“Early Sodium Intake in Preterm Newborns; Randomized Clinical Trial”

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Introduction

Hyponatremia is a common complication among preterm infants, renal losses of sodium contribute to the development of hyponatremia in preterm newborns. Sodium imbalances impact in newborns outcome. There is controversy about the time of initiation and the requirements of sodium in premature infants. Hypothesis: early (24 hours of life) sodium supplementation (5mEq/kg/day) prevents the develop of hyponatremia in preterm infants.

This study is a randomized controlled trial in infants less than 35 weeks gestation admitted to the Newborn Intensive Care Unit at Children Hospital in Saltillo Coahuila Mexico.

Infants receive at 24 hours of life; sodium (5mEq/kg/day) versus less than 1mEq/kg/day. Weight, serum and urine sodium, serum chloride, serum and urine creatinine, serum chloride, bicarbonate and glucose are monitored daily during the first 3 days of life. Patients are assessed for hyponatremia, hypernatremia, weight change, sepsis, necrotizing enterocolitis and intraventricular hemorrhage.

Objectives:

1. Compare the risk of hyponatremia in the first 72hrs of life, in preterm newborns with early sodium intake and late sodium intake.
2. Compare the risk of hypernatremia in the first 72hrs of life, in preterm newborns with early sodium intake and late sodium intake.
3. Assess the change in serum sodium in preterm newborns with early sodium intake and late sodium intake.
4. Assess the weight change in preterm newborns with early sodium intake and late sodium intake.
5. Assess the development of complications (sepsis, necrotizing enterocolitis, intraventricular hemorrhage, mortality) in preterm newborns with early sodium intake and late sodium intake.

Study design and statistical analysis

This study is a randomized controlled trial.
Eligibility criteria:
Preterm infants <35 weeks of gestation.
Less than 24 hours of life.

Exclusion criteria:
Urinary malformations
Congenital abdominal wall defect
Intestinal atresia / obstruction
Congenital heart defect

The eligible patients will be simple randomized in two groups:

1. Comparation: Sodium administration, enteral and/or parenteral less than 1mEq/kg/day starting on day of life one.
2. Intervention: Sodium administration, enteral and/or parenteral of 5mEq/kg/day starting on day of life one.

At admission, gestational age and sex and birth weight will be recorded. Weight will be evaluated every 24 hours for 3 days.

Blood samples will be taken every 24 hours for 3 days to assess serum sodium, creatinine, glucose, sodium bicarbonate and serum chloride levels.

Urine samples will be taken every 24 hours for 3 days to assess urine sodium and urine creatinine levels.

The incidence of hyponatremia, hypernatremia, change of serum sodium and weight change will be evaluated and compared between groups during this time frame (72hrs).

The patients will be following through hospital stay to record the development of sepsis, necrotizing enterocolitis, intraventricular hemorrhage and mortality.

The distribution of variables will be assessed with Shaphiro Wilk test, normally distributed data will be compared with t test or Chi squared test and those with abnormal distribution with Mann-Whitney U test or Fisher exact test. The risk of hyponatremia and hypernatremia will be expressed using relative risk.

The change of serum sodium, creatinine, chloride, sodium bicarbonate, glucose levels and weight will be evaluated using repeated measures ANOVA or Kruskal-Wallis test depending on data distribution.

Exploratory analysis will include sodium balance (according to sodium intake and urinary excretion), urine output and total fluid administration.

IBM SPSS Statistics (IBM Corp. Released in 2013. IBM Statistics for Windows, Version 21.0. Armonk NY: IBM Corp.) will be used for statistical analysis. A p-value <0.05 will be considered statistically significant.

Definitions:

Hyponatremia: Serum sodium <130mEq/L

Hypernatremia: Serum sodium >150mEq/L

Change in serum sodium: The difference between serum sodium (at 48 and 72hrs) and initial serum sodium.

Weight change: The difference between weight (at 24, 48 and 72hrs) and birth weight.

Sepsis: Positive blood culture and/or 5 days of continuous antimicrobial therapy.

Necrotizing enterocolitis: Necrotizing enterocolitis according to Bell staging (II or grater).

Intraventricular hemorrhage: Bleeding into the brain´s ventricular system (intracranial ultrasound).

Mortality: Death during hospitalization.

References

Wang J, Xu E, Xiao Y. Isotonic versus hypotonic maintenance IV fluids in hospitalized children: a meta-analysis. Pediatrics. 2014 Jan;133(1):105-13. doi: 10.1542/peds.2013-2041. Epub 2013 Dec 30.

Bhatia J. Fluid and electrolyte management in the very low birth weight neonate. J Perinatol. 2006 May;26 Suppl 1:S19-21.

Moritz ML, Ayus JC. Hyponatremia in preterm neonates: not a benign condition. Pediatrics. 2009 Nov;124(5):e1014-6. doi: 10.1542/peds.2009-1869. Epub 2009 Oct 26.

Balasubramanian K, Kumar P, Saini SS, Attri SV, Dutta S. Isotonic versus hypotonic fluid supplementation in term neonates with severe hyperbilirubinemia - a double-blind, randomized, controlled trial. Acta Paediatr. 2012 Mar;101(3):236-41. doi: 10.1111/j.1651-2227.2011.02508.x. Epub 2011 Nov 19

Al-Dahhan J, Haycock GB, Nichol B, Chantler C, Stimmler L. Sodium homeostasis in term and preterm neonates. III. Effect of salt supplementation. Arch Dis Child. 1984 Oct;59(10):945-50.

Gawlowski Z, Aladangady N, Coen PG. Hypernatraemia in preterm infants born at less than 27 weeks gestation. J Paediatr Child Health. 2006 Dec;42(12):771-4.

Lönnqvist PA. III. Fluid management in association with neonatal surgery: even tiny guys need their salt. Br J Anaesth. 2014 Mar;112(3):404-6. doi: 10.1093/bja/aet436. Epub 2013 Dec 23.

Oh W. Fluid and electrolyte management of very low birth weight infants. Pediatr Neonatol. 2012 Dec;53(6):329-33. doi: 10.1016/j.pedneo.2012.08.010. Epub 2012 Oct 12. Review.

Hartnoll G, Bétrémieux P, Modi N. Randomised controlled trial of postnatal sodium supplementation on oxygen dependency and body weight in 25-30 week gestational age infants. Arch Dis Child Fetal Neonatal Ed. 2000 Jan;82(1):F19-23.

Hartnoll G, Bétrémieux P, Modi N. Randomised controlled trial of postnatal sodium supplementation on body composition in 25 to 30 week gestational age infants. Arch Dis Child Fetal Neonatal Ed. 2000 Jan;82(1):F24-8.

Lorenz JM, Kleinman LI, Kotagal UR, Reller MD. Water balance in very low-birth-weight infants: relationship to water and sodium intake and effect on outcome. J Pediatr. 1982 Sep;101(3):423-32.

Costarino AT Jr, Gruskay JA, Corcoran L, Polin RA, Baumgart S. Sodium restriction versus daily maintenance replacement in very low birth weight premature neonates: a randomized, blind therapeutic trial. J Pediatr. 1992 Jan;120(1):99-106.

Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R; Parenteral Nutrition Guidelines Working Group; European Society for Clinical Nutrition and Metabolism; European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN); European Society of Paediatric Research (ESPR). 1. Guidelines on Paediatric Parenteral Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). J Pediatr Gastroenterol Nutr. 2005 Nov;41 Suppl 2:S1-87.

Bolisetty S, Osborn D, Sinn J, Lui K; Australasian Neonatal Parenteral Nutrition Consensus Group. Standardised neonatal parenteral nutrition formulations - an Australasian group consensus 2012. BMC Pediatr. 2014 Feb 18;14:48. doi: 10.1186/1471-2431-14-48.