



Chloramphenicol use in Ophthalmic Practice

RANZCO Position Statement

This position statement has been reviewed and endorsed by the RANZCO Public Health Committee and RANZCO Therapeutics Committee

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Background

Chloramphenicol, is a commercially available topical antibiotic, and has been in clinical use since 1949¹. It has a broad spectrum of activity against many Gram positive and Gram negative organisms, but is bacteriostatic, rather than bactericidal, and importantly, lacks activity against *Pseudomonas aeruginosa*².

Chloramphenicol has an important role in the management of bacterial conjunctivitis, prophylactically in the post-operative period, and in the setting of minor corneal trauma. It has little role in the treatment of microbial keratitis, especially in contact lens wearers who are at risk of *Pseudomonas* infections. It should also be noted that Chloramphenicol is also the most commonly used first line antibiotic for any condition presenting as 'red eye' to general practitioners, other non-ophthalmic medical practitioners, and pharmacists. This includes non-infective causes such as episcleritis and iritis^{3,4}.

In Australia, chloramphenicol was reclassified from a Schedule 4 to a Schedule 3 (S3) medication in 2010. Schedule 4 medications are prescribed by registered medical practitioners or endorsed optometrists. Schedule 3 medications are available to the public from a pharmacist without a prescription. The rationale behind the rescheduling of ophthalmic chloramphenicol preparations was to reduce patient waiting periods for initiating treatment and patient presentations to general practices and emergency departments⁵. Such benefits of improved patient access to topical chloramphenicol preparations was argued to outweigh the risks of the projected small percentage of misdiagnosis and inappropriate use as a significant proportion of common red-eye conditions are benign and due to self-limiting cases of bacterial, viral or allergic conjunctivitis^{5,6}. Improved accessibility of chloramphenicol preparations facilitates patient ability to self-diagnose and treat conjunctivitis. However, appropriate treatment requires health professionals to be diligent in adhering to protocols and exercising appropriate clinical judgment for supplying this medicine⁶.

At the time that Chloramphenicol was changed to Schedule 3, both the Australian Medical Association (AMA), and the Royal Australian and New Zealand College of Ophthalmologists (RANZCO) expressed strong disapproval of the decision to reschedule chloramphenicol⁷. The concern was based on the fact that pharmacists have not been trained in the diagnosis of eye disease, and do not have the appropriate equipment to properly examine an eye. Following consultation with the Optometric Association of Australia, a protocol was developed to guide pharmacists in the provision of ocular chloramphenicol.

In New Zealand the situation is similar to Australia as Chloramphenicol was recently made available over the counter (OTC). There are a number of vision threatening causes of the red eye, including microbial keratitis, acute glaucoma, and uveitis, and initial inappropriate treatment with OTC chloramphenicol could lead to a worse outcome for these patients.

Especially in microbial keratitis, OTC treatment will delay appropriate intensive topical therapy, and may also prevent accurate diagnosis because of alteration in viability of causative organisms and lower rate of positive cultures on corneal scrape.

In general, antibiotic use without specific accurate clinical diagnosis, is to be discouraged because of the increasing development of antibiotic resistance in the community. OTC use goes against this policy.

Ophthalmic Use of Chloramphenicol

The Therapeutic Goods Administration (TGA) has approved chloramphenicol for the 1) treatment of bacterial conjunctivitis, and 2) use under medical supervision in the treatment of other superficial ocular infections caused by chloramphenicol sensitive organisms. The manufacturer does not recommend over-the-counter (OTC) chloramphenicol use under the following circumstances: Presence of photophobia, severe eye pain, reduced vision, and contact lens wear, amongst other conditions.

Microbial keratitis, for example, is an ophthalmic emergency, and a significant cause of ocular morbidity. In this context, anti-microbial therapy is essential for preserving vision, as prompt treatment limits damage to the cornea⁸. Prompt institution of anti-microbial therapy relies on early diagnosis of infection, knowledge of the likely infecting microbe, and the availability of effective anti-microbial agents^{10,11}. The mainstay of treatment is intensive topical antibiotics, commenced before results of corneal culture become available. The two options are monotherapy with commercially available fluoroquinolones, or dual therapy with fortified cephalosporin-aminoglycoside combination.

Patients who wear contact lenses are at greater risk of bacterial keratitis and infection by resistant organisms than the general population^{9,10}. Further, the most common organism isolated is the gram-negative bacterium, *Pseudomonas*, which is typically not sensitive to chloramphenicol. Therefore, empirical treatment for conjunctivitis with chloramphenicol in this cohort of patients is not recommended, as this antibiotic will likely be ineffective and delay specialist review and initiation of more appropriate treatment^{9,10,11}.

The database of Adverse events from 2015-2017 records 17 Chloramphenicol adverse events of which 9 relate to visual, keratitis or inappropriate use of the drug. Only 4 of these appear to be associated with the topical chloramphenicol. However, further supporting evidence highlighting the increasing incidence of adverse events resulting from an increased likelihood of negative corneal cultures and delayed presentation of keratitis are the annual surveillance reports. The Sydney Eye Hospital is in the process of publishing keratitis data from the last 5 years¹².

Recommendations

In order to prevent inappropriate use of chloramphenicol in the future, ophthalmologists have an obligation to report such adverse events to the TGA via the Australian Adverse Drug Reaction Reporting System, and in doing so, advocate for more stringent criteria in prescription of ophthalmic antibiotics.

There are several 'red flag' risk factors for microbial keratitis: contact lens use, significant dry eye, topical corticosteroid use, recent eye trauma or surgery. Patients presenting with such red flag symptoms should be urgently referred for specialist treatment without initiating topical chloramphenicol.

The extent to which non-ophthalmic health professionals such as pharmacists screen for red flag symptoms should be determined.

Ophthalmologists should continue to educate non-ophthalmic health professionals, including general practitioners and pharmacists, on the symptoms and signs of microbial keratitis, associated risk factors, and the need for prompt consultation with an ophthalmologist, who is the only medical specialist with the requisite training and resources to diagnose and manage this sight-threatening condition.

Lessons from Practice

- Patients presenting with acute red eye symptoms are at risk of misdiagnosis, with sight-threatening consequences. Therefore, adherence to guidelines and thorough review of patient history and symptoms by all health professionals is imperative when considering the use of ophthalmic chloramphenicol
- Infective conjunctivitis is *not* typically associated with severe eye pain, progressive vision loss, or photophobia. These symptoms should act as ‘red flags’ for the treating health professional, pointing to potentially serious microbial keratitis.
- Contact lens wear, significant dry eye, topical corticosteroid use, recent eye trauma or surgery are all ‘red flag’ risk factors for microbial keratitis, and should be elicited in the patient’s history prior to commencement of chloramphenicol.
- In the presence of ‘red flag’ symptoms or risk factors, no treatment should be provided, and the patient should be immediately referred to avoid delaying appropriate assessment and treatment

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