Acanthamoeba Keratitis and Its Associated Risk Factors in Farabi Eye Hospital of Tehran

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Abstract

***Purpose*:** Acanthamoeba keratitis (AK) is a sight-threatening corneal infection with a rapidly increased incidence since 1990s along with the growing popularity of contact lenses. In this study we aimed to study patients with AK and its associated risk factors in Farabi Eye Hospital of Tehran, focusing on those with more severe corneal involvement.

***Methods*:** Patients with clinical or laboratory diagnosis of AK at the cornea clinic of Farabi Eye Hospital during April 2009 to March 2010 were studied regarding their demographics, and clinical characteristics, corneal infection risk factors, and suboptimal hygiene practices. Linear regression analysis was applied to determine factors affecting the stage of corneal involvement at presentation.

***Results*:** Twenty five patients (4 males and 21 females) with 27 involved eyes were identified during the one year study. Cosmetic contact lenses accounted for the most common potential risk factor of AK (85.2%). Most of the patients (92.6%) reported a history of antibacterial treatment before the presentation. Only four patients (16%) did not report any suboptimal hygiene practice. In the linear regression model only the first visual acuity (VA) at presentation, and the duration of symptoms were independently associated with the stage of disease.

***Conclusion*:** The high number of patients presented with AK in our study suggests a possible outbreak of the disease in Tehran, which is highly associated with cosmetic contact lenses.

***Keywords*:** Acanthamoeba, Contact Lens, Cornea, Keratitis

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Introduction

Acanthamoeba keratitis (AK), a painful sight-threatening corneal infection, is caused by a free-living amoeba distributed widely in the soil and water resources.[1] After AK being first introduced by Naginton in 1973,[2] its incidence initiated to rapidly increase in 1990s along with the growing popularity of contact lenses, specially in the developed countries.[3] 208 cases of AK reported in the US between 1973 and 1988 and 85% of them wore contact lens,[4,5] it is generally believed that contact lens use (particularly when lenses are worn while swimming or when users have poor lens hygiene) is a prominent risk factor.[6] Other well-known risk factors include poor lens hygiene, use of certain types of contact lens disinfection products, water contamination, and even the type of hydrogel lens material.[6] Although AK is extremely rare, with reported US annualized incidence rates ranging between 1.65 to 2.01 cases per million contact lens wearers, it may be up to 15 times more common in the United Kingdom, the Europe, and Hong Kong.[6] Non-specific clinical presentations accompanied by the poor microbial isolation make the diagnosis difficult moreover the treatment is even more challenging due to the cystic nature of Acanthamoeba which makes it resistant to the conventional antimicrobial treatments.[7] Physicians must consider AK in case of atypical keratitis based on clinical suspicion, and the diagnosis must be confirmed by laboratory tests including confocal microscopy, polymerase chain reaction, or cultures with positive results after corneal scraping or biopsy.[3]

Epidemiologic findings provide us with more knowledge on AK risk factors and help to find appropriate preventive strategies[1]; hence, in this study we aimed to investigate patients with AK in Farabi Eye Hospital of Tehran considering its associated risk factors. We also evaluated predisposing risk factors resulting in a more severe corneal involvement.

Methods

After obtaining the university ethics committee approval, we began a clinical trial studying the effects of polyhexamethylene biguanide treatment on visual outcomes in patients with AK. Patients referring to the cornea clinic of Farabi Eye Hospital were selected as the study population. Farabi Eye Hospital is a tertiary referral eye specialty care centre in Tehran, Iran, affiliated to Tehran University of Medical Sciences with thousands of annual visits. The patients were planned to be followed up for a period of at least six months after the treatment. This is a preliminary report of the patients characteristics presented with AK during one year (April 2009 to March 2010) at our institute.

The patients with signs and symptoms suggestive for AK were evaluated using in vivo confocal microscopy and laboratory culture of Acanthamoeba from corneal scraps or, if not possible, from the contact lens case solution. Patients with clinical or laboratory diagnosis of AK were enrolled during the first year of study. The following features were recorded at presentation: age, sex, chief complaint, eye(s) involved, symptoms and signs at presentation, duration from symptom onset till presentation, the season of symptom onset, previous treatment, history of contact lens use and its type, frequency of lens use, and risk factors of Acanthamoeba infection including use of contaminated lens (described as use of lens after falling on the ground), exposing the lens to tap water, swimming or showering with the lens, borrowing or lending lens from/to others, overnight wear, and dry contact lens use.

The first visual acuity (VA) was measured by an optometrist and the stage of the disease was determined by a single expert ophthalmologist (FR) according to the depth of corneal involvement using a slit-lamp (Hagg-Streit 900; Koeniz, Switzerland). Stage I was defined as to one or more of the three following conditions: (i) epithelial stippling or elevated line; (ii) epithelial irregularity; (iii) pseudodendrites. Anterior stromal infiltration was considered as stage II, and stage III was determined as either deep stromal or ring infiltration.

Statistical analysis

SPSS software version 14.00 (SPSS Inc., Chicago, IL) was used for statistical analysis. Quantitative variables are presented as median (range) and qualitative data was expressed in number (percent). χ^2 test for proportion was applied to check any

seasonality of AK by comparing the proportion of patients with symptom presentation in each season. A linear regression analysis with the stage of AK as the dependent variable was made after adjusting for the variables of interest including age, sex, symptom presentation in warmer seasons (i.e. summer), frequency of lens use, number of suboptimal hygiene practice risk factors, corneal culture with positive results, first VA at presentation (inserted in the model as logarithm of the minimum angle of resolution (logMAR)), and the duration of symptoms at presentation to determine any factors affecting the stage of corneal involvement at presentation. P-value<0.05 was considered as statistically significant.

Results

Among the 25 patients with AK, (4 males and 21 females) age ranging from 14 to 36 (median: 21), two (8%) presented with bilateral involvement; thus 27 eyes were included. Thirteen patients (52%) had AK of the right eye only and 10 (40%) ones had only the left eye disease. In vivo confocal microscopy was diagnostic in 26 (96.2%) eyes, while a positive culture was obtained from 22 (82.5%) eyes with a percent agreement of 77.8%.

The potential risk factors identified for the infectious keratitis in our patients were listed in table 1. Cosmetic contact lens wearers included 85.2% of the cases. The most frequent chief complaint was ocular pain. Twenty five patients (92.6%) had a history of antibacterial treatment before presentation and 12 (44.4%) had used topical steroids (Table 1). Only 4 patients (16%) did not report any suboptimal hygiene practice. A half of the lens wearers had washed their lenses with tap water, and 42.3% reported wearing a contaminated lens (Table 2).

Eleven eyes (40.7%) presented in stage I, 7 (25.9%) in stage II and 9 (33.3%) in stage III of corneal involvement. The frequency of lens wearing among the lens users were shown in figure 1 exhibiting their stages of the disease as well. All patients who used contact lens 1-2 times monthly were diagnosed as the 1th stage of AK. Seventy-five percent of patients who used contact lens only ones diagnosed as 2th stage of AK. Those in the third stages of AK except one have used contact lens at least 1-2 times weekly. The only patient who did not use contact lenses presented as stage II. The linear regression model adjusted for desired variables revealed that logMAR and the duration of symptoms were independently associated with worse stages of the disease; using the stepwise method, a significant model emerged ($F_{2,21}$=13.98, p<0.001, adjusted R square=0.530). Significant variables were shown in table 3.

As is shown in figure 2, most cases reported summer as the season of symptom onset; however, χ^2 test for proportions did not show any significant priority for any season (p=0.13 for summer and winter).

Table 1. Potential risk factors of Acanthamoeba keratitis, chief complaints and pre-diagnosis medications in the study population (number of eyes=27)

Potential risk factors		Number of eyes (n; %)
	Cosmetic contact lens	23 (85.2%)
	Soft optical contact lens	3 (11.1%)
	Infectious water	1 (3.7%)
Chief complaint		
	Ocular pain	15 (55.6%)
	Decreased vision	2 (7.4%)
	Redness	3 (11.1%)
	Burning or foreign body sensation	3 (11.1%)
	Tearing	2 (7.4%)
	Photophobia	2 (7.4%)
Drug history at presentation		
	Antibacterial therapy	25 (92.6%)
	Corticosteroid therapy	12 (44.4%)
	Anti-Acanthamoeba therapy	7 (25.9%)
	Antiviral therapy	9 (33.3%)

Table 2. Suboptimal hygiene practice among the lens users (number of eyes=26)

	Number of eyes (n; %)
Contaminated lens	11 (42.3%)
Exposing the lens to tap water	13 (50.0%)
Swimming or showering with the lens	7 (26.9%)
Sharing of the lenses with others	6 (23.1%)
Overnight wear	6 (23.1%)
Dry contact lens use	6 (23.1%)

Table 3. Significant variables in the linear regression model adjusted for desired variables using the stepwise method ($F_{2,21}$=13.98, p<0.001, adjusted R square=0.530)

Predictor variable	Unstandardized coefficients (B)	Beta	t	P-value
Constant	1.114	-	5.509	<0.001
logMAR*	0.901	0.593	3.965	0.001
Duration of symptoms	0.013	0.326	2.182	0.041

*: logarithm of the minimum angle of resolution

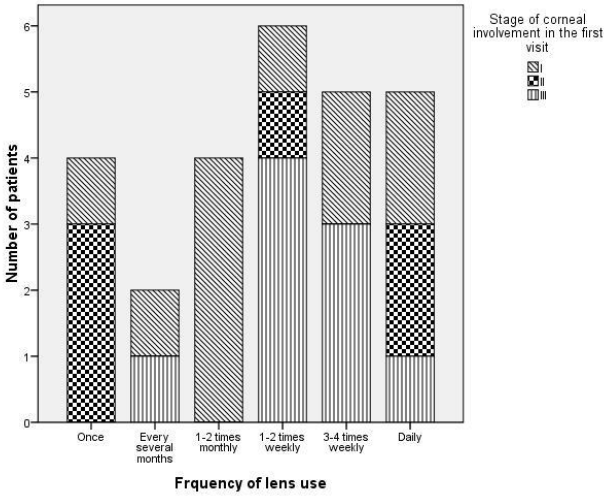

Figure 1. Frequency of lens wearing and the stages of the disease (number of eyes=26)

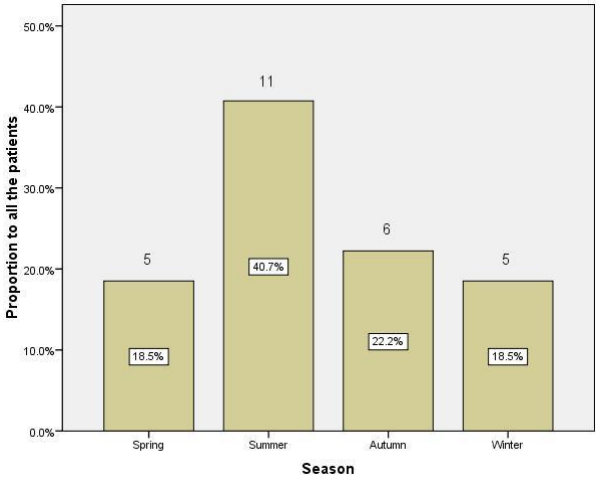

Figure 2. Number of patients presenting in each season and their proportion to all the patients

Discussion

In this study we investigated patients with AK in Iran, their demographic characteristics, and the risk factors affecting the stage of corneal involvement. Among the 25 patients (27 eyes involved) with AK, (4 males and 21 females) age ranging from 14 to 36 (median: 21), female/male ratio was $^{21}/_{4}$ and the right eye was more involved (right/left ratio=$^{13}/_{10}$). The mean age in other studies has been reported 28-30 years, and female proportion as 30% to 65% of all cases.[8,11,12] This difference could be due to this issue that most contact lens user in Tehran are young female who use contact lens for cosmetics purpose. In cosmetic contact lenses accounted for the most common potential risk factor of AK; a half of the patients reported washing their lenses with tap water, and 42.3% used contaminated ones.

After Rezeaian et al[9] study which reported 49 cases of AK in an Iranian population during ten years from 1997 to 2007, it is the first time to report such a high rate of this corneal infection in Iran. They investigated the Acanthamoeba positive cultures referred to the Department of Parasitology of Tehran

University of Medical Sciences which mainly consisted of the specimens from Farabi Eye Hospital (i.e. our study setting). McAllum et al reported a dramatic increase in AK cases during the eight years of their study in Canada[10]; however, the highest number they reported was 14 in 2005. Similar reports are available from different states of the US.[12-15] Non-specific clinical presentations leading to delayed diagnosis, complicated treatment and also the devastating trend of the disease make the increased AK incidence a big concern. Twenty seven eyes involved in our study during just one year, indicate a possible AK outbreak in Iran. However, increased knowledge of AK, developing diagnostic methods, and performing the study in a referral hospital may justify this possibly high incidence.

The most important risk factor for AK in this study was found to be cosmetic contact lenses accounting 85.2% of the identified risk factors; soft optical contact lenses and infectious water came next with 11.1% and 3.7%, respectively. The high prevalence of contact lens use in patients with AK is consistently reported in other studies.[1,4,5,10-14] However, to our knowledge, there is no report of such a high number of AK resulting from cosmetic contact lenses. As cosmetic contact lenses are not classified as medical devices in Iran, their sale is not restricted by the Health Ministry; hence, cosmetic contact lenses are widely available through clothing shops, novelty stores, hairdressers, and even local markets with an increasing popularity. These users are less likely to be provided with adequate professional information regarding safe use and potential ocular complications and to receive proper eye examination. AK treatment is estimated to cost from $8000 for an uncomplicated case to $50,000 for those needing corneal graft[14] to the health systems: hence, it is suggested to highly consider AK in contact lens users presenting with atypical keratitis manifestations,[3] and a red or painful eye in a cosmetic contact lens wearer must be fully evaluated by an ophthalmologist for AK.[14]

Two patients (8%) had bilateral eye involvement which could result from the contamination of the contact lens solution or the frequent use of cosmetic contact lenses (up to 3-4 times weekly). This is reported in other studies to range from 2.4% to 11%.[1,9,15] Ocular pain was the most frequent chief complaint in our patients (55.6%); while it was more frequently (85%) found in another study.[9] Contact lens exposure to tap water is reported to be a considerable risk factor for AK in contact lens wearers.[10,17]

In a study- on tap water in Iran 94 samples of cold and warm tap- water were collected from different wards of hospitals in 13 cities of Iran in 2007-2008. Acanthamoeba was found in 45 samples (48%). Thirty-four and 11 positive samples were collected from cold and warm tap water, respectively. Samples with a temperature of 20-30°C containing 0-2 ppm free residual chlorine, and pH of 6-7.4 showed the most coincidence to the positive cases. The greatest proportion of positive samples was obtained from Mashhad hospitals, while all samples collected from Arak and Semnan hospitals had negative results.[18] Domestic tap water, specially when supplied from roof storage tanks, is a source of Acanthamoeba contamination. People who use contact lens should be aware of the risks associated with Acanthamoeba in tap water supplied from water storage tanks.[18]

However we identified a half of our patients to practice suboptimal contact lens hygiene and 42.3% used dust contaminated lenses. This indicates patients' poor knowledge in our society about contact lens storage and hygiene. However, in a national study recently performed in the US, no association was reported between tap water exposure of the lenses and AK.[11]

As AK is a rare cause of keratitis compared to other pathogens, in many occasions the patients are mistakenly treated by antibacterial, antiviral or antiherpetic agents before the definite diagnosis.[19,20] In our study population, 92.6% had received antibacterial therapy and 33.3% antiviral treatment before the presentation, and only 25.9% were given anti-Acanthamoebal drugs; 44.4% had also received a course of corticosteroid therapy. Antibacterial and steroid therapy in other studies were fewer but none had impressed conclusive treatment results.[7] AK is reported to be more prevalent during the warmer seasons, specially during the summer.[10] Although the most frequent season for patients with AK in this study was summer (Figure 2), the difference between summer and winter (as the seasons with highest and

lowest symptom presentation respectively) was not statistically significant. This could be due to smaller study population and limited duration (one year) of our study. In other studies the summer was reported as the most frequent season for AK symptom presentation.[4-8]

Tu et al investigated prognostic factors associated with a worse visual outcome and concluded that corneal disease staging at presentation is highly predictive of worse visual outcome.[7] As a result, we assessed factors affecting the stage of corneal involvement at presentation, as a strong independent predictor of final visual outcome after treatment, using a linear regression model. Only the first VA at presentation and the duration of symptoms were independent predictors of the stage of disease. Other studies have also suggested early diagnosis of AK to result in favorable visual outcomes.[20,21] However, Tu et al did not find the duration of symptoms as a strong predictor of final visual outcome when compared to the stage of corneal involvement; they claimed patient recall of the symptoms to be subjective and unreliable due to non-specific characteristics of AK presentation.[7]

Corneal ulcer smear and culture are the standard diagnostic methods for AK; however, confocal microscopy is known as a non-invasive beneficial means in early diagnosis and management of AK.[22] Kanavi et al reported a sensitivity and specificity of 100% and 84% respectively for confocal microscopy in AK diagnosis compared to corneal and/or contact lens case solution smear and culture.[23] Applying both methods in our study, confocal microscopy and culture were diagnostic in 96.2% and 82.5% of the patients, respectively with a percent agreement of 77.8% which shows a good agreement between the two methods.

As Farabi Eye Hospital is a referral eye specialty hospital, number of patients referred to our clinics could not provide an accurate estimation for AK incidence assessment. Other limitations of this study included the lack of complete knowledge of the number of previous AK cases in our center which prevented any accurate judgment about the trend of the disease in the past years. Besides, a collaborative case-control study by parasitology department, eye clinical hospital and eye research center would result in a more precise assessment of the AK risk factors. However, in order to prevent underestimation of AK cases we used both confocal microscopy and corneal culture as the diagnostic tests.

Conclusion

Following a previous study in Iran, the possibly high incidence of AK in our center suggests a possible outbreak of the disease, parallel to the reported outbreaks in the developed countries, which is highly associated with cosmetic contact lenses. Considering the progressive rate of cosmetic contact lens use in our country, we strongly recommend restricting the sale of these lenses to be included in national health policies, as well as improving the public knowledge on lens storage and hygiene.

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