

ADRENALINE ACID TARTRATE INJECTION

1:1 000 (1 mg/mL)

Presentation

Adrenaline injection contains no antimicrobial agent. It should be used only once and any residue discarded. It is a clear, colourless solution and should not be used if it is coloured.

Adrenaline 1:1000

Adrenaline acid tartrate equivalent to adrenaline 1:1000 (1 mg/1 mL) with sodium metabisulfite and sodium chloride in Water for Injections BP; Sodium hydroxide or hydrochloric acid is used for pH adjustment, pH 2.8 to 3.6.

Uses

Actions

Adrenaline acts on both alpha and beta adrenergic receptors of tissues innervated by sympathetic nerves, except the sweat glands and arteries of the face. It is the most potent alpha receptor activator. Adrenaline stimulates the heart to increased output; raises the systolic blood pressure; lowers diastolic blood pressure; relaxes bronchial spasm and mobilises liver glycogen, resulting in hyperglycaemia and possibly glycosuria.

Pharmacokinetics

Parentally administered adrenaline has a rapid onset and short duration of action. The circulating drug is metabolised by the liver and other tissues. The majority is taken up and metabolised by sympathetic nerve endings. Adrenaline is excreted in the urine, mainly in the form of metabolites.

Adrenaline crosses the placenta but not the blood-brain barrier. It is also distributed into breast milk (see USE IN PREGNANCY and USE IN LACTATION).

Indications

Adrenaline 1:10,000 is used as an adjunct in the management of cardiac arrest.

Adrenaline 1:1,000 is the drug of choice in the emergency treatment of acute severe anaphylactic reactions due to insect bites, drugs and other allergens. It may also be used for the symptomatic relief of respiratory distress due to bronchospasm.

Dosage and Administration

The 1:1,000 (1 mg/1 mL) injection is preferably administered subcutaneously. It may also be administered intramuscularly but not in the buttocks.

In emergency situations, adrenaline may be injected very slowly intravenously but **only** as the dilute solution 1:10,000.

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Cardiac Arrest

Adults.

The recommended dose is 1 mg intravenously, using 10 mL of the 1:10,000 solution. This may be repeated every 3-5 minutes. If given through a peripheral line, each dose should be followed by a flush of 20 mL of IV fluid to ensure delivery of the drug to the central compartment. Intracardiac administration is no longer recommended.

Children.

The recommended dose is 10 micrograms (0.1 mL of the 1:10,000 solution) per kg bodyweight administered intravenously. This may be repeated every 3-5 minutes.

Severe Anaphylaxis or Asthma

Adults.

The usual initial dose is 100 to 500 microgram (0.1 to 0.5 mL of the 1:1,000 solution) SC or IM. SC doses may be repeated at 20 minute to 4 hour intervals depending on the response of the patient and the severity of the condition.

In severe anaphylactic shock, slow and cautious IV administration may be necessary to ensure absorption of the drug. A dose of 100 to 250 microgram (1 to 2.5 mL of the 1:10,000 solution) may be administered. Alternatively 25 to 50 microgram (0.25 to 0.5 mL of the 1:10,000 solution) may be given IV every 5 to 15 minutes following an initial dose of 500 microgram SC or IM.

Children.

10 microgram (0.01 mL of 1:1,000 solution) per kg body weight SC, repeated if necessary at intervals of 20 minutes to 4 hours depending on the response of the patient and the severity of the condition. Single paediatric doses should not exceed 500 microgram.

Contraindications

- Known hypersensitivity to sympathomimetic amines
 - Shock (other than anaphylactic shock)
 - Cardiac dilatation and coronary insufficiency
 - Hypertension
 - Ischaemic heart disease
 - Arrhythmias
 - Cerebral arteriosclerosis
 - Diabetes mellitus
 - Hyperthyroidism
 - Narrow angle (congestive) glaucoma
 - Organic brain damage
 - Pheochromocytoma
 - During general anaesthesia with halogenated hydrocarbons or cyclopropane
 - With local anaesthesia in fingers, toes, ears, nose or genitalia - there is a danger of vasoconstriction producing sloughing of tissues in these areas.
 - Labour - it may delay the second stage by inhibiting spontaneous or oxytocin-induced contractions of the pregnant human uterus.
 - Conditions in which vasopressor drugs may be contraindicated e.g. thyrotoxicosis.
 - In obstetrics when maternal blood pressure is in excess of 130/80 mmHg.
- (See also INTERACTIONS)

Warnings and Precautions

Other beta-agonist sympathomimetics

Allow sufficient time to elapse before or after administering another beta-agonist sympathomimetic agent to avoid additive effects.

Disease states

Use with extreme caution in the elderly, and in patients with cardiovascular disease, phenothiazine induced circulatory collapse, cerebrovascular insufficiency, diabetes,

hypertension, chronic lung disease, angina pectoris, prostatic hypertrophy, psychoneurosis or hyperthyroidism.

Use with extreme caution in patients with long standing bronchial asthma and emphysema who have developed degenerative heart disease. Anginal pain may be induced when coronary insufficiency is present. Syncope has occurred following administration to asthmatic children. In patients with parkinsonian syndrome the drug increases rigidity and tremor.

General anaesthesia

Concurrent use with cyclopropane, halogenated hydrocarbon or similar volatile anaesthetics may produce fatal ventricular arrhythmias.

Diabetic patients

A greater increase may be produced in heart rate, blood glucose, lactate, glycerol and free fatty acids when adrenaline is administered to diabetic patients with autonomic neuropathy than in diabetics without neuropathy.

Circulatory Support

When adrenaline is used for circulatory support, correction of hypervolaemia, metabolic acidosis, and hypoxia or hypercapnia should be carried out beforehand or concomitantly.

Sodium metabisulfite

This product contains sodium metabisulfite, which may cause allergic reactions in susceptible individuals. The possibility of an allergic reaction to sodium metabisulfite should be considered in asthmatic patients who show paradoxical worsening of their condition following use of the drug.

GANGRENE

Inter-arterial administration must be avoided as marked vasoconstriction may result in gangrene.

Local ischaemic necrosis can occur from repeated injections in one site.

Use in Pregnancy

Adrenaline has been administered to a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

However, the use of adrenaline during labour is contraindicated because it may delay the second stage by inhibiting spontaneous or oxytocin-induced contractions of the pregnant human uterus.

Use in Lactation

Adrenaline is excreted in the breast milk. The use of adrenaline in breast-feeding women is therefore not recommended.

Adverse Effects

Adrenaline may cause reactions such as fear, anxiety, tenseness, restlessness, disorientation, impaired memory, confusion, irritability, hallucinations and psychotic states. Headache, weakness, dizziness, anorexia, nausea and vomiting and difficulty in micturition with urinary retention may also occur.

Muscle tremor and hypokalaemia, psychomotor agitation, pallor, respiratory difficulty, hyperglycaemia, sweating, hypersalivation, cold extremities and insomnia have also been reported.

Adrenaline causes E.C.G. changes including a decrease in T-wave amplitude in all leads in normal persons.

Palpitations, tachycardia (sometimes with anginal pain) and cardiac arrhythmias may also occur along with hypertension which in some instances may induce reflex bradycardia as can vasodilation with flushing and hypotension. Ventricular fibrillation may occur and severe hypertension may lead to cerebral haemorrhage and pulmonary oedema.

Overdosage or inadvertent IV injection of usual subcutaneous doses of adrenaline may cause hypertension. Cerebrovascular or other haemorrhage and hemiplegia may result, especially in geriatric patients. Inadvertent IV injection of adrenaline has also been reported to have caused convulsions, metabolic acidosis, and renal failure with anuria.

Repeated injections of adrenaline can cause necrosis as a result of vascular constriction at the injection site. Tissue necrosis may also occur in the extremities, kidneys and liver.

Prolonged use or overdosage of adrenaline can result in severe metabolic acidosis.

Pulmonary oedema has been associated with excessive parenteral administration of adrenaline and following topical aerosol application.

Gas gangrene which can be fatal has been reported following intramuscular injection of adrenaline into the buttock or thigh. This appears to have been due to clostridium organisms on the skin being deposited into muscle tissue during injection, with the vasoconstrictor properties of adrenaline enhancing the effects of the infection (see DOSAGE AND ADMINISTRATION).

High doses may result in ventricular arrhythmias.

Rigidity and tremor may be exacerbated in patients with Parkinsonism.

Syncopal episodes have been reported in children.

Psychiatric disorders may be exacerbated.

Interactions

Other Sympathomimetic Agents

Adrenaline should not be administered concomitantly with other sympathomimetic agents because of the possibility of additive effects and increased toxicity.

Rapidly Acting Vasodilators

These can counteract the marked pressor effects of adrenaline.

General Anaesthetics

Administration of adrenaline in patients receiving cyclopropane, halogenated hydrocarbon or similar volatile general anaesthetics that increase cardiac irritability and seem to sensitise the myocardium to adrenaline, may result in arrhythmias including ventricular premature contractions, tachycardia or fibrillation and acute pulmonary oedema if hypoxia is present.

Cardiovascular Drugs

Adrenaline should not be used in patients receiving high dosage of other drugs, eg. quinidine, digoxin and other cardiac glycosides, that can sensitise the heart to arrhythmias.

Antihypertensive Therapy

Special care is advisable in patients receiving antihypertensive therapy as severe hypertension may result.

Alpha Blockers

The administration of adrenaline to patients receiving alpha blockers may result in both hypotension and cardiac-accelerating effects.

Beta Blockers

The administration of adrenaline to patients receiving non-selective beta blockers (eg. propranolol) may result in severe hypotension, followed by a reflex bradycardia, due to stimulation of adrenergic receptors.

CNS and Other Drugs

Tricyclic antidepressants, some antidepressants, some antihistamines and thyroid hormones may potentiate the effects of adrenaline, especially on heart rhythm and rate. Patients on MAOIs should not receive sympathomimetic treatment.

Drugs Causing Potassium Loss

The hypokalaemic effect of adrenaline may be potentiated by other drugs that cause potassium loss, including corticosteroids, potassium-depleting diuretics and aminophylline or theophylline; patients receiving high doses of beta₂-adrenergic agonists concomitantly should have their plasma-potassium concentration monitored.

Hypoglycaemic Agents

Adrenaline induced hyperglycaemia may lead to loss of blood sugar control in diabetic patients treated with hypoglycaemic agents.

Overdosage

Symptoms

Overdosage with adrenaline produces a rapid rise in blood pressure resulting in cerebrovascular haemorrhage, cardiac arrhythmias leading to ventricular fibrillation and death. Pulmonary oedema may also lead to death because of the peripheral constriction and cardiac stimulation produced.

Treatment

To counteract the pressor effects of adrenaline, use rapidly acting vasodilators, for instance nitrates or α -blocking agents.

Pharmaceutical Precautions

Incompatibilities

Adrenaline is incompatible with oxidising agents, alkalis, copper, zinc, iron, silver and other metals.

Adrenaline has been reported to be incompatible with solutions containing the following: aminophylline, ampicillin sodium, amylobarbitone sodium, ascorbic acid, benzylpenicillin potassium, calcium chloride, calcium gluconate, cephalothin sodium, chloramphenicol sodium succinate, chlortetracycline hydrochloride, corticotrophin, diazepam, digitoxin, ergometrine maleate, erythromycin gluceptate, frusemide, hyaluronidase, hydrocortisone sodium succinate, methicillin sodium, nitrofurantoin, noradrenaline acid tartrate, novobiocin sodium, pentobarbitone sodium, procaine, prochlorperazine edisylate, promazine hydrochloride,

sodium bicarbonate, sulfadiazine sodium, suxamethonium chloride, tetracycline hydrochloride, vancomycin hydrochloride, vitamin B complex with ascorbic acid, warfarin sodium.
This list is not intended to be comprehensive. Refer to standard texts for further information.

Medicine Classification

Restricted Medicine

Package Quantities

1.0 mg/mL (1:1000) 1 mL glass ampoules in packs of 5 and 50

Shelf Life And Storage Conditions

Store below 25 °C and protect from light.
1:1000 syringes have a shelf-life of 18 months.

Further Information

Nil.

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Date of Preparation

5 May 2016