PRESCRIBING INFORMATION

Pr ATROPINE INJECTION BP

0.4 mg / mL, and 0.6 mg / mL atropine sulfate solution

For intramuscular, intravenous and subcutaneous use

Anticholinergic

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DATE OF PREPARATION:
April 22, 2022

Control number: 262701

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ACTION AND CLINICAL PHARMACOLOGY

Atropine is commonly classified as an anticholinergic or parasympatholytic drug. More precisely however, it is termed an antimuscarinic agent since it antagonizes the muscarinic-like actions of acetylcholine and other esters.

Atropine inhibits the muscarinic actions of acetylcholine on structures innervated by postganglionic cholinergic nerves, and on smooth muscles which respond to endogenous acetylcholine but are not so innervated. The major action of atropine is a competitive antagonism which can be overcome by increasing the concentration of acetylcholine at receptor sites of the effector organ (e.g. by using anticholinesterase agents which inhibit the enzymatic destruction of acetylcholine). The receptors antagonized by atropine are the peripheral structures that are stimulated or inhibited by muscarine (i.e. exocrine glands and smooth and cardiac muscle). Responses to postganglionic cholinergic nerve solution also may be inhibited by atropine, but this occurs less readily than with responses to injected (exogenous) choline esters.

Atropine induced parasympathetic inhibition may be preceded by a transient phase of stimulation, especially on the heart where small doses first slow the rate before characteristic tachycardia develops due to paralysis of vagal control. In clinical doses (≈ 1 mg), atropine does not depress the CNS, but may stimulate the medula and higher cerebral centres. Although mild vagal excitation occurs, the increased respiratory rate and (sometimes) increased depth of respiration produced by atropine are probably the result of bronchiolar dilatation. Accordingly, atropine is an unreliable respiratory stimulant and large or repeated doses may depress respiration.

Adequate doses of atropine abolish various types of reflex vagal cardiac slowing or asystole. The drug also prevents or abolishes bradycardia or asystole produced by injection of anticholinesterase agents or other parasympathomimetic drugs, and cardiac arrest produced by stimulation of the vagus. Atropine may also lessen the degree of partial heart block when vagal activity is an etiologic factor. In some patients with complete heart block, the idioventricular rate may be accelerated by atropine: in others, the rate is stabilized. Occasionally, a large dose may cause atrioventricular block and nodal rhythm.

Atropine injection in clinical doses counteracts the peripheral dilatation and abrupt decrease in blood pressure produced by choline esters. However, when given by itself, atropine does not exert a striking or uniform effect on blood vessels or blood pressure. Systemic doses slightly raise systolic and lower diastolic pressures and can produce significant postural hypotension. Such doses also slightly increase cardiac output and decrease central venous pressure. Occasionally,

therapeutic doses dilate cutaneous blood vessels, particularly in the blush area (atropine flush), and may cause hyperthermia due to suppression of sweat gland activity in infants and small children.

Atropine disappears rapidly from the blood flow following injection and is distributed throughout the body. Much of the drug is destroyed by enzymatic hydrolysis, particularly in the liver and from 13 to 50% is excreted unchanged in the urine. Traces are detected in various secretions, including milk. Atropine readily crosses the placental barrier and enters the fetal circulation.

INDICATIONS AND CLINICAL USES

Atropine Injection BP is indicated for:

- Reduction of secretions of the respiratory tract before anesthesia
- Prevention and treatment of bradycardia caused by excessive vagal stimulation.
- Antidote for cholinesterase inhibitors and for poisoning from muscarinic mushrooms (e.g. amanita)
- Antidote to organophosphate poisoning.
- During cardiopulmonary resuscitation to treat excessive vagal tone.

CONTRAINDICATIONS

Angle-closure glaucoma, prostatic hypertrophy, gastrointestinal obstruction, pyloric stenosis, except in doses ordinarily used for preanesthetic medication.

Atropine Injection BP is contraindicated in patients known to be hypersensitive to the product.

WARNINGS

Atropine is a highly potent drug and due care is essential to avoid overdosage, especially with intravenous administration. Children are more susceptible than adults to the toxic effects of anticholinergic agents (agitation, confusion, drowsiness).

PRECAUTIONS

Conventional systemic doses may precipitate acute glaucoma in susceptible patients, convert partial organic pyloric stenosis into complete obstruction, and lead to complete urinary retention in patients with prostatic hypertrophy.

Atropine should be used only with extreme caution in febrile children, or in high ambient temperatures, because of the danger of hyperpyrexia. Atropine should be used cautiously in all patients with fever.

Atropine should be used with caution in conditions characterized by tachycardia such as thyrotoxicosis, cardiac insufficiency and in cardiac surgery where it may further accelerate the heart rate.

Conventional systemic doses may cause thickening of bronchial secretions and formation of dangerous mucous plugs in patients with chronic lung disease.

Use with caution in all individuals over 40 years of age. Atropine may cause mental confusion, especially in the elderly.

Doses of atropine up to 1 mg are mildly stimulant to the central nervous system (CNS). Higher doses may induce mental disturbances and depression of the CNS. Children and elderly people are particularly susceptible.

The effects of atropine may be enhanced by the concomitant administration of other drugs with anticholinergic properties such as tricyclic antidepressant, MAOI's, phenothiazines, amantadine, some antihistamines, butyrophenones and disopyramide. Reduced gastrointestinal motility caused by atropine may affect the absorption of other drugs such as mexiletine and ketoconazole. Atropine induced dry mouth may prevent dissolution of sublingual preparations such as the nitrates, reducing their effectiveness.

Pregnancy:
Atropine sulfate crosses the placenta. Studies in humans have not been done and only limited information is available from animal studies. Intravenous administration of atropine during pregnancy or at term may cause tachycardia in foetus. However, data from a limited number of pregnancies have not shown adverse events on the pregnancy, the fetus or the newborn. Nevertheless, atropine should be given to a pregnant woman only if clearly needed.

Lactation:
Trace amounts of atropine is excreted in breast milk and may cause antimuscarinic effects in the infant. Lactation may be inhibited.

ADVERSE EFFECTS

Most adverse events are due to the antimuscarinic actions of atropine and are dose related. Common adverse events include: tachycardia, dry and hot skin, mydriasis, light sensitivity, blurred vision, dry mouth, dysphagia, constipation, headache, insomnia, restlessness and dizziness. Patients with Down's syndrome appear to have an increased susceptibility to atropine.

Less common adverse events include bradycardia following low-dose atropine (as low dose may be parasympathomimetic), palpitations, arrhythmias, paradoxical heart block, hypertension, increased myocardial ischemia; ataxia, confusion, agitation, somnolence, seizures and psychosis; vomiting, impaired GI motility and ileus; urinary retention; increased intraocular pressure and

cycloplegia; and rarely severe allergic reactions including anaphylaxis. Elderly patients are more prone to hallucinations, delirium, agitation and confusion.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

Symptoms of overdosage include flushing and dryness of the skin, dilated pupils, dry mouth, tachycardia, hypertension, rapid respiration, hyperpyrexia, nausea, vomiting. Symptoms of CNS stimulation may include restlessness, confusion, hallucinations, paranoid and psychotic reactions, incoordination, delirium and occasionally convulsions. In severe overdose, CNS depression may occur with coma, circulatory and respiratory failure and death.

In the event of overdosage, diazepam may be considered to control marked agitation and convulsions. Large doses for sedation should be avoided because central depressant action may coincide with the depression occurring late in atropine poisoning.

The fatal adult dose of atropine is not known. In children, 10 mg or possibly even less may be fatal. With doses as low as 0.5 mg, symptoms of overdosage may occur.

DOSAGE AND ADMINISTRATION

Atropine can be administered by intravenous, intramuscular or subcutaneous injection. The intravenous administration is the preferred route for life-threatening indications.

Pre-anesthesia:
Adults: 0.3-0.6 mg
Children: 0.01-0.02 mg/kg

Antidote to cholinesterase inhibitors and in amanita mushroom poisoning:
Adults: 0.6-1.2 mg. Can be repeated every 2 hours until muscarinic signs disappear or until signs of atropine toxicity occur.

Antidote to organophosphate poisoning:
Adults: 2 mg.
Children: 0.02 mg/kg
Can be repeated every 5-10 minutes until signs of poisoning are sufficiently lessened or until signs of atropine toxicity occur.

Administration:
Examine the ampoule contents before injection. DO NOT USE if solution shows haziness, particulate matters, discolouration, or leakage. Discard unused portion.

AVAILABILITY

Atropine Injection BP 0.4 mg/mL: Each mL of sterile solution contains atropine sulfate 0.4 mg, sodium chloride 8.9 mg (for isotonicity), water for injection and may contain sulfuric acid (to adjust pH). Ampoules of 1 mL, boxes of 10.

Atropine Injection BP 0.6 mg/mL: Each mL of sterile solution contains atropine sulfate 0.6 mg, sodium chloride 8.9 mg (for isotonicity), water for injection and may contain sulfuric acid (to adjust pH). Ampoules of 1 mL, boxes of 10.

STORAGE

Store at room temperature (15 to 30°C). Protect from freezing. Protect from light.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Questions or concerns?
Contact Hikma Canada Limited at 1-800-656-0793.

This leaflet was prepared by Hikma Canada Limited, Mississauga, ON L5R 3P9

Date of Preparation: April 22, 2022