Incidence, Risk Factors, and Clinical Characteristics of Infectious Keratitis Due to Contact Lens Supplied without Prescription: Systematic Review of Primary Reports

1st auther: Dareen Talal alahmadi Co aurhers: Basil Talal Alahmadi Ahlam Mohammed Al sharafi Ibtisam Yunus Alruwaili

Abstract:

Background

The over-the-counter sale of CLs is allowed in some European and most of Asian countries. These unregulated sources of supply were reported to be associated with lack of proper knowledge and adequate compliance to CL guidelines. Therefore, we performed this systematic review to synthesis evidence from the published literature about the incidence, risk factors, and clinical characteristics of microbial keratitis due to CL supplied without prescription.

Methods

We searched PubMed, Scopus, Web of Science and EBSCO databases from inception to 20 December 2017 using different combinations of keywords. We included primary reports which reported the incidence, risk factor, or clinical characteristic of patients presented with MK as a result of unregulated CL supply. No limitations were made on patient's age, gender, or study language. The authors independently extracted the following data from each of the included study.

Results

Twenty studies (Case reports =17, prospective studies =3) were included in the present systematic review. The sample size of the included studies ranged from one patient to 2083 patients, and the patients' age ranged from 13 to 30 years old. Eighty-one patients were reported to wear CLs for better cosmetic appearance, while 58 patients used the CL for refractory error without prescription. Over-the-counter supply accounted for 73% of cases, whereas 17% borrowed or shared lenses and 6% obtained lenses through the Internet. Eighteen patients presented with Acanthamoeba keratitis. The risk of MK increased in patients who had obtained their lenses from Internet or mail-order suppliers compared with optometrists.

Conclusion

In conclusion, CLs from unregulated sources of supply are associated with increased risk of MK and visual impairment. The risk factors associated with the greatest increased in the risk CL-related MK were using cosmetic CL wear and overnight wear and soft lens use. Further well-designed studies are still needed to quantify the association between the CLs from unregulated sources of supply and MK.

Keywords: Contact lens; Infectious keratitis; risk factors; incidence.

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1 INTRODUCTION

Previous reports estimated that the number of contact lens (CLs) wearers approximate 300 million wearers worldwide[1]. CL modalities can be utilized for wide varieties of indications, mainly for myopia correction (orthokeratology lenses) and better cosmetic appearance.[2] Although the orthokeratology lenses wearers undergo close monitoring from their eye care practitioners, cosmetic CLs are largely supplied without prescription, especially among young population[3]. The over-the-counter sale of CLs is allowed in some European and most of the Asian countries[4]. These unregulated sources of supply were reported to be associated with

lack of proper knowledge and adequate compliance with CL guidelines[5]. As a result of inadequate handling and poor CL hygiene, CL may act as a vector for the transmission of different types of bacteria, with the subsequent infection of the cornea. CL-related microbial keratitis (MK) is an established, potentially serious, complication among CL wearers[6].

The current body of evidence suggested that the yearly incidence of MK is about 2–4 per 10,000 wearers of daily soft CL and 20 per 10,000 wearers of overnight soft CL[7]. The occurrence of MK was linked to a large number of pathways including contaminated storage case, hands, eyelids, cosmetic eye

products and contact with contaminated water[8]. Epidemiologic studies showed that gram-negative organisms, particularly Pseudomonas aeruginosa, is the most common retrieved pathogen among cases with MK. However, corneal infiltration with rare pathogens, as amoebae, may lead to sever MK with permanent visual impairment[9].

There is a growing number of published reports suggested an increased incidence of MK among CL wearers who have obtained their lenses from unregulated sources of supply. Dinc et al, reported that 49% of young CL wearers obtained their lenses without a prescription and 54% had their information about CLs from unreliable sources[10]. Stapleton and colleagues reported that unregulated supply of CL increased the risk of MK significantly (Odds ratio 4.76; p<0.001). In addition, the literature shows a large number of case-reports which described the occurrence of MK among CL wearers from unregulated supply[8].

Therefore, we performed this systematic review to synthesis evidence from the published literature about the incidence, risk factors, and clinical characteristics of MK due to CL supplied without a prescription.

2 MATERIAL AND METHODS

We performed this review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [11].

3 LITERATURE SEARCH STRATEGY

We searched PubMed, Scopus, Web of Science and EBSCO databases from inception to 20 December 2017 using different combinations of the following search query: "Keratitis"[MeSH] AND "Contact Lens"[MeSH]. We also manually scanned references of relevant review articles for any additional data.

4 STUDY SELECTION AND ELIGIBILITY CRITERIA

After duplicates removal, the authors reviewed titles and abstracts of retrieved records. Potentially eligible studies were retained for full-text screening. We included primary reports which reported the incidence, risk factor, or clinical characteristic of patients presented with MK as a result of unregulated CL supply. No limitations were made on patient's age, gender, or study language. We excluded review articles, theses, dissertations and conference abstracts.

5 DATA EXTRACTION

The authors independently extracted the following data from each of the included study: (1) Study design, (2) Population's characteristics, (3) Sample Size, (4) Lens type, (5) complications, and (6) causative organisms.

6 QUALITY ASSESSMENT OF THE INCLUDED STUDIES

The quality of each of the included prospective studies was assessed according to Newcastle-Ottawa Scale tool which included the following domains: selection, comparability, and exposure/outcome. Each domain was judged based on the standardized manual and each item was given a star if it fulfilled the criteria[12].

7 RESULTS

We retrieved 4244 unique citations after the online databases search. Out the retrieved citations, 54 potentially eligible studies were retained for full-text screening, from which 20 studies (Case reports =17, prospective studies =3) were included in the present systematic review. **Figure 1** shows the PRISMA flow chart.
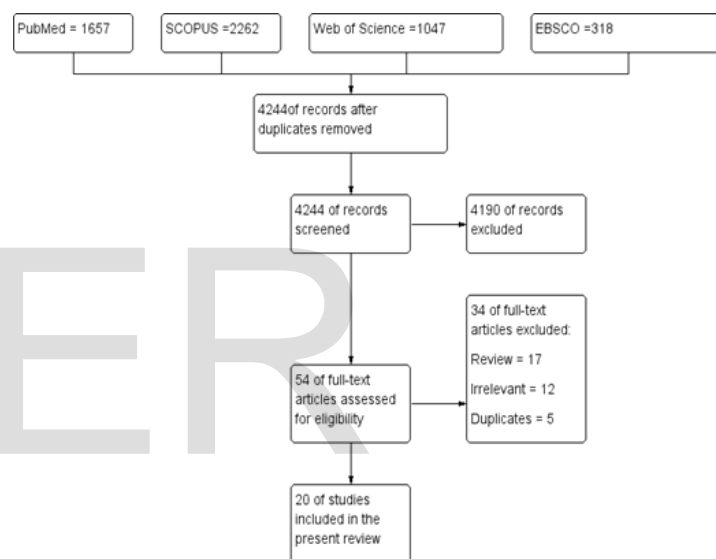
The quality of the included prospective studies were from moderate to high according Newcastle-Ottawa Scale tool. **Table.1** shows the summary of quality assessment.

Table.1: Newcastle Ottawa Scale for the included prospective studies

Author, year	Selection Bias	Comparability	Exposure

	Representativeness of the exposed cohort	Selection of the non- exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	1) Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Stapleton 2012[13]	*	*	*	*		*	*	*
Sauer 2011[14]	*	*	*	*		*	*	*
Stapleton 2008[7]	*	*	*	*		*	*	*

8 INCIDENCE OF MK

In the present review, we yielded only three prospective studies after comprehensive database search[5, 7, 13]. Stapleton and colleagues conducted a prospective, 12-month, surveillance study in Australia. They reported that the annualized incidence of MK per 10.000 wearers was 1.2% in daily rigid gas-permeable CL; 1.9% in daily wear soft CL wearers. The highest reported incidence rate of MK was associated with overnight wear of silicone hydrogel CL (25.4%)[7]. Based on their results, Stapleton and colleagues concluded that the new lens types did not reduce the incidence of MK.

Sauer and colleagues compared the occurrence of MK between cosmetic CL wearers and the wearers of other types of CL, they found that cosmetic CL wearers account for approximately 13% of all cases of MK and this type of patients is less likely to be instructed on appropriate lenses use and basic hygiene rules[5].

9 CLINICAL CHARACTERISTICS AND COMPLICATIONS OF MK PATIENTS:

We retrieved a total of 17 case reports which identified specific cases of ocular complications secondary to the wearing of CLs obtained from unregulated sources of supply, invalid prescription, or without the supervision of eye care practitioner[15–30]. The sample size of the included studies ranged from one patient to 2083 patients, and the patients' age ranged from 13 to 30 years old. Eighty-one patients were reported to wear CLs for better cosmetic appearance, while 58 patients used the CL for refractory error without prescription. Over-the-counter supply accounted for 73% of cases, whereas 17% borrowed or shared lenses and 6% obtained lenses through the Internet. Regarding the causative organisms, 61 patients developed a MK that is caused by an organism other than amebae, and 18 patients presented with Acanthamoeba keratitis. Stapleton

Table.2: The demographic and clinical characteristics of included studies.

Author, year	Study Design	Population	Sample Size	Age	Lens Type	
					No of patients with Plano (cosmetic) Lens	No of patients with unregulated Refractive Lens
Ray 2013[15]	Case report	CL user presented with a polymicrobial keratitis	1	14	1	-
Stapleton 2012[8]	A prospective, 12-month, pop-	Cases: patients with moderate and severe MK in daily wear CL in Australia over a 12-	1180	NA		-

8   Risk Factors for MK idence of MK

The association between the occurrence of MK and a number of independent risk factors was extensively studied in the included studies. Stapleton and colleagues found a five times higher rate of MK in patients who had obtained their lenses from Internet or mail-order suppliers compared with optometrists; in addition, they found a significant association between MK and overnight use, poor storage case hygiene, smoking, <6 months wear experience, and higher socioeconomic class [7].

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Tseng 2008[19]	Case report	MK Patients who purchased a brand new box of daily disposable lenses from a retail store.	1	18	1	-
Lee 2007[23]	Case report	Patient with a history of wearing cosmetic CL presented with keratitis.	1	17	1	-
Colin 2006[28]	Case report	MK in patients wearing Plano cosmetic CL	1	20	1	-
Gagnon 2006[24]	Case report	Patient with a history of wearing cosmetic CL presented with keratitis.	1	24	1	-
Li 2006[25]	Case report	Patient with a visual loss following Pseudomonas keratitis from novelty CL wear	1	13	1	-
Steinemann 2005[31]	Case series	Patients who developed MK after wearing Plano decorative CL.	12	17.3 ± 4.51*	12	-
Connell 2004[29]	Case report	A patient who developed Acanthamoeba keratitis after colored cosmetic CL wear.	1	18	1	-
Steinemann 2003[26]	Case series	Patients who developed MK after unlicensed CL.	6	23 ± 6.9*	6	-
Snyder 1991[30]	Case report	Cases of severe microbial keratitis associated with the use of cosmetic CL.	5		5	-
Johns 1988[27]	Case report	Emmetropic individual presented with Pseudomonas corneal ulcer associated with colored cosmetic contact lenses	1	14	1	-
			3574		81	58

Author, year	Risk Factor		Complication		
	Poor CL Hygiene	Extended Wear	MK (non-AK)	AK	Other
Ray 2013[15]	1	1	1	-	-
Stapleton 2012[8]	-	90	90	-	-
Sauer 2011[14]	-	-	28	4	-
Singh 2011[16]	13	4	13	-	-
Guyomarch 2010[20]	3	3	4	1	-
Van Zyl 2010[17]	3	-	3	-	-
Mckelvie 2009[21]	1	1	-	1	-
Kerr 2008[22]	1	1	-	1	-
Sousa 2008[18]	1	1	-	1	-
Stapleton 2008[7]	-	-	285		-
Tseng 2008[19]	1	1	-	1	-
Lee 2007[23]	1	1	-	1	-
Colin 2006[28]	1	-	-	1	-
Gagnon 2006[24]	1	-	-	1	-
Li 2006[25]	1	-	1		
Steinemann 2005[31]	4	10	3	1	8
Connell 2004[29]	1	1	1	-	-
Steinemann 2003[26]	4	3	3	3	-
Snyder 1991[30]	3	3	3	2	-
Johns 1988[27]	1	1	1	-	-

Sauer and colleagues found a significant association between poor education and increased risk of MK among cosmetic CL wearers. In addition, CL dispensed by a friend, a local market, or internet only was associated with higher risk of MK[5]. Poor CL hygiene and extended CL wear were reported as the major risk factors for MK in the most of included case reports.

Table.3 showed the distribution and risk factor of MK.

8 DISCUSSION

MK is an established vision-threatening complication of daily CL wearers. There is a consensus in the published literature that the risk of CL-related MK is greater among those who fail to adequately adhere to CL usage guidelines[32]. Such lack of proper compliance was linked to CL supplied from unregulated sources of supply[14]. In the present review, we included 20 studies who addressed the incidence, clinical characteristics, and risk factors of MK related to CL from unregulated sources of supply. The incidence of MK was reported to be higher and more severe than the prescribed CL. Lenses supplied from Internet or mail-order, overnight use, poor storage case hygiene, smoking, <6 months wear experience, and higher socioeconomic class were significant risk factors for MK.

As mentioned before, CL modalities can be utilized mainly for myopia correction and better cosmetic appearance[2]. Due to lack of refractive power, Plano CL for cosmetic purposes is not considered to be medical devices in many European and Asian countries, despite the recent regulations in the United States, the United Kingdom, Australia, and Canada[33, 34]. In the present review, 58% of the patients purchased Plano CL from the unregulated sources of supply for cosmetic purposes. This finding runs in concordance with Singh and colleagues who found that cosmetic CL are frequently provided without a medical prescription, and sold without any disinfecting solutions or instructions[16]. In addition, Young and colleagues found that 94% of MK cases had worn Plano cosmetic lenses[3]. Another report showed similar results[5, 35].

These unregulated sources of supply were extensively reported as a risk factor acute vision-threatening infections; a previous multicenter case-control study showed that cosmetic CL wearers exhibited a high relative risk (odds ratio =1.37) for acute vision-threatening infections[36]. Similarly, Lam and colleagues reported that cosmetic CL wearers showed a higher incidence of Acanthamoeba keratitis compared to non-cosmetic CL wearers[37]. Moreover, Young and colleagues performed a systematic review to collect the existing literature regarding complications associated with CLs from unregulated sources of supply. They concluded that wearers of cosmetic CLs have an increased risk of poorer lens hygiene and infectious keratitis[3].

Acanthamoeba keratitis is a serious form of keratitis that may aggressively affect both eyes leading to blindness. The association between Acanthamoeba keratitis and CLs is widely established within the literature[22]. The incidence of Acanthamoeba keratitis was reported to be low in Korea (0.33 per 10000 CL wearers), Holland (0.05 per 10000 CL wearers) and the USA. However, a higher (1.49 per 10000 CL wearers) was reported in Scotland[38]. Previous reported have linked

the increased risk of Acanthamoeba keratitis with poor lens hygiene and compliance with CL guidelines[39]. In the present review, we included 18 cases of Acanthamoeba keratitis (22.8% of the total cases of MK). This high incidence of Acanthamoeba keratitis in our study may be attributed to the lack of proper lens hygienic measures among wearers of CL from unregulated sources of supply. Similar to our findings, Young and colleagues identified ten published case reports of Acanthamoeba keratitis among CL wearers from unregulated sources of supply, the CLs were either available as over-the-counter supply or shared with a friend[3].

In the present review, we identified a number of risk factors of MK among CLs obtained from unregulated sources of supply. The most commonly reported risk factors were overnight use, poor storage case hygiene, and internet supply of CLs. It can be assumed that a strong relationship exists between these factors. As mentioned before, wearers of CLs from unregulated sources of supply tend to show a poor compliance with CL handling guidelines. Hence they tend to show unfavourable behaviours and poor CLs hygiene; which leads to the significant increase in the risk of MK[8]. The previous systematic review showed that a high proportion of CLs-related complications, including the non-keratitis cases, were associated with two or more risk factors, and the most commonly encountered risk factors were a failure to disinfect lenses, overnight wear, solution misuse, and poor case hygiene[3].

The present review has certain strength points. We have conducted a comprehensive search of four medical databases and identified clear eligibility criteria. In addition, we followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement during the preparation of the present review[11]. However, we acknowledge that our review has limitations as well. Most of our included studies were case reports which may affect the quality of the present review. Moreover, we could not compare the clinical characteristics between the Acanthamoeba keratitis and non-Acanthamoeba keratitis patients due to lack of the available data.

In conclusion, CLs from unregulated sources of supply are associated with increased risk of MK and visual impairment. There is an established link between obtaining the CLs from unregulated sources and poor CL hygiene. The risk factors associated with the greatest increased in the risk CL-related MK were using cosmetic CL wear and overnight wear and soft lens use. Further well-designed studies are still needed to quantify the association between the CLs from unregulated sources of supply and MK.

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