

Calcium Chloride

Calcium chloride dihydrate 1000 mg/10 mL Solution for Injection

Presentation

Calcium Chloride Injection is a clear, colourless, sterile solution of calcium chloride dihydrate in Water for Injection, with a pH of between 5.0 and 8.0. Calcium Chloride Injection is available in 10 mL vials containing 1,000 mg calcium chloride dihydrate,. Each gram of calcium chloride dihydrate represents approximately 6.8 mmol (13.6 mEq) calcium and 13.6 mmol (13.6 mEq) chloride. Each mL of the 10 mL vial contains 0.68 mmol (1.36 mEq) calcium.

Uses

Actions

Calcium is essential for the maintenance of the functional integrity of the nervous, muscular and skeletal systems, and cell membrane and capillary permeability. This cation is an important activator in many enzymatic reactions and is essential to a number of physiological processes including the transmission of nerve impulses; contraction of cardiac, smooth and skeletal muscles; renal function; respiration; and blood coagulation. Calcium also plays a regulatory role in the release and storage of neurotransmitters and hormones, in the uptake and binding of amino acids, in cyanocobalamin (vitamin B12) absorption and in gastrin secretion.

The calcium of bone is in constant exchange with the calcium of plasma. Plasma calcium concentration is kept within narrow limits by an endocrine control mechanism involving parathyroid hormone, calcitonin and Vitamin D. Under the influence of this control mechanism, calcium may be released from bone if plasma calcium decreases, and may be sequestered into bone if plasma calcium rises. Thus, on a chronic basis, normal mineralisation of bone requires adequate amounts of total body calcium.

Pharmacokinetics

The normal concentration range of calcium in plasma is 2.15 - 2.6 mmol/L.

Approximately 99% of total body calcium is contained in the bones and teeth, primarily as hydroxy apatite $[Ca_{10}(PO_4)(OH)_2]$, with small amounts of calcium carbonate and amorphous calcium phosphates. The remaining 1% is contained in other body tissues and fluids.

Approximately 50% of calcium in plasma is in the physiologically active, ionised form, 45% is bound to protein (principally albumin) and 5% is complexed with phosphates, citrates and other anions. For a change in serum albumin of 1 g/dL, the calcium concentration may change about 0.02 mmol/dL. Hyperproteinaemia is associated with increased total serum concentration of calcium; in hyperproteinaemia, total serum calcium concentration decrease. Acidosis results in increased concentration of

ionic calcium, while alkalosis promotes a decrease in the ionic serum calcium concentration.

Approximately 80% of calcium is excreted via faeces and consists of non absorbed calcium and calcium secreted via bile and pancreatic juice into the lumen of the gastrointestinal tract. The remaining 20% of calcium is excreted renally. More than 95% of the calcium filtered by the renal glomeruli is reabsorbed in the ascending limb of the loop of Henle and the proximal and distal tubules. Urinary excretion of calcium is decreased by parathyroid hormone, thiazide diuretics and Vitamin D and increased by calcitonin, other diuretics and growth hormone.

Indications

Parenteral administration of calcium is indicated in the treatment of hypocalcaemia where a rapid increase in plasma calcium is required, such as in hypocalcaemic tetany and tetany due to parathyroid deficiency.

Intravenous calcium is also indicated to antagonise the cardiotoxicity of hyperkalaemia.

Dosage and Administration

Calcium Chloride Injection should not be administered if the solution is cloudy or contains particles. After use, the unused portion of each vial must be discarded. The injection should not be given via the subcutaneous or intramuscular route.

Use in one patient on one occasion only.

Each mL of Calcium Chloride Injection contains approximately 0.68 mmol of calcium ions and 1.36 mmol chloride ions.

To aid in converting: 1 g elemental calcium = 25 mmol elemental calcium = 50 mEq elemental calcium = 3.7 g calcium chloride.

Calcium chloride must be administered slowly via a small needle into a large vein at a rate not exceeding 0.35 - 0.7 mmol (0.7 - 1.4 mEq)/ minute to avoid venous damage and to prevent a high concentration of calcium reaching the heart and causing syncope. The injection should be stopped if the patient experiences pain or redness at the injection site as this may indicate extravasation of the drug.

It is recommended that the patient remain recumbent for a short time after the intravenous injection of calcium. The dose, and dose rate, should be individualised according to the patients condition using frequent determinations of plasma calcium concentrations.

Acute Hypocalcaemia

Adults: An initial dose of 3.5-7 mmol (7-14 mEq) calcium is recommended repeated every 1-3 days as necessary.

Children: An initial dose of 0.5-3.5 mmol (1-7 mEq) calcium/kg is recommended. The dose may be repeated every 1-3 days as necessary.

Hypocalcaemic Tetany

Adults: An initial dose of 2.25-8 mmol (4.6-16 mEq) calcium is recommended, repeated until a response is achieved.

Children: An initial dose of 0.25-0.35 mmol (0.5-0.7 mEq) calcium/kg, is recommended, repeated every 6-8 hours until a response is achieved.

Hyperkalaemia with Secondary Cardiac Toxicity:

Adults: An initial dose of 1.1 -7 mmol (2.25-14 mEq) calcium is recommended. The dose may be repeated after 1-2 minutes if necessary. ECG should be monitored during administration.

Contraindications

The administration of calcium salts is contraindicated where hypercalcaemia, hypercalcuria or severe renal disease are present.

Due to the increased risk of arrhythmias, intravenous calcium administration is contraindicated in patients with ventricular fibrillation.

Administration of calcium salts is also contraindicated in patients with renal calculi, since it may exacerbate the condition, and in patients with sarcoidosis, since it may potentiate the hypercalcaemia which may occur in this condition.

The administration of calcium preparations is also contraindicated in digitalised patients (see Drug Interactions).

Calcium Chloride Injection should never be administered orally to infants since it may result in severe irritation to the gastrointestinal tract.

Warnings and Precautions

Solutions of calcium salts, particularly calcium chloride, are irritant and should not be administered intramuscularly or subcutaneously or into peri vascular tissue, since severe necrosis or sloughing may occur. The injection should be stopped if the patient complains of discomfort. Direct injection into heart tissues should be avoided.

Intravenous calcium chloride must be administered slowly via a small needle into a large vein, at a rate not exceeding 0.3 -0.7 mmol per minute, to avoid venous damage and to prevent a high concentration of calcium reaching the heart and causing syncope. Continuous ECG monitoring should be performed when using calcium salts to antagonise cardiac toxicity associated with hyperkalaemia.

Intravenous administration of calcium chloride may cause vasodilatation, which may result in a moderate fall in blood pressure.

Since calcium chloride is acidifying, caution should be extended in administering intravenous calcium chloride in conditions where acidification may cause problems, such as renal disease, cor pulmonale, respiratory acidosis, or respiratory failure.

Caution should be extended in administering intravenous calcium solutions in conditions where there may be an increased risk of hypercalcaemia, such as chronic renal function impairment, dehydration, or electrolyte imbalance.

Since calcium salts may increase the risk of cardiac arrhythmia, caution should be extended in administering intravenous calcium preparations in patients with cardiac disease.

Laboratory Tests

Careful monitoring of serum calcium levels is advised at frequent intervals during therapy to ensure that normal serum calcium levels are not exceeded. Urinary calcium concentrations may also need to be monitored to avoid hypercalcuria since hypercalcuria can occur in the presence of hypocalcaemia.

Use in Pregnancy

Animal reproduction studies have not been conducted with this product. It is not known whether this product can cause foetal harm when administered to a pregnant woman or can affect reproductive capacity. Therefore, Calcium Chloride Injection is not recommended during pregnancy.

Use in Lactation

Calcium is a normal constituent of breast milk, but it is not known whether calcium chloride is distributed into breast milk. Therefore, Calcium Chloride Injection is not recommended during lactation.

Adverse reactions

Solutions of calcium salts, particularly calcium chloride may cause venous irritation when injected intravenously. Local reactions such as skin redness or rash and pain may indicate extravasation which can lead to severe necrosis. Tissue calcification has also been reported.

Excessive intravenous administration of calcium chloride may cause hypercalcaemia, but this is rare except in cases of chronic renal failure. Adverse reactions associated with hypercalcaemia include: thirst, nausea, vomiting, constipation, polyuria, abdominal pain, muscle weakness, mental disturbances and in severe cases, cardiac arrhythmia and coma.

Too rapid injection of calcium chloride may cause the patient to experience hot flushes, chalky taste, peripheral vasodilation, a decrease in blood pressure and abnormal heart activity (bradycardia, arrhythmia, syncope) (see Dosage and Administration).

If calcium chloride is injected into the myocardium, cardiac tamponade or pneumothorax, leading to ventricular fibrillation, may result.

Drug Interactions

Cardiac Glycosides/Digitalis:

Since the inotropic and toxic effects of intravenous calcium chloride and cardiac glycosides are synergistic, concurrent use may increase the risk of arrhythmia.

Calcium Channel Blockers:

Concurrent use of calcium salts in quantities sufficient to raise the serum calcium concentrations above normal with calcium channel blocking agents may reduce the response to verapamil and probably other calcium channel blockers.

Calcium containing or Magnesium containing Medications:

Concurrent use with other calcium-containing or magnesium containing medications may increase the risk of hypercalcaemia or hypermagnesemia, especially in patients with renal disease.

Neuromuscular Blocking Agents:

Concurrent use with parenteral calcium salts usually reverses the effects of nondepolarising neuromuscular blocking agents; also concurrent use with calcium salts has been reported to enhance or prolong the neuromuscular blocking action of tubocurarine.

Overdosage

Clinical Features

Hypercalcaemia may occur when large doses of calcium salts are given, especially in patients with renal failure. Symptoms associated with hypercalcaemia include: thirst, nausea, vomiting, constipation, polyuria, abdominal pain, muscle weakness, mental disturbances and, in severe cases, cardiac arrhythmia and coma.

Treatment

Plasma concentrations exceeding 2.6 mmol/L are considered hypercalcaemia. Plasma calcium concentrations should be monitored at frequent intervals to guide therapy.

For mild cases of overdose, treatment involves immediately discontinuing administration of calcium chloride and other calcium-containing medications.

For more serious cases, (plasma concentration > 2.9 mmol/L) the following measures may be required:

- rehydration with 0.9% sodium chloride infusion
- use of non-thiazide diuretics to increase calcium excretion
- monitoring of serum potassium and magnesium levels; early use of replacement therapy
- monitoring of cardiac function; use of beta-blockers to protect the heart against arrhythmia
- haemodialysis may need to be considered.

Pharmaceutical Precautions

Storage

Store below 30°C.

Incompatibilities

Tetracyclines:

Calcium salts may complex with tetracyclines, and therefore tetracyclines and calcium salts should not be mixed for parenteral administration.

Magnesium Sulfate:

Mixing calcium salts with magnesium sulfate may cause precipitation of calcium sulfate and therefore magnesium sulfate and calcium salts should not be mixed for parenteral administration.

Phosphate-containing Medications:

Mixing calcium salts with phosphates may cause precipitation of calcium phosphate and therefore phosphate-containing medications and calcium salts should not be mixed for parenteral administration.

Carbonate-containing Medications:

Mixing calcium salts with carbonates may cause precipitation of calcium carbonate and therefore carbonate-containing medications and calcium salts should not be mixed for parenteral administration.

Tartrate-containing Medications:

Mixing calcium salts with tartrates may cause precipitation of calcium tartrate and therefore tartrate-containing medications and calcium salts should not be mixed for parenteral administration.

Compatibilities

Calcium chloride is reported to be compatible with glucose 5% and sodium chloride 0.9%.

Medicine Classification

General sale medicine.

Presentation

Packs of 10 vials

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