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A multi-country outbreak of fungal keratitis associated with a brand of contact lens solution: the Hong Kong experience

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Summary
Objectives: Starting in mid-2005, an increase in fungal keratitis caused by *Fusarium spp* was observed among contact lens wearers in Hong Kong, Singapore, and the USA. The objective of this study was to describe the outbreak and to determine any association with the use of Bausch & Lomb (B&L) ReNu® contact lens solution.
Methods: We defined a case as a disposable contact lens user with ophthalmologist-diagnosed keratitis and a positive culture of *Fusarium spp* reported to the Department of Health from January 1, 2005 to May 31, 2006. We identified cases through inpatient discharge data and the electronic laboratory databases of all public hospitals, and from physician reporting. Controls were recruited from three outpatient clinics. Risk factors were collected using a standardized questionnaire and analyzed by univariate analysis and binary logistic regression.
Results: From January 2005 through May 2006, we identified 33 cases of Fusarium keratitis. Most were in young adults (mean age 28 years) who presented with eye pain (100%), redness (84%), photophobia (41%), and tearing (34%). Twenty-four cases and 86 controls were recruited in the case—control study. By logistic regression, B&L ReNu solution showed the strongest association with being a case (adjusted odds ratio 26.1, 95% confidence interval 3.0—225.3) after adjusting for potential confounders.
Conclusion: Using B&L ReNu contact lens solution was strongly associated with Fusarium keratitis among disposable contact lens users in Hong Kong. B&L ReNu with MoistureLoc® was permanently withdrawn from the market globally in May 2006.

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Introduction

Microbial keratitis is the most devastating complication of contact lens wearing and may result in permanent vision loss from corneal scarring or perforation. Contact lens-related fungal keratitis is a severe corneal infection caused by fungi such as *Fusarium spp*, *Aspergillus spp*, and *Acremonium spp*. It has rarely been reported in the healthy soft contact lens wearing population.[1,2] Patients may require corneal transplantation if anti-fungal medication fails. Risk factors associated with microbial keratitis in contact lens wearers include overnight wear, duration of continuous overnight wear, lower socio-economic class, smoking, and poor lens hygiene practice, specifically in daily wear lenses.[3]

In late August 2005, the Centre for Health Protection (CHP), Department of Health of Hong Kong, became aware of an apparent increase in the number of cases of contact lens-related microbial keratitis among patients who attended public hospitals in one region of Hong Kong. Following this, the CHP initiated an investigation along with the doctors in public hospitals to determine whether there were any similar cases of contact lens-related microbial keratitis in other hospitals, and started monitoring the inpatient hospital discharge trend of contact lens-related microbial keratitis. The initial investigation suggested that many patients with fungal keratitis caused by *Fusarium spp* were disposable contact lens users and had reported a history of using a commercial contact lens solution, namely Bausch & Lomb (B&L) ReNu®.

We describe herein the epidemiological details of the cases, and we present the findings of a case—control study conducted in February—March 2006 in Hong Kong, which helped to ascertain the risk factors associated with the development of Fusarium keratitis among disposable contact lens users.

Materials and methods

We actively identified patients having Fusarium keratitis from inpatient discharge diagnosis data and the electronic laboratory records of all the public hospitals in Hong Kong. We also received reports from both public and private ophthalmologists. A case was defined as a contact lens user who had clinical features compatible with fungal keratitis diagnosed by an ophthalmologist, with a positive culture of *Fusarium spp* obtained from corneal scraping, reported to the Department of Health from January 1, 2005 to May 31, 2006. We interviewed the cases by telephone using a standardized questionnaire to collect epidemiological and clinical information.

A retrospective unmatched case—control study was conducted in February—March 2006. To focus our investigation on the risk factors for the development of Fusarium keratitis among disposable soft contact lens users, our case definition was restricted to those cases of contact lens-related Fusarium keratitis reported to the CHP who were using disposable soft contact lenses (7-day, 2-weekly, or monthly). In March, urgent epidemiological information was needed to assist in making a public health decision and hence only cases reported from January 1, 2005 to March 31, 2006 were included in the case—control study. Controls were recruited from the attendees of the three family clinics of the Department of Health from February to March 2006. The Department of Health family clinics are general outpatient clinics for civil servants and their family members. We invited attendees who used disposable soft lenses (7-day, 2-weekly, or monthly) in the past 1 year to be controls; they had to have used the same brand of contact lens disinfectant solution over the past 6 months, before the voluntary suspension of B&L ReNu solution by the company. We excluded attendees who had had eye diseases related to the wearing of contact lenses in the past 1 year.

A standardized questionnaire was developed taking reference from a similar study in Singapore. Information concerning demographics, the choice and usage of contact lenses, the choice and usage of contact lens solution, and lens hygiene practice before onset of symptoms were elicited. Trained public health nurses administered the questionnaire to the cases by telephone interview. Two medical officers and five trained public health nurses approached potential controls in the waiting halls of the three family clinics and obtained verbal consent from them before administering the questionnaire through face-to-face interview. Issues of voluntary participation, confidentiality, and anonymity were emphasized before the interview. No clinical specimen was taken from the controls.

Data analysis was performed using SPSS version 13.0 and SAS Enterprise Guide 2.0. Univariate analysis (*t*-tests, Pearson Chi-square tests, or Fisher's exact tests) was used to assess the variation/association of predictive values with case status. Selected variables that demonstrated variation/association with a *p*-value of less than 0.2 were entered into a binary logistic regression model. In selecting variables into the regression model, forward selection (likelihood ratio) was used. Adjusted odds ratios (AOR) and their 95% confidence intervals (95% CI) were estimated. For all statistical tests, association was considered statistically significant at $p < 0.05$. A hygiene score (11—50) was developed in collaboration with the Singapore Ministry of Health, based on 10 questions (available on request) concerning lens hygiene practice, with a higher score signifying better hygiene practice. The score was analyzed as a continuous variable.

Results

Up until May 31, 2006, a total of 33 cases of contact lens-related Fusarium keratitis were reported to the CHP. Sixty-four percent (21/33) were female, and the age range of all cases was 16—51 years (mean 28 years). Twenty-five (75.8%) required hospital admission and at least two cases required corneal transplantation. Figure 1 shows the number of case hospital admissions/consultations by month. Thirty-two of these patients were successfully interviewed. They presented with eye pain (100%), redness (84%), photophobia (41%), tearing (34%), foreign body sensation (31%), and blurring of vision (28%). Among these 32 patients, 30 patients were disposable contact lens users (7-day, 2-weekly, or monthly), while two patients used conventional soft lens. Twenty-nine out of 32 (90.6%) patients recalled that they solely used B&L ReNu contact lens solution before the onset of their symptoms. The patients were using different batches of B&L ReNu solution, as evidenced by the different lot numbers of the solutions. Among them, 27 (93.1%) patients could specify the product line to be B&L ReNu with MoistureLoc® on repeated