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CLASSES

Parasympathomimetic Ophthalmological Surgical Aids

DEA CLASS

Rx

DESCRIPTION

Direct-acting parasympathomimetic ophthalmic agent; naturally-occurring neurohormone that mediates nerve impulse transmission at cholinergic sites.
Used intraocularly to produce rapid miosis during ophthalmic surgery.

COMMON BRAND NAMES

Miochol-E

HOW SUPPLIED

Miochol-E Intraocular Inj Pwd F/Sol: 20mg

DOSAGE & INDICATIONS

For miosis induction in cataract surgery, in penetrating keratoplasty, iridectomy and other anterior segment ocular surgery where rapid miosis may be required.

Intraocular dosage (Miochol-E 1% solution)

Adults

In most cases, 0.5 to 2 mL of the 1% intraocular solution instilled into the anterior chamber produces satisfactory miosis. Intraocular irrigation with the drug must be gentle. Note that the syringe filter supplied with Miochol-E has a priming volume of 0.6 mL (approximately). For prolonged miosis, a second application may be used.

MAXIMUM DOSAGE

Adults

20 mg (2 mL of 1% Miochol-E solution) intraocularly per eye is usually sufficient. A second application may be needed for prolonged miosis.

Geriatric

20 mg (2 mL of 1% Miochol-E solution) intraocularly per eye is usually sufficient. A second application may be needed for prolonged miosis.

Adolescents

Safety and efficacy have not been established.

Children

Safety and efficacy have not been established.

Infants

Safety and efficacy have not been established.

Neonates

Safety and efficacy have not been established.

DOSING CONSIDERATIONS

Hepatic Impairment

No dosage adjustments are needed for intraocular use.

Renal Impairment

No dosage adjustments are needed for intraocular use.

ADMINISTRATION

Ophthalmic Administration

Directions for Preparing MIOCHOL-E (acetylcholine chloride):

Aqueous solutions of acetylcholine chloride are unstable. Prepare solution immediately before use.
Sterile unless package is open or broken. Do NOT gas sterilize.
Inspect the unopened blister, vial and ampule to ensure that they are all intact. Peel open the blister under a sterile field. Maintain sterility of the outer containers of the vial and ampule during preparation of solution.
Aseptically attach a sterile 18-20 gauge, beveled needle to the luer tip of a sterile disposable syringe with a twisting motion to assure a secure fit.
Break open the ampule containing the diluent. The One Point Cut (OPC) ampule must be opened as follows: Hold the bottom part of the ampule with the thumb pointing to the colored dot. Grasp the top of the ampoule with the other hand, positioning the thumb at the colored dot, and press back to break at the existing cut under the dot.
Remove the needle protector and withdraw the diluent from the ampule into the syringe. Discard the ampule.
Remove and discard the cap from the top of the vial.
Insert the needle through the center of the vial stopper, and transfer the diluent from the syringe to the vial. Shake gently to dissolve the powder.
Slowly withdraw the solution from the vial through the needle into the syringe. Discard the needle.
Aseptically open the syringe filter pouch, and attach the filter onto the luer tip of the syringe with a twisting motion to assure a secure fit.
Aseptically attach a sterile blunt tip irrigation cannula to the male luer of the filter prior to intraocular irrigation.
Discard the filter appropriately after use.
Do not reuse the syringe filter.
Do not aspirate and inject through the same filter.
Do not use solution which is not clear and colorless. Discard any solution that has not been used.

Administration of MIOCHOL-E (acetylcholine chloride):
Instill into the anterior chamber before or after securing one or more sutures. Instillation should be parallel to the iris face and tangential to pupil border.
Instillation should be gentle; avoid forceful jet administration.
If there are no mechanical hindrances, the pupil starts to constrict in seconds and the peripheral iris is drawn away from the angle of the anterior chamber. Any anatomical hindrance to miosis must be released to permit the desired effect of the drug. In most cases, 0.5 to 2 mL produces satisfactory miosis. Note that the syringe filter supplied with Miochol-E has a priming volume of 0.6 mL (approximately).
In cataract surgery, use Miochol-E only after delivery of the lens.
Discard any solution that has not been used.

STORAGE

Miochol-E:
- Protect from freezing
- Store between 39 to 77 degrees F

CONTRAINDICATIONS / PRECAUTIONS

General Information

Acetylcholine use is contraindicated in any patient with a known hypersensitivity to acetylcholine or any of the product components.

Iritis

Acetylcholine use should be avoided in patients with acute iritis and acute inflammatory disease of the anterior chamber. Cholinergic miotics might worsen inflammation in these situations.

Children, infants, neonates

The safety and efficacy of intraocular acetylcholine in neonates, infants, and children (including adolescents) has not been established according to the manufacturer.

Pregnancy

Safe use of this drug during pregnancy has not been established. Therefore, before use of acetylcholine in pregnant women or women of childbearing potential, the potential benefits should be weighed against possible risks to mother and fetus.

Breast-feeding

It is not known whether acetylcholine is excreted in human milk. Acetylcholine via intraocular administration typically results in low systemic concentrations; therefore, it is unlikely that nursing infants would be exposed to clinically significant amounts via breast milk. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

ADVERSE REACTIONS

Severe

optic atrophy / Delayed / 1.0-10.0
corneal opacification / Delayed / 1.0-10.0
corneal degeneration / Delayed / 1.0-10.0
bradycardia / Rapid / Incidence not known
bronchospasm / Rapid / Incidence not known

Moderate

corneal edema / Early / 1.0-10.0
dyspnea / Early / Incidence not known
hypotension / Rapid / Incidence not known

Mild

diaphoresis / Early / Incidence not known
flushing / Rapid / Incidence not known
headache / Early / Incidence not known

DRUG INTERACTIONS

Ambenonium Chloride: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase

inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Amoxapine: (Major) Amoxapine may antagonize some of the effects of parasympathomimetics. However, bethanechol has occasionally been used therapeutically to offset some of the adverse antimuscarinic effects of cyclic antidepressants. Due to their anticholinergic actions, some cyclic antidepressants, such as amoxapine, may potentially antagonize the therapeutic actions of cholinergic agonists.
Anticholinergics: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine; Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine; Difenoxin: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine; Diphenoxylate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine; Edrophonium: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided. (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Atropine; Hyoscyamine; Phenobarbital; Scopolamine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Belladonna Alkaloids; Ergotamine; Phenobarbital: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Belladonna; Opium: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Benztropine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Chlordiazepoxide; Clidinium: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Cholinesterase inhibitors: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Dicyclomine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Disopyramide: (Moderate) Disopyramide possesses clinically significant antimuscarinic properties and these appear to be dose-related. It is possible that disopyramide could antagonize the muscarinic actions of cholinergic agonists. Clinicians should be alert to this possibility.
Donepezil: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Donepezil; Memantine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Edrophonium: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Flavoxate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Galantamine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Glycopyrrolate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Glycopyrrolate; Formoterol: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Homatropine; Hydrocodone: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Hyoscyamine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Indacaterol; Glycopyrrolate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Maprotiline: (Major) Maprotiline may antagonize some of the effects of parasympathomimetics. However, bethanechol has occasionally been used therapeutically to offset some of the adverse antimuscarinic effects of cyclic antidepressants. Due to their anticholinergic actions, some cyclic antidepressants like maprotiline may potentially antagonize the therapeutic actions of the cholinesterase-inhibitors used for the treatment of dementia.
Mepenzolate: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Methscopolamine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Neostigmine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Oxybutynin: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Physostigmine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Propantheline: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Pyridostigmine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Rivastigmine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Scopolamine: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and

cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Tacrine: (Major) Cholinergic agonists can cause additive pharmacodynamic effects if used concomitantly with cholinesterase inhibitors. Concurrent use is unlikely to be tolerated by the patient and should be avoided.
Tricyclic antidepressants: (Moderate) Tricyclic antidepressants (TCAs) may antagonize some of the effects of parasympathomimetics (e.g., cholinesterase inhibitors) due to their anticholinergic activity. However, parasympathomimetics like bethanechol have occasionally been used historically to offset some of the adverse peripheral antimuscarinic (anticholinergic) effects of TCAs, such as dry mouth, constipation, or urinary retention. For years, physostigmine was used as an adjunct to the treatment of TCA overdose; however, its efficacy was limited to addressing anticholinergic effects. Additionally, case reports suggest that harmful effects such as seizures and bradyarrhythmias progressing to asystole, especially in patients with cardiac conduction abnormalities at baseline, are possible. For these reasons, physostigmine is no longer considered a standard of care in the treatment of TCA overdose.
Trihexyphenidyl: (Major) The muscarinic actions of drugs known as parasympathomimetics, including both direct cholinergic receptor agonists and cholinesterase inhibitors, can antagonize the antimuscarinic actions of anticholinergic drugs, and vice versa.
Trospium: (Moderate) Pharmacologically, parasympathomimetic drugs enhance muscarinic/cholinergic function. Because trospium is an antimuscarinic, the muscarinic actions of drugs known as parasympathomimetics, including direct cholinergic agonists, could be antagonized when used concomitantly with trospium.

PREGNANCY AND LACTATION

Pregnancy

Safe use of this drug during pregnancy has not been established. Therefore, before use of acetylcholine in pregnant women or women of childbearing potential, the potential benefits should be weighed against possible risks to mother and fetus.

It is not known whether acetylcholine is excreted in human milk. Acetylcholine via intraocular administration typically results in low systemic concentrations; therefore, it is unlikely that nursing infants would be exposed to clinically significant amounts via breast milk. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

MECHANISM OF ACTION

Acetylcholine is a direct-acting parasympathomimetic ophthalmic agent used to produce miosis during ophthalmic surgery. It is a naturally occurring neurohormone that helps transmit nerve impulses at all cholinergic sites including somatic and autonomic nerves. Direct application of acetylcholine causes contraction of the sphincter muscles of the iris. This results in miosis and contraction of the ciliary muscle thereby leading to accommodation. Miosis occurs promptly and lasts for approximately 10 minutes.

PHARMACOKINETICS

Acetylcholine chloride is administered intraocularly. Precise pharmacokinetic data are not available. When applied to the intact eye, natural cholinesterase rapidly breaks the drug down more rapidly than it can penetrate the cornea.

Other Route(s)

Intraocular route:
Acetylcholine is applied directly to the iris where it is absorbed immediately and produces miosis within seconds. Miosis lasts for approximately 10 minutes. Topical ocular instillation of acetylcholine to the intact eye causes no discernible response as cholinesterase destroys the molecule more rapidly than it can penetrate the cornea.