MINIMS® OXYBUPROCAINE EYE DROPS

Name of Medicine:

Oxybuprocaine Hydrochloride

Description:

Composition: Active. Benoxinate (oxybuprocaine) HCl USP.
Inactive. Water—Purified and Hydrochloric acid.
No preservatives are contained in the formulation.

Chemical Structure

Minims Benoxinate (oxybuprocaine) hydrochloride is a local, surface anaesthetic of the ester type. It is a white or off-white crystal or crystalline powder, odourless or with a slight characteristic odour. It is freely soluble in water, alcohol and chloroform and practically insoluble in ether. Aqueous solutions have a pH of 4.5 to 6.

The solution is available as a 0.4% (4mg/mL) single-use, clear, colourless sterile ophthalmic solution.

Chemical name: 2-Diethylaminoethyl-4-amino-3-butoxybenzoate hydrochloride.
Formula: C_{17}H_{28}N_{2}O_{3}.HCL  MW 344.9
CAS 99-43-4 (oxybuprocaine); 5987-82-6 (hydrochloride).

Pharmacology:

Surface or topical anaesthesia blocks conduction of sensory, motor and autonomic nerve fibres, the excitability of nociceptors and the conducting system of the heart. A 0.4 % solution of Benoxinate has been shown to give effective surface anaesthesia in short ophthalmological procedures. Sensation of pain is locally and reversibly reduced, with the possibility of temperature and pressure sensitivity also affected. Anaesthetic activity is ten times that of cocaine and twice that of tetracaine (amethocaine).

Surface anaesthesia occurs in approximately one minute with 0.4% intra-ocular solution, and peak response is between 1 and 15 minutes. Anaesthesia persists for about 20 to 30 minutes, with full corneal sensitivity taking 40 minutes or more to return.
Benoxinate has demonstrated a concentration-related inhibition of platelet-activating-factor-induced aggregation of human blood samples taken from volunteers. 50% inhibition was demonstrated at 170 micromoles.

A 1% Benoxinate solution demonstrated significant bactericidal activity against *Pseudomonas aeruginosa*, *Escherichia coli*, *Haemophilus influenza* and *Streptococcus pneumonia*.

Benoxinate, like several local anaesthetics, competitively inhibits the exchange transport of glucose in human erythrocytes.

**Pharmacokinetics:**

Most local anaesthetics are readily absorbed through mucous membranes and through damaged skin. Local anaesthetics at tissue pH can diffuse through connective tissue and cellular membranes to reach the nerve fibre where ionisation can occur. Benoxinate is metabolized by esterases in the plasma and, to a lesser extent, in the liver. There are at least nine metabolites, with 3-butoxy-4-aminobenzoic acid making up 70 – 90 %. Their activity is unknown. Urinary excretion of the drug and its metabolites at 9h after an oral dose is approximately 90%.

**Indications:**

To produce local anaesthesia in the eye for short ophthalmological procedures.

**Contraindications:**

Known hypersensitivity to anaesthetics in this group.
Concomitant infection of the eye.
Patient instillation of drug. To be given only by a clinician.

**Warnings:**

Benoxinate eye drops should not be used for prolonged periods. Frequent or chronic use may result in severe corneal damage, keratitis and acquired tolerance. NOT FOR INJECTION – Topical ophthalmic use only.

**Precautions:**

The anaesthetized eye should be protected from dust and bacterial contamination.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. This blocks the passage of the drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa. It is especially advisable in children.

This preparation may cause transient blurring of vision. Patients should be advised not to drive or operate hazardous machinery until their vision is clear.

Benoxinate has the potential to cause severe corneal damage and morbidity.
Use of benoxinate 1% solution for long term ventilator bronchoscopy had no effect on cardiovascular function, but produced a decline in mean arterial oxygen pressure (paO2) from 100 to 78, which persisted for over 30 minutes in one patient.

Anaesthesia of the respiratory system with benoxinate has rarely resulted in hypersensitivity reactions including lung oedema.

Carcinogenicity/Mutagenicity
No data is available regarding the carcinogenicity or mutagenicity of Benoxinate in humans.

Use in Pregnancy: (Category D)
Safety for use in pregnancy has not been established. The use of Minims Benoxinate eye drops should be used only when it is considered essential by a physician.

Use in Lactation
No studies have established the safety of Minims Benoxinate eye drops during lactation. This medication should therefore be used only when it is considered essential by a physician.

Interactions
Metabolism of local anaesthetics derived from esters may be inhibited by anticholinesterases and thus prolong the effects of Benoxinate. Ester - type local anaesthetics may competitively enhance the neuromuscular blocking action of suxamethonium.

Adverse Reactions:

Ocular
Instillation of drops commonly causes a transient stinging or burning sensation.

Stromal infiltration, oedema, candida keratitis, disciform keratitis and peripheral corneal ring formation have all been reported as a result of the frequent use of Benoxinate.

Frequent or chronic use can also result in acquired tolerance, epithelial cell damage irreversible apical cell damage at the level of the corneal endothelial cells and keratitis.

Local anaesthetics are known to inhibit the rate of movement of corneal epithelial cells migrating to cover wounds.

Reductions in tear film stability have also been documented as a result of Benoxinate treatment.

A fibrinous iritis has been observed in two patients following minor surgery, believed to be the result of drug entering the anterior chamber.

Cardiovascular
One incidence of sinus bradycardia after one drop of 0.4% benoxinate solution was instilled into each eye occurred in one patient.
Central Nervous System
Abuse or overdose of benoxinate may cause sedation, confusion, agitation, euphoria, disorientation, hearing, visual or speech disorders, paraesthesia, muscle twitching and if severe enough seizures, respiratory depression and coma. These symptoms would be very rare in therapeutic doses.

Gastrointestinal
Occasional nausea, vomiting and dysphagia have been observed during therapy.

Immunological
Use of local anaesthetics of the ester type, especially when frequent, has the potential to cause allergic reactions including contact allergy, urticaria and angioneurotic oedema.

Dosage and Administration:

All Patients
One drop of 0.4% benoxinate solution instilled into each eye has been shown sufficient for tonometry after one minute. Addition of a further drop after 90 seconds provides adequate anaesthesia for fitting of a contact lens. To obtain a deeper anaesthetic effect, further drops may be instilled at intervals of no less than 90 seconds. For most procedures one to two drops is sufficient, however for removal of foreign bodies or minor surgery, three to six drops is suggested.

One drop a minute for 10 minutes was shown to provide adequate anaesthesia for patients undergoing pterygium surgery.

One drop instilled in each eye of a 0.2% benoxinate solution prior to tonometry, was shown to be sufficient in patients over 40 years, suggesting that older patients may achieve sufficient anaesthetic effect with a lower dose of drug.

Corneal sensitivity is normal again after about 1 hour

Each Minims unit should be discarded after a single use.

Overdosage:

Overdose of any local anaesthetic may cause various serious neurological, cardiovascular and respiratory events. These are overwhelmingly associated with oral and parenteral use/abuse, and are unlikely to occur in therapeutic, topical doses. Treatment for the various clinical effects is complex, however cessation of drug and supportive management including oxygen, intravenous fluids and management of any seizures is essential.

Presentation:

Single use clear colourless sterile eye drops available in cartons of 20 units. Each unit contains approximately 0.5mL

AUST R 32259
MINIMS Oxybuprocaine Product Information

Storage:

Store at 2°C to 8°C. (Refrigerate. Do not freeze.) Do not expose to strong light.

Poisons Schedule: S4 - Prescription Only Medicine

Name and address of Sponsor.

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