 80 ml/kg/d and ≥ 1500 g at 60 ml/kg/d on day 1 irrespective of whether they were AGA or SGA. Fluids were then increased by 20 ml/kg/d till day 5 and then 160 ml/kg/d on day 6 and 7 provided acceptable goals like weight loss of 1–3% per day, serum sodium of 135–145 meq/L, urine output of 1–3 ml/kg/hour and urine specific gravity of 1.005–1.015, were met. Urine output was estimated 6th hourly by weighing wet nappies in a nappy weighing scale (Indosaw, Osaw) with a sensitivity of 0.1 g. Fluids were relaxed by an additional 20 ml/kg/day if weight loss was > 3% per day, urine output was <1 ml/kg/hr in the preceding 6 hours, serum sodium was >145 meq/L and hematocrit was > 65%. In neonates receiving phototherapy 10 ml/kg/day extra fluids were prescribed.

Fluids were not increased if there is no weight loss or weight gain or there were features of congestive Heart failure or patent ductus arteriosus (PDA). In case of excessive weight gain (>5%), fluids were reduced by 20 ml/kg/day from the earlier prescription. In the first 48 hours of post natal life, 10% dextrose (5% used in case the capillaryblood glucose was > 125 mg/dL) was used. Isolyte *P* was given from day 3 onwards provided baby had lost 5% body weight. Feeds were started when the infant was hemodynamically stable and the abdomen was soft, had normal bowel sounds and there was no altered gastric aspirate.

Daily fluids prescribed and received; vital parameters like heart rate, respiratory rate and blood pressure; weight and urine output; evidence of PDA, necrotizing enterocolitis (NEC), jaundice, polycythemia and intraventricular hemorrhage (IVH) were recorded. Daily fluids included IV fluids, enteral feeds, drugs, total parenteral nutrition, blood products and fluid boluses. The biochemical parameters recorded were electrolytes (recorded 12th hourly if on IV fluids and then 24th hourly till day 7), renal function tests once daily and hematocrit 12th hourly. The enrolled neonates were followed up for the 1st seven days of life. They were managed in unhumidified single and double walled incubators. Clinical criteria (presence of cardiac murmur, increased precordial activity, wide pulse pressures with bounding pulses, worsening respiratory status) in addition to echocardiographic evidence was used to define a hemodynamically significant PDA.

Necrotizing enterocolitis was defined and staged as per modified Bell's criteria (11). IVH was diagnosed by cranial ultrasound, done in asymptomatic neonates on day 1, 4 and 7 or any time, if IVH was clinically suspected. Further grading of IVH was as per Papile's criteria.[12] The research protocol was approved by KBNIMS research ethics committee.

Sample size

A convenient sample size of 100 was chosen.

Outcome measures

Primary: To determine whether the total amount of fluids received by the neonates in the 1st 7 days of life resulted in normal post natal weight loss and serum electrolytes and to determine the number of instances when there was a discrepancy between the fluids prescribed and received.

Secondary outcomes: To determine the frequency of morbidities like PDA, IVH, NEC, jaundice, polycythemia and hyponatremia.

Statistical analysis

Fluid volumes were compared by Students "*t*" test and various morbidities were compared by chi-square test. Fischer's exact test was used wherever required. Mann-Whitney U-test was used for comparing nonparametric variables. Subgroup analysis was performed according to AGA and SGA status.

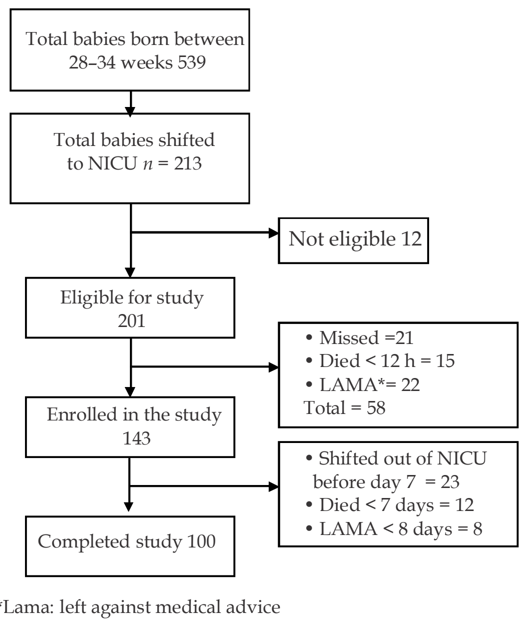
Results

539 neonates were born between 28 and 34 weeks during the study period. Out of these 213 neonates were admitted in the NICU. 143 neonates were enrolled and 100 completed the study. The detailed flow chart is given in Fig. 1. Table 1 shows the demographic characteristics of the study population. Thirty neonates were SGA. The mean (S.D) birth weight and gestational age of AGA neonates was 1392 ± 298 g and 31 ± 1.5 wks respectively and that of SGA neonates was 1064 ± 173g and 31.6 ± 1.3 wks respectively.

Table 1: Demographic characteristics of study subjects

Variable	All subjects (*n* = 100)
Birth weight (grams)	1302 ± 278
Gestation (weeks)	31.4 ± 1.5
SGA (*n* and %)	30 (30)
AGA (*n* and %)	70 (70)
Antenatal steroids (*n* and %)	66 (66)
Oxytocin to mother (*n* and %)	51 (51)
Vaginal delivery (*n* and %)	65 (65)
Male:female	2.1 : 1

Values are expressed in Mean ± SD and *n* (%)



*LAMA : left against medical advice

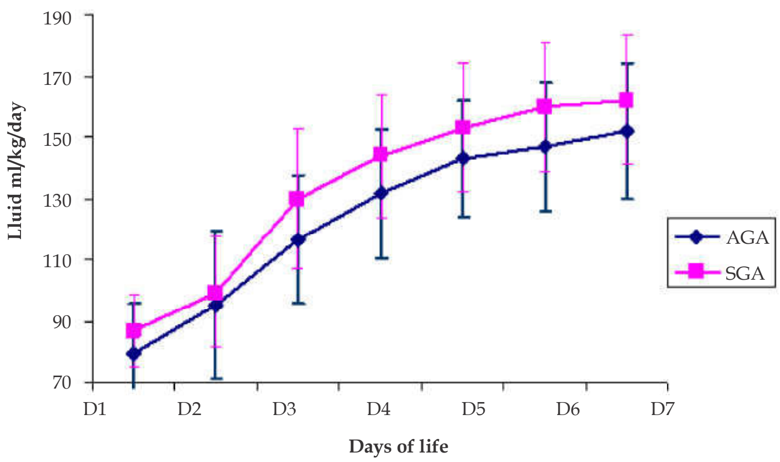
Fig. 1: Patient flow during the study

The cumulative median weight loss during the study period was 8.6%. AGA neonates lost significantly more (p = 0.006) than SGA (9.3% vs 4%). Table 2 gives the total fluid prescribed and received in the study population and the corresponding mean serum sodium values. There was no significant difference on any study day between the fluids advised and received and the mean serum sodium was also within normal limits. SGA neonates received significantly more fluids than AGA neonates on 1, 3, 4, 5 and 6 (Fig. 2). During the study period fluid prescriptions were made 609 times and there were 85 instances (14%) where there was discrepancy between the prescribed and received fluids. On 40 occasions neonates received more fluids than prescribed (extra boluses – 10); blood and blood products not deducted from total fluids 13; feeds introduced but not deducted -17. On 45 occasions neonates received less than prescribed fluids (not received the amount of feeds charted - 11; IV fluids deducted for feeds prescribed but feeds not received – 23; feeds stopped but IV fluids not increased - 11.

Table 2: Fluids and electrolytes in all infants (n = 100)

Study day	Fluids prescribed in ml/kg/d (mean ± S.D)	Fluids received in ml/kg/d (mean ± S.D)	Serum sodium in mEq/L (mean ± S.D)
1	81.3 ± 9	81.4 ± 13	136.2 ± 7.7
2	97.3 ± 15	96 ± 19.7	137.4 ± 6.9
3	119 ± 18.9	119.8 ± 23	137.7 ± 8.2
4	133.6 ± 18.9	134.8 ± 21	136.8 ± 6.3
5	143 ± 22	145.6 ± 21	137.3 ± 6.3
6	147.4 ± 23.9	150.5 ± 21.6	136 ± 7.5
7	152.8 ± 19	154.9 ± 22	136.2 ± 4.2

p = not significant on any day between fluids prescribed and received



The "p" values are <0.05 on study days 1, 3,4 and 6

Fig. 2: Fluid received (ml/kg/d) in AGA and SGA neonates.

The morbidities encountered in the study population are given in (Table 3). All morbidities, were not statistically different between the SGA and AGA neonates.

Table 3: Comparison of morbidities in AGA and SGA

Morbidity	AGA (n = 70)	SGA (n = 30)	All (n = 100)	p-value
PDA	18 (25.7)	7 (23.3)	25 (25)	0.89
IVH	12 (17)	3 (10)	15 (15)	0.34
NEC	2 (2.8)	3 (10)	5 (5)	0.41
Jaundice	5 (6)	3 (10)	8 (8)	1.00
Polycythemia	7 (9.3)	4 (13.3)	11 (11)	0.19

All figures expressed as n (%)

*p < 0.05 considered significant

Discussion

The current study shows that our policy of prescribing 80 ml/kg/day fluids for < 1500 g and 60 ml/kg/d for ≥ 1500 g babies on day 1 of life and further increments decided by daily changes in weight, serum sodium and urinary parameters, resulted in normal fluid and electrolyte balance.

What constitutes appropriate fluid therapy in preterm neonates is controversial with experts Suggesting varied fluid and electrolyte regimens (13). We used a fluid regimen that is based on known physiological principles of fluid therapy and with allowances given for our local practice for nursing these neonates in an unhumidified environment. Rather than following an arbitrary approach we altered the fluid therapy dictated by changes in clinical condition.

In the absence of differing guiding principles regarding fluid management in SGA neonates, we used the same regimen in them too.

Five randomized controlled trials (RCT) and their subsequent meta-analysis have addressed the issues of appropriate fluid therapy in preterm neonates and the impact of varying the fluid intake on clinical outcomes.[14–19] These studies used different and often overlapping fluid volumes as part of their fluid strategy. Meta-analysis of these 5 RCT's showed significant advantages in a restrictive fluid strategy in premature neonates. Restricted fluids significantly reduced the risk of PDA, NEC and showed a trend towards reduced bronchopulmonary dysplasia, IVH and death.19 The mean daily fluid intake in our study was 125.7 ml/kg over the entire study period. To know whether our fluid regimen was "liberal" or "restricted" is important as it might influence important clinical outcomes. Comparison with the 5 RCT's in the Cochrane meta-analysis showed that our regimen was similar to the "liberal" fluid group of 4 RCT's,[15–18] whereas the 5 th RCT by Bell et al.[14] had the restricted fluid group with fluid volume similar to ours. In the Bell et al trial the incidence of PDA and NEC was significantly reduced in the "restricted" fluid group, which received comparable fluids as ours. In none of the 4 other RCT's, a fluid regimen similar to ours resulted in a significant increase in clinical morbidities compared to the more restricted fluid regimen. Our fluid regimen cannot be called "liberal" as our neonates were nursed in unhumidified incubators like in the Bell[14] trial and unlike the 4 other trials, which used humification. That may have resulted in higher fluid intake due to higher insensible water losses in our babies. Also we included a significant number of SGA neonates, with morbidities, more likely to require higher fluid.

Our fluid regimen resulted in normal sodium levels on all study days and cumulative weight loss was also within acceptable limits. The appropriateness of any fluid regimen is judged by the clinical and biochemical parameters that we monitored in our study, of which weight is the most important.[13] Rapid changes in weight reflect changes in the extracellular fluid compartment with abnormal persistence being linked to various morbidities.[20–22] A recent observational study in 102 extremely low birth weight neonates showed that when a post natal weight loss is within acceptable ranges, then there is no significant increase in morbidities.[23] In this study maximal weight loss did not correlate well with the fluid intake in the 1st 7 days of life. The result suggests that targeting a permissible range of weight loss with fluid volume adjustments, rather than having fixed fluid intakes, could possibly help in avoiding hydration related morbidities in the extremely premature neonates. The permissible limits of weight loss in very low birth weight neonates are not certain, but generally upto 1–3% per day amounting to a cumulative weight loss of 5–15 % is acceptable. The cumulative weight loss of 8.6% in our study appears well within accepted limits, again highlighting the effectiveness of our fluid policy.

As fluid therapy has been linked to various clinical morbidities like PDA, NEC and IVH, we monitored these in our study. In addition jaundice and polycythemia were also seen, as they generally mandate fluid increments. As we did not compare different fluid regimens, we cannot compare various morbidities. But when our incidence of morbidities was compared with other studies using similar fluid regimens.[14–18] the incidence appears to be similar.

AGA neonates received mean daily fluids at 122.9 ml/kg and SGA at 130.5 ml/kg. It is important to study SGA neonates because their morbidities and fluid dynamics could be different from AGA neonates. This issue is more important in a developing country like ours where a significant proportion of low birth weight neonates are SGA (24). We found polycythemia was slightly higher but not statistically significant in the SGA neonates compared to AGA neonates, which is an expected outcome considering the increased erythropoiesis generally seen in this population.[25]

As per our fluid protocol, neonates with polycythemia received 20 ml/kg extra fluids, which could explain the differences in fluid received between the two groups. SGA neonates had a cumulative weight loss of 4% during the study period. The permissive post natal weight loss in SGA neonates is again controversial but is expected to be less than the AGA neonates, as there is less post natal volume contraction[26] and potential for rapid catch up growth.[27] This fluid regimen did not significantly increase the incidence of other morbidities in SGA neonates.

In our study we also looked at discrepancies in the fluids prescribed and received as part of a periodic quality assurance exercise. We believe that these errors could be linked to less number of resident doctors and nurses being available in a very busy NICU. The strength of our study is that our fluid policy was simple and easy to practice and effective in neonates between 28 and 34 wks of gestation. One important limitation was that bronchopulmonary dysplasia and mortality were not looked at as outcomes. Future study should be able to find out appropriate fluid regimens in AGA and SGA of extremely low birth weight neonates as the survival is improving in these babies.

What is already known?

- Restricted fluid intake in preterm neonates results in lower incidence of clinical morbidities.
- What this study adds?
- The fluid regimen used by us results in appropriate fluid and electrolyte balance with a similar incidence of morbidities in sick preterm neonates.

Abbreviations

VLBW - very low birth weight,

IV – intravenous fluid,

NICU - neonatal intensive care unit,

PDA - patent ductus arteriosus,

NEC - necrotizing enterocolitis,

IVH - intraventricular hemorrhage,

AGA - Appropriate for gestation,

SGA - small for gestation,

RCT - randomized controlled trial.

NICU-neonatal intensive care unit

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