Data Sheet

ARGININE HYDROCHLORIDE INJECTION 5%

Presentation

Arginine hydrochloride injection is a 5% solution of arginine hydrochloride in Water For Injection. The product contains no preservatives or other excipients. It is presented as a clear and colourless solution in a 500 ml glass bottle with a non-latex stopper.

Uses

Actions

Infusion of arginine hydrochloride, a natural amino acid, stimulates growth hormone secretion from the pituitary inducing a rise in the plasma level of human growth hormone (HGH) in subjects with intact pituitary function. The rise is usually diminished or absent in subjects with impairment of this function.

Pharmacokinetics

Normal basal plasma levels of arginine are 2 mmol/ml. After IV infusion of 30 g over a 30-minute period in adults, levels of 8 mmol/ml are reached 20 - 30 minutes after the infusion is started and remain above 4 mmol/ml for an hour. Increased plasma levels of growth hormone occur after 1 - 2 hours. Arginine is metabolised in the liver by hydrolytic cleavage to ornithine and urea. Arginine is almost totally renally reabsorbed.

Indications

Arginine hydrochloride 5% is indicated for the evaluation of pituitary growth hormone reserve.

Dosage and administration

The intravenous dose for adults is 30 g (600 ml) and for children is 0.5 g/kg (10 mL/kg). The intravenous infusion of arginine hydrochloride is part of the test for measurement of pituitary reserve of HGH and, for successful administration of the test, clinical conditions and procedures should be as follows:

1. The test should be scheduled in the morning following a normal night's sleep and an overnight fast should continue through the test period.
2. Patients must be placed at bed rest for at least 30 minutes before the infusion begins. Care should be taken to minimise apprehension and distress. This is particularly important in children.
3. Arginine hydrochloride injection should be infused through an indwelling needle or soft catheter placed in an anticubital, or other suitable, vein. Blood samples should be taken by venipuncture from the other arm.
4. A desirable schedule for drawing samples is at -30, 0, 30, 60, 90, 120 and 150 minutes.
5. Arginine hydrochloride injection should be infused beginning at time zero at a uniform rate that will permit the recommended dose to be administered in 30 minutes.
6. Blood samples should be promptly centrifuged and the plasma stored at - 20 ℃ until assayed by one of the published radioimmunoassay procedures.
7. Diagnostic test results showing a deficiency of pituitary reserve for HGH should be confirmed with a second test with arginine hydrochloride, or one may elect to confirm with the insulin hypoglycaemia test. A waiting period of one day is advised between tests.

Contraindications

Arginine hydrochloride is contraindicated in patients with allergic tendencies and hyperchloraemic acidosis.

Warnings and precautions

General Precautions

Arginine hydrochloride injection is hypertonic (approximately 400 mOsm/kg) and can irritate the tissues. Care should be used to ensure administration through a patent catheter within a patent vein. Excessive rates of infusion may result in local irritation and in flushing, nausea or vomiting. Inadequate dosing or prolongation of the infusion may diminish the stimulus to the pituitary and nullify the test.

Use with caution in patients with renal disease or anuria. Arginine can be metabolised resulting in nitrogen-containing products for excretion. The temporary effects of a high nitrogen load on the kidneys, particularly those with renal impairment, should be considered before administering arginine hydrochloride.

Use with caution in patients with electrolyte imbalance. The chloride content of arginine hydrochloride is 237 mmol/L of solution and the effect of infusing this amount of chloride into patients with electrolyte imbalance should be evaluated before the test is undertaken.

A suitable antihistamine should be available for use if an allergic reaction occurs.

Severe, potentially fatal hyperkalaemia has occurred following arginine hydrochloride therapy for metabolic alkalosis in several patients with severe hepatic disease who had recently received spironolactone. Severe hyperkalaemia in these patients probably resulted from an arginine-induced extracellular shift of potassium from cells, impaired hepatic metabolism of arginine, and/or a spironolactone-induced decrease in renal excretion of the ion. Patients receiving a potassium-sparring diuretic are at an increased risk of arginine-induced hyperkalaemia, therefore combined use of the drug should be avoided.

Basal and post stimulation levels of HGH are elevated in patients who are pregnant or taking oral contraceptives.

Pregnancy and lactation

Reproduction studies have been performed in rabbits and mice at doses 12 times the human dose and have revealed no evidence of impaired fertility or harm to the foetus due to arginine hydrochloride. There have been no adequate or well controlled studies for the use of arginine hydrochloride in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should not be used during pregnancy.

It is not known whether intravenous arginine hydrochloride could result in significant quantities of arginine in breast milk. Systemically administered amino acids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when arginine hydrochloride is administered to nursing women.

Effects on ability to drive and use machines

As patients are required to fast for this test and as nausea is a common side effect of arginine hydrochloride use, it is advisable not to drive or to use machinery on the day of the test.

Geriatric use

Clinical studies of arginine did not include a sufficient number of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported experience has not identified differences between the elderly and younger patients.

Adverse effects

Following 1670 infusions of arginine hydrochloride in pre-market studies, non-specific side effects affected 3% of patients. The side effects included nausea, vomiting, headache, flushing, numbness and local venous irritation.

In addition:

- One patient experienced an allergic reaction which was manifested as a confluent macular rash with reddening and swelling of the hands and face. The rash subsided after the infusion was terminated and an antihistamine administered.
- One patient had an apparent decrease in platelet count from 150,000 to 60,000.
- One patient with a history of acrocyanosis had an exacerbation of this condition following infusion of arginine hydrochloride.

Leakage of IV solutions of arginine hydrochloride into the surrounding tissue may cause necrosis and superficial phlebitis.

Exacerbation of sickle cell anaemia, and elevations of BUN and serum creatine and creatinine may occur following administration of arginine hydrochloride.

Spontaneous reports of adverse reactions associated with arginine hydrochloride use in the post-market setting have been reported. The reactions detailed in the reports include:

- hypersensitivity reactions
- injection site reactions
- haematuria
- cerebral oedema
- vomiting
- headache
- lethargy
- perioral tingling
- decreased platelet count
- exacerbation of acrocyanosis

Nasal obstruction and discharge, choking, sweating, and increased pulse rate have also been reported during IV arginine administration and may have represented an allergic reaction to the drug.

Local post-market surveillance has indicated that nausea is the most common side effect. Appetite loss is common, possibly due to nausea.

Interactions

Oestrogens and progestin-oestrogen combination oral contraceptives may elevate growth hormone response.

Medroxyprogesterone acetate may reduce growth hormone response. Norethindrone may reduce insulin response.

Some reports suggest that arginine may intensify antihypertensive medications and may increase the chance of dizziness and light-headedness. Thiazide diuretics xylitol and aminophylline may increase insulin response and the latter two may reduce glucagon response.

Sulfonylurea oral antidiabetic agents may suppress plasma glucagon response.

Overdosage

Errors in dosage calculations, leading to overdosage, can have very serious and sometimes fatal effects. There have been reports of overdose resulting from medication error, including reports with fatal outcomes. Therefore care must be taken in checking dosage calculations to avoid overdose.

Overdosage may cause a metabolic acidosis with hyperventilation to a degree depending upon the extent of the dosage. Mild acidosis will be compensated and base deficit will return to normal following completion of the infusion. If the condition persists or is severe, the deficit should be determined and corrected by a calculated dose of an alkalinizing agent.

Pharmaceutical precautions

Instructions for use

Do not use unless the solution is clear and free from particles. Discard any leftover solution. Due to the risk of an allergic reaction, a suitable antihistaminic drug should be available where arginine hydrochloride is used. Arginine hydrochloride is a diagnostic aid and is not intended for therapeutic use. Arginine hydrochloride injection should be administered only by intravenous infusion because of its hypertonicity.

Incompatibilities

None known.

Shelf life

The product has a shelf life of 36 months form the date of manufacture. Store at or below 25 ℃. Do not freeze. Use immediately after opening.

Medicine classification

General sale medicine

Package quantities

500 ml bottles.

Name and address

Distributed in New Zealand by:
Biomed Limited
52 Carrington Road
Point Chevalier
Auckland.
Telephone 0800 833 133

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