

Clinical Technique

Evaluation of surveillance methods for an epidemiological study of contact lens related microbial keratitis

Lisa Keay BOptom,^{1,2} Katie Edwards BAppSci(Optom),^{1,2} Garry Brian FRANZCO,³ Thomas Naduvilath PhD^{1,2} and Fiona Stapleton PhD^{1,2}

¹Cornea and Contact Lens Research Unit, School of Optometry and Vision Science, ²Vision Cooperative Research Centre, and ³International Centre for Eyecare Education, University of New South Wales, Sydney, New South Wales, Australia

ABSTRACT

Purpose: To evaluate surveillance methods in a pilot epidemiological study of contact lens related microbial keratitis (MK) cases identified by ophthalmic practitioners in Australia and New Zealand between May and August 2003 inclusive.

Methods: Twelve ophthalmologists and 55 optometrists from rural and metropolitan locations were sent a study information pack with postal reporting forms. After 2 months, practitioners were emailed a link to a website for Internet reporting. After 4 months, practitioners were prompted by email and then by telephone if a response was not received. Passive response rates were the rate of returns after posting information and emailing the website link. Active response rates included personalized email and telephone follow-up.

Results: Ten cases of MK were identified by optometrists and five by ophthalmologists. The passive response rates were 79% and 58% for the first and second reporting periods, respectively. There was a lower response rate in the second reporting period compared to the first ($P = 0.02$). With active surveillance the response rate increased to 97% and 96%. A large proportion of optometrists (62%) and ophthalmologists (55%) used the website for at least one reporting period. Internet reporting was used by all New Zealand practitioners (5/5).

Conclusions: A surveillance study to estimate the incidence of contact lens related MK in Australia and New Zealand is feasible and acceptable. Internet-based reporting offers a reliable, rapid and cost-effective means of running a large scale, international surveillance study. Active surveillance methods are necessary to enhance reporting rates.

Key words: corneal ulceration, Internet, microbial keratitis, response rate, surveillance.

INTRODUCTION

Microbial keratitis (MK) is a rare but debilitating complication of contact lens wear and many studies have shown increased risk with overnight contact lens use.^{1–6} Estimates of the incidence of MK with daily and extended wear of soft contact lenses have proven to be remarkably consistent across time.^{2,3} It is widely agreed that surveillance techniques are best suited to estimating the incidence of rare disease where cohorts would otherwise be large and potentially unmanageable.^{7,8}

Silicone hydrogel contact lenses were first licensed for 30 nights continuous wear in Australia and New Zealand in 1999 and now have significant market penetration in both countries.⁹ Although premarket clinical trials^{10–12} and physiological studies^{13,14} demonstrate that hypoxia has been eliminated with silicone hydrogel lenses, it is not known whether this will result in a protective effect against the risks or severity of MK. There are now published case reports of MK with silicone hydrogel contact lenses.^{15–17} It is therefore timely to examine for the first time the incidence rates with these new contact lens materials and wear modalities.

Internet reporting has not been utilized as a means of gathering data from practitioners in Australian ophthalmological surveillance studies¹⁸ or the many previously reported studies of contact lens related MK.^{2,3,5,19–21} The US federal agency for the Center for Disease Control and Prevention (CDC) advocates the future national standardization of public health surveillance systems with the electronic handling of data in the interests of speed and efficiency in managing large volumes of data.²² The present study examines for the first time use of Internet-based surveillance methods in Australian and New Zealand eye care.

■ Correspondence: Ms Lisa Keay, CCLRU, Level 5, Rupert Myers Building, Gate 14 Barker Street, University of NSW, Sydney, NSW 2052, Australia.

Email: l.keay@visioncrc.org

Presented at the 2003 Australasian Ophthalmic and Visual Sciences Meeting, Melbourne, Australia, 29–30 November 2003.

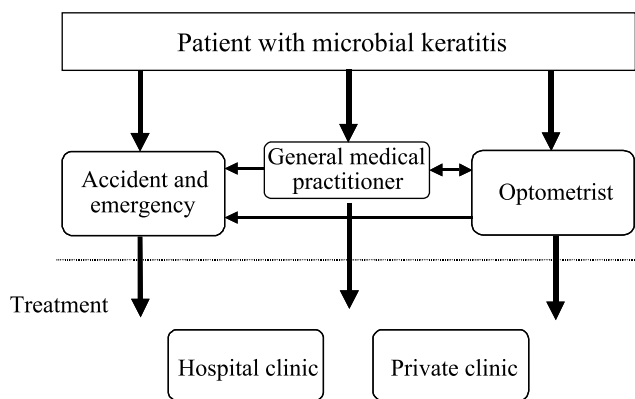


Figure 1. Health-care options and referral pathways for a patient with microbial keratitis.

In both Australia and New Zealand, optometrists fit the majority of contact lenses. However ophthalmologists usually manage MK. Figure 1 describes the referral pathways for patients with MK through the ophthalmic health care system. Generally, patients either present to a hospital accident and emergency department or to a primary care practitioner such as an optometrist or general medical practitioner. Patients presenting to a primary care practitioner are usually referred for ophthalmological management because of the specialized nature of treatment for which only a few optometrists are licensed (those in the states of Victoria and Tasmania in Australia).

Once diagnosed, intensive broad-spectrum antibiotic therapy commences with patients either hospitalized for treatment or managed as outpatients in hospital or private clinics. There is some suggestion that since the introduction of topical fluoroquinolones in the 1990s, there has been a trend towards successful treatment of ulcers in private ophthalmological practice²³ with a reduction in cases presenting at tertiary referral centres.²⁴ Accurate surveillance studies for contact lens related MK must therefore include private as well as hospital clinics.

There are approximately 850 ophthalmologists practising in Australia and New Zealand including trainees, and in excess of 3600 optometrists. Involving both professions increases the likelihood of capturing all cases and increases the accuracy of estimates of incidence rates. As optometrists in Australia and New Zealand provide the bulk of refractive eye care, their inclusion also contributes valuable information on disease morbidity including visual outcomes.

We sought to field-test the feasibility of Internet and postal reporting methods for a future national surveillance study of both Australia and New Zealand in a 4-month pilot study between May and August 2003 inclusive. A small group of ophthalmologists and optometrists were recruited to participate. Secondary purposes of this pilot study were to increase the specificity of the case definition and refine the active follow-up methods for practitioners.

METHODS

Practitioners

We attempted to contact 85 practitioners by telephone or email to inform them about the pilot study and ascertain interest in field-testing the surveillance methods. Practitioners were selected to represent rural and urban areas and also to include practitioners involved in the management of large numbers of contact lens wearers or anterior eye disease. If the practitioner was interested, a study pack was sent. Nine practitioners declined participating in the pilot study, mainly due to time commitments (4/9). One practitioner was on leave from his hospital clinic, one was waiting on ethics approval from a local human research ethics committee and the remaining three refused participation for miscellaneous reasons. Of the remainder not recruited, nine could not be contacted by telephone within the study's limited time-frame. The final set of practitioners for the pilot study comprised 12 ophthalmologists and 55 optometrists. Email addresses for correspondence were available for 11/12 ophthalmologists and 52/55 optometrists.

Case definition of contact lens related MK

The clinical case definition of contact lens related MK used was: 'presumed infection of the cornea by replicating microbes, characterized by a corneal epithelial defect and inflammation of the underlying corneal stroma, which requires treatment with topical antibiotics'. Eligible subjects were 15–64 years of age and were wearing contact lenses for the correction of simple refractive errors, excluding keratoconus or aphakia at the time of the event. Subjects were excluded if they were wearing contact lenses for medical indications.

Study design

Practitioners were asked to report at the end of each 2-month reporting period, regardless of whether or not they had seen a case of MK. Response rates were compared between the first and second period and between the professions using Fisher's Exact Test.

The practitioners could report to the study centre via a postal form supplied in the initial study pack or via the study website. The website address and a practitioner ID and password were supplied via email at the end of each reporting period.

Case information

Once a case was identified, more detailed case information was sought. The practitioner approached the patient to sign a consent form agreeing both to release medical information to the study centre and to be interviewed over the telephone. With consent, the practitioner completed case

Table 1. Response rates for passive and active surveillance for ophthalmic practitioners ($n = 67$)

Period	Passive surveillance No. responses (%)	Active surveillance No. responses (%)	<i>P</i> -value*
Period 1	53 (79.1)	65 (97.0)	0.008
Period 2	39 (58.2)	64 (95.5)	<0.001
<i>P</i> -value*	0.02	1.00	

*Fisher's exact test.

reporting forms detailing the clinical presentation, treatment course and visual outcome of the event. These forms were supplied in the original study pack but could also be downloaded from the website.

The University of New South Wales Human Research Ethics Committee approval was obtained prior to the study and the investigation was conducted in accordance with the tenets of the Declaration of Helsinki, as revised in 2000.

Active versus passive surveillance

Once a practitioner had agreed to participate, no further phone contact was made; however, those practitioners with email addresses were invited to use the website address for Internet reporting at the end of both reporting periods. After the second reporting period had elapsed, passive response rates were calculated for both periods. All practitioners who had not responded were then contacted by telephone or email to prompt their participation. Active surveillance response rates were then calculated.

Qualitative data

During the pilot study, many practitioners voluntarily provided feedback on their impressions of the study. Qualitative data was informally gathered via phone, email and written correspondence. When the non-responders were contacted at the end of the study, their criticisms and impressions of the study were sought.

RESULTS

Response rates

The response rates for the two professions were not different ($P > 0.5$) for either reporting period; therefore, results are reported for the aggregate group of ophthalmic practitioners ($n = 67$). The passive response rates were generally poor for each reporting period (Table 1), but improved to acceptable levels after the practitioners were prompted to respond. Active surveillance response rates were >85% for both professions. A reduction in the passive response rate with time was noted in both professions between reporting period 1 and 2 ($P = 0.02$).

During the pilot program, one ophthalmologist left his position to return overseas and hence only completed the first reporting period. A second ophthalmologist only participated in the second reporting period as ethics approval within the local institution was still pending during the first period. The number of ophthalmologists was therefore maintained at 12 for both periods. The non-responders included a practitioner on sick leave, one on recreational leave at the time of active follow-up and another with whom phone and email contact could not be established.

Use of Internet reporting

The proportion of practitioners opting for Internet reporting was used to gauge the preference for this method. More than half of the practitioners used the Internet to report. Of the 11 ophthalmologists who were emailed a link to Internet reporting, 55% used the Internet for at least one of the reporting periods. Of the subgroup of 52 optometrists who were emailed the link to the website, 62% used Internet reporting.

Case information

Over 4 months, 15 cases were reported to the study centre. There were no instances of duplicate reporting. Ophthalmologists reported five cases and optometrists reported ten cases. The majority of these cases had complete case information (80%). For three cases, practitioners were unable to obtain patient consent. Therefore, for these patients, full case information was not available to the study and no phone interview was conducted. Review of the clinical presentation indicated the diagnosis was equivocal in two cases and a third case was of viral keratoconjunctivitis in a contact lens wearer, amounting to a predictive value positive of 80% for contact lens related MK (12/15).

Of the five cases reported by ophthalmologists, two were managed in hospital clinics and three in private clinics. All ten cases reported by optometrists were referred for treatment: three to hospital clinics, five to private clinics and two to general practitioners. Clinical information for the two general practitioner managed cases indicated that the lesions were possibly sterile.

Qualitative data

Of the practitioners who expressed an opinion ($n = 6$), all felt the forms were easy to read and simple to complete. One practitioner was opposed to the inclusion of an interview with patients, citing possible problems with future complaints about invasion of privacy.

A total of 35 non-responders were contacted to prompt their response. Five of these practitioners had delayed responding as they were collating information on a case. All who were successfully contacted were able to supply their response over the phone if they had no cases to report.

When cases were reported, basic details were noted with further details following by post or email. As expected, reaching practitioners by phone during working hours required multiple phone calls. Four practitioners referred the researcher to associates familiar with their caseload including orthoptists and nominated colleagues within the practice location.

The majority of discussions on study design were regarding differential diagnosis. Some of the practitioners expressed concerns about under-reporting and being able to detect all cases of MK by surveying ophthalmology and optometry. Two practitioners expressed concerns that cases would be managed through casualty departments and not reviewed as outpatients or admitted to specialized ophthalmic clinics for treatment.

DISCUSSION

The results from this study confirmed the feasibility of the surveillance methods. Internet reporting was well received, but could not replace postal reporting as only a little over half of the practitioners used Internet reporting.

The response rate met acceptable levels for surveillance studies (>85%) but required active surveillance to achieve this.²⁴ Although active surveillance involves greater expense,²⁵ it will be necessary in the national study to ensure accuracy of incidence estimates. Once cases were identified, a small proportion had incomplete case information, which compromises data quality.²⁴ Careful explanation about the study design and importance of obtaining informed consent will be required to minimize the impact of incomplete data.

The diagnosis of some cases reported in the pilot study was equivocal. However, subsequent review of each case was carried out to stratify them by severity and confirm confidence in diagnosis. In response to the concerns about differential diagnosis, an additional variable was added to the case information. This characterized confidence in the diagnosis of infective versus sterile lesions. The CDC describes the 'predictive value positive' attribute of a study as a key performance indicator in a surveillance system.²⁴ The predictive value positive is defined as the proportion of reported cases that actually have the health-related event under surveillance.

In response to this pilot study, the diagnostic criteria were refined in an attempt to increase specificity. Diagnostic criteria were simplified to cases that were either culture proven or, if not, to have at least one of the following features: located within the central 4 mm of the cornea, associated with significant progressive pain, or associated with a significant anterior chamber response. These criteria are also in use in a parallel case-control study at Moorfields Eye Hospital in London. Adopting the same criteria will enable comparison of risk factors between the two centres.

The fact that a significant proportion of cases were managed in private clinics reinforces the need to include private clinic rather than solely hospital-based practitioners.

In response to concerns about not being able to detect cases managed in casualty departments, a decision was made to survey trainees registered with RANZCO as well as fully trained ophthalmologists. Both professions reported cases and this supported the inclusion of ophthalmology and optometry in the full study, both for completeness of information and as an audit to ensure all cases are detected. Although we did not see duplicate reporting in the pilot study, we do expect this to occur in the national study. In the pilot there was only a small number of participating practitioners making it very unlikely that more than one of the practitioners would see the same patient. All case information included at least date of birth, patient initials and date of event. In the full study, duplicate cases will be identified through this means, together with geographical location.

The ratio of ophthalmologists to optometrists in the pilot study aligned closely with the ratio of ophthalmologists to optometrists in each country. One possible criticism of the predictive value of this pilot study is that practitioners were personally recruited by phone or email contact and that this is not planned for the national study, where letters of invitation will be sent by post. In the national study, recruitment may not be as thorough and this may impact the participation rate. To address this, awareness of the study will be marketed at scientific and continuing education conferences and press releases in the professional media.

This pilot study has demonstrated the feasibility of Internet and postal reporting for a surveillance study examining contact lens related MK in Australia and New Zealand. Outcomes of such research will contribute to the understanding of contact lens related MK in the context of recently released contact lenses and the re-introduction of overnight contact lens wear. Information gathered through this research will be of benefit to those fitting contact lenses for optimal patient care in the interests of prevention of disease.

FEEDBACK

Comments from readers on the design and interpretation of this pilot study are welcomed. Please contact us via the CCLRU (telephone: 1800 883365 in Australia, 0800 777116 in New Zealand; email: mkstudy@mk.cclru.org; website: <http://www.mk.cclru.org>).

ACKNOWLEDGEMENTS

This study is funded in part by the Institute for Eye Research and the Australian Federal Government via the Cooperative Research Centres program.

We would like to thank the practitioners involved in the pilot study, the Microbial Keratitis Study Group international steering committee, the Royal Australian and New Zealand College of Ophthalmologists, Optometrists Association of Australia and New Zealand Association of Optometrists for their support, Jermyn Chan for administrative assistance, Selim Soytemiz for website design and I-media for graphic design.

REFERENCES

1. Schein OD, Buehler PO, Stamler JF, Verdier DD, Katz J. The impact of overnight wear on the risk of contact lens-associated ulcerative keratitis. *Arch Ophthalmol* 1994; **112**: 186–90.
2. Poggio E, Glynn R, Schein OD *et al*. The incidence of ulcerative keratitis among users of daily-wear and extended-wear soft contact lenses. *N Engl J Med* 1989; **321**: 779–83.
3. Cheng K, Leung S, Hoekman H *et al*. Incidence of contact-lens-associated microbial keratitis and its related morbidity. *Lancet* 1999; **354**: 181–5.
4. Dart JKG, Stapleton F, Minassian D. Contact lenses and other risk factors in microbial keratitis. *Lancet* 1991; **338**: 650–53.
5. Lam DS, Houang E, Fan DS *et al*. Incidence and risk factors for microbial keratitis in Hong Kong: comparison with Europe and North America. *Eye* 2002; **16**: 608–18.
6. Nilsson SEG, Montan PG. The annualised incidence of contact lens induced keratitis in Sweden and its relation to lens type and wear schedule: Results of a 3-month prospective study. *CLAO J* 1994; **20**: 225–30.
7. Schein O. Assessing the safety of the new 30-night contact lenses. *Eye Contact Lens* 2003; **29**: S157–9.
8. Stapleton F. Contact lens-related microbial keratitis: what can epidemiological studies tell us? *Eye Contact Lens* 2003; **29**: S85–9.
9. Edwards K, Keay L, Stapleton F, Wong R, Naduvilath T. National survey of contact lens wear. *Proceedings of the 10th Scientific Meeting in Optometry*. Melbourne, Australia, July 2003; 26.
10. Papas E, Vajdic C, Austen R, Holden BA. High-oxygen-transmissibility soft contact lenses do not induce limbal hyperaemia. *Curr Eye Res* 1997; **16**: 942–8.
11. Nilsson SEG. Seven-day extended wear and 30-day continuous wear of high oxygen transmissibility soft silicone hydrogel contact lenses. A randomized 1-year study of 504 patients. *CLAO J* 2001; **27**: 125–36.
12. Brennan NA, Coles C, Comstock TL, Levy B. A 1-year prospective clinical trial of balafilcon A (Purevision) silicone hydrogel contact lenses used on a 30-day continuous wear schedule. *Ophthalmology* 2002; **109**: 1172–7.
13. Cavanagh HD, Ladage PM, Yamamoto K *et al*. Effects of material O₂ transmissibility on tear film and corneal epithelium after daily and extended contact lens wear in rabbit and man. *Cornea* 2000; **19**: S79.
14. Lin MC, Graham AD, Polse KA, McNamara NA, Tieu TG. The effects of one-hour wear of high-Dk soft contact lenses on corneal pH and epithelial permeability. *CLAO J* 2000; **26**: 130–33.
15. Lim L, Loughnan MS, Sullivan LJ. Microbial keratitis associated with extended wear of silicone hydrogel contact lenses. *Br J Ophthalmol* 2002; **86**: 355–7.
16. Whiting M, Raynor M, Morgan P, Galloway P, Tole D, Tullo A. Continuous wear silicone hydrogel contact lenses and microbial keratitis. *Eye* 2004; **18**: DOI:10.1038/sj.eye.6701364.
17. Lee K, Lim L. *Pseudomonas* keratitis associated with continuous wear silicone-hydrogel soft contact lens. *Eye Contact Lens* 2003; **29**: 255–7.
18. Vajdic CM, Krickler A, Giblin M *et al*. Eye color and cutaneous nevi predict risk of ocular melanoma in Australia. *Int J Cancer* 2001; **92**: 906–12.
19. Huang E, Lam D, Fan D, Seal DV. Microbial keratitis in Hong Kong: relationship to climate, environment and contact-lens disinfection. *Trans R Soc Top Med Hyg* 2001; **95**: 361–7.
20. Radford CF, Lehmann O, Dart JKG. *Acanthamoeba* keratitis: multicentre survey in England 1992–1996. *Br J Ophthalmol* 1998; **82**: 1387.
21. Rahi JS, Edelsten C. The British Ophthalmological Surveillance Unit: the study of uncommon ophthalmic disorders made easier. *Eye* 1997; **11**: 766–7.
22. Centres for Disease Control and Prevention (CDC): Guidelines Working Group. Updated guidelines for evaluating public health surveillance systems. *MMWR* 2001; **50**: 1–35.
23. Jeng BH, McLeod SD. Microbial keratitis. *Br J Ophthalmol* 2003; **87**: 805–6.
24. Cohen EJ, Fulton JC, Hoffman CJ, Rapuano CJ, Laibson PR. Trends in contact lens-associated corneal ulcers. *Cornea* 1996; **15**: 566–70.
25. Vogt RL, La Rue D, Klaucke DN, Jillson DA. Comparison of an active and passive surveillance system of primary care providers for hepatitis, measles, rubella and salmonellosis in Vermont. *Am J Public Health* 1983; **73**: 795–7.