The role of contact lenses and ocular TRAUMA in determining Acanthamoeba Keratitis: a case-control study in Italy

ELENA PACELLA(1), FERNANDA PACELLA(1), DAVID IMPALLARA(3), VITTORIO SCAVELLA(3), PAOLO TURCHETTI(2), CARMEN PIRAINO(1), CHIARA BRILLANTE(1), ANNA MARIA LOMBARDI(3), MARIA DE GIUSTI(3)

ABSTRACT

BACKGROUND: Acanthamoeba Keratitis (A.K.) is a rare secondary infection due to Acanthamoeba (A) invading the cornea. Cofactors of risk may include TRAUMA and contact lenses (CL). The objectives of this observational study are to evaluate the occurrence of A.K. in patients accessing the Department of Special Senses of the Teaching Hospital “Policlinico Umberto I” of Rome with ocular infections during the period from 2005 to 2011, and the role played by risk factors which included contact lenses, TRAUMA, sex and age.

METHODS: A case-control study involving 714 subjects was conducted (350 male and 364 female). All of the patients underwent a thorough ocular examination with confocal microscopy and a review of their medical history to outline relevant variables (contact lens and TRAUMA). Statistical analysis calculated the frequency distribution and the Odds ratio (OR) (95%CI) for the risk factors “contact lenses” (CL) and “TRAUMA”. The Odds ratio (95%CI) was adjusted for age and sex through Logistic Regression.

RESULTS: Out of 714 patients, 11 patients (7 male and 4 female) with a mean age of 34.09 years (19 to 51 years old) were found to be affected by A.K. The age group most afflicted ranged from 30 to 51 years old. Statistical analysis produced a crude OR equal to 17.68 (95%CI 2.25-138.89) for CL-A.K. and OR equal to 7.71 (95%CI 0.89-66.75) for Ocular TRAUMA-A.K. Logistic Regression performed to adjust OR for age and sex showed the following values, respectively: OR*=82.54 (95%CI 3.04-2239.58) and OR*=11.52 (95%CI 1.19-111.76).

CONCLUSIONS: The data highlights an increase in A.K. cases during the 6 year study period. The association between this pathology and the use of contact lenses and/or TRAUMA has been statistically proven. The strength of this association increases when the Odds Ratio (OR*) is adjusted for the confounding risk factors of age and sex. When dealing with the topic of Acanthamoeba Keratitis, it is important to remember that educating patients on proper hygiene practice for contact lenses is the first step towards preventing A.K. The results obtained are important because they are derived from the first Italian case-control study on A.K.

Key words: Keratitis, Acanthamoeba, Contact lens, TRAUMA

CORRESPONDING AUTHOR: Elena Pacella, MD - Department of Sense Organs, Faculty of Medicine and Dentistry - La Sapienza University of Rome - Viale Regina Elena 324 - 00161 Rome (ITALY) - Phone: +39 06 49973302-03-05 - Fax: +39 06 49975304 - e-mail: elena.pacella@uniroma1.it
INTRODUCTION

Acanthamoeba Keratitis (A.K.) is a rare secondary infection due to Acanthamoeba (A) invading the cornea, which, in developed countries, mainly strikes contact lens (CL) wearers (1,2). Acanthamoeba is a protozoan that is resistant to environmental stress and easily found in potentially contaminated settings, such as fresh water and salt-water sources in pools and thermal springs, air conditioner filters and contact lens (CL) solution.

Identified species of Acanthamoeba are divided into 3 morphological groups: group I (including non-pathogenic organisms for humans), group II (including A. castellani, A. hatchetti, A. polyphaga, A. quina and A. rhysodescapable capable of causing serious keratitis) and group III (A. culbertsoni, which does not act as an infective agent) (3).

The first observation of Acanthamoeba Keratitis was reported in literature by Nagington in 1974 (4). However, it wasn’t until the late 1980’s that comprehensive clinical knowledge of this pathology was attained, when the number of indicated cases notably increased. This increase was linked to the escalating use of contact lenses (CL) (5,6,7).

Cofactors of risk may include TRAUMA, abrasion by a contaminated foreign body or even contact lenses (CL) themselves, which present a favorable pathway for parasites to directly penetrate the cornea.

The increased diffusion of the disease calls for early diagnosis due to the seriousness of anatomo-clinical manifestations, often underestimated at first glance. In fact, the initial phases of A.K., characterized by fluctuating epithelial defects, epithelial opacities, pseudo-dendrites, bulbar hyperemia and intense ocular pain, can simulate dendritic keratitis in different ways (8).

During the progression of the infection, stromal ulcerations, ruptures and a characteristic stromal ring infiltrate may appear, as well as perineural infiltrates which are pathognomonic indices of A.K.

Therefore, diagnosis must be timely because the amoeba produces a devastating alteration that, if not adequately treated, tends to reoccur even after surgical intervention by keratoplasty. Hence, it is essential to examine the cornea in vivo with confocal microscopy. Possible indications of Acanthamoeba Keratitis must be confirmed through laboratory exams using samples taken by scraping the epithelium and the stroma, or obtained through biopsy of the injured stroma (with a small blade) (9).

A case-control study was conducted with the scope of evaluating:

a) the occurrence of A.K. in patients with ocular infections under care at the Department of Special Senses of the general hospital “Policlinico Umberto I” of Rome during the time period between January 2005 and October 2011.

b) the role of risk factors including contact lenses (CL), TRAUMA, sex and age.

METHODS

Patients and setting

A case-control study was conducted on a group of 714 patients(350 male and 364 female) affected by different types of corneal alterations who accessed the Department of Special Senses of the Teaching Hospital “Policlinico Umberto I” of Rome during the time period between January 2005 and October 2011.

Patients underwent complete clinical examination (Visual acuity with ETDRS Table chart, anterior segment of the eye with slitlamp and corneal confocal microscopy with Nidek Confoscan) of the anterior segment, and sample cultures obtained to single out Acanthamoeba. A thorough review of their medical history was assessed paying particularly to information regarding the use of contact lenses (CL) and the occurrence of ocular TRAUMA, which compelled patients to seek medical help. Results were reported using recommendations outlined by STROBE (10).

Statistical analysis

Data inserted into an excel database and analyzed using the statistical software SPSS 19.0 for Windows. Statistical analysis was used to create frequency tables and to calculate the Odds ratio (95%CI) for the risk factors “contact lenses” (CL) and “TRAUMA”. In addition, the Odds ratio (95%CI) was adjusted for the confounding factors “age” and “sex” through Logistic Regression.

RESULTS

For this case-control study, 714 subjects (350 male and 364 female) were included. In
particular, 246 patients were afflicted in both eyes, while the rest showed monocular ailments (for a total of 960 eyes).

Medical history evaluation revealed that 37.00% of subjects (264 patients out of 714) wore contact lenses (CL), while 1.40% (10 patients out of 714) reported ocular TRAUMA. Out of 714 patients, 406 (56.86%) had been diagnosed with early phase bacterial keratitis with a clinical outline that included redness, conjunctival injection, minor anterior chamber reaction, minor pain and photophobia. This group was excluded from our study.

Another 244 patients (34.17%) presented signs of stromal infiltrations and notable anterior chamber reaction with hypopyon. They were evaluated using confocal microscopy and corneal swab, which permitted us to exclude the presence of A.K.. These subjects were also excluded from our study.

The remaining group, which included 64 patients (9.00% of the total number), was admitted to hospital for the severity of their clinical manifestations (corneal ulcers). Confocal microscopy, corneal scraping and corneo-conjunctival swabs were carried out on all patients.

Out of 64 subjects, 53 (82.81%) were excluded from the study because of negative test results when tested for Acanthamoeba.

Only 11 patients, of which 7 were men and 4 were women (17.00% of those admitted or 1.54% of the total number), were diagnosed with A.K.. Ten cases were diagnosed using confocal microscopy with confirmation by corneal scraping. One case, initially thought to be negative after testing with confocal microscopy, was later diagnosed through corneal scraping.

The 11 patients affected by A.K. (16 eyes in total) had an age range between 19 and 51 years of age (34.09 mean years old) and were otherwise in good general physical condition.

Six patients had unilateral disturbances, while 5 patients had problems in both eyes. Ten patients (90.90%) were soft contact lens (CL) wearers: 6 admitted not following appropriate standard hygiene procedures, using unsuitable solutions to clean contact lenses (CL) (saliva or tap water), 3 were swimmers and 1 had associated the onset of symptomatology with ocular TRAUMA while wearing contact lenses (CL).

The patient who did not wear contact lenses (CL) reported an accidental TRAUMA caused by an organic/plant source in his medical history that had occurred a few days before being admitted (during objective examination, severe palpebral swelling, secretion, granulomatous stromal reaction and corneal microcysts were noted).

In all patients, initial symptomatology was characterized by photophobia associated with intense and disproportionate pain with relative to clinical signs. Objectively, stromal infiltrates were associated with epitheliopathy in 6 eyes and anterior uveitis in 2 eyes. Perineural infiltrates were found in 2 cases and the characteristic ring infiltrate in only one patient.
Anti-amoebic treatment with PHMB (poliacetalsilbiguanide) was initiated immediately after diagnosis was confirmed.

The patients responded in various ways to therapy. There was anatomico-clinical improvement in 9 cases after 3 weeks, while in 2 cases surgical intervention with full-thickness keratoplasty was necessary due to scarring.

Visual acuity improved after 3 months in 10 patients out of 11, including 1 of the 2 subjects who had undergone keratoplasty. The other patient who underwent keratoplasty had to undergo another round of surgery to recuperate complete function due to graft rejection after nine months.

Corneo-conjunctival swabs allowed us to study the etiology of the remaining 53 admitted patients:

- 28 patients- 37 eyes (44.00% of those admitted) presented bacterial keratitis (in particular 18 patients for Staphylococcus aureus, 7 for Pseudomonas aeruginosa and 3 for Coagulase Negative Staphylococcus (CoNS)).
- 16 patients- 22 eyes (26.00% of those admitted) revealed viral keratitis (in particular 10 for type 1 Herpes simplex and 6 for Varicella zoster virus).
- 9 patients- 13 eyes (13.00% of those admitted) demonstrated fungal keratitis (in particular 6 for Aspergillus and 3 for Fusarium).

The logistic regression model was used to evaluate the association between CL-A.K. (contact lenses and A.K.) and TRAUMA-A.K. (recent ocular TRAUMA and A.K.). It highlighted a statistically significant association between contact lenses (CL) usage and A.K. (Table 1). In 10 out of 11 cases (90.90%) of A.K., the patient was a contact lens (CL) wearer with a crude OR equal to 17.68 (95%CI 2.25-138.89). Ocular TRAUMA was also revealed to be a risk factor with evidence in 1 out of 11 cases (9.09%) and a crude OR equal to 7.71 (95%CI 0.89-66.75).

An association was statistically seen to exist between exposition to certain risk factors (CL, TRAUMA) and A.K., even if it was more significant for CL where the OR (CL-A.K.)= 17.68 (95%CI 2.25-138.89) was higher in comparison to that for TRAUMA where the OR (TRAUMA-A.K.)=7.6 (95%CI 0.89-66.75).

The strength of this association increases when the Odds Ratio (OR*) is adjusted for the confounding risk factors of age and sex through Logistic Regression. The association CL-A.K. and TRAUMA-A.K. produced an OR of 82.54 (95%CI 3.04-2239.58) and 11.52 (95%CI 1.19-111.76), respectively

The time trend of A.K. prevalence showed that its occurrence had steadily increased during the 6 years observation period. It went from 1.09% (one case out of 91 patients) in 2005 to 3.06% (3 cases out 98 patients) in 2011 with a higher prevalence observed during the last two years from 2010 to 2011 (Figure 1).

**DISCUSSION**

In Italy, infections triggered by parasites are often attributed to immigrant patients while, in reality, they may affect all citizens (11).

Parasitic infections of the cornea, such as A.K., until recently were considered to be typical of low-level socio-sanitary regions. During recent years, however, cases of A.K. have increased even in industrialized countries. It is estimated that there are 180 cases a year in Italy (12), while in England numbers have jumped from 1 to 3 cases for every 100 000 residents (13, 14, 15).

The data from our study, concord with international trends, and highlight an increase in A.K. cases during the 6 years considered in this study, increasing from 0.99% (5 cases/504 patients) in the first 4 years to 3.01% (6 cases/199 patients) in the last two years alone (Figure 1).
This phenomenon seems to be linked to 4 factors: the increase in the number of CL wearers, which in Italy alone accounts for 2,000,000 people, the increase in migratory fluctuations of non-EU populations into Europe, the increase in the number of immunosuppressive pathologies such as AIDS, and the increase of tourism towards tropical countries (2). In addition, the diffusion of specific instrumental investigations, such as the confocal microscopy, enables us to increase the number of A.K. diagnoses that may have been underestimated in the past, particularly before the 1970’s and 1980’s (16, 17, 18).

In examining the 11 patients with A.K., a close association is noted between pathology and predisposing factors, such as CL use (10 cases) and TRAUMA (1 case), which create a favorable pathway for parasites to enter the cornea. This is in agreement with various epidemiological studies, such as the retrospective study conducted at Toronto Western Hospital (19) and a study conducted at Princess Alexandra Hospital in Australia (20), which both reported that more than 90.00% of affected subjects were CL wearers. It also agrees with the analysis carried out at Hong Kong Eye Hospitals that supported the correlation between infection, CL use and TRAUMA (21).

In this study, an association was statistically evidenced between exposition to certain risk factors (CL, TRAUMA) and A.K., even if it is more significant for CL where OR values were higher ((CL-A.K.) = 17.68 (95%CI 2.25-138.89)) in comparison to those for TRAUMA (TRAUMA-A.K.) = 7.71 (95%CI 0.89-65.75)). The strength of this association increases when the Odds Ratio (OR*) is adjusted for the confounding risk factors of “age” and “sex”.

This association can be attributed in part to the increase of CL wearers because of better manageability of CL, and the reduced costs of CL nowadays, and in part to the improper use of CL (at night or while swimming). Bad hygienic practices are also included as possible reasons for this increase (8 out of 10 patients evaluated confessed to washing their contacts with tap water or unsuitable solutions). The cornea on which a CL is placed undergoes hypoxia and micro-TRAUMA. The diffusion of silicone hydrogel contact lenses (22), which facilitate the adhesion of the parasite due to penetrating oxygen, is also to be added to the list of possible risk factors as well.

The factors listed above notably expose CL wearers to the parasite. It has been demonstrated that 100% of healthy subjects present IgG against Acanthamoeba (23).

Acanthamoeba Keratitis, therefore, must be suspected in all subjects that complain of strong disproportionate eye pain, that show anatomo-pathological alterations, and who are CL wearers or have experienced eye TRAUMA in the past.

It is recommended to carefully check the patient’s medical history and examine how patients use and conserve their CL. These observations, along with anatomo-clinical and laboratory evaluations, allow us to avoid the serious complications that arise from the disease (hypopyon, corneal scarring, nodular scleritis, cataract from metabolic alterations (24) and optic neuritis). This also guarantees early diagnosis of A.K. and permits the prescription of targeted treatment.

CONCLUSION

The data obtained coincides with scientific evidence underlining the importance of educating patients about proper hygiene practice for the use of contact lenses, that is the first step towards preventing A.K.

We still only have access to a small number of records, and so it is reasonable to hypothesize that, in the coming years, further studies may examine the problem in more depth. Nonetheless, the results obtained are of considerable importance being that they are derived from the first Italian case-control study on A.K.
References


(20) Jae Yee Ku MBChB,Fiona M Chan FRANZCO and Peter Beckingsale FRANZCO.Acanthamoebakeratitis cluster: an increase inAcanthamoeba keratitis in Australia, Journal compilation 2009 Royal Australian and New Zealand College of Ophthalmologists: 181-190.


