Risk Factors for Contact Lens Related Microbial Keratitis: A Case-Control Study

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Objective: *To evaluate the risk factors that may contribute to microbial keratitis in contact lens wearers.*
Material and Method: *This prospective case-control study included 52 patients with contact lens related keratitis treated between 1 December 2006 and 15 October 2007 at the Faculty of Medicine, Siriraj Hospital. Controls were sixty-three contact lens users attending with disorders unrelated to contact lens wear. All subjects with informed consent were interviewed about demographic data, types of contact lens and contact lens solutions, contact lens use past the recommended replacement date, overnight wear, and lens hygiene. Odds ratio (OR, estimates of relative risks) and 95% confidence interval (CI) were calculated through multivariable logistic regression analysis.*
Results: *The use of contact lens past the replacement date caused the highest risk of developing microbial keratitis (OR = 9.1; CI 1.8-45.4, p = 0.005). Overnight wear of lenses (OR = 2.9, CI 1.3-6.2, p = 0.012) and poor lens hygiene (OR = 2.3, CI 1.0-5.1, p = 0.007) significantly increased the risk of microbial keratitis, respectively. None of the other risk factors showed a significant association.*
Conclusion: *The significant risk factors for contact lens related microbial keratitis in the present study were the use of contact lens past the replacement date, overnight wear, and poor lens hygiene. Thus, the appropriate advice of contact lens care and usage may reduce the risk of microbial keratitis in contact lens wearers.*

Keywords: *Contact lens, Microbial keratitis, Risk factor, Infection*

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Contact lens (CL) is a very popular form of vision correction and cosmetic purpose. However, it can lead to some complications such as allergic conjunctivitis, corneal hypoxia, corneal neovascularization, and infectious keratitis[1]. Of all CL related complications, microbial keratitis is the most hazardous complication of CL wear and may result in permanent visual loss from corneal scarring or perforation[2-4]. Recently, the number of patients wearing contact lens (CL) has increased over the past few decades[5], due to widespread advertisement and unregulated sale of CL. Furthermore, substandard quality of contact lenses in general stores or the markets are sold without control in children. Consequently, CL related microbial keratitis has been increasing continuously. Some patients, who have severe keratitis, not responding to the antimicrobial agents, need the urgent corneal transplantation. It does alert us to be highly aware of CL related microbial keratitis. The information reported herein will be beneficial to prevent or decrease this serious complication.

This prospective, single center, case-control study was conducted to investigate the risk factors for CL related microbial keratitis in Bangkok, including types of CL and CL solutions, CL use past the replacement date, overnight wear and lens hygiene.

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Material and Method

Study design and data collection

The authors conducted a prospective case-control study between December 1, 2006 and October 15, 2007 at the outpatient department and with hospitalized patients at the Faculty of Medicine, Siriraj Hospital, Mahidol University in Bangkok.

The present study was approved by an Institutional Review Board/Ethics Committee and

conformed to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all subjects.

Cases

Cases were defined as patients with presumed microbial keratitis associated with the use of contact lenses for refractive error correction, as diagnosed by the corneal specialists. Patients who were wearing contact lenses for therapeutic reasons, aphakia, or keratoconus were excluded. The severity of microbial keratitis was classified according to the modification of Jones' grading criteria[6].

Controls

Hospital-based control subjects were contact lens wearers for the correction of refractive error and had been wearing lenses at least once a week for not less than 3 months before the interview. Control subjects were randomly selected from the subjects attending the general outpatient department of Siriraj Hospital, with disorders unrelated to contact lens wear.

Risk factor assessment

The interviewer (YT) used the same record form and took approximately 15 minutes to interview each case or control subject. The form included demographic data such as age, sex, details about the type, brand of CL and CL solutions, the use of the current contact lens past the recommended replacement date, overnight wear, and lens hygiene.

Overnight wear was defined as sleeping overnight with CL at least once before the interview.

Lens hygiene was classified as "optimal" or "suboptimal". "Optimal" hygiene practices included washing hands prior to handling lenses, daily mechanical lens cleaning and rinsing, daily case cleaning and disinfection with fresh solution on every lens removal for extended wear soft contact lens, or rigid contact lens use. If the subjects did not perform any one of these aspects, the authors classified hygiene as "suboptimal".

Statistical analysis

All statistical analysis was performed using SPSS software (version 10.0; SPSS Inc., Chicago, IL). Student t-test and Chi-square test were used for descriptive and univariable analyses of potential risk factors. Thereafter, the risk factors that were significant at $p < 0.05$ were considered for further multivariable testing. Multivariable logistic regression was carried out to calculate odds ratios (OR, estimates of relative risks) and 95% confidence interval (CI). Factors in the final model were considered significant at $p < 0.05$.

Results

Fifty-two cases met the present study criteria. Sixty-three control subjects were enrolled. Table 1 shows characteristics of the present study subjects and univariable analyses of potential risk factors between cases and control groups. Due to the small number of cases and control subjects, an association between microbial keratitis and each type of CL or CL solution could not be shown to have significance. Presentation of cases was dependent of CL use past the replacement date, lens hygiene, and overnight wear. Using multivariable logistic regression, risk factors for microbial keratitis were the use of CL beyond the replacement date, overnight wear of CL and "suboptimal" lens hygiene, respectively as shown in Table 2.

Mild, moderate and severe degree of microbial keratitis were 12cases (23.1%), 18 cases (34.6%), and 22 cases (42.3%) respectively. Thirty-nine of 52 (75%) cases were positive culture results. Twenty-eight lesions were polymicrobial. Positive cultures for bacteria were 39 cases (39/52, 75%), which were Pseudomonas aeruginosa (27/39, 69.2%), Serratia marcescens (12/39, 30.8%), Klebsiella pneumoniae (4/39, 10.3%), Stenotrophomonas maltophilia (4/39, 10.3%), Proteus mirabilis (2/39, 5.1%), Bacillus cereus (2/39, 5.1%) and Staphylococcus aureus (1/39, 2.6%). One case had positive culture for fungus and two cases were diagnosed as fungal keratitis due to clinical findings and successful treatments with antifungal agents. Four cases had positive cultures for acanthamoeba (4/39, 10.3%).

Discussion

Microbial keratitis is the most serious complication of CL wear. Many factors, including younger age, male, type of CL, lens care system, poor hygiene, smoking and failure to achieve the intended wearing schedule, may increase the possibility of this infection[7-10]. In the present study, age of the patients was not a risk factor for microbial keratitis during the present study period, although previous studies have found that the higher risk of infection is associated with youth[7-10]. This could be due to small number of cases and controls, resulting in inability to divide into 10-year interval age groups. The authors compare mean age of both groups.

Table 1. Characteristics of the study subjects and univariable analyses of potential risk factors between cases and control groups

Characteristic	Cases (n = 52), n (%)	Control (n = 63), n (%)	p-value
Age (mean ± SD) (range, yrs)	26.6 ± 7.7 (13, 52)	28.9 ± 6.7 (19, 59)	0.217
Gender			0.331
Male	12 (23.1)	9 (14.3)	
Female	40 (76.9)	54 (85.7)	
Contact lens type			
Conventional soft CL	2 (3.8)	6 (9.5)	
Daily and 2 weekly disposible	4 (7.7)	5 (8.0)	
Monthly disposible	46 (88.5)	52 (82.5)	
Contact lens solutions			
Did not use CL solution	0 (0)	2 (3.2)	
Unknown solution	3 (5.8)	0 (0)	
Complete	29 (55.8)	13 (20.6)	
Renu Multiplus	8 (15.4)	23 (36.5)	
Duna	5 (9.6)	8 (12.7)	
Solo-Care	4 (7.7)	3 (4.8)	
Opti-Free	3 (5.8)	13 (20.6)	
Clean-Care	0 (0)	1 (1.6)	
The use of the current CL past the replacement date	12 (23.1)	2 (3.2)	0.003
Overnight wear	34 (65.4)	25 (39.7)	0.011
Lens hygiene			0.019
Optimal	19 (36.5)	38 (60.3)	
Suboptimal	33 (63.5)	25 (39.7)	

CL = contact lens

Table 2. Relative risks of significant exposure factors for contact lens related microbial keratitis

Risk factors	Relative risk (95% CI)	p-value
CL use past the replacement date	9.1 (1.8-45.4)	0.005
Overnight wear	2.9 (1.3-6.2)	0.012
Suboptimal lens hygiene	2.3 (1.0-5.1)	0.007

Regarding gender, male was not a risk factor for infection as in previous reports[2,10,11]. Some studies have found such an association to be significant[7]. The present study could not demonstrate the relationship of male to microbial keratitis because few cases were male in both groups.

The significant risk factors for microbial keratitis in the present study are CL use past the replacement date, overnight wear of CL and suboptimal lens hygiene, respectively. CL use beyond the recommended replacement date was the highest risk factor for infection in the present study. Previous studies have found a similar association[11,12]. The reason may be due to a torn CL or a CL defect when using it beyond the recommended replacement date and an increase in microbial colonizations and debris deposits on its surface[1]. These contaminations induce the inflammatory and allergic reactions, accompanied by corneal hypoxia and microtrauma to corneal epithelium. All of these can promote the invasion of microbes into the cornea [1].

Overnight wear of CL and poor lens hygiene are well-established risk factors for microbial keratitis[5,8,10,13-17] and are associated with an increase in risk in these subjects. These two factors have been postulated to cause microbial keratitis by microbial contamination of lens and lens-care systems, corneal hypoxia, reducing tear exchange, increasing micro-trauma to the corneal epithelium resulting in an increase in the penetration of microorganisms[1].

Concerning CL types and CL solutions, an insufficient number and many various types of CL and CL solutions could not be analyzed separately. However, 1 month disposable soft CL was more popular among CL users than any other types of CL. Even though silicone hydrogel CL allow higher levels of oxygen to the cornea, the earlier studies have shown that the risk of the infection in overnight wear is the

same as for hydrogel CL[18,19]. In the present study, cases mostly used Complete (29/52, 55.8%), whereas controls used Renu Multiplus (23/63, 36.5%) more than any other types of CL solutions. Concerning only Renu CL solution, 8 cases (15.4%) and 23 controls (36.5%) used Renu Multiplus. No one used Renu MoistureLoc due to its unavailability in Thailand.

In the present study, culture-positive rate could be achieved up to 75% (39/52), which is higher than that observed in earlier studies[17,20,21]. However, it is close to that reported in other tertiary referral hospitals[10,22]. This may be due to more severe lesions referred to the authors' hospital, providing enough tissues for cultures.

Twenty-eight cases (28/39, 71.8%) had polymicrobial infection. Most commonly isolated bacteria is Pseudomonas aeruginosa (27/39, 69.2%), similar to most previous reports in Asia, the United States and Europe[5]. Acanthamoeba was found in four cases (4/39, 10.3%), as the second most common microbes. This is less frequent than that shown in Hong Kong (5/21, 23.8%)[5]. This may be due to the environment and the climate. Fungal keratitis was found in three cases (3/52, 5.8%) in almost one year of the present study, which is not an abnormal increase in fungal keratitis associated with CL wear. The present study was conducted during the time of the outbreaks of Fusarium keratitis associated with CL wear, reported from Singapore, Hong Kong and the United States in 2006[23-26]. However, the present study did not demonstrate an abnormal increase in fungal keratitis. The reason may be that all of that Fusarium keratitis was strongly associated with the use of a specific CL solution, Renu with MoistureLoc (Bausch & Lomb)[23-26], which was not available in Thailand.

In the authors' opinion, the present study could indirectly support that the authors have not found an increase in fungal keratitis related CL wear due to unavailable Renu MoistureLoc in Thailand during that period. After this event, Renu MoistureLoc was withdrawn from the market globally.

From the present study, the results support the importance of wearing CL schedule as recommended by the CL Company, properly cleaning and caring CL and not sleeping overnight with CL. These considerations would decrease the incidence of CL related microbial keratitis. Recently, the Food and Drug Administration of Thailand implements the law that all contact lenses are restricted medical devices that require a prescription for purchase. Selling them without a prescription is punishable. Therefore, it is hoped that this law will be in successful practice and CL related microbial keratitis will be decreased. However, the CL users and CL practitioners should pay high attention to the risk factors of infection that the authors have shown in the present study.

Potential limitations in the present study are the use of a possibly unrepresentative hospital population, and definition of cases. The authors feel that our tertiary care hospital population provide a sample of patients and control subjects from a large area of Thailand especially in the central part. That would reduce an appreciable source of bias. Regarding the definition of cases, the authors used clinical diagnosis of presumed microbial keratitis, because many clinically suspected microbial keratitis have negative culture results[17,20,21].

Conclusion

CL use beyond the replacement date, poor lens hygiene and overnight wear carries a greater risk of microbial keratitis.

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Potential conflicts of interest

None.

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ปัจจัยเสี่ยงของการเกิดกระจกตาติดเชื้อจากการใส่เลนส์สัมผัส: การศึกษาโดยมีกลุ่มควบคุม

วิภาวี บูรณพงศ์, ภิญนิตา ตันธุวนิตย์, พนิดา โกสียรักษ์วงศ์, ยิ่งพันธุ์ ธาราวัชรศาสตร์

วัตถุประสงค์: *เพื่อศึกษาปัจจัยเสี่ยงของการเกิดกระจกตาติดเชื้อในผู้ใส่เลนส์สัมผัส*

วัสดุและวิธีการ: *การศึกษานี้เป็นแบบไปข้างหน้าโดยมีกลุ่มควบคุม ทำการศึกษาในผู้ป่วยจำนวน 52 ราย ที่พบกระจกตาติดเชื้อเกี่ยวข้องกับการใส่เลนส์สัมผัสที่มารับการรักษาที่โรงพยาบาลศิริราช ระหว่างวันที่ 1 ธันวาคม พ.ศ. 2549 ถึงวันที่ 15 ตุลาคม พ.ศ. 2550 กลุ่มควบคุมคือ ผู้ใส่เลนส์สัมผัสจำนวน 63 ราย ที่มาโรงพยาบาลศิริราชด้วยความผิดปกติอื่นที่ไม่เกี่ยวข้องกับการใส่เลนส์สัมผัส ผู้เข้าร่วมงานวิจัยทุกรายถูกสัมภาษณ์เกี่ยวกับข้อมูลส่วนบุคคล, ชนิดของเลนส์สัมผัสและน้ำยาเลนส์สัมผัส, การใส่เลนส์สัมผัสเกินวันที่กำหนด, การใส่เลนส์สัมผัสนอนทั้งคืน และการทำความสะอาดเลนส์สัมผัส คำนวณค่า odds ratio (OR) และ 95% confidence interval (CI) เพื่อหาปัจจัยเสี่ยงดังกล่าว โดยวิเคราะห์แบบ multivariable logistic regression*

ผลการศึกษา: *การใส่เลนส์สัมผัสเกินวันที่กำหนด เป็นปัจจัยเสี่ยงสูงสุดของการเกิดกระจกตาติดเชื้อ (OR = 9.1; CI 1.8-45.4, p = 0.005) การใส่เลนส์สัมผัสนอนทั้งคืน และการทำความสะอาดเลนส์สัมผัสไม่ถูกต้อง เพิ่มโอกาสเสี่ยงของการเกิดกระจกตาติดเชื้ออย่างมีนัยสำคัญทางสถิติตามลำดับ (OR = 2.9; CI 1.3-6.2, p = 0.012), (OR = 2.3; CI 1.0-5.1, p = 0.007) จากการศึกษาไม่พบปัจจัยอื่นที่มีผลต่อการเกิดกระจกตาติดเชื้อจากเลนส์สัมผัสอย่างมีนัยสำคัญทางสถิติ*

สรุป: *ปัจจัยเสี่ยงสำคัญของการเกิดกระจกตาติดเชื้อจากการใส่เลนส์สัมผัสในการศึกษานี้ คือ การใส่เลนส์สัมผัสเกินวันที่กำหนด, การใส่เลนส์สัมผัสนอนทั้งคืน และการทำความสะอาดเลนส์สัมผัสไม่ถูกต้อง ดังนั้นการให้คำแนะนำในการดูแลรักษา และการใช้เลนส์สัมผัสอย่างถูกต้อง เหมาะสม อาจลดการเกิดกระจกตาติดเชื้อในผู้ใส่เลนส์สัมผัส*