SCIENTIFIC REPORT

Bacterial contamination of ophthalmic solutions used in an extended care facility

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Br J Ophthalmol 2007;**91**:1308–1310. doi: 10.1136/bjo.2007.115618

Aim: To assess the frequency of contamination of ophthalmic solutions in a long-term care facility and to describe the characteristics of contaminated solutions.

Methods: One hundred and twenty-three ophthalmic solutions used for patient treatment in a long-term care facility were cultured for bacteria. The culture results were analysed according to the therapeutic class of the solution, how long the bottle had been in use and the appearance of the bottle on visual inspection.

Results: 10 (8%) of the 123 multiple-dose solutions were contaminated with bacteria: 4 (50%) of 8 steroid-containing anti-inflammatory solutions, 2 (33%) of 6 combination antimicrobial and steroid-containing anti-inflammatory solutions, 2 (6%) of 34 solutions for treatment of glaucoma, and 2 (4%) of 57 medications for ''dry eye''. None of the mydriatic, miotic or non-combination antimicrobial solutions was contaminated. *Proteus mirabilis* was identified in 8 (80%) of the 10 contaminated solutions. Only 30% of the contaminated solution bottles were classified as ''dirty'' bottles when the bottles were visually inspected. Neither the length of time the solutions had been in use nor the appearance of the bottle predicted contamination.

Conclusions: 8% of ophthalmic solutions used in a long-term care facility were contaminated with bacteria, most frequently *Proteus mirabilis*. Compared with solutions not containing steroids, steroid solutions were 5.8 times more likely to be contaminated (RR = 5.84, 95% CI: 2.42 to 14.10, $p<0.002$). The frequent contamination during reuse of certain steroid-containing ophthalmic solutions raises the question of whether single-use solutions might be preferred for these and other classes of ocular drugs.

We previously reported a systemic *Serratia marcesens* infection in a patient receiving an ophthalmic solution contaminated with the same micro-organism.[1] Ophthalmic solutions used for both diagnostic and therapeutic purposes have been found to be contaminated with bacterial pathogens and associated with ocular infections.[2–16] Eye diseases are common in patients residing in long-term care facilities and ophthalmic solutions are frequently prescribed. In this study, we assessed the frequency of bacterial contamination of ophthalmic solutions used in a long-term care facility and the characteristics associated with contaminated solutions.

METHODS

The pharmacy records of five randomly selected wards of a 400-bed long-term care facility were reviewed to identify patients receiving ophthalmic solutions. The routine procedure in the pharmacy was to assign two bottles of each ophthalmic solution to each individual patient. One is used immediately and the second bottle is stored in the pharmacy. After the first is in use for one week it is replaced by the second bottle and returned to the pharmacy for re-examination by the pharmacist. If the returned bottle appears unfit for use based on the subjective determination of the cleanliness of the bottle and its tip, it is discarded. Bottles considered fit for use are stored for use as replacements the following week and used until empty. Each bottle of ophthalmic solution is only administered to one patient and is discarded at the manufacturer's printed date of expiration.

The solutions contained in previously opened squeeze-type bottles currently in use were cultured by placing five drops of each solution in 5 ml of enriched thioglycolate medium. Bacteria were identified to the species level using standard laboratory techniques. The number of days since the bottle was opened was noted and the visual appearance of the bottle was observed as ''clean'' or ''dirty.'' A bottle was considered dirty if the cap was missing, the label was worn, or dried medication or dirt was present on the cap or surface of the bottle. Solutions in unopened bottles were not cultured.

The differences in appearance, solution type, and patient history between sterile and contaminated solutions were compared using the Fisher's exact test for proportions. The student t test was used to compare differences in means. Relative risks and 95% confidence intervals were computed using EPI INFO 6.0 (CDC).

RESULTS

One hundred and twenty-three ophthalmic solutions in use for 47 patients residing on five wards of a long-term care facility were cultured. Solutions from 10 (8%) of the 123 bottles (95% CI: 3.2 to 12.8%) grew bacteria. Contaminated solutions included four (50%) of the eight anti-inflammatory steroid-containing solutions, two (33%) of six combination antimicrobial and steroid-containing anti-inflammatory solutions, two (6%) of the 34 glaucoma medications and two (4%) of the 57 lubricant solutions for ''dry eye''. None of the four mydriatic, 11

Table 1 Frequency of contamination of therapeutic ophthalmic solutions according to type of solution

Medications used by study patients	Number studied	Number contaminated (%)
Anti-inflammatory containing steroids	8	4 (50)
Combination anti-inflammatory/ antimicrobial solutions	6	2 (33)
Glaucoma medications	34	2 (6)
Lubricants (solution for dry eye)	57	2 (4)
Mydriatics	4	0
Miotics	11	0
Antimicrobial solutions	3	0
Total	123	10 (8)

miotic or three antimicrobial solutions were contaminated (table 1).

Compared with solutions not containing steroids, steroid solutions were 5.8 times more likely to be contaminated (RR = 5.84, 95% CI: 2.42 to 14.10, p<0.002). All of the anti-inflammatory steroid-containing solutions cultured were of identical composition provided by a single manufacturer. Of the six combination antimicrobial/anti-inflammatory steroid-containing medications, the two that were contaminated contained sulfacetamide sodium, and the four that were sterile contained polymyxin B and neomycin as the antibiotic component.

The 10 contaminated solutions were prescribed for seven patients (table 2). *Proteus mirabilis* was present in eight of 10 contaminated solutions. The other two solutions grew coagulase-negative Staphylococcus in one and gram-positive bacilli in the other. Of the eight solutions contaminated with *Proteus mirabilis*, six had more than one micro-organism present: *Klebsiella pneumoniae* was cultured from three solutions, gram-positive cocci (not further identified) were cultured from two solutions and *Clostridium perfringens* was cultured from one solution. In two (Patients B and F), both bottles of the same type of solution were contaminated with bacteria, and in one patient (Patient F), two different types of solutions were contaminated with three different micro-organisms.

Data on the appearance of the bottles and the number of days the bottles had been in use were available for 120 of the 123 bottles cultured. There were 18 bottles classified as dirty and 102 bottles classified as clean. Visual inspection only identified three (30%) of the 10 contaminated solutions as having dirty bottles. Contaminated solutions were present in three (17%) dirty bottles and seven (7%) clean bottles. Bottles that appeared dirty (n = 18) had been in use for 91.6 (SD 42.7) days, while bottles that appeared clean (n = 102) were in use 56.1 (SD 53.8) days (p = 0.005). Compared with bottles classified as clean, dirty bottles were 2.5 times more likely to be contaminated with bacteria (RR = 2.42, 95% CI: 0.57 to 10.29, p>0.05).

DISCUSSION

Ophthalmic solutions are presumed sterile when first opened. Prior studies have presented data on the potential risks of contaminated ophthalmic solutions. Contact lens care systems of asymptomatic patients have been found to be contaminated with a variety of pathogens,[2] and bacterial contamination of solutions used for soaking and wetting contact lenses have been associated with the development of keratitis and corneal ulcers.[3–7] Recently, a worldwide outbreak of *Fusarium* keratitis led to the recall of Bausch & Lomb's ReNu with MoistureLoc contact lens storage solution that had been identified as harbouring the *Fusarium* fungus.[7] Therapeutic solutions have also been found to be contaminated, with reported rates as high as 31%,[10] and such contamination has resulted in keratitis or postoperative bacterial endophthalmitis.

In this study contamination of therapeutic ophthalmic solutions occurred predominantly in steroid-containing solutions. Schein *et al.* found the highest contamination rates in β-blockers, steroid-containing drops and ocular lubricants.[12] Hovding *et al.* found contamination in 13% of solutions containing cortisone acetate but in none of the solutions containing prednisolone acetate (0.5%).[8] If increased risk of contamination in steroid-containing solutions is confirmed in additional studies, it would suggest that particular attention be paid to these medications. The disproportionate contamination rate of corticosteroid-containing solutions raises the possibility of a common source of contamination including the manufacturing process. Our study was not designed to resolve this issue because unopened bottles were not cultured.

The finding in this study of *Proteus mirabilis* in 80% of the contaminated solutions differs from that of Hovding and coworkers who found gram-positive organisms (coagulase-negative staphylococci) most frequently.[8] Schein *et al.*, however, found gram-negative organisms, *Pseudomonas, Proteus* and *Serratia* species being slightly more represented among the nine species isolated, more commonly in contaminated solutions.[12]

Staphylococcus epidermidis and various aerobic and anaerobic bacteria have been isolated from the conjunctival sac and are thought to originate from the normal flora of the eyelids.[16] Other organisms that have been cultured from the lid, lashes and conjunctiva include *Proteus mirabilis* among many others.[13]

It is possible that the ophthalmic solutions are contaminated by organisms in the eye that originate from the face, nose or hands. The type of bottle used may also be a relevant factor affecting contamination. All of the solutions cultured in this study came from multi-dose squeeze-type bottles. Development of the squeeze-type dropper bottle rather than a corked bottle with a separate pipette was intended to reduce the risk of solution contamination because it allowed delivery of the medication without opening the bottle.[15] Other investigators have suggested that pipette-type dispensers decrease the rate of contamination.[18]

Hovding.[8] and Aslund[17] showed that handling of eye drops by people trained to do so led to less contamination of the medication. This is an area for further study especially in extended care facilities where patients may or may not be able to use their own medications. Since most of the patients receiving ophthalmic solutions in this study were routinely seen by an ophthalmologist, the ophthalmology clinic visit may be a valuable time to review the proper use of these medications.

Neither visual inspection of the bottles nor the number of days the bottle had been in use predicted contamination. The estimated risk of contamination was, however, based on only 10 contaminated bottles. A larger sample size would be required for more precise estimates of risk.

The frequent contamination during reuse of certain steroid-containing ophthalmic solutions raises the question of whether single-use solutions might be preferred for these and other classes of ocular medications.

Table 2 Contaminated solutions and details of cultures

Patient (n = 7)	Type of solution (n = 10)	Organism(s) in culture
A	1. Anti-inflammatory (steroid)	1. *Klebsiella pneumoniae* 2. *Proteus mirabilis*
B	2. Lubricant dry eyes	1. *Klebsiella pneumoniae* 2. *Proteus mirabilis*
	3. Lubricant dry eyes	1. *Proteus mirabilis*
C	4. Anti-inflammatory (steroid)	1. *Proteus mirabilis*
D	5. Anti-inflammatory (steroid)	1. *Klebsiella pneumoniae* 2. *Proteus mirabilis*
E	6. Glaucoma	1. Staphylococcus-coagulase negative
F	7. Combination anti- inflammatory/ antimicrobial	1. *Proteus mirabilis*
	8. Combination anti-inflammatory/ antimicrobial	2. Gram-positive cocci*
	9. Anti-inflammatory	1. *Proteus mirabilis* 2. Gram-positive cocci* 3. Large gram-positive bacilli*
G	10. Glaucoma	1. *Proteus mirabilis* 2. *Clostridium perfringens*

*Not further identified.

ACKNOWLEDGEMENTS

We would like to thank Dr Frank Palmieri for his assistance.

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Competing interests: None declared.

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Accepted 3 March 2007
Published Online First 2 May 2007

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