Oxybuprocaine (benoxinate)

Newborn use only

2023

Alert	Prolonged ophthalmic use is not recommended due to risk of severe keratitis and corneal adverse effects. For short procedure use only.
Indication	Local anaesthesia for eye examination [including RetCam3™] and procedures [laser] in newborn infants in conjunction with other pharmacological and/or non-pharmacological analgesia methods.
Action	Local anaesthetic.
Drug type	Ester-type local anaesthetic.
Trade name	Minims® Oxybuprocaine hydrochloride 0.4% w/v
Presentation	Oxybuprocaine hydrochloride 0.4% single-use, preservative-free, eye drop, approximately 0.5 mL per minim.
Dose	One drop each eye as required 1–5 minutes prior to examination. Complete examination within 20 to 30 minutes of administration. Further drops may be needed to achieve a complete anaesthetic effect.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No information. Hepatic impairment – No information.
Maximum dose	No information.
Total cumulative dose	
Route	Topical instillation into the eyes.
Preparation	Not applicable.
Administration	Apply pressure to the lacrimal sac during and for 60 seconds after instillation of eye drop to minimise systemic absorption. Wipe away excess medication.
Monitoring	
Contraindications	Hypersensitivity to any of the components of the preparation. Eye infection.
Precautions	The cornea may be damaged by prolonged or frequent application of anaesthetic eye drops. Prolonged use of topical ophthalmic local anaesthetics has been associated with severe keratitis and permanent corneal opacification and scarring with accompanying reduction of visual acuity or visual loss. Systemic toxicity typical of local anaesthetics could occur if sufficient amounts were absorbed systemically. 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.
Drug interactions	Metabolism may be inhibited by anticholinesterases with prolongation of the effects of oxybuprocaine. May competitively enhance the neuromuscular blocking action of suxamethonium
Adverse reactions	Transient stinging or burning sensation. Fibrinous iritis. Limited safety data in infants. Inappropriate and frequent use might cause corneal ulcerations and perforations.
Compatibility	No information.
Incompatibility	No information.
Stability	Discard immediately after use.
Storage	Store in refrigerator at 2 °C to 8 °C. Do not freeze. Protect from light.
Excipients	
Special comments	Anaesthesia persists for about 20 to 30 minutes. Corneal sensitivity is normal again after about one hour
Evidence	**Efficacy:** **Eye examination for ROP:** Several cohort studies reported the use of 0.4% Oxybuprocaine eye drops for screening of retinopathy of prematurity (ROP). Lorenz et al used Oxybuprocaine eye drops for local anaesthesia in 2,444 eyes of 1,222 preterm babies to facilitate retinal imaging using the wide-angle digital fundus camera for assessment of ROP. The mean gestational age of infants at birth was 30 weeks and birth weight was 1395 gm. Of the total 3,230 image sets, 97.6 % were of enough quality as per the preset quality criteria and 2.4% images required a repeat examination. (1) In a prospective study, Li et al investigated the incidence of ROP in 3000 preterm infants using 0.4% oxybuprocaine eye drops for analgesia to facilitate examination of eyes using a digital camera. The authors did not report any limitations of medications used for either local anaesthesia or mydriasis and cycloplegia. (2)

	However, the data form randomised control studies on efficacy of Oxybuprocaine eye drops for ROP examination is limited. Sun et al, in a small RCT, studied the efficacy of human gentle touch as a way of comforting and reducing PIPP scores in preterm infants during ROP examination. In both experimental and control arms, all preterm infants received oxybuprocaine 0.4% eye drops as local analgesia as their standard policy. Addition of human gentle touch improved PIPP scores during ROP examination and no adverse events were reported in either arm. In another RCT of developmental care measures (NIDCAP) in preterm infants undergoing ROP examination, oxybuprocaine was used in both treatment arms in 20 infants prior to examination. (4,5) Both treatment arms had significant increases in neonatal pain scores in response to eye examination. There is more evidence for use of proxymetacaine (proparacaine) eye drops during ROP examination. Three RCTs in newborn infants have evaluated the effects of proxymetacaine hydrochloride 0.5% ophthalmic solution during ROP examination.(6,7) Proxymetacaine eye drops prior to examination were effective in reducing pain responses and/or the number of infants with high pain scores on eye examination. However, the effect was not great and a substantial proportion of infants still had high pain scores. Another RCT compared topical anaesthetic eye drops (proxymetacaine hydrochloride 0.5% ophthalmic solution) to oral sucrose during ROP examination. There was no difference between pain scores. (8,9) A systematic review of these studies concluded that although there is evidence that topical eye anaesthetic at least 30 seconds prior to the procedure reduces pain, its effect is incomplete and screening remains a painful procedure.(10) **Conclusion:** There is no single pain intervention recommended for ROP examinations. (11) A multimodal approach to eliminating pain is recommended.(5) The Pain Study Group of the Italian Society of Neonatology 2009 recommended, in the case of RetCam3™ screening, applying local anaesthesia with oxybuprocaine 0.4% or tetracaine (amethocaine) 1% eye drops. (12) **Laser treatment of ROP:** A multicentre, observational study compared local anaesthesia with oxybuprocaine versus intravenous pentazocine versus intravenous fentanyl versus air, oxygen and sevoflurane inhalation.(13) Heart rates were elevated in oxybuprocaine and pentazocine groups; systemic blood pressures were elevated in oxybuprocaine, pentazocine and fentanyl groups; and poor analgesic efficacy was found in the oxybuprocaine, pentazocine and fentanyl groups. However; the air, oxygen and sevoflurane inhalation group experienced hypothermia, enteral feeding intolerance and apnoea more frequently. **Conclusion:** Oxybuprocaine alone provides inadequate analgesia for laser treatment. The Pain Study Group of the Italian Society of Neonatology 2009 recommended, for laser therapy for ROP, in general, combine a local anaesthetic with general anaesthesia.(12) **Safety** Older patients describe stinging for 10 seconds after instillation of oxybuprocaine eye drops. (14) There is more evidence for the use of proxymetacaine 0.5% eye drops than oxybuprocaine for ROP screening. However, single use proxymetacaine eye drops are not currently available in Australia and NZ. Proxymetacaine 0.5% is available as 15 mL bottle with preservative benzalkonium chloride. Topical local anaesthetics currently used in ophthalmology, including proxymetacaine and oxybuprocaine, are mostly free of reported complications. Systemic side effects have not been documented with them. However, inappropriate use by patients might cause corneal ulcerations and perforations. Known hypersensitivity to a local anaesthetic drug itself or its preservative is a contraindication for topical local anaesthetic use. (15) **Pharmacokinetics** Pharmacokinetics relate to adult data. Oxybuprocaine 0.4% has an intra-ocular surface anaesthesia onset after approximately 1 minute and peak anaesthesia between 1 and 15 minutes. Corneal sensitivity is normal again after about one hour. (16) Anaesthesia persists for about 20 to 30 minutes. Oxybuprocaine is metabolised by plasma and liver esterase enzymes and predominantly excreted in urine. (16)
Practice points	
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