Pre-existing blindness in a cohort of patients with bacterial keratitis

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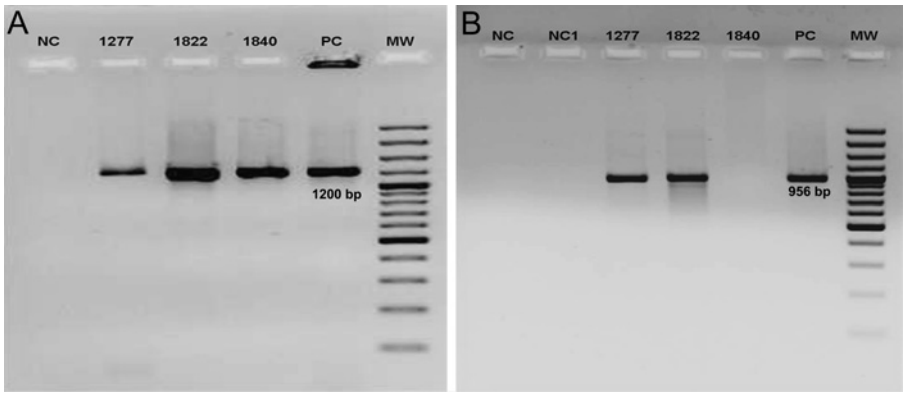

Figure 1 (A) Representative gel picture of microsporidia PCR showing amplification of 1200 bp product from three patients (1277, 1822 and 1840). (B) Representative gel picture of adenovirus PCR showing amplification of 956 bp product from two patients (1277 and 1822). There is no amplification from patient no. 1840. NC, negative control; PC, positive control; NC1, negative control from first round PCR used as a template in second round PCR; MW, 100 base pair molecular weight DNA ladder.

two samples (5.7%). Thirty-one out of 35 microsporidial amplicons were identified as *Vittaforma corneae* and the four adenovirus PCR positive amplicons were identified as HAdV serotype 8.

This study, involving a modest sample of 35 patients with EKC, showed that a small number of patients (6/35, 17.1%) harboured the adenovirus along with microsporidia in the corneal lesions. This co-existence has not been suggested earlier in patients with EKC and opens a door to further research on the interaction between these diverse groups of organisms. Microsporidia are known to survive in a variety of insects, especially those found in water bodies. This seems to be the most plausible explanation for the rise in the incidence of EKC during the rainy season when the insect population increases. Increased incidence of microsporidial keratoconjunctivitis during the rainy season has also been documented from central India.[5] It is possible that this phenomenon exists in all parts of India and is peculiar to tropical and subtropical parts of the world.

Adenoviruses are intracellular organisms and although humans are the only known host of the virus, we hypothesise that the viruses may reside in the microsporidia infecting insects in nature and concomitantly increase in the environment during rains. This possibility has been alluded to in a report by Visvesvara *et al* who observed growth of adenovirus in co-culture with microsporidia (*Enterocytozoon bieneusi*) in a mammalian cell culture inoculated with duodenal biopsy or aspirates from patients with intestinal microsporidiosis.[6] It is possible that these two organisms co-exist in nature and we believe that our observation calls for further research to unravel the interaction between these two types of organisms.

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Competing interests None.

Ethics approval This study was conducted with the approval of the IRB at L V Prasad Eye Institute, Hyderabad.

Contributors PK performed the PCR and sequencing for all samples. SS received the financial grant, provided the concept and design for the study, performed the microscopy and culture studies, and wrote the manuscript. SD and SKS examined the patients and collected the clinical samples. SK and AM processed the samples in the laboratory, collected data and helped in the analysis.

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INTRODUCTION

Microbial keratitis is an important cause of visual loss worldwide, although the resulting blindness is generally assumed to be monocular.[1 2] Vision loss secondary to microbial keratitis will have a greater impact in patients with concurrent poor vision in the fellow eye. In this report, we analyse the prevalence of pre-existing blindness in patients screened for the NIH-sponsored Steroids for Corneal Ulcers Trial (SCUT, clinicaltrials.gov NCT00324168), (unpublished data) the degree of vision loss and the cause of blindness in the fellow eye.

METHODS

All patients with culture-positive bacterial corneal ulcers at the Aravind Eye Care System (Madurai, Coimbatore and Tirunelveli), Dartmouth Medical School and the F.I. Proctor Foundation, University of California San Francisco, between September 2006 and February 2010 were included. Patients excluded for poor vision in their other eye were identified from the SCUT database. Case review was performed for all available charts meeting this exclusion criterion. Descriptive statistics were performed using Stata 10.0. Ethical approval was granted by the University of California San Francisco, Dartmouth Medical School and Aravind Eye Hospital.

RESULTS

Of 1769 patients screened for the trial, 119 were excluded due to vision worse than 6/60

Table 1 Visual acuity at presentation and primary cause of vision loss in the non-infected eye of 78 patients with unilateral corneal ulcer and poor vision in the non-infected eye

Cause of vision loss	N (%)	Visual acuity, logMAR (median, IQR)
Corneal opacity	30 (38%)	1.85 (1.5–2.0)
Cataract	14 (18%)	1.75 (1.7–1.9)
Retinal disease	5 (7%)	1.7 (1.1–1.9)
Glaucoma	4 (5%)	1.85 (1.8–1.95)
Enucleation	5 (6%)	2.0 (2.0–2.0)
Endophthalmitis	1 (1%)	NA*
Other†	15 (19%)	2.0 (1.7–2.0)
Total	78	1.9 (1.7–2.0)

*Acuity not available.
†Includes phthisis bulbi of unknown cause, failed previous penetrating keratoplasty and bullous keratopathy.

in their fellow eye (6.7%), 112 of whom (94%) were from India. Charts were available for 78 (65%) patients. Of these, 56 (72%) had pre-existing unilateral blindness in the eye without the current ulcer. The remainder had pre-existing bilateral blindness. Median age was 64 years (IQR 56–70 years), and 50 (64%) patients were men. Of 46 patients for whom geographical data were available, 37 (80%) lived in a rural setting. Median visual acuity in the fellow eye was logMAR 1.9 (light perception, IQR logMAR 1.7 (count fingers) to 2.0 (no light perception), table 1). Median visual acuity in the eye with a current corneal ulcer was logMAR 1.7 (count fingers, IQR logMAR 0.8 (6/40) to 1.8 (count fingers)). The most common cause of pre-existing loss of vision in the fellow eye was corneal opacity (table 1).

COMMENT

The prevalence of unilateral blindness has been estimated to be approximately 1–2% in developing countries.[2–4] Reasons for unilateral blindness commonly include cataract and corneal scar.[5] In this study, we found a prevalence of pre-existing blindness in the eye without the presenting ulcer of 6.7%, most of which was unilateral. The primary cause of vision loss was corneal opacity, and the degree of vision loss was severe. Patients who had a previous corneal injury or infection may be more at risk for a subsequent similar event because of occupation or access to care. For most of these patients, there is little potential for recovery of vision. The median age of patients excluded due to blindness in the fellow eye was higher than those included in the SCUT study, and a higher proportion of patients were men (unpublished data). Older male patients may be at increased risk for bilateral blindness secondary to keratitis.

The absence of data from 35% of the cases identified as having poor visual acuity in the unaffected eye may bias our estimates of the severity and cause of vision loss. Despite these limitations, these data suggest that corneal ulceration may result in more bilateral blindness than previously thought. We conservatively defined poor vision in the fellow eye as worse than 6/60 in this study; a less stringent definition would increase our estimates of patients with fellow eye visual impairment, as well as the potential impact of monocular visual loss associated bacterial keratitis. Further study of corneal ulceration in patients with pre-existing blindness is warranted and prevention of corneal ulceration and effective early treatment is especially important.

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Competing interests None.

Ethics approval This study was conducted with the approval of the ethics committees of University of California San Francisco, Dartmouth Medical School and Aravind Eye Care System.

Contributors CEO designed the study and data collection tools, cleaned, analysed and interpreted data, drafted and revised the manuscript. AS helped to design data collection tools, collected data, interpreted, drafted and revised the manuscript. MS designed data collection tools, collected data, oversaw data collection for the entire study and revised the manuscript. CMT-K designed data collection tools, collected data and revised the manuscript. JM collected data and revised the manuscript. MR collected data and revised the manuscript. RR collected data and revised the manuscript. EJE collected, analysed and interpreted data and revised the manuscript. JDC helped to design study, collected data and revised the manuscript. NRA helped to design study and data collection tools, analysed and interpreted data and revised the manuscript. TML helped to design study and data collection tools, collected data, analysed and interpreted data and revised the manuscript. MEZ designed study and data collection tools, collected data, analysed and interpreted data and drafted and revised the manuscript.

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Authors' response

We would like to thank Dr Rao and colleagues for their interest and comments regarding our study.[1] In their letter, they pointed out two major issues concerning studies on long-term perimetric fluctuation: the definition of stability of the disease and the methods used to calculate fluctuation.

Dr Rao and colleagues claimed that the use of morphological data would have been desirable to define progression, as commonly done in studies on progression when both morphological and functional data are available (ie, progression is defined by means of morphological criteria in order to analyse the performance of functional parameters and vice versa).

In clinical practice, it is very common to find patients with a stable optic nerve head at stereophotography (the morphological standard) showing progressive visual field tests, regardless of the stage of the disease. We acknowledge that the sensitivity of morphological progression is strongly dependent on the instruments and criteria used and that automated analysis may enhance it, but consensus on progression criteria of the so-called high-technology devices is still missing.

Most importantly, if morphological data had been used to define progression in our study, this strategy would have generated misleading results because it does not allow a precise division of functional true change (progression) from functional false change (fluctuation). If progressing visual field tests had been included in the analysis due to the absence of morphological progression, data on 'fluctuation' would have been erroneously higher, because they would also reflect progression, which is clearly a methodological bias. In other words, we confirm that when calculating fluctuation of a parameter, it is mandatory to exclude progression for it.

We agree with Dr Rao and colleagues that the exclusion of stable patients who fell in different stages of the glaucoma staging system resulted in lower estimates of fluctuation. We decided to exclude these subjects (n=9/170) at the beginning of the study because data presentation would have been cumbersome and the interpretation very difficult.

We also agree that the method used to calculate fluctuation was one of the several possible. It had the advantage of providing a 'number' for the whole field (and we showed that this may be useful to discriminate normal from borderline cases with similar mean deviation), but it also had the disadvantage, as correctly pointed out in the letter, of ignoring very useful information about localised visual field defects.

Finally, we would like to briefly comment on the implications of statistics on this paper. We are aware of the limits of statistics: for large numbers, 1 test over 20 may be deemed as significant just by chance,

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Notes