Calcium Gluconate 2018

Newborn Use only

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. Calcium gluconate in glass vials should not be used for repeated or prolonged treatment due to the high aluminium content.
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 Gluconate Injection [Phebra] 10% injection (calcium 0.22 mmol/mL)
Maximum Dose	3 mmol/kg/day[25]
Presentation	Calcium gluconate 10% 10 mL vial contains 0.22 mmol/mL of elemental calcium.[23]
Dosage/Interval	**Hypocalcaemia, hyperkalaemia, magnesium toxicity, calcium channel blocker overdose** IV or IO: Elemental Calcium - 0.15 mmol/kg (= 0.7mL/kg of **UNDILUTRED** 10% calcium gluconate). Repeat as necessary. **Maintenance IV calcium therapy – Titrate to serum calcium levels** IV bolus: Elemental Calcium – 0.15 mmol/kg/dose 4-6 hourly (maximum daily dose 3 mmol/kg/day) **Exchange transfusion: Administer if hypocalcaemia:** **IV:** Elemental calcium 0.23 mmol/kg (= 1 mL/kg of **UNDILUTED** Calcium gluconate 10%); repeat as necessary.
Route	IV (via a central line where possible). Oral (see separate guideline 'Calcium- ORAL')
Preparation/Dilution	**Calcium gluconate – IV intermittent** Draw up 4.5 mL (1.0 mmol) and add 5.5 mL of sodium chloride 0.9%, glucose 5% or glucose 10% 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 gluconate – cardiac arrest (secondary to hyperkalaemia, hypocalcaemia, hypermagnesaemia or calcium channel blocker)** Infuse undiluted over 5 – 10 minutes via a central line (if possible).
Administration	**Calcium gluconate – IV intermittent** In cardiac arrest secondary to hypocalcaemia, hyperkalaemia, magnesium toxicity or calcium channel blocker overdose, 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 calcium. 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%, glucose 10%, Hartmann's, sodium chloride 0.9% Y-site: Amifostine, amiodarone, aztreonam, bivalirudin, ceftaroline fosamil, cisatracurium, dexmedetomidine, doripenem, filgrastim, granisetron, heparin sodium, hydrocortisone sodium succinate, labetalol, linezolid, midazolam, milrinone, piperacillin-tazobactam (EDTA-free), potassium chloride, remifentanil.
Incompatibility	Fluids: Fat emulsion Y-site: Adrenaline (epinephrine) hydrochloride, cefalotin, ceftriaxone, clindamycin, dexamethasone, dobutamine, flucloxacillin, fluconazole, foscarnet, indometacin, methylprednisolone sodium succinate, metoclopramide, mycophenolate mofetil, sodium bicarbonate, thiopentone, carbonate, phosphate and sulfate salts. **Do not mix with any medication that contains phosphates, carbonates, sulfates or tartrates.**
Stability	Calcium gluconate is a supersaturated solution and may precipitate in the vial at room temperature. Inspect the vial before use. 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) + 0.025 x (40 – albumin (g/L))

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[23]
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%). Calcium gluconate solution in glass containers contains almost 200 times more aluminium than calcium gluconate in plastic containers, due to the solution leaching aluminium from the glass. The Paediatric Medicines Expert Advisory Group recommended that these products should no longer be used for repeated or prolonged treatment of children or those with impaired renal function. [19] 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.[20]

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