SODIUM CHLORIDE 3%

Newborn use only

2021

Alert	Osmolarity: 1027 mOsm/L.[1] Sodium supplementation is not always appropriate and fluid restriction may be appropriate in the management of hyponatraemia. Treatment should always be tailored to the cause.
Indication	Treatment of hyponatraemia.
Action	Sodium is the major cation of extracellular fluid.
Drug type	Sodium chloride 3% contains 30 g/L sodium chloride, equivalent to 0.5 mmol/mL of sodium.
Trade name	Sodium chloride 3%
Presentation	Sodium chloride 3% – 250mL and 1000 mL.
Dose	**Severe hyponatraemia < 120 mmol/L or symptomatic hyponatraemia** IV: Sodium chloride 3% at 0.5 mmol/kg/hour (1 mL/kg/hour) until symptoms abate or serum sodium ≥ 120 mmol/L.* Then give sodium chloride 3% at 0.15 mmol/kg/hour (0.3 mL/kg/hour) for 48 hours or until desired serum sodium is achieved. Therapeutic goal is to increase serum sodium by 7 mmol/L/day *1 mL/kg sodium chloride 3% will raise serum sodium by approximately 1 mmol/L.[2] **IV supplementation** Start at 2–4 mmol/kg/day and increase as required.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No information. Hepatic impairment – No information.
Maximum dose	
Total cumulative dose	
Route	IV
Preparation	**Not applicable**.
Administration	Can be given undiluted as an infusion, preferably through large vein.
Monitoring	Local IV site for signs of extravasation. Serum sodium as per clinical team's recommendation.
Contraindications	No information.
Precautions	Impaired renal function, cardiac insufficiency, pre-existing oedema with sodium retention.
Drug interactions	No information.
Adverse reactions	Hypernatraemia, volume overload, congestive heart failure, respiratory distress. Hyperchloraemia, hypercalciuria. Disseminated intravascular coagulation (DIC) is associated with inadvertent injections of sodium chloride into blood vessels of the uterus or placenta due to hypernatraemic shock; not reported in infants. Osmotic demyelinating syndrome. Fever. IV site: Extravasation, phlebitis, venous thrombosis.
Compatibility	**IV Fluids:** Glucose 5%, glucose 10%, glucose 5% in sodium chloride 0.9%, glucose 5% in sodium chloride 0.45%, sodium chloride 0.9%, sodium chloride 0.45%. **Y site**: No information.
Incompatibility	**IV Fluids:** Fat emulsion. **Y site**: No information. Amino acid solutions – No information.
Stability	
Storage	Store at room temperature, 20–25°C
Excipients	
Special comments	Osmolarity of undiluted hypertonic sodium chloride is > 1000 mOsm/L, posing the risk of extravasation for peripheral IV solutions.[3,4] Monitor for extravasation when infused peripherally at higher rates.

	Total body water is traditionally calculated as weight x 0.6 in children. Greater total body water content in newborns should be considered and therefore should be calculated as weight x 0.75.[2,5]
Evidence	<u>IV correction for severe and/or symptomatic hyponatraemia</u> The body of evidence to base recommendations in this clinical setting is extremely limited, particularly in neonatal populations. Recommendations are based on expert opinion, which have been extrapolated from adult consensus guidelines[6,7] and take into account specific neonatal safety concerns (see Safety below). In acute hyponatraemia, where the risk of sequelae is greater than that of osmotic demyelination, the correction should be rapid.[8] Aim to increase serum sodium by 1–2 mmol/L per hour until symptoms abate or a safe level of serum sodium is achieved (≥ 120 mmol/L).[9] Once the safe level is achieved, suggested subsequent goals are 6–8 mmol/L in 24 hours, 12–14 mmol/L in 48 hours and 14–16 mmol/L in 72 hours.[10] (LOE IV, GOR C) <u>Sodium deficit calculation</u> Deficit in mmol = (desired sodium – serum sodium) x total body water Total body water is traditionally calculated as weight x 0.6 in children. Greater total body water content in newborns should be considered and therefore should be calculated as weight x 0.75.[2,5] (LOE IV, GOR C) <u>Oral supplementation</u> A randomised, controlled trial of 4 mmol/kg/d of sodium versus placebo from DOL 7 to 35 in infants born 24–31 weeks (53 infants) showed higher serum sodium levels and increased weight gain in the intervention group.[11] A randomised, controlled trial of 4 mmol/kg/d of sodium versus placebo from DOL 4 to 14 in infants born at 29–34 weeks (20 infants) showed higher serum sodium levels and increased weight gain in the intervention group.[12] There are also three case-control studies that report similar findings with respect to serum sodium levels and growth in preterm infants supplemented with oral sodium.[13-15] A systematic review comparing higher versus lower sodium intake for preterm infants is in progress.[16] These findings support the use of oral sodium supplements to correct hyponatraemia and potentially improve growth. (LOE II, GOR B) <u>Safety</u> An historical case-control study identified 42/350 (12%) ELBW NICU admissions with an episode of hyponatraemia (Na < 125 mmol/L [range 113–124]) that lasted > 6 hours (median 1.5 days).[17] Rates of abnormal head ultrasound (IVH or PVL) and abnormal neurological examination were higher in the hyponatraemic group ($p < 0.03$; $p < 0.001$ respectively). Correction ≥ 0.5 mmol/L/h showed a trend toward higher rates of abnormal neurological examination. In paediatric and adult populations, multiple cohort studies and reviews have concluded that in patients with chronic hyponatraemia (≥ 48 hours), neurologic sequelae due to osmotic demyelination are associated with more rapid rates of correction.[7,9] In summary, rapid correction of hyponatraemia may be detrimental to neurological outcome during myelination of the newborn brain.[17] In adult populations, osmotic demyelination syndrome can usually be avoided by limiting correction of chronic hyponatremia to < 10 to 12 mmol/L in 24 hours and to < 18 mmol/L in 48 hours. These estimates should be regarded as approximate limits and not goals of therapy.[7] (LOE IV, GOR C) <u>Osmolarity and Osmolar load</u> A retrospective, matched-cohort study of 352 children ≤ 18 years evaluated the incidence of phlebitis or infiltration associated with peripheral administration of parenteral nutrition with an osmolarity >1000 mOsm/L vs ≤1000 mOsm/L.[18] There were 151 neonates in the study. There were no differences between patients who did or did not develop adverse events in terms of age or weight. Administration of PPN with osmolarity >1000 mOsm/L vs ≤ 1000 mOsm/L significantly increased infiltration (17% vs 7%; odds ratio [OR], 2.47; 95% confidence interval [CI], 1.24–4.94; $p = 0.01$) and the combined composite end point of phlebitis or infiltration (45% vs 34%; OR, 1.65; 95% CI, 1.07–2.54; $p = 0.02$). In multivariate analysis, osmolarity >1000 mOsm/L was an independent risk factor for developing complications (OR, 1.67; 95% CI, 1.08–2.52; $p = 0.02$).[18] (LOE III, GOR C)

	A prospective, observational study in adults suggests that osmolar load (i.e. number of milliosmoles per hour, calculated as osmolarity x infusion rate) is a better predictor than osmolarity alone for phlebitis.[19] They found an osmolarity rate of 84–99 mOsm/hour was associated with a 4–27% rate of phlebitis. They did not report on other injuries such as extravasation. The infusion rates suggested in our formulary have low osmolar load and are considered to carry minimal risk of phlebitis (Consensus opinion).
Practice points	
References	1. Micromedex solutions. Accessed on 18 July 2017. 2. Zieg J. Evaluation and management of hyponatraemia in children. Acta Paediatr 2014;103:1027-34. 3. Dugan S, Le J, Jew RK. Maximum tolerated osmolarity for peripheral administration of parenteral nutrition in pediatric patients. Journal of Parenteral and Enteral Nutrition. 2014 Sep;38(7):847-51. 4. Timmer JG, Schipper HG. Peripheral venous nutrition: the equal relevance of volume load and osmolarity in relation to phlebitis. Clinical Nutrition. 1991 Apr 1;10(2):71-5. 5. Modi N, Bétrémieux P, Midgley J, Hartnoll G. Postnatal weight loss and contraction of the extracellular compartment is triggered by atrial natriuretic peptide. Early Hum Dev 2000;59:201-8. 6. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol 2014; 170: G1–47. 7. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. Am J Med 2007;120:S1-21. 8. Marcialis MA, Dessi A, Pintus MC, Irmesi R, Fanos V. Neonatal hyponatremia: differential diagnosis and treatment. J Matern Fetal Neonatal Med 2011;24:75-9. 9. Assadi F. Hyponatremia: a problem-solving approach to clinical cases. J Nephrol. 2012;25(4):473-80. 10. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. Semin Nephrol 2009;29:282-99. 11. Isemann B, Mueller EW, Narendran V, Akinbi H. Impact of Early Sodium Supplementation on Hyponatremia and Growth in Premature Infants: A Randomized Controlled Trial. Jpen: Journal of Parenteral & Enteral Nutrition 2016;40:342-9. 12. Vanpee M, Herin P, Broberger U, Aperia A. Sodium supplementation optimizes weight gain in preterm infants. Acta Paediatr. 1995;84:1312-1314. 13. Sulyok E, Rascher W, Baranyai Z, Ertl T, Kerekes L. Influence of NaCl supplementation on vasopressin secretion and water excretion in premature infants. Biology of the Neonate 1993;64:201-8. 14. Ayisi RK, Mbiti MJ, Musoke RN, Orinda DA. Sodium supplementation in very low birth weight infants fed on their own mothers milk, I: effects on sodium homeostasis. East Afr Med J. 1992;69:591-595. 15. Al-Dahhan J, Haycock GB, Nichol B, Chantler C, Stimmler L. Sodium homeostasis in term and preterm neonates. Arch Dis Child 1984;59:945-950. 16. Chan W, Chua MYK, Teo E, Osborn DA, Birch P. Higher versus lower sodium intake for preterm infants (Protocol). Cochrane Database of Systematic Reviews 2017: CD012642. 17. Bhatty S, Tsirka A, Bigini-Quinn P, La Gamma EF. Does Hyponatremia Result in Pontine Myelinolysis and Neurological injury in Extremely Low Birth Weight (ELBW) Micropremies?† 825. Pediatric Research 1997;41:140. 18. Clark E, Giambra BK, Hingl J, Doellman D, Tofani B, Johnson N. Reducing risk of harm from extravasation: a 3-tiered evidence-based list of pediatric peripheral intravenous infusates. Journal of Infusion Nursing 2013;36:37-45. 19. Pereira-da-Silva L, Henriques G, Videira-Amaral JM, Rodrigues R, Ribeiro L, Virella D. Osmolality of solutions, emulsions and drugs that may have a high osmolality: aspects of their use in neonatal care. The Journal of Maternal-Fetal & Neonatal Medicine 2002;11:333-338.

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