Tobramycin 0.3% Topical

Newborn use only

2022

Alert	Tobramycin eye drops are not recommended for routine empirical treatment of bacterial conjunctivitis in neonates. Use under close supervision and in consultation with an ophthalmologist.
Indication	Treatment of bacterial conjunctivitis. For prophylaxis following intra-ocular injection for ROP
Action	Inhibit protein synthesis by irreversibly binding to the 30S ribosomal subunit and causing cell membrane damage. Concentration-dependent bactericidal effect.
Drug type	Aminoglycoside.
Trade name	Tobrex
Presentation	Eye drop, 0.3% (3 mg/mL tobramycin) 5 mL drop-tainer bottle Eye ointment, 0.3% (3 mg/mL tobramycin), 3.5g ophthalmic tube
Dose	Dose frequency depends upon severity of infection and response to treatment.(1) **First 48 hours:** 1 eye drop every 2–4 hours in the affected eye and, if clinical improvement, **From day 3 up to day 7**: 1 drop 4 times daily. Eye ointment may be used as an adjunct to drops at night, or as a single agent 3 times daily.
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – Not applicable. Renal impairment – Not applicable. Hepatic impairment – Not applicable.
Maximum dose	
Total cumulative dose	
Route	Topical
Preparation	Not applicable
Administration	Instil 1 eye drop into the affected eye(s) by gently tapping or pressing the base of the bottle with your forefinger. After administering eye drop, gently press against the inner corner of eye to reduce systemic absorption. If other eye drop(s) are administered, wait for 5 minutes between drops.
Monitoring	Total serum aminoglycosides if concomitant systemic treatment
Contraindications	Hypersensitivity to tobramycin or any of the product ingredients
Precautions	Allergic reaction to an ocular aminoglycoside; cross-allergenicity may occur
Drug interactions	Topical beta lactam inactivates tobramycin
Adverse reactions	Ocular irritation and superficial punctate keratitis Delayed corneal epithelial wound healing Retinal toxicity (if there is leakage through corneoscleral wound) Hypersensitivity reactions
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	
Storage	Store below 25°C. Discard container 4 weeks after opening.
Excipients	Tobrex (tobramycin) Eye Drops: contain boric acid, sodium sulfate, sodium chloride, tyloxapol, sodium hydroxide and/or sulphuric acid (to adjust pH) and purified water, benzalkonium chloride 0.01% (0.1 mg) as preservative. Tobrex (tobramycin) Eye Ointment: contains mineral oil and petroleum base, chlorobutanol 0.5% (5 mg) as preservative.
Special comments	Safety and effectiveness in children below the age of 1 year have not been established. Concurrent and/or sequential use of Tobrex with other drugs with neurotoxic or ototoxic potential should be avoided. Do not use Tobrex simultaneously with a topical beta lactam type antibiotic as this is likely to result in inactivation of tobramycin. Tobramycin eye drops are supplied in a round DROP-TAINER container which requires user to press the bottom of the bottle instead of squeezing the sides to dispense a drop of medication.
Evidence	**Background** A 2012 epidemiological study conducted in a Level III-IV NICU in the USA, identified gram negative bacteria to be the causative agent in 38% of infants with bacterial conjunctivitis (2). Topical tobramycin is frequently used for targeted treatment of serious bacterial conjunctivitis caused by gram-negative bacilli,

	such as pseudomonas aeruginosa (3). **Efficacy** Limited evidence is available on topical antibiotics for bacterial conjunctivitis in neonates. There was no trial that specifically assessed topical tobramycin in bacterial conjunctivitis in neonates. Aminoglycoside treatment is therefore not recommended as the first-line antibiotic therapy for empirical treatment of neonatal bacterial conjunctivitis. **Tobramycin vs placebo** A 2012 Cochrane review identified improvement in clinical and microbiological remission with topical antibiotic therapy. Topical antibiotics were of benefit in improving 'early' clinical (RR 1.36, 95% CI 1.15 to 1.61) and microbiological (RR 1.55, 95% CI 1.37 to 1.76) remission rates. (4) A further 2017 Cochrane review on topical treatments for blepharokeratoconjunctivitis in children, identified one study which compared the use of topical tobramycin with placebo, loteprednol etabonate, and combination therapy in 137 children. The study was deemed to be at high risk of attrition bias due to selective outcome reporting, however all groups showed a reduction in blepharokeratoconjunctivitis with no significant differences between the groups. The tobramycin and placebo groups did not report any adverse events with treatment (5). **Tobramycin vs alternative agent** A double-masked randomised trial was conducted to compare the efficacy and safety of tobramycin and gentamicin ophthalmic ointment in the treatment of superficial external eye disease in the adult population (n=77). Results demonstrated that 97% of the tobramycin treated patients and 91.3% of the gentamicin treated patients were clinically cured or improved. Tobramycin eradicated or controlled 87.8% of the bacterial infections vs. 77.4% for gentamicin. There was also a 9.3% adverse reaction rate with tobramycin vs. 17.6% with gentamicin (6). A systematic review comparing the use of azithromycin 1-1.5% ophthalmic solution with tobramycin 0.3% eye drops, concluded that azithromycin eye drops were more effective than tobramycin 0.3% eye drops in short duration dosing (⩽5 days) (RR 1.13; 95% CI: 1.008, 1.28), whereas on increased duration (>5 days), azithromycin was as effective as tobramycin (RR 1.007; 95% CI: 0.96, 1.05). There was no significant difference in the efficacy of resolution of infection between 2 treatments (RR 0.99; 95% CI: 0.96, 1.018) (7). A double blinded RCT compared the use of topical tobramycin with topical ciprofloxacin in 257 children, Microbiological eradication was observed in 90.1% of the ciprofloxacin group and 84.3% of the tobramycin group (P = 0.29). Clinical judgement identified 87.0% of the ciprofloxacin patients and 89.9% of the tobramycin patients as clinically cured on day 7 (p>0.5). There were no serious adverse medical events attributable to either treatment (8). **Safety** Adverse effects has been uncommon with ophthalmic solutions for neonatal bacterial conjunctivitis (4). A study by Cagle et al hypothesized that whilst aminoglycoside ophthalmic solutions are safe to use, the use of tobramycin ophthalmic solution is associated with less frequent adverse reactions than topical gentamicin, due to the preservatives used in gentamicin ointment (methyl and propyl paraben) (9). The most frequent reported side effects with tobramycin 0.3% solution have been hypersensitivity and localized eyelid itching and swelling. This has been reported in 0.3% of patients using tobramycin ophthalmic solution (3).
Practice points	**ANMF consensus:** Proven bacterial conjunctivitis in the neonatal population should be treated with appropriate topical antibiotics to prevent progression of disease. Limited evidence is available to support the use of tobramycin as an empirical therapy for neonatal bacterial conjunctivitis, therefore its use should be recommended by ophthalmologists and for serious infections not responding to treatment with other agents. Higher strengths of tobramycin eye drops (0.9–1.4%) are used for treating bacterial keratitis and are prepared by some pharmacies.
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