

SODIUM CHLORIDE 23.4%

Newborn use only

2020

Alert	Osmolarity: Sodium chloride 23.4%: 8010 mOsm/L ¹ . High risk of extravasation if administered undiluted. 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					
Drug type	Sodium chloride 23.4% contains 234 g/L sodium chloride, equivalent to 4 mmol/mL of sodium.				
Trade name	Sodium chloride 23.4%.				
Presentation	Sodium chloride 23.4% – 10 mL vial. Can be used for both IV and oral routes.				
Dose	<p><u>Severe hyponatraemia < 120 mmol/L or symptomatic hyponatraemia</u></p> <p>IV: CAUTION—CANNOT BE GIVEN UNDILUTED. REFER TO PREPARATION/DILUTION SECTION FOR DETAILS Infuse sodium chloride at 0.4 mmol/kg/hour until symptoms abate or sodium ≥ 120 mmol/L Then infuse sodium chloride at 0.15 mmol/kg/hour for 48 hours or until desired sodium is achieved Therapeutic goal is to increase sodium by 7 mmol/L/day.</p> <p><u>IV supplementation</u> Start at 2–4 mmol/kg/day and increase as required</p> <p><u>Oral supplementation</u> Start at 2–4 mmol/kg/day (0.5–1 mL/kg/day) and increase as required, divided into 3–12 doses.</p>				
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No information. Hepatic impairment – No information.				
Maximum dose					
Total cumulative dose					
Route	IV, PO				
Preparation	<p>IV infusion: Draw up 5 mL (20 mmol sodium) of 23.4% sodium chloride and add 45 mL of water for injection to make a final volume of 50 mL with a final concentration of 0.4 mmol/mL. Infusion at 1 mL/kg/hour = 0.4 mmol/kg/hour (9.6 mmol/kg/day).</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Infusion Strength</th> <th style="text-align: center;">Prescribed amount</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">1 mL/kg/hour = 0.4 mmol/kg/hour</td> <td style="text-align: center;">5 mL of sodium chloride 23.4% and make up to 50 mL of water for injection</td> </tr> </tbody> </table> <p style="text-align: center;">*1 mL/kg of 0.4 mmol/mL of sodium chloride will raise serum sodium by 0.8 mmol/L.²</p> <p>Oral: Sodium chloride 23.4% vials or oral preparation supplied by pharmacy.</p>	Infusion Strength	Prescribed amount	1 mL/kg/hour = 0.4 mmol/kg/hour	5 mL of sodium chloride 23.4% and make up to 50 mL of water for injection
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Administration	<p>IV: Infusion only. Must be diluted as above prior to IV infusion.</p> <p>Oral: To be given mixed with feeds. Divide the daily oral dose into 3–12 doses, aiming for a small but practical volume.</p>				
Monitoring	IV: Local IV site for signs of extravasation. Oral: Signs of gastric irritation. Serum sodium as per clinical team’s recommendation.				
Contraindications	Oral: Infants who are not any enteral nutrition, acute gastrointestinal illness including ileus, necrotising enterocolitis, intestinal obstruction.				
Precautions	Impaired renal function, cardiac insufficiency, pre-existing oedema with sodium retention.				
Drug interactions	No information.				

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Adverse reactions	<p>Hypernatraemia, volume overload, congestive heart failure, respiratory distress.</p> <p>Hyperchloraemia, hypercalciuria.</p> <p>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.</p> <p>Osmotic demyelinating syndrome.</p> <p>Fever</p> <p>IV site: Extravasation, phlebitis, venous thrombosis.</p> <p>Oral: Gastric irritation.</p>
Compatibility	<p>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%.</p> <p>Y site: No information.</p>
Incompatibility	<p>IV Fluids: Fat emulsion.</p> <p>Y site: No information.</p> <p>Amino Acid solutions – No information.</p>
Stability	<p><u>Oral solution:</u> Supplied by pharmacy has 7-day expiry from manufacture and 24 hours after opening.</p> <p><u>Vials:</u> 24-hour expiry after opening</p>
Storage	<p>IV: Store at room temperature, 20–25°C.</p> <p>Oral solution: Refrigerate (2–8°C)</p> <p>Vials: Store at room temperature, 20–25°C, once opened refrigerate vials ((2–8°C)</p>
Excipients	
Special comments	<p>Osmolarity of undiluted hypertonic sodium chloride is > 1000 mOsm/L, posing the risk of extravasation for peripheral IV solutions.^{3,4} So, local consensus was to bring the osmolarity of IV preparation to 2.4% sodium chloride that has 0.4 mmol/L of sodium and an estimated osmolality of 855 mOsm/L.</p> <p>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}</p>
Evidence	<p><u>IV correction for severe and/or symptomatic hyponatraemia</u></p> <p>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</p> <p>Aim to increase sodium by 1–2 mmol/L per hour until symptoms abate or a safe level of 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)</p> <p>Dosage and infusion rate recommendations in this formulary are extrapolated from the rate of rise expected with sodium chloride 3%² and are as follows:</p> <p>0.5 mmol/mL of sodium chloride (i.e. sodium chloride 3%), when administered at 1 mL/kg, will raise serum sodium by 1 mmol/L.</p> <p>0.4 mmol/mL of sodium chloride (i.e. diluted sodium chloride in this formulary), when administered at 1 mL/kg, will raise serum sodium by 0.8 mmol/L.</p> <p><u>Sodium deficit calculation</u></p> <p style="text-align: center;">Deficit in mmol = (desired sodium – serum sodium) x total body water</p> <p>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)</p> <p><u>Oral supplementation</u></p> <p>A randomised, controlled trial of 4 mmol/kg/d (0.4 mL/kg per dose of 2.5 mmol/mL sodium chloride) of sodium versus placebo from DOL 7 to 35 in infants born 24–31 weeks (53 infants) showed higher sodium levels and increased weight gain in the intervention group.¹¹ A randomised, controlled trial of 4 mmol/kg/d (concentration not specified) of sodium versus placebo from DOL 4 to 14 in infants born at 29–34 weeks (20 infants) showed higher 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 sodium levels and growth in preterm infants supplemented with oral sodium.¹³⁻¹⁵ A systematic review comparing</p>

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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)

Safety

An historical, case-control study identified 42/350 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 hyponatremic 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 hyponatraemia 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)

Osmolarity and Osmolar load

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 vs ≤ 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 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

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	<p>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. <i>East Afr Med J.</i> 1992;69:591-595.</p> <p>15. Al-Dahhan J, Haycock GB, Nichol B, Chantler C, Stimmler L. Sodium homeostasis in term and preterm neonates. <i>Arch Dis Child</i> 1984;59:945-950.</p> <p>16. Chan W, Chua MYK, Teo E, Osborn DA, Birch P. Higher versus lower sodium intake for preterm infants (Protocol). <i>Cochrane Database of Systematic Reviews</i> 2017: CD012642.</p> <p>17. Bhatti 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. <i>Pediatric Research</i> 1997;41:140.</p> <p>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. <i>Journal of Infusion Nursing</i> 2013;36:37-45.</p> <p>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. <i>The Journal of Maternal-Fetal & Neonatal Medicine</i> 2002;11:333-338.</p>
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