Calcium chloride 10%

Newborn Use only

2021

Alert	Multiple forms of calcium exist with varying amounts of elemental calcium expressed in varying units. Therefore, careful attention is required in prescription and administration of calcium to avoid over- or under-dosing. **Conversion factor for elemental Ca: 1 mg = 0.02 mmol = 0.05 mEq.** **Prescribe calcium in mmol/kg/dose (not in mL/kg/dose)** Calcium can slow the heart rate and precipitate arrhythmias. In cardiac arrest, calcium may be given by rapid intravenous injection. In the presence of a spontaneous circulation give it slowly. Do not give calcium solutions and sodium bicarbonate simultaneously by the same route to avoid precipitation. Calcium chloride 10% may be preferred over calcium gluconate 10% for rapid IV administration.
Indication	Asymptomatic or symptomatic hypocalcaemia. Hyperkalaemia. Exchange transfusion. Magnesium toxicity. Calcium channel blocker overdose. Supplementation in parenteral nutrition (beyond the scope of this guideline).
Action	Calcium is essential for the functional integrity of the nervous, muscular, skeletal and cardiac systems and for clotting function. It antagonises the cardiotoxic effects (arrhythmias) of hyperkalaemia, hypermagnesaemia and calcium channel blockers.
Drug Type	Mineral.
Trade Name	Calcium Chloride Injection (Phebra) 10%
Presentation	Calcium chloride 10% 10 mL vial (1 mL contains 100 mg calcium chloride equivalent to 0.68 mmol of elemental calcium).
Dosage	**Prescribe calcium in mmol/kg/dose (not in mL/kg/dose)** **Maintenance IV calcium therapy – IV intermittent** Elemental Calcium – 0.15 mmol/kg/dose 4-6 hourly (maximum daily dose 3 mmol/kg/day). Titrate to serum calcium levels **Hypocalcaemia, hyperkalaemia, magnesium toxicity, calcium channel blocker overdose (All may lead to cardiac arrest)** IV or IO: Elemental Calcium - 0.15 mmol/kg (= 0.2mL/kg of **UNDILUTED** 10% calcium chloride). Repeat as necessary. **Exchange transfusion**: Administer if hypocalcaemia: IV: Elemental calcium 0.23 mmol/kg (=0.3mL/kg of **UNDILUTED** 10% calcium chloride) Repeat as necessary.
Maximum Dose	IV – 3 mmol/kg/day21
Route	IV (via a central line where possible) IO Oral (see separate guideline 'Calcium- ORAL').
Preparation	**Calcium Chloride – IV intermittent** Draw up 1.5 mL (1.02 mmol of elemental calcium) and add 8.5 mL sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a concentration of 0.1 mmol/mL. Infuse dose over 10–60 minutes via a central line (if possible). **Calcium Chloride – cardiac arrest** Infuse undiluted over 5 – 10 minutes via a central line (if possible).
Administration	**Calcium chloride – IV intermittent** In cardiac arrest, calcium may be given by rapid intravenous injection. In the presence of a spontaneous circulation give it slowly. Infuse dose over 10–60 minutes (5-10 minutes in cardiac arrest) via a central line (if possible and compatibilities permit). If NO central access is available, consult the Neonatologist on service before administering via peripheral route. If administering peripherally give via a large vein. In poorly perfused patients, consider diluting the infusion further (two-fold) and infuse over at least TWO hours.

	MUST NOT be injected intra-arterially, intramuscularly or subcutaneously.
Monitoring	Continuous ECG monitoring to monitor heart rate and rhythm (stop infusion if HR < 100 bpm). Measurement of ionised calcium preferred over total or corrected calcium concentration. Blood gas machines measure ionised calcium directly and are more accurate than the main pathology laboratory which calculates the ionised calcium from a complex formula. Observe IV tubing for precipitates. Observe IV insertion site for extravasation. Correct hypomagnesaemia if present.
Contraindications	Caution in patients with renal or cardiac impairment.
Precautions	Do not give calcium solutions and sodium bicarbonate simultaneously by the same route to avoid precipitation. Ensure IV calcium is administered at a different time to phosphates, carbonates, sulfates or tartrates (precipitates can occur).
Drug Interactions	Ceftriaxone (may cause insoluble precipitates and can be fatal), digoxin (serious risk of arrhythmia and cardiovascular collapse), thiazide diuretics (increased risk of hypercalcaemia), ketoconazole (decreased ketoconazole effect).
Adverse Reactions	Rapid administration is associated with bradycardia or asystole. Rash, pain, burning at injection site, cutaneous necrosis with extravasation (give via central line unless otherwise instructed by a neonatologist) Nephrolithiasis with long term use. Gastric irritation, diarrhoea and NEC have occurred during oral therapy with hyperosmolar preparations (must be diluted if used orally. See separate guideline Calcium – ORAL)
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9% Y-site: Aciclovir, adrenaline (epinephrine) hydrochloride, amikacin, aminophylline, amiodarone, atropine, azithromycin, benzylpenicillin (penicillin G), calcium gluconate, cefotaxime, ceftaroline fosamil, clindamycin, ciclosporin, dexmedetomidine, digoxin, dobutamine, dopamine, erythromycin lactobionate, esmolol, famotidine, fentanyl citrate, fluconazole, furosemide, ganciclovir, gentamicin, heparin, insulin (regular), linezolid, lorazepam, metronidazole, midazolam, morphine sulfate, noradrenaline (norepinephrine), phenobarbital sodium, piperacillin-tazobactam, potassium acetate, potassium chloride, rocuronium, sodium nitroprusside, suxamethonium, vancomycin, vecuronium bromide, verapamil.
Incompatibility	Fluids: Lipid emulsion. For TPN solutions: No information; seek advice from TPN manufacturer. Y-site: amphotericin B conventional colloidal, amphotericin B lipid complex, amphotericin B liposome, ampicillin, azathioprine, , cefazolin, ceftazidime, ceftriaxone, dexamethasone, diazepam, diazoxide, folic acid, foscarnet, haloperidol lactate, hydralazine, hydrocortisone sodium succinate, indomethacin, ketorolac, magnesium sulfate, meropenem-vaborbactam, methylprednisolone sodium succinate, pantoprazole, phenytoin sodium, phosphate salts, propofol, sodium bicarbonate, thiopentone. **Do not mix with any medication that contains phosphates, carbonates, sulfates or tartrates.**
Stability	IV diluted solution: Do not use if discoloured, cloudy, turbid or if a precipitate is present. Discard remaining solution after use.
Storage	Ampoule: Store below 25°C.
Special Comments	Hypocalcaemia defined as a serum total calcium concentration below 1.875 mol/L [7.5 mg/dL] or ionized calcium less than 1.2 mmol/L.[1] Blood gas machines measure ionised calcium directly and are more accurate than the main pathology laboratory which calculates the ionised calcium from a complex formula. Corrected calcium is calculated (when albumin < 40 or > 45) by the formula: Measured Ca (mmol/L) + (40 – albumin (g/L) x 0.025)

Consider use of hyaluronidase for treatment of extravasation injuries

Calcium salt equivalents of elemental calcium

Salt	***Elemental Ca***		
Calcium chloride 10% 1 mL	1.36 mEq	27.3 mg	0.68 mmol
Calcium gluconate 10% 1 mL	0.46 mEq	9.3 mg	0.22 mmol[18]
Salt 1g			
Calcium Acetate	12.6 mEq	253 mg	6.30 mmol
Calcium Carbonate	19.9 mEq	400 mg	9.96 mmol
Calcium Citrate	10.5 mEq	211 mg	5.26 mmol
Calcium Chloride	13.6 mEq	273 mg	6.80 mmol
Calcium Glubionate	3.29 mEq	66 mg	1.64 mmol
Calcium Gluceptate	4.08 mEq	82 mg	2.04 mmol
Calcium Gluconate	4.65 mEq	93 mg	2.32 mmol

Evidence summary

Hypocalcaemia:

Hypocalcaemia may be defined as a serum total calcium concentration <1.875 mmol/L (7.5 mg/dL) or ionized calcium < 1.2 mmol/L.[1] Calcium concentrations decrease transiently after birth.[2-4] Early neonatal hypocalcaemia occurs within the first 3 days of life and is common in premature infants with 26% to 50% having levels < 1.75 mmol/L (7 mg/dL).[2-4] Most infants will be asymptomatic, with hypocalcaemia detected only on routine chemistries. They may present with symptoms of neuromuscular irritability including tremulousness, tetany, exaggerated startle response, seizures and laryngospasm, and nonspecific symptoms such as apnea.[1, 3]

Efficacy:

Treatment of hypocalcaemia: In normocalcaemic infants, a randomised trial of calcium chloride 10% (2.5 mg/kg) vs calcium gluconate 10% (7.5 mg/kg) reported an equal effect on calcium concentrations.[5] However, in 49 critically ill, hypocalcaemic infants (age 1 day to 17 years), calcium chloride 0.136 mEq/kg per dose resulted in a greater increase in ionised calcium and blood pressure than calcium gluconate 0.136 mEq/kg per dose. The group receiving calcium chloride had an increase in MAP of nearly 6 mm Hg ($p < 0.05$). No change in blood pressure was seen in the group receiving calcium gluconate.[6] In 104 newborns with late symptomatic hypocalcaemia after artificial feeding with a full-cream evaporated milk were randomly allocated to calcium gluconate 10% 10 ml orally vs phenobarbitone 75 mg 6-hourly orally for 48 hours vs magnesium sulphate 50% 0.2 mL/kg intramuscularly on two occasions 12 hourly. The plasma calcium levels rose in all groups, but infants treated with magnesium sulphate had higher plasma-calcium concentrations after 48 hours' treatment and fewer convulsions during and after the treatment period.[7]

Prevention of hypocalcaemia: In preterm and sick newborn infants, the addition of calcium gluconate 10% at 4 ml/kg/day [0.93 mmol/day calcium] to maintenance fluids for 120 hours resulted in a reduction in hypocalcaemia incidence (15% vs 48% ionised Ca <0.7 mmol/l) but an increased incidence of extravasation with tissue damage (35% vs 10%). The benefit of intravenous calcium was short lived and associated with a significant risk of local tissue necrosis.[8]

Recommendation:

Routine addition of calcium to maintenance fluids cannot be recommended in high risk babies.[8](LOE II GOR C)

Treatment of newborns with acute or symptomatic hypocalcaemia is accomplished best by the intravenous infusion of calcium salts - 10% calcium gluconate (9.3 mg/mL of elemental calcium) is used most commonly. In asymptomatic newborns, treatment is indicated when the total serum calcium concentration < 1.5 mmol/L (6 mg/dL) in the preterm infant and less than <1.75 mmol/L (7 mg/dL) in the term infant. Calcium supplementation can be given either by the intravenous or oral route, depending on the clinical status of the infant. [1] [Expert opinion].

Treatment in cardiac arrest: Calcium is not commended for use in neonatal resuscitation by ILCOR or ANZCOR.[9, 10] Evidence from three LOE 2 studies in children and five LOE 5 adult studies failed to document an improvement in survival to hospital admission, hospital discharge, or favourable

	neurological outcome when calcium was administered during cardiopulmonary arrest in the absence of documented hypocalcaemia, calcium channel blocker overdose, hypermagnesaemia or hyperkalaemia. [11, 12] [Expert Consensus Opinion] ***ANZCOR Paediatric recommendation:*** Calcium may be used as an inotropic or vasopressor but it has no place in the management of an arrhythmia unless it is caused by hyperkalaemia, hypocalcaemia, hypermagnesaemia or calcium channel blocker. It should not be given routinely at a cardiac arrest and is associated with worse outcome. [11] [Expert Consensus Opinion] **Arrhythmia caused by hyperkalaemia, hypocalcaemia or hypermagnesaemia, or hypotension caused by calcium channel blocker:** In a case series, extremely premature infants with arrhythmia secondary to hyperkalaemia were all initially successfully treated with an intravenous bolus of calcium (dose not reported). [13, 14] ***ANZCOR Paediatric guideline:*** Calcium (0.15 mmol/kg) is the antidote to hypotension caused by a calcium channel blocker.[9] The intravenous or intraosseous dose is 0.2mL/kg of 10% calcium chloride or 0.7mL/kg of 10% calcium gluconate. [11] [Expert Consensus Opinion] **Exchange transfusion:** Exchange transfusion with blood stored in citrate causes a fall in ionised calcium concentrations.[15, 16] Current supplies of Australian Red Cross Blood Service whole blood contain citrate, whereas packed red cells contain saline, adenine, glucose and mannitol. A quasi-random trial of 30 infants undergoing exchange transfusion for hyperbilirubinaemia with CPD stored whole blood with intervention group receiving 1 mL 10% calcium gluconate for every 100 mL blood reported the intervention group had a significant increase in total and ionised calcium whereas control group had a fall in total and ionised calcium. However, the difference was not clinically important.[17] Conclusion: A systematic review concluded there is no good-quality evidence to support or reject continual use of calcium during exchange transfusion with citrated blood.[18] **Safety:** The addition of calcium gluconate 10% at 4 ml/kg/day [0.93 mmol/day calcium] to intravenous maintenance fluids increased incidence of extravasation with tissue damage (35% vs 10%).[8] Calcium can slow the heart rate and precipitate arrhythmias. In cardiac arrest, calcium may be given by rapid intravenous injection. In the presence of a spontaneous circulation give it slowly. Do not give calcium solutions and sodium bicarbonate simultaneously by the same route to avoid precipitation.[19]
References	1. Cote' CJ, Drop LJ, Daniels AL, Hoaglin DC. Calcium chloride versus calcium gluconate: comparison of ionization and cardiovascular effects in children and dogs. Anesthesiology 1987;66(4):465-70. 2. MHRA Public Assessment Report. Calcium gluconate injection 10% in 10 ml glass containers: risk of aluminium exposure. September 2010 3. Maisels MJ, Li TK, Piechocki JT, Werthman MW: The effect of exchange transfusion on serum ionized calcium. Pediatrics 1974; 53:683–686. 4. Wieland P, Duc G, Binswanger U, Fischer JA. Parathyroid hormone response in newborn infants during exchange transfusion with blood supplemented with citrate and phosphate: effect of iv calcium. Pediatr Res 1979;13(9):963-8.) 5. Greer FR. Calcium and Phosphorus and the Preterm Infant. NeoReviews 2016;17(4): e195-e202; DOI: 10.1542/neo.17-4-e195 6. Nelson N, Finnstrom O. Blood exchange transfusions in newborns, the effect on serum ionized calcium. Early Human Development 1988;18(2-3):157-64. 7. Scott SM, Ladenson JH, Aguanna JJ, Walgate J, Hillman LS. Effect of calcium therapy in the sick premature infant with early neonatal hypocalcemia. J Pediatr 1984;104(5):747-51. 8. Porcelli PJ Jr, Oh W. Effects of single dose calcium gluconate infusion in hypocalcemic preterm infants. Am J Perinatol 1995;12(1):18-21. 9. Brown DR, Salsburey DJ. Short-term biochemical effects of parenteral calcium treatment of early-onset neonatal hypocalcemia. J Pediatr 1982;100(5):777-81. 10. 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;41 Suppl 2:S1-87..

	11. Agostoni C, Buonocore G, Carnielli VP, De Curtis M, Darmaun D, Decsi T, Domellof M, Embleton ND, Fusch C, Genzel-Boroviczeny O, Goulet O, Kalhan SC, Kolacek S, Koletzko B, Lapillonne A, Mihatsch W, Moreno L, Neu J, Poindexter B, Puntis J, Putet G, Rigo J, Riskin A, Salle B, Sauer P, Shamir R, Szajewska H, Thureen P, Turck D, van Goudoever JB, Ziegler EE, ESPGHAN Committee on Nutrition. Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr 2010;50(1):85-91. 12. Christmann V, de Grauw AM, Visser R, Matthijsse RP, van Goudoever JB, van Heijst AF. Early postnatal calcium and phosphorus metabolism in preterm infants. J Pediatr Gastroenterol Nutr 2014;58(4):398-403. 13. 16. Calcium chloride – Micromedex. Accessed online 24/09/2021. 17. Calcium gluconate – Micromedex. Accessed online 24/09/2021. 18. Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia 2014. Accessed on 24/09/2021. 19. Calcium equivalents. http://www-users.med.cornell.edu/~spon/picu/calc/cacalc.htm. Accessed on 7 06 2016 20. Smits-Wintjens VEHJ, Rath MEA, van Zwet EW, Oepkes D, Brand A, Walther FJ, Lopriore E. Neonatal morbidity after exchange transfusion for red cell alloimmune hemolytic disease. Neonatology 2013;103:141–147. 21. Koletzko B, Goulet O, Hunt J, Krohn K, Shamir R. 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). Journal of pediatric gastroenterology and nutrition. 2005;41 Suppl 2:S1-87.

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