Letter to the Editor

Incidence of chloramphenicol use and the effect on corneal scrape results in bacterial keratitis

Fiona Pearce MBBS,¹ Nathan Wong MBBS¹ and Elsie Chan FRANZCO^{1,2}

¹ Corneal Unit, Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia

² Centre for Eye Research Australia, University of Melbourne, Melbourne, Victoria, Australia

Correspondence: Dr Fiona C Pearce, Royal Victorian Eye and Ear Hospital, 32 Gisborne Street, East Melbourne, Victoria 3002, Australia

Email: dfpearce@gmail.com

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Robaei et al. have previously reported a significant increase in the use of ocular chloramphenicol in Australia since it was re-classified to a Schedule 3 medication in 2010.(1) The authors also reported two cases of bacterial keratitis with delayed presentation and poor outcomes in the context of prior chloramphenicol use.(2)

We conducted a retrospective review on cases of bacterial keratitis seen at the Emergency Department of the Royal Victorian Eye and Ear Hospital, Melbourne, Australia between May 2015 and February 2016. The aim of this study was to determine the incidence and effect of chloramphenicol use on corneal scrape results and outcomes in bacterial keratitis. Participants were identified using the hospital's diagnostic coding and St Vincent's Pathology's microbiology databases. Cases were excluded if there was an infiltrate size less than 1mm², prior treatment with topical antibiotics other than chloramphenicol or an insufficient specimen on the pathology report. Results were compared between those treated with chloramphenicol and those who had no prior treatment. Statistical analysis was performed using SPSS software (version 23, IBM Corp., Armonk, NY) with descriptive statistics, chi-squared testing, and independent samples t tests.

109 cases were included in the study, and the results are summarised in table 1. 34 patients (31%) were treated with topical chloramphenicol prior to presentation, for a mean of 3.81 days. This is consistent with the proportion seen in the United Kingdom, where chloramphenicol has been available over the counter since 2005.(3) Those using chloramphenicol took longer to present after symptom onset (7.15 vs 5.04 days; $p=0.082$), although there was no significant difference in infiltrate size between groups (5.4mm² vs 6.9mm², $p=0.52$). Bourkiza et al have similarly reported delayed presentation following

chloramphenicol use in patients with Pseudomonal keratitis, although, in contrast to our study, they also report a larger ulcer size in this group.(3)

Despite an additional 600,000 units of chloramphenicol sold in the first 12 months since it was made available over the counter, Robaei et al. found that the number of prescriptions from doctors decreased.(1) In our study, 74% of patients using chloramphenicol were prescribed the treatment by a medical practitioner (19 General Practitioners; 5 Ophthalmologists; 1 Emergency Physician). Four (11.8%) of these patients had risk factors for microbial keratitis: three were contact lens wearers and one had a corneal graft. Of the seven patients recommended chloramphenicol by their pharmacist or optometrist, six (85.7%) had risk factors for microbial keratitis: three were contact lens wearers, two had previous microbial keratitis and one had a corneal graft.

Gram stains were positive in 37 samples (34%) and cultures were positive in 84 (77%). The most commonly isolated Gram-positive organism was *Staphylococcus aureus* (16%). The most commonly isolated Gram-negative organisms were *Moraxella* species (12%). There was no significant difference in Gram stain results between groups, however culture positivity was less common if chloramphenicol was used prior to corneal scraping ($p=0.04$). Resistance to chloramphenicol occurred in 8 isolates, four (5%) of which were obtained after chloramphenicol treatment. Six were Gram-negative organisms and two were Gram-positive.

Prior use of chloramphenicol affected the probability of obtaining a positive culture in bacterial keratitis. In addition, it was associated with delayed presentations to Ophthalmology services. However, it did not result in worse

outcomes in our study as the time to healing and final visual acuity were similar ($p>0.05$) between the two groups (Table 1). A number of non-ophthalmic health professionals recommended using chloramphenicol for ocular symptoms, despite risk factors for microbial keratitis. This supports concerns raised by Robaei et al., thereby suggesting a role for further education around safe use of chloramphenicol in the community.

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TABLE

Table 1. Comparison of microbial keratitis cases treated with or without prior chloramphenicol.

	Treatment	No Treatment	P-value
Patients	34 (31%)	75 (69%)	
Age (years)	52 ± 23	58 ± 22	0.23
Sex			
Male	17 (50%)	44 (59%)	0.40
Female	17 (50%)	31 (41%)	
Symptom duration (days)	7.2 ± 6.4	5.0 ± 5.5	0.08
Initial BCVA [†]	6/38	6/48	0.12
Infiltrate size (mm ²)	5.4 ± 6.7	6.9 ± 12.6	0.52
Gram-stain			
GP	4 (12%)	13 (17%)	0.46
GN	7 (21%)	13 (17%)	0.68
Nil	23 (68%)	49 (65%)	0.81
Culture			
Positive	22 (65%)	62 (83%)	0.04
Negative	12 (35%)	13 (17%)	
Resistance to CPL	4 (12%)	4 (5%)	0.25

Major complications			
Enucleation	1 (3%)	1 (1%)	0.68
Corneal perforation	1 (3%)	4 (5%)	0.58
Time to healing (days)	37.1 ± 17.0	38.8 ± 5.3	0.75
Final BCVA [†]	6/24	6/38	0.51

[†] Best corrected visual acuity is reported as Snellen equivalent.

BCVA, best corrected visual acuity; GP, Gram positive; GN, Gram negative; CPL, chloramphenicol.

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Author/s:

Pearce, F;Wong, N;Chan, E

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