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Acute Bacterial Conjunctivitis

ABSTRACT

Acute bacterial conjunctivitis is encountered frequently in optometric practice. The condition often resolves on its own without any treatment.

Although it is a self-limiting condition, current initial treatment for bacterial conjunctivitis is the application of a broad-spectrum topical antibiotic. While the use of antibiotics is associated with improved rates of early clinical remission, and early and late microbiological remission; its benefit in improving clinical outcome remains minimal. When prescribing antibiotics, clinician should ensure better patient compliance to minimise the growth of drug resistance.

This report describes a patient who had been diagnosed with bacterial conjunctivitis, whose condition remained unresponsive when both chloramphenicol and tobramycin were prescribed. Different types of antibiotics and their modes of action are discussed. Possible drug adverse reactions are also included.
INTRODUCTION

Acute bacterial conjunctivitis is characterised by conjunctival injection and purulent ocular discharge accompanied with foreign body sensation. Most patients are treated empirically with topical broad-spectrum antibiotics. Although recent systematic review and meta-analysis had concluded that the use of antibiotics in bacterial conjunctivitis only offers marginal benefit in improving clinic outcome, they are still widely prescribed as they can prevent the recurrence and the spread to the unaffected eye; reduce patient’s anxiety and symptoms.

This case report describes a patient whose condition remained unresponsive with chloramphenicol therapy and had subsequently developed an adverse reaction when the anti-bacterial therapy was changed to tobramycin.

CASE REPORT

A 34 year old white female presented with complaints of sticky eyelids, watery and green ocular discharge, redness, soreness and slightly blurred vision in both eyes. The symptoms started 2 weeks ago; the right eye was affected first. She was prescribed with chloramphenicol (0.5%) initially, but as no improvement was reported, it was replaced by tobramycin; improvement was only noticeable on the first day. She then had ocular swab taken for polymerase chain reaction (PCR) testing and was advised not to use tobramycin until the confirmation of results. She reported on the visit that the left eye now felt worse and noticed an increase in green discharge but a decrease in redness since the drop discontinuation. Prior ocular history included a metal foreign body removal from the right eye 10 years ago. She had flu 3 weeks ago but is in good health now, was not atopic and she was not taking any medications.

Vision

OD  6/6    OS  6/5

Slit lamp examination


OS:  360 degree conjunctival injection grade 3. Multiple white nodules at the limbus. Mild follicular change of the inferior palpebral conjunctiva. No anterior chamber inflammation.

Other investigation

Polymerase chain reaction (PCR) testing confirmed negative results for: Adenovirus, Varicella-Zoster virus, Herpes Simplex virus and Chlamydia trachomatis.
Diagnosis

A tentative diagnose of bacterial conjunctivitis was made based on the signs and symptoms.

Differential Diagnosis

**Viral Conjunctivitis** is associated watery discharge, conjunctival edema and hyperaemia, and occasional small sub-conjunctival haemorrhages. Tender palpable pre-auricular lymph node may be present.²⁻³ While both conditions share some similarities in symptoms, PCR testing has confirmed negative results for viral conjunctivitis.

**Hyperacute Bacterial Conjunctivitis** is characterised by an abrupt onset and a copious purulent discharge with marked conjunctival chemosis and eyelid swelling.²⁻³ The difference in both the type and amount of discharge has ruled out the possibility of this condition.

**Chlamydial Conjunctivitis** maybe acute or subacute in onset and are often unilateral initially. The condition is usually associated with stringy, mucopurulent discharge.¹⁻³ A pre-auricular node is often present on the affected side.¹⁻³ In this particular case, PCR testing dismissed such possibility.

**Allergic Conjunctivitis** is characterised by a red itchy eye with watery discharge and is often encountered in patients with atopic disease.¹⁻³ In this case, the hallmark symptom itchiness was not present; the green ocular discharge also suggested the condition is more of bacterial nature than allergy.

**Superficial Keratitis** Although both condition present with conjunctival hyperaemia, in this case the absence of multiple punctate epithelial lesions has ruled out the possibility of superficial keratitis.

**Blepharitis** is a common condition of the lid margin. It is often associated with itching, burning, mild mucous discharge, conjunctive injection and crusting around the eyes.²⁻³ However, its critical sign crusty, red and thickened eyelid is missing in this case; therefore it is not consistent with a diagnosis of blepharitis.

**Episcleritis** is characterised by the rapid onset of sectoral redness with mild pain in one or both eye.¹⁻³ Discharge, if present, is watery. These symptoms are inconsistent with the diffused conjunctival injection and green purulent discharge observed in this patient.

**Scleritis** is usually associated with moderate to severe ocular pain and the underlying sclera is pink.²⁻³ Both of these are not present in this case.

**Acute Angle-closure Glaucoma** is associated with a painful red eye with a pronounced elevation of intraocular pressure.¹⁻³ The patient in this case did not report experiencing any pain, frontal headache and the pupil is normal rather than
moderately dilated. Also the presentation of acute angle-closure glaucoma is often unilateral.

Acute Anterior Uveitis The hallmark of acute anterior uveitis is missing, there were no presence of inflammatory cells and protein aqueous flare in the anterior chamber of both eyes.

Management

Ofloxacin was prescribed to replace tobramycin due to suspecting toxic reaction to Tobrex (tobramycin). Patient was asked to instil one drop of ofloxacin into the left eye q2h on the day, to reduce the dosage to qid the next day if the condition improves, the right eye is to be treated with ofloxacin qid. A review appointment was scheduled in one week time.

DISCUSSION

Acute bacterial conjunctivitis is a contagious disease caused by one or more bacterial species. Both gram-positive and gram-negative organisms can cause acute bacterial conjunctivitis. S.aureus, S pneumonia, and H.influenzae are most frequently associated with acute bacterial conjunctivitis. Bacterial conjunctivitis induced by gram-negative bacteria is generally more severe. Acute bacterial conjunctivitis usually starts in one eye with ocular irritation, mucopurulent or purulent discharge and conjunctival hyperaemia. The other eye may become involved a few days after the first eye.

Although many cases of acute bacterial conjunctivitis are self-limiting and resolve without treatment. Topical antibiotics are usually prescribed as they do provide symptomatic relief, shorten the disease duration, reduce the risk of developing complications, prevent the infection spread and hasten microbial remission.

It would be ideal to perform laboratory testing on all case of infectious conjunctivitis so the exact etiology can be identified and a more effective treatment can be used to treat the condition. However in practice, treatment of bacterial conjunctivitis is often initiated before speciation of the ocular pathogen. Hence an antibiotic with broad spectrum would be considered as the first line treatment.

Sulfonamides, once a mainstay of treatment are no longer used for treating bacterial conjunctivitis. The sulphonamides are broad spectrum drugs, however their anti-infective activity is inhibited by the para-aminobenzoic acid in purulent exudates, and also many patients are allergic to sulfa drugs.

Chloramphenicol achieves bacteriostasis by inhibiting protein synthesis. It is effective against a broad spectrum of bacteria. It is also useful in treating anaerobes, mycoplasma, rickettsia, Chlamydia, and spirochete species. Its linkage to possible aplastic anaemia has however limited its use in the US market. The risk
posed by the use of topical chloramphenicol has remained debatable. Several literature reviews have concluded that there are insufficient epidemiological and scientific data to implicate the use of topical chloramphenicol in the causation of aplastic anaemia.\textsuperscript{12,14,15} However, a full medication history should be taken and that the patient should be asked whether there is any personal or family history of blood disorder when prescribing chloramphenicol.\textsuperscript{12,14,15}

Bacitracin, developed in 1943, is bactericidal for most gram-positive bacteria including \textit{S.aureus}.\textsuperscript{8} Polymyxin B, on the other hand has excellent bactericidal activity against most gram negative organisms \textit{Pseudomonas}.\textsuperscript{8,11} When combined, a broad spectrum antibiotic can be achieved for treating acute bacterial conjunctivitis.\textsuperscript{8,11} Another effective combination is the combination of bacitracin, polymyxin B and Neomycin. Neomycin belongs to the aminoglycosides group, it has a broad spectrum anti-bacterial activity and works by inhibiting bacterial protein synthesis. However, the relative high rate of delayed, type IV hypersensitivity reaction caused by neomycin has limited its use in treating bacterial conjunctivitis.\textsuperscript{8,11}

Other aminoglycosides, gentamicin and tobramycin, also exhibits broad spectrum anti-bacterial activity and both are bactericidal against most gram-negative bacteria and some gram-positive bacteria.\textsuperscript{8} Although they can also cause allergic reactions similar to those seen with neomycin, but the adverse rates are lower. A study done by Leibowitz \textit{et al} investigated the efficacy and safety of tobramycin and gentamicin ophthalmic ointment in treating superficial external eye disease and concluded that tobramycin exhibited an advantage in the adverse event rate when compared to gentamicin, this difference is possibly either due to the toxicity difference between the two drugs or difference in their preservative systems.\textsuperscript{16} This journal article also described the common symptoms of adverse reactions including tearing, burning, itching, photophobia, conjunctival erythema, edema of the lid, and chemosis.\textsuperscript{16} All these symptoms were mild and resolved quickly when the aminoglycosides therapy was halted.\textsuperscript{16} When prescribed for bacterial conjunctivitis, gentamicin, or tobramycin solution are instilled as one drop four times daily for 5 to 7 days.\textsuperscript{8} A rather interesting study performed by Powell investigated the efficacy and toxicity of gentamicin, netilim, and tobramycin on different dosing frequency in animal models with acute pneumonia and found that intermittent dosing of a higher concentrated aminoglycosides may be less toxic and equally efficacious as frequent dosing,\textsuperscript{17} whether this will have any implication on the ophthalmic application remained unanswered.

Azithromycin, a second generation macrolide works by inhibiting bacterial protein synthesis and possessing broad spectrum action against most gram-positive pathogens as well as chlamydia species.\textsuperscript{8,11} Because of its prolonged intracellular half life, it has a rather user friendly dosing frequency, dosage is one drop twice daily for two days, then once daily for five more days.\textsuperscript{8,11} Cohereau \textit{et al} conducted a study to compare the efficacy and safety of azithromycin with tobramycin in treating purulent bacterial conjunctivitis and found a 3 day treatment with azithromycin 1.5%
was as effective and as safe as tobramycin for 7 days, a slightly higher clinical cure was observed on patients prescribed with azithromycin at day 3, the study also suggested that azithromycin may be a better choice when it comes to managing paediatric bacterial conjunctivitis.\(^7\)

Fluoroquinolones are rapidly dominating the world of bacterial infection management. It works by inhibiting bacterial DNA synthesis, which leads to cell death.\(^8\) They are used for a broad range of infections due to their excellent gram-positive, gram-negative coverage. Currently ciprofloxacin, ofloxacin, levofloxacin, gatifloxacin, and moxifloxacin are available as ocular fluoroquinolone solutions.\(^8,11\)

Both ciprofloxacin and ofloxacin exhibits a similar bactericidal potency and spectrum. Both have been compared with tobramycin when it comes to the management of bacterial conjunctivitis. Gwon \textit{et al} compared the efficacy and safety of 0.3% ofloxacin with 0.3% tobramycin when treating patients with external bacterial ocular infection and concluded that ofloxacin is able to diminish the severity of symptoms more rapidly than tobramycin.\(^18\) When compared with gentamicin, ofloxacin also exhibited a higher improvement rates both clinically and microbiologically, and the adverse reaction is less than that reported for gentamicin.\(^19\) Ciprofloxacin, on the other hand has also been shown to be as effective and safe as tobramycin when it comes to treating paediatric bacterial conjunctivitis.\(^5\) Levofloxacin, a third-generation fluoroquinolone have expanded activity against gram-positive bacteria and atypical pathogens when compared with ofloxacin and ciprofloxacin.\(^20\) Its efficacy in microbial eradication rates was also evident when compared with ofloxacin in a population with bacterial conjunctivitis.\(^21\)

Emergent resistance to the antibiotics has always been a major concern. Block \textit{et al} investigated the level of resistance in \textit{H.influenzae} and \textit{S.pneumoniae} in vitro and found that ciprofloxacin, ofloxacin and tetracycline were the most active while the aminoglycosides were intermittently active, sulfamethoxazole possessed no activity against either pathogen.\(^22\)

The development of fourth generation fluoroquinolones is hence pivotal in combating the increasing resistance to the older generation drugs. Both gatifloxacin and moxifloxacin are developed in view of enhanced tissue penetration, a better coverage against gram-positive organisms while maintaining coverage against gram-negative organisms.\(^8,23\) Moxifloxacin also has the advantage of a more patient friendly dosing regimen, it is prescribed 3 times daily for 7 days.\(^8\) Moxifloxacin also possess the advantage of not containing preservative because of the inherent antibacterial and antifungal activities of its formulation.\(^8,23\)

The ultimate key in preventing resistance is simply to avoid using antibiotics unless there is a clear indication to do so. As resistant mutants are more likely to arise after exposure of a bacterial subpopulation to repeated sub-lethal doses of an antibiotic, a
A bactericidal dose of antibiotics should be maintained until the therapy is discontinued. In this case report, the patient was first given chloramphenicol in view of its broad spectrum against both gram-positive and gram-negative bacteria, despite its broad antibacterial spectrum, there was no improvement in patient’s symptom, and hence the use of tobramycin was initiated. Unfortunately the patient had an adverse reaction to the aminoglycoside, this was evident when she noted that the discontinuation of tobramycin had reduced ocular hyperaemia, but resulted an increase in ocular discharge. PCR was performed to rule possible viral and chlamydia infection. This was deemed necessary as her condition was unresponsive to prescribed therapy. The ophthalmologist had a strong suspicion that the condition was caused by a gram-negative bacteria due to the nature of ocular discharge, therefore prescribed ofloxacin as it has a relatively strong antibacterial activity against gram-negative organisms.

In conclusion, bacterial conjunctivitis often resolves on its own. While epidemiologic data suggests that topical antibiotics accelerate bacterial eradication and help resolve the signs and symptoms of bacterial conjunctivitis, the use of topical antibiotics offers only marginal benefit in improving clinical outcomes. As clinicians, we should always assessing patient’s history, signs and symptoms carefully before prescribing topical antibiotics, patient should also be advised to follow the dosing regimen to minimise the development of drug resistance.
REFERENCES


