Results of case-control studies support the association between contact lens use and Acanthamoeba keratitis

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Background: Acanthamoeba keratitis (AK) is ever more frequently reported in industrialized countries. The loss of the corneal surface integrity consequent to secondary microtrauma produced by the use of contact lens (CL) favors the penetration of the parasite into the corneal tissue.

Objectives: A scientific review was performed to investigate the association of CL wear as an Acanthamoeba keratitis (AK) risk factor.

Methods: A computerized screening of 7834 Medline articles (4623 from PubMed; 3211 from Scopus) used a strict selection criteria of case-control studies involving CL wear and/or trauma.

Results: The search yielded five case-control studies published from 1995 to 2012. All studies included showed a statistically significant positive association between AK and CL use, with a combined odds ratio (OR) of 10.21 (95%, confidence intervals [CI]; 3.57–27.64).

Statistical analysis: All studies included showed a statistically significant positive association between AK and CL use, though with differing OR values.

Conclusion: Though rare, AK should be held in higher consideration when ophthalmologists are faced with CL users exhibiting simplex-like lesions associated with circular stromal infiltrates and disproportionate ocular pain in respect to the objective clinical picture.

Keywords: keratitis, contact lens, Acanthamoeba

Introduction
Keratitis is an infective process of the cornea which may lead to serious visual impairments.¹ The microbiological etiology of the disease is varied and may be of viral, mycotic, or parasitic origin.²

Corneal parasitic infections, which were – up to recently – thought to be associated mostly with poor sociosanitary conditions, are ever more frequent in industrialized countries.¹³⁻⁵

Acanthamoeba (A) is a resistant protozoan often found in proximity to freshwater or saltwater sources, in swimming pools, thermal baths, air-conditioning filters, and in contact lens (CL) cleansing solutions.⁶⁻⁸ The first observation of Acanthamoeba keratitis (AK) was reported by Nagington in 1974,⁹ but it wasn’t until 1975 that a causal relationship between AK and A was reported by Visvesvara et al.¹⁰ The species of Acanthamoeba that produces the most serious forms of keratitis in humans are Acanthamoeba castellanii, A. hatchetti, A. polyphaga, A. quina, and A. rhysodes.¹¹

Risk cofactors are particularly associated to the loss of the integrity of the corneal surface,¹² be it consequent to trauma or abrasions from an external contaminated...
object or a secondary microtrauma produced by the use of CL, which both favor the penetration of the parasite into the corneal tissue. Moreover, even the exposure to environmental pollution could be associated to the developing of this keratitis, as reported by Lalitha et al.

There are wide differences in the incidence of the condition around the world and over time, which include the changing CL solution market and local environmental issues, such as water storage and disinfection.

Nevertheless, KA is still a health problem that needs to be clearly faced, according to Ibrahim et al.

The first phases of AK are characterized by fluctuating epithelial defects, epithelial opacity, pseudodendritis, and bulbar hyperaemia, symptoms which resemble the dendritic keratitis often seen with herpes simplex infection; and these symptoms produce intense eye pain.

The evolution of the infection causes a stromal ulceration, lysis, and the characteristic circular and perineural infiltrates of the stroma as typical markers of AK. The diagnosis of this condition must be made quickly, because it is a potentially devastating condition which, if untreated, may return even after surgical intervention.

**Objectives**
The aim of our study was to review the scientific literature regarding the association between CL use and AK, considering that the use of CL has become more widespread. We aimed to perform a pooled analysis of studies where the results could be combined. The main reason for this is to offer support for the development and communication of preventive strategies (technical brochures conveyed through territorial medicine and pharmacies), focused on implementing targeted educational programs among CL users. This awareness may help alert specialists about markers associated to an appropriate and early diagnosis of AK.

**Methods**

**Identification of relevant studies**
The Internet medical databases used for the search were PubMed and Scopus. On Medline and Scopus, we used the keywords “Acanthamoeba keratitis,” “contact lens,” “trauma,” and “case control” linked by the Boolean operators and/or applying the following two algorithms:1 “Acanthamoeba keratitis,” and/or “contact lens,” and/or “case-control study,” and “Acanthamoeba keratitis” and/or “contact lens” and/or “microtrauma.”

The identification of relevant studies was carried out within the time window from January 1995 to February 15, 2012, and was restricted to the English language. We only selected studies that clearly reported the following criteria – CL, trauma, and AK – that measured health outcomes on the basis of association measures (odds ratio [OR]). We excluded papers that did not meet these criteria.

Data extracted included first authors, publication year, nation, study design, sample size, OR of cases and controls, and 95% confidence intervals (CI).

**Data extraction**
To perform the review, we extracted data related to infection by Acanthamoeba keratitis in CL wearers. Extracted data regarded persistent infection, defined by the detection of ulcers in one or more consecutive medical control visits.

**Statistical analysis**
Pooled analysis was performed using the random-effects model, since heterogeneity was found between studies (P for homogeneity = 0.053). The pooled OR was calculated as the back-transformation of weighted mean of transformed ORs using DerSimonian–Laird weights.

**Results**

**Identification of relevant studies**
From Medline, we retrieved 7834 articles (4623 from PubMed and 3211 from Scopus). After sorting for duplicates, removing ineligible studies through PRISMA methods (Liberati et al.), and screening for titles and abstracts, we were left with twelve eligible full-text articles. Moreover, after a first analysis, seven of these full-text papers were excluded because of the lack of data regarding the association measures we were most interested in. This criteria led to a strict selection of sorted articles. PubMed is a highly sensitive search tool and retrieves many articles, although in a much less selective way. If the same article was found in more than one database, it was only used once. The eligible papers were obtained as full text.

The process of data extraction was performed by two independent researchers.

In the end, five studies were included in the systematic review (Figure 1). All studies were case-control studies published from 1995 to 2012.

The sample size ranged from 89 to 714 individuals. Three studies were published in the USA, one in Italy, and one in the UK. The characteristics of each study are shown in Table 1.

ORs ranged from 3.57 (95%, CI; 1.86–6.87), Verani et al. to 27.64 (95%, CI; 6.46–135.54), Radford et al. The five
Table 1 Results of case-control studies of keratitis caused by *Acanthamoeba* published from 1995 to 2012

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Nationality</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radford CF et al</td>
<td>1995</td>
<td>UK</td>
<td>12</td>
<td>378</td>
<td>27.64</td>
<td>6.46</td>
<td>135.54</td>
</tr>
<tr>
<td>Meier PA et al</td>
<td>1998</td>
<td>USA</td>
<td>31</td>
<td>11</td>
<td>1.48</td>
<td>228.1</td>
<td>228.1</td>
</tr>
<tr>
<td>Joslin CE et al</td>
<td>2007</td>
<td>USA</td>
<td>38</td>
<td>100</td>
<td>13.16</td>
<td>3.55</td>
<td>35.57</td>
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<tr>
<td>Verani JR et al</td>
<td>2009</td>
<td>USA</td>
<td>72</td>
<td>140</td>
<td>3.57</td>
<td>1.86</td>
<td>6.87</td>
</tr>
<tr>
<td>Pacella E et al</td>
<td>2012</td>
<td>Italy</td>
<td>11</td>
<td>703</td>
<td>17.68</td>
<td>2.25</td>
<td>138.89</td>
</tr>
<tr>
<td>Pooled data</td>
<td></td>
<td></td>
<td>164</td>
<td>1379</td>
<td>10.21</td>
<td>4.01</td>
<td>25.99</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; CI, confidence interval.
The number of cases recorded and described in the literature is notably on the increase,\textsuperscript{16–20} and the aim of this study was to report the information pertinent to CL users and inform them about the diffusion and resistance of \textit{Acanthamoeba} spp. in freshwater sources, including tap water.

A correct prevention envisages a scrupulous cleaning of CLs and their correct use, using ad hoc communication strategies that use the most efficient means of communication (information leaflets in pharmacies, doctor’s waiting rooms, etc.).\textsuperscript{1,25}

**Conclusion**

Because of the disease’s rare nature, it should be held in higher consideration when the ophthalmologist is faced with a CL user exhibiting simplex-like lesions associated with circum stromal infiltrates and disproportionate ocular pain in respect to the objective clinical picture. The temporal trend of publications has shown a steady increase from 1984 to the current time, testifying the interest in this rare disease among members of the international scientific community. In any case, we recommend that case-control studies need to be intensified to support risk evaluation, management, and communication better.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**