Comparison of Isotonic Versus Hypotonic Fluids in Neonates on Maintenance Fluid Therapy

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Abstract

Introduction: In neonates, the use of hypotonic fluids is a widely accepted practice to maintain hydration and electrolyte balance, particularly after surgery. However, this approach can increase the risk of hyponatremia due to the lower sodium content in hypotonic solutions compared to blood plasma. This makes neonates more vulnerable to sodium imbalances if not properly monitored. While hypotonic fluids are commonly used, there is growing consideration of isotonic alternatives to reduce the risk of electrolyte disturbances and improve safety in neonatal care.

To evaluate and compare the outcomes of using isotonic versus hypotonic fluids in neonates receiving maintenance fluid therapy following surgery.

Study place and duration**:** Department of Pediatric Surgery, Holy Family Hospital, Rawalpindi from January 2023 to December 2023.

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Materials and Methods: Total 84 cases were enrolled in the study who underwent surgery and admitted in neonatal intensive care unit. Infants were randomly divided in two groups. Group I was given isotonic/normal saline with 5% dextrose in 0.9% saline. Group H was given hypotonic saline with 5% dextrose in 0.45% saline. Neonates were followed up and hyponatremia was noted. Data analysis will be done by using SPSS software version 25.0.

Results: In Isotonic saline solution, the mean age of neonates was 6.21 ± 6.19 days. In Hypotonic saline solution, the mean age of neonates was 3.84 ± 3.50 days. In Isotonic saline solution, hyponatremia was developed in 2 (4.8%) cases, hypernatremia in 9 (21.4%) cases, while 31 (73.8%) neonates maintained normal serum sodium level. In Hypotonic saline solution, hyponatremia was developed in 11 (26.2%) cases, hypernatremia in 0 (0%) cases, while 31 (73.8%) neonates maintained normal serum sodium level. The difference in both groups was found to be significant ($p<0.05$).

Conclusion: The risk of hyponatremia is higher with hypotonic saline solution when used as maintenance fluid after surgery in pediatric population.

Keywords

- isotonic saline, hypotonic saline
- neonates
- maintenance fluid therapy
- surgery
- hyponatremia

Introduction

The primary objective of the perioperative fluid strategy is to restore normal physiological balance, known as "homeostasis," by achieving optimal fluid volume in the central circulation and providing appropriate electrolyte levels based on the child's specific requirements. These requirements may arise from factors such as preoperative fasting and losses resulting from renal, cutaneous, gastrointestinal, and third space sources.[1]

Children possess an elevated metabolic rate, a greater ratio of surface area to weight, and a more rapid respiration, leading to significant fluid depletion and therefore necessitating a greater fluid intake. [2]

Proper fluid management is crucial for ensuring sufficient blood flow to tissues and maintaining a stable internal environment, particularly in perioperative situations and critically sick infants. The pediatric population is diverse; thus, a single formula may not be enough. Therefore, both the quantitative and qualitative aspects of fluid management should be determined depending on the child's physiology, pathology, and surgical requirements.[3] Fluid treatment should aim to maintain sufficient organ perfusion without inducing electrolyte imbalances, pulmonary fluid accumulation, or tissue swelling. An intraoperative fluid strategy encompasses maintenance treatment, blood loss replacement, and compensation for both insensible and sensible water loss resulting from surgery and anesthesia.[4-5]

Fluid management in neonates having major surgery is intricate and is affected by factors such as gestational age, postnatal age, physiological development of organ systems, kind of operation, concurrent sickness, and blood loss.[6] Moreover, the presence of prematurity exacerbates these difficulties, since the organ systems are underdeveloped and the composition of bodily fluids differs from that of a healthy full-term infant. The majority of the information comes from the newborn who is severely sick. Therefore, it is important to be careful when applying this data to the neonate who is receiving surgery.[7]

Different formulations of intravenous fluid are accessible. These solutions may be classified as either isotonic or hypotonic in relation to plasma. Isotonic solutions such as normal saline, ringer lactate, and acetate, closely resemble the osmolality of plasma, which ranges from 270 to 310 mOsm/L. On the other hand, hypotonic solutions like 0.45% and 0.18% normal saline have a lower osmolality. The extensive range of maintenance fluids is a challenge for clinicians in selecting the optimal intravenous maintenance fluid treatment for their patients.[8, 9] There is significant incidence of iatrogenic hyponatremia in children receiving a hypotonic solution containing 38 mmol/l of sodium. Hyponatremia may result in fatality and enduring brain impairment for those who survive. Numerous investigations have been carried out on youngsters who need intravenous administration of fluids for ongoing treatment. The majority of the findings indicated that the hypotonic solution is linked to an increased likelihood of iatrogenic hyponatremia.[10-11]

According to this, we planned this study to get the evidence in favor of more appropriate saline solution to maintain the serum sodium level on neonates. So that in future, better maintenance fluid option can be adopted to improve the serum sodium level after surgery and reduce risk of deranged serum sodium level that may cause severe disability and mortality.

To compare the outcome of isotonic versus hypotonic fluids in neonates on maintenance fluid therapy after surgery.

Materials and Methods

Study design: Randomized controlled trial

Study place and duration: Department of Pediatric Surgery, Holy Family Hospital, Rawalpindi from January 2023 to December 2023.

Sample size: Sample size of 84 cases was estimated by keeping 80% power of study, 5% significance level and percentage of hyponatremia i.e. 22% with hypotonic saline and 1.9% with isotonic saline. [12]

Sampling technique: Non-probability, consecutive sampling

Inclusion Criteria: Neonates of age 1-28 days, either gender underwent surgery and admitted to neonatal intensive care unit were enrolled in the study.

Exclusion criteria: Neonates already taking normal saline, enrolled in another trial, very low birth weight neonate (birth weight <1.5 kg)

Data collection and analysis: After approval from ethical review board of institute, 84 neonates were enrolled in the study from neonatal intensive care unit. Informed consent was taken from parents to record information and demographics (age, gender, weight of baby, residence, procedure performed) were recorded. Then neonates were randomly divided in two groups by using random number table. Group I was given isotonic / normal saline with 5% dextrose in 0.9% saline. Group H was given hypotonic saline with 5% dextrose in 0.45% saline. Blood sample was taken before surgery and was sent to hematology department for assessment of serum sodium levels. Then surgical procedure was done and patients were shifted to neonatal intensive care unit after the procedure. Neonates were followed-up there for 24 hours. After 24 hours, blood sample was taken before and sent to hematology department for assessment of serum sodium levels. Reports were assessed and level were recorded. If serum sodium level <135 mEq/L, then hyponatremia was noted. Hypernatremia (serum sodium level>145 mEq/L) was also noted. Other complications including edema were also noted. Data analysis will be done by using SPSS software version 25.0. Hyponatremia and complications were calculated as frequency and percentage. Tables and graphs were made to present the data.

Result

In Isotonic saline solution, the mean age of neonates was 6.21 ± 6.19 days. In Hypotonic saline solution, the mean age of neonates was 3.84 ± 3.50 days. In Isotonic saline solution, there were 14 (33.3%) male neonates and 28 (66.7%) female neonates. In Hypotonic saline solution, there were 21 (50%) male neonates and 21 (50%) female neonates. In Isotonic saline solution, the mean weight of neonates was 2.95 ± 0.46 kg. In Hypotonic saline solution, the mean weight of neonates was 2.60 ± 0.47 kg. In Isotonic saline solution, out of 42 neonates, 39 (92.9%) were delivered on term, 2 (4.8%) had preterm birth and 1 (2.4%) had post-term birth. In Hypotonic saline solution, out of 42 neonates, 38 (90.5%) were delivered on term, 3 (7.1%) had preterm birth and 1 (2.4%) had post-term birth. In Isotonic saline solution, 7 (16.7%) neonates were delivered spontaneously through vaginal delivery while 35 (83.3%) were delivered through cesarean section. In Hypotonic saline solution, 16 (38.1%) neonates were delivered spontaneously through vaginal delivery, while 26 (61.9%) were delivered through cesarean section **(Table 1).**

Out of 84 cases, hyponatremia developed in 13 (15.5%) cases, hypernatremia in 9 (10.7%) cases, while 62 (73.8%) neonates maintained normal serum sodium levels **(Figure 1).**

In Isotonic saline solution, hyponatremia was developed in 2 (4.8%) cases, hypernatremia in 9 (21.4%) cases, while 31 (73.8%) neonates maintained normal serum sodium levels. In Hypotonic saline solution, hyponatremia was developed in 11 (26.2%) cases, hypernatremia in 0 (0%) cases, while 31 (73.8%) neonates maintained normal serum sodium levels. The difference in both groups was found to be significant ($p<0.05$). In Isotonic saline solution, edema was noted in 1 (2.4%)

neonate. In Hypotonic saline solution, edema was noted in 9 (21.4%) neonates. The difference in both groups was found to be significant ($p<0.05$) **(Table 2).**

Table 1: Basic characteristics of neonates enrolled in the study

	Group	
	Isotonic saline solution	**Hypotonic saline solution**
n	42	42
Mean Age (in days)	6.21 ± 6.19	3.84 ± 3.50
Gender		
Male	14 (33.3%)	21 (50%)
Female	28 (66.7%)	21 (50%)
Mean Weight (kg)	2.95 ± 0.46	2.60 ± 0.47
Maturity		
Term	39 (92.9%)	38 (90.5%)
Preterm	2 (4.8%)	3 (7.1%)
Post-term	1 (2.4%)	1 (2.4%)
Mode of delivery		
Normal vaginal delivery	7 (16.7%)	16 (38.1%)
Cesarean delivery	35 (83.3%)	26 (61.9%)

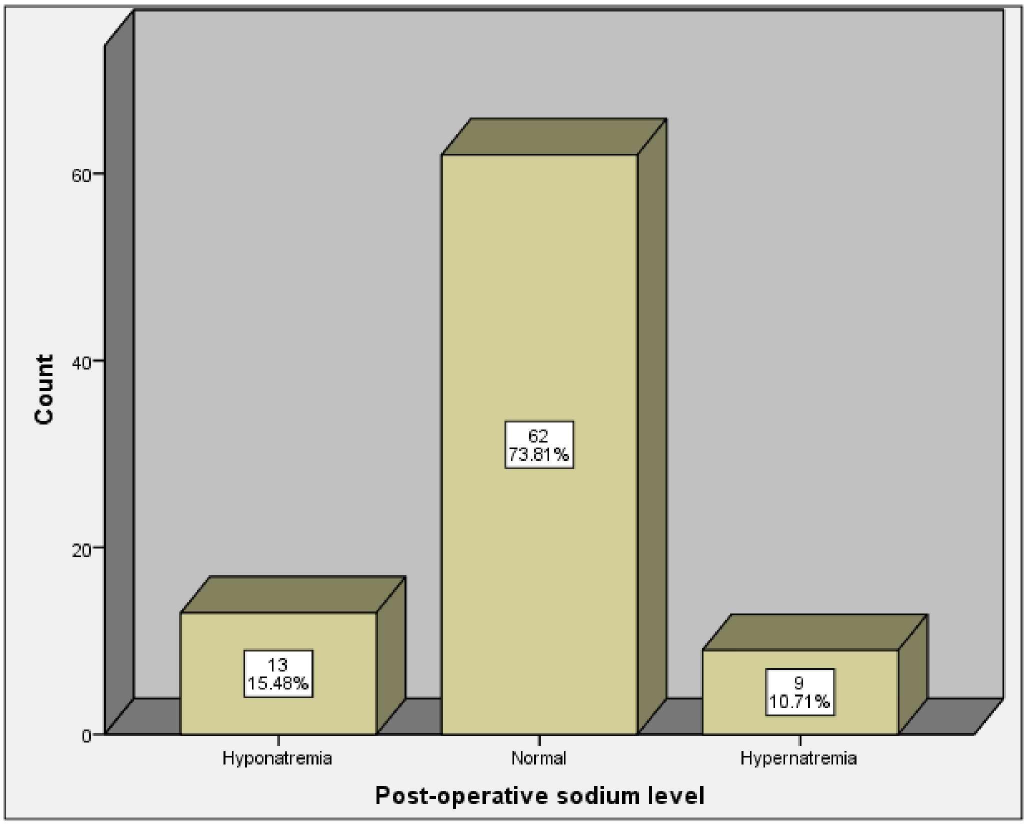

Figure 1: Hyponatremia observed in neonates (n = 84)

Table 2: Comparison of outcome in both groups

		Group		P-value
		Isotonic saline solution	**Hypotonic saline solution**	
n		42	42	
Serum sodium levels	**Hyponatremia**	2 (4.8%)	11 (26.2%)	0.000
	Normal	31 (73.8%)	31 (73.8%)	
	Hypernatremia	9 (21.4%)	0 (0%)	
Complications	**Yes (Edema)**	1 (2.4%)	9 (21.4%)	0.007
	No	41 (97.6%)	33 (78.6%)	

Discussion

Sodium is the primary positively charged ion found outside of cells and plays a crucial role in determining the concentration of solutes in the blood. Thus, maintaining homeostasis is crucial for the maintenance of plasma volume. Furthermore, alterations in plasma volume lead to abnormal blood sodium levels.[13] The regulation of plasma volume is primarily controlled by the antidiuretic hormone, which has a significant impact on sodium balance.[13-14] The primary trigger for the release of antidiuretic hormone under normal physiological circumstances is an elevation in serum osmolarity. Additionally, it is released in reaction to several non-osmotic triggers, including dehydration, stress, and pain.[14] These stimuli often lead to an increase in release of antidiuretic hormone, which in turn decreases the excretion of water and causes dilutional hyponatremia in hospitalized children.[15]

In our trial, we observed that hyponatremia occurred in 13 (15.5%) cases, out of which 2 (4.8%) cases received isotonic saline solution and 11 (26.2%) cases received hypotonic saline solution. Hypernatremia developed in 9 (10.7%) cases, and all those cases were present in isotonic saline solution group, while none of them developed hypernatremia in hypotonic saline solution group. The calculated difference in both groups was significant (p<0.05), and isotonic saline solution was found to be more safe than hypotonic saline solution in maintaining normal serum saline concentration.

Therefore, children who are admitted to the hospital are very susceptible to develop hyponatremia. Due to the decreased concentration of electrolytes in hypotonic solutions compared to plasma, the risk is increased while administering hypotonic intravenous maintenance fluid treatment.[16] On the other hand, isotonic solutions more accurately resemble the sodium content in the blood plasma.[9] Consequently, they are linked to a reduced likelihood of hyponatremia and minimal alterations in blood electrolytes and osmolarity.[17]

McNab et al. ran a study and discovered that those who were given isotonic fluid had a significantly reduced risk of hyponatremia compared to those who did not get it (17% vs 34%; RR 0.48; 95% CI 0.38 to 0.60, good quality evidence). It is uncertain if there is an increased risk of hypernatremia when isotonic fluids are administered (4% vs 3%; RR 1.24; 95% CI 0.65 to 2.38, nine trials, 937 participants, poor quality data), however the absolute number of patients experiencing hypernatremia was modest. The majority of studies included safety limitations in their methodology, which hindered thorough examination of severe adverse events.[18] Robles et al. discovered that after 8 hours, the average serum sodium level was lower in the group that received the hypotonic solution [0.45% saline 134.90 (2.3) mmol/L] compared to the group that received the isotonic solution [0.9% saline 137.98 (2.8) mmol/L] ($P < 0.0001$). The occurrence of hyponatremia was more frequent in the hypotonic groups treated with 0.45% saline (22%) compared to those treated with 0.9% saline (1.9%), with a statistically significant difference ($P = 0.006$). No disparities were seen in terms of additional negative outcomes or duration of hospitalization across the groups.[12]

Kumar et al. ran an experiment in which they evaluated the blood sodium level at various time intervals. The researchers discovered that the occurrence of hyponatremia after 12 hours in children who received half-normal saline was comparable to those who received normal saline (6% vs 4.8%; Relative risk (RR) 1.2; 95% CI 0.3.0-4.8; $p = 0.73$). The occurrence of hyponatremia at 24 hours in children who received half-normal saline was somewhat greater compared to those who received normal saline, but the difference was not statistically significant

(14.3% vs 6%; relative risk 2.6; 95% confidence interval 0.9-7.8; p = 0.07). Their findings indicate that using half-normal saline as a maintenance intravenous fluid does not lead to a substantially higher likelihood of hyponatremia in pediatric kids under the age of 5 who are admitted to general wards.[19]

However, Omiofo et al. performed a separate experiment and documented contradictory findings. The study findings revealed a 4% occurrence of hyponatremia in patients receiving hypotonic maintenance fluid, whereas a 5% occurrence was seen in the isotonic maintenance groups. The occurrence of hyponatremia was similar in individuals who received hypotonic and isotonic intra-operative maintenance fluids (P = 1.000).[20]

A meta-analysis of 33 randomized trials, involving 5049 patients, revealed that isotonic maintenance fluid significantly decreased the risk of mild hyponatremia within both 24 hours or less (RR = 0.38, 95% CI [0.30, 0.48], P < 0.00001; high quality of evidence) and more than 24 hours (RR = 0.47, 95% CI [0.37, 0.62], P < 0.00001; high quality of evidence). The beneficial impact of isotonic fluid was consistent across the majority of analyzed subgroups. The use of isotonic maintenance fluid in newborns substantially raised the likelihood of hypernatremia (relative risk = 3.74, 95% confidence interval [1.42, 9.85], p-value = 0.008). Furthermore, it caused a substantial rise in serum creatinine within 24 hours (mean difference = 0.89, 95% confidence interval [0.84, 0.94], P < 0.00001) and a reduction in blood pH (mean difference = -0.05, 95% confidence interval [-0.08 to -0.02], P = 0.0006). The hypotonic group had lower levels of mean serum sodium, serum osmolarity, and serum chloride during the first 24 hours. The two fluids exhibited similarity in serum potassium levels, duration of hospitalization, blood glucose levels, and the likelihood of negative outcomes.[17]

In our trial, we observed that edema occurred in 10 cases, out of which 1 (2.4%) neonate was from isotonic saline solution groups while 9 (21.4%) neonates were from hypotonic saline solution group. The difference in both groups was found to be significant (p<0.05) and again isotonic saline solution was found to be safer in reducing the risk of postoperative complications than hypotonic saline solution.

The existing data does not support the conventional approach of giving a hypotonic saline solution as a kind of ongoing intravenous fluid treatment for children who are admitted to the hospital. While there is no universally optimal intravenous fluid composition for all children, it seems that an isotonic saline solution is the preferable option for administering maintenance intravenous fluid treatment to the overall pediatric population.[21]

Conclusion

The risk of hyponatremia is higher with hypotonic saline solution wen used as maintenance fluid after surgery in pediatric population. But further trials should be done in local population with large sample size and more electrolytes should be considered to improve outcome of maintenance fluid in neonates to prevent mortality and severe morbidities.

Ethical Consideration

This study has been registered at ClinicalTrials.gov with the international registration number NCT06484608.

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Conflict of interests

All authors declare that they have no conflict of interest

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