Ethicholine Injection

Description

Ethicholine Injection is a sterile, clear, colourless solution consisting of 50 mg suxamethonium chloride in each mL of Water for Injections BP.

Pharmacology

Suxamethonium is a depolarizing, noncompetitive, skeletal muscle relaxant. As with acetylcholine, it combines with nicotinic cholinoceptors to produce depolarization. This depolarization may be experienced as painful muscle fasciculation. Subsequent inhibition of neuromuscular transmission will occur if adequate concentration of suxamethonium remains at the motor end plate. The result of this is flaccid paralysis. The paralysis is selective, initially involving in order of occurrence, the levator muscles of the face, muscles of the glottis and finally the intercostals and the diaphragm and all other skeletal muscles.

When suxamethonium is given over a prolonged period of time, the characteristic depolarizing neuromuscular block (phase 1 block) may change to a block with characteristics superficially resembling a nondepolarizing block. Suxamethonium causes a slight, transient increase in intraocular pressure.

Pharmacokinetics

Suxamethonium has a rapid onset and a short duration of action. It acts in about 30 seconds following intravenous injection and has a duration of action averaging 4 to 6 minutes.

Suxamethonium is hydrolysed by pseudocholinesterases in plasma and body tissues; only a small proportion of the dose is excreted in the urine unchanged. Suxamethonium does not readily cross the placenta following administration of normal doses.

Pharmacogenomics

RYR1 and CACNA1S are polymorphic genes and multiple pathogenic variants have been associated with malignant hyperthermia susceptibility (MHS) in patients receiving succinylcholine, including suxamethonium. Case reports as well as *ex vivo* studies have identified multiple variants in RYR1 and CACNA1S associated with MHS. Variant pathogenicity should be assessed based on prior clinical experience, functional studies, prevalence information, or other evidence (see section *Contraindications* and *Warnings*).

Indications

Ethicholine Injection is indicated for the production of skeletal muscle relaxation during operative and manipulative procedures, and in conjunction with electroshock therapy. The short duration of action of the drug is ideally suited for procedures requiring only brief relaxation such as endotracheal intubation, endoscopic examinations, orthopaedic manipulations, short surgical procedures such as tonsillectomies and electroshock therapy. The drug is also indicated to provide muscular relaxation during surgical techniques of longer duration.

Contraindications

Ethicholine Injection is contraindicated in patients who are burnt, severely hyperkalaemic, or known to have atypical pseudocholinesterase. Ethicholine Injection is also contraindicated in patients with penetrating wounds of the eye, in patients with a personal or family history of malignant hyperpyrexia, in massively traumatised patients or those with extensive muscle degeneration, such as in recent paraplegia. Ethicholine Injection should not be administered to patients with known hypersensitivity to the drug. Ethicholine Injection is contraindicated in patients with known or suspected genetic susceptibility to malignant hyperthermia (see section *Warnings* and *Pharmacogenomics*).

Warnings

The use of Ethicholine Injection is inadvisable in patients with low serum pseudocholinesterase concentrations such as may occur in patients with liver disease, malnutrition, severe anaemia, burns and in persons exposed to organophosphorus insecticides or weedkillers.

If eye drops containing long-acting cholinesterase inhibitor drugs such as ecothiopate iodide, dyflos, or demecarium bromide are used within a period of one month prior to an operation, the decreased serum cholinesterase levels may preclude the use of Ethicholine Injection.

The use of Ethicholine Injection is also inadvisable in patients with advanced myasthenia gravis, neurological defects, or myopathies.

In susceptible individuals, succinylcholine may trigger malignant hyperthermia, a skeletal muscle hypermetabolic state leading to high oxygen demand. Fatal outcomes of malignant hyperthermia have been reported.

The risk of developing malignant hyperthermia increases with the concomitant administration of succinylcholine and volatile anaesthetic agents. Ethicholine Injection can induce malignant hyperthermia in patients with known or suspected susceptibility based on genetic factors or family history, including those with certain inherited ryanodine receptor (RYR1) or dihydropyridine receptor (CACNA1S) variants (see section *Contraindications* and *Pharmacogenomics*).

Signs consistent with malignant hyperthermia may include hyperthermia, hypoxia, hypercapnia, muscle rigidity (e.g., jaw muscle spasm), tachycardia (e.g., particularly that unresponsive to deepening anaesthesia or analgesic medication administration), tachypnoea, cyanosis, arrhythmias, hypovolaemia, and haemodynamic instability. Skin mottling, coagulopathies, and renal failure may occur later in the course of the hypermetabolic process.

Successful treatment of malignant hyperthermia depends on early recognition of the clinical signs. If malignant hyperthermia is suspected, discontinue all triggering agents (i.e., volatile anaesthetic agents and succinylcholine), administer intravenous dantrolene sodium, and initiate supportive therapies. Consult prescribing information for intravenous dantrolene sodium for additional information on patient management. Supportive therapies include administration of supplemental oxygen and respiratory support based on clinical need, maintenance of haemodynamic stability and adequate urinary output, management of fluid

and electrolyte balance, correction of acid base derangements, and institution of measures to control rising temperature.

Precautions

Ethicholine Injection should be used with caution in patients with cardiac disease, those suffering from severe trauma or electrolyte imbalance, those receiving quinine or who have been recently digitilised as serious cardiac arrhythmias or cardiac arrest may be induced, those with pre-existing hyperkalaemia, paraplegic patients, and those who have suffered severe burns.

Ethicholine Injection should be used with caution, if at all, during ocular surgery and in patients with glaucoma.

The drug should be employed with caution in patients with fractures or muscle spasm because the initial muscle fasciculations may cause additional trauma.

When prolonged apnoea follows a single dose of suxamethonium chloride, neostigmine should not be given. Neostigmine and other anticholinesterase drugs are not antidotes to suxamethonium chloride but would normally have the effect of intensifying the depolarising effect. However, in some cases of prolonged apnoea, especially following large doses of Ethicholine by intravenous infusion, a state of 'dual block' may be responsible. In dual block, the muscle relaxation is due to nondepolarising blockade and is reversible with neostigmine. To investigate this possibility, the short-acting anticholinesterase drug, edrophonium, should be given; a transitory return of muscle power confirms the presence of dual block, which can then be reversed with neostigmine.

Sinus tachycardia and raised blood pressure have occurred following continuous infusion of suxamethonium chloride. Care should be taken with patients receiving systemic antibiotics such as streptomycin, neomycin, kanamycin, tobramycin, framycetin, amikacin, gentamicin, colistin and the polymyxins, as the action of suxamethonium chloride can be potentiated.

Ethicholine Injection may increase intragastric pressure, which may result in regurgitation and possible aspiration of stomach contents.

Use in Neonates, Infants and Children

Neonates and premature infants may be relatively resistant to Ethicholine Injection.

Intravenous bolus administration in infants or children may result in profound bradycardia, or rarely, asystole. As in adults, the incidence of bradycardia in children is higher following a second dose. The occurrence of bradyarrhythmias may be reduced by pretreatment with atropine. It has been suggested that continuous infusion is unsafe in children and neonates because of the risk of inducing malignant hyperpyrexia. In seriously burnt children, suxamethonium can precipitate gross cardiac arrhythmias and cardiac arrest. This can be prevented by the prior administration of 6 mg of tubocurarine, 5 minutes before giving suxamethonium.

Use in the Elderly

Caution is required because of the possible cardiovascular effects of depolarising agents.

Use in Pregnancy

Category A*. Serum pseudocholinesterase concentrations are reduced in pregnancy and pregnant patients may show increased sensitivity to the drug.

Category A = Drugs which have been taken by a large number of pregnant women and women of childbearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.*

Use in Lactation

No problems have been documented in relation to the administration of suxamethonium during lactation.

Nevertheless, if it is to be given to women who are breast feeding, the benefits to the mother must be weighed against the potential adverse effect on the infant before administration.

Drug Interactions

1. Kanamycin, tobramycin, gentamicin, neomycin, and streptomycin have all been shown to produce a neuromuscular blockade that may enhance the blockade produced by Ethicholine Injection.

2. Prolonged use of eyedrops containing long-acting cholinesterase inhibitors may result in reduced activity of pseudocholinesterase, thereby enhancing the effect of suxamethonium (see **Warnings**).

3. Both Polymixin B and colistin can produce neuromuscular blockade.

4. Clindamycin may have some neuromuscular blocking activity.

5. Cyclophosphamide may decrease pseudocholinesterase levels in plasma, thereby enhancing the effects of suxamethonium.

6. Suxamethonium appears to potentiate the effects of digitalis glycosides with respect to both conduction and increased ventricular irritability.

7. Low doses of frusemide may possibly enhance the neuromuscular blocking activity of Ethicholine Injection.

8. Magnesium possesses neuromuscular blocking activity.

9. Large doses of procaine may competitively inhibit the metabolism of Ethicholine Injection.

10. The concurrent use of suxamethonium and quinidine may induce serious cardiac arrhythmias.

Compatibilities/Incompatibilities

Suxamethonium chloride is reported to be unstable in alkaline solutions and to decompose in solutions with a pH greater than 4.5. Suxamethonium chloride is reported to be compatible with 5% dextrose injection and 0.9% sodium chloride injection.

It is reported that suxamethonium chloride should not be mixed with short-acting barbiturates in the same syringe or administered via the same line during IV infusion.

Since suxamethonium chloride is reported to be fairly quickly hydrolysed and destroyed by the alkalinity of thiopentone and moreover, since the initial contractions produced are painful if the thiopentone has not taken full effect, suxamethonium should be injected immediately after thiopentone and also from a different syringe.

Adverse Reactions

Common Side Effects

1. Transient muscle fasciculations before relaxation.
2. Increases in intraocular and intragastric pressure.
3. Post-operative pain.
4. Bradycardia, tachycardia, hypertension and hypotension, often associated with arrhythmias.
5. Suxamethonium has muscarinic effects and may cause an increase in bowel movements and salivary, bronchial and gastric secretions.

Uncommon Side Effects

1. Hypersensitivity reactions to the drug.
2. Malignant hyperpyrexia in patients with a genetic predisposition to this syndrome.

Dosage and Administration

Ethicholine Injection is usually administered by the intravenous route.

Intravenous Injection

Ethicholine Injection is given by intravenous injection in single doses ranging from 0.4 mL to 2 mL according to the depth and duration of relaxation required. For adults, the average dose for intubation is from 1 mL to 1.6 mL; for electroconvulsive therapy 0.8 mL to 1.5 mL and for manipulations 1.6 mL.

The dose of Ethicholine Injection is dependent upon the degree of muscular relaxation required and the response of individual patients. A dose of 1 mg/kg will produce muscular relaxation in about 60 seconds and has a duration of action of about 10 minutes.

Intravenous Infusion

Longer periods of relaxation for major surgical operations may be produced if Ethicholine Injection is given by repeated intermittent injection or by continuous intravenous infusion. A

1 mg/mL to 2 mg/mL solution may be prepared by the addition of Ethicholine Injection to sodium chloride 0.9% injection or to dextrose 5% injection immediately before use. The rate of infusion ranges from 2 to 6 mg of suxamethonium (40 to 120 drops of the 0.1% dilution and 20-60 drops of the 0.2% dilution of Ethicholine Injection per minute; the average being 3 mg (60 drops of the 0.1% dilution and 30 drops of the 0.2% dilution) per minute.

Intramuscular Injection

For infants and in other patients in whom a suitable vein is not accessible, the drug may be administered by deep intramuscular injection, preferably high into the deltoid muscle.

Up to 2.5 mg/kg body weight, but no more than 150 mg total dose should be given to adults and children by the IM route.

Note: an initial test dose of 0.1 mg/kg may be used to determine the sensitivity of the patient to Ethicholine Injection and individual recovery time.

To avoid distress to the patient Ethicholine Injection should not be administered before unconsciousness has been induced and should always be accompanied by assisted respiration.

After administration of Ethicholine Injection, the lungs must be inflated for about one minute, with either pure oxygen or a 50% mixture of oxygen and nitrous oxide, to allow time for the full effect of the relaxant to develop before laryngoscopy, intubation or administration of a local anaesthetic.

Inflation of the lungs must be continued after intubation until spontaneous respiration returns.

Overdosage

Symptoms

Apnoea and prolonged muscle paralysis are the main and most serious effects of overdosage.

Management of Overdosage

It is essential to maintain the airway and adequate ventilation until spontaneous respiration occurs. Assisted respiration sufficient for full oxygenation, yet avoiding excessive elimination of carbon dioxide, should be maintained until paralysis passes off. This should be combined with light narcosis, e.g., with nitrous oxide-oxygen mixture.

If the blockade is a Phase II block, which is indicated by a fading of responses to successive peripheral nerve stimulation, neostigmine may be used to reverse the block.

The use of neostigmine to reverse a Phase II block is a decision which depends on the subject and the experience and judgement of the doctor. If neostigmine is used, its administration should be preceded by that of atropine to protect against any muscarinic effects which may otherwise be elicited.

Storage

Store at 2°C - 8°C.

Refrigerate. Do not freeze. Protect from light.

Presentation

Ethicholine Injection is available as follows:

Strength	**Pack size**
suxamethonium chloride 100 mg/2 mL	50 ampoules

Name and Address of Product Owner

Hospira Australia Pty Ltd
1 Lexia Place
Mulgrave VIC 3170
Australia

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