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BACTERIAL CONTAMINATION OF USED EYE DROPS AND KNOWLEDGE ON SAFE USAGE AMONG GLAUCOMA PATIENTS AT TERTIARY HOSPITAL, SRI LANKA

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ABSTRACT

Background: When ophthalmic solutions are used improperly, then it is more likely to be contaminated with bacteria which may result in permanent vision loss or blindness.

Method: This study was a descriptive cross - sectional laboratory-based study. It was conducted to determine the bacterial contamination of multidose eye drops and influence of patients' knowledge on safety usage techniques and socio demographic factors among glaucoma patients, who were attending an eye clinic, Teaching Hospital, Jaffna. Thirty-five patients who were from Nallur and Jaffna area divisional secretory divisions were included in this study. Used eye drop bottles of glaucoma patients were collected by visiting their homes. Interviewer-administered questionnaire was used to collect the data. The study was done between July and August 2017. Data were analyzed using SPSS version 21.

Results: Overall contamination rate of used eye drops was 22.9% (n=8). Regarding knowledge on safe usage of eye drops, 34.3% (n=12) of participants had good knowledge and 54.3% (n=19) participants had average knowledge. The level of knowledge on safe usage of eye drops showed a statistically significant association with contaminated eye drops. Sociodemographic factors did not show a significant association on patients with contaminated eye drops.

Conclusion: Bacterial contaminated eye drops were identified among glaucoma patients. Patients should be trained on proper handling of eye drops and educate them about serious problems due to improper usage.

Key words: Bacterial contamination, glaucoma patients, eye drops, knowledge, safe usage

INTRODUCTION

Background

Glaucoma is a progressive optic neuropathy caused by the death of the retinal ganglion cells and is currently the leading cause of irreversible blindness. (Katherine and Georgios, 2015; Tham et al., 2014). In the worldwide second leading cause of blindness is glaucoma, largely due to primary open-angle glaucoma (Resnikoff S et al., 2004). There are over 60 million people affected by glaucoma in this world (Tham Y-CC et al., 2014). The medication management of glaucoma primarily depends on the administration of topical ocular medications (Tony et al., 2007). The most common method of ocular drug delivery is a topical application of eye drops to the conjunctival sac and they are widely used for anterior chamber of the eye and as well

as deeper intraocular structures. The beneficial effects of eye drops are relative ease and non – invasiveness self - administration, direct targeting to the desired site, by passing the first-pass metabolism and minimizing systemic side effects. The British National Formulary (BNF) states that multidose eye drops for domiciliary use should not be used for more than 4 weeks after the first opening. Generally, a container of eye drops may be used for approximately one month for domiciliary purposes and if they used in hospital wards, they should not be used not more than one week.

Improper use eye drops resulting in contamination. Contaminated eye drops are a serious risk factor for ocular infections (Geyer O et al., 1995). Most potential sites of contamination of eye drops are tip, cap, inside the head space and expelled drops (Schein OD et al., 1992). The microorganisms may be infected when the bottle comes into touching base with fingers, lids, conjunctiva, or cornea (Nentwich MM et al., 2007). The moist nozzle acts as a reservoir for microbes. When the patient accidentally touches it to the eyelids during use, contaminants may consequently travel to other portions of the bottle including the cap, bottle top, and the bottle contents (Geyer et al., 1995). Many patients, especially those with poor vision and coordination, accidentally touch their eyes or skin with the dropper or tip of the bottle, which could contaminate the container (Geyer et al., 1995). Commonly high risk of contamination is possible when handling the multidose eye drops by elderly patients due to touch the eyelid or conjunctiva with the container and contaminated by microbial flora of the skin and conjunctiva (Dietlein TS et al., 2008). Protective measures employed to lessen this risk are hand washing, using alcohol hand gels, avoidance of contact with the eye or lids, discarding any contaminated vial and recapping the bottle immediately after use.

A small population of bacteria, normally coagulase negative staphylococci (CNS) naturally supports to ocular surface of healthy individuals, which are believed to exist as Commensals on the mucosa and lid borders (Geyer O et al., 1995); (Jokl DH et al., 2007). Under ideal conditions, there is little or no opportunistic bacterial colonization of the conjunctiva or cornea, because of the washing effect of the tears (Nentwich MM et al., 2007), (Porges Y et al., 2004). Endophthalmitis due to eye droppers contaminated with Pseudomonas pyocyanea (Prof.Culloch JC., 1943) as well as some cases of keratitis caused by Serratia contaminated eye drop caps and droppers have been reported (Templeton WC et al., 1982). Bacteria isolated from contaminated bottles include usual conjunctival flora and other potential pathogens such as Staphylococcus aureus and Pseudomonass sp (Jokl DHK et al., 2007).

Contaminated eye drops cause serious risk factor for ocular infections. It results in increasing the morbidity, and extending the treatment and hospital stay, thus, increasing the total cost of treating a particular eye disorder of a patient. The current study is to determine the bacterial contamination of multi dose eye drops among glaucoma patients and factors influencing them.

LITERATURE REVIEW

Bacterial contamination of eye drops

A cross-sectional study was done by Mostafa Feghhi et al., (2007) to study the incidence of fungal and bacterial contaminations of using 287 randomly collected used eye drop products in Ahvaz, Iran. The microbial contamination was 17.8%, with the highest rate (24.6%) and the lowest rate (9.0%) noted with day 1

and day 3 samples, respectively. The most contaminated part of the eye drop products was the caps (45.9%) followed by droppers (41.0%) and residual contents (13.1%). Another cross-sectional study was done by Mohammad reza fazelid et al., (2004) to study on microbial contamination of preserved ophthalmic drops in outpatient departments and the possibility of an extended period of use in Iran. The most contaminated part was residual contents (50%), whereas a lower contamination rate (31.5%) was obtained in eye drop caps ($p<0.001$). The isolated bacteria were Staphylococcus epidermidis, Staphylococcus aureus, Micrococcus spp, Bacillus spp, Corynebacterium spp and Streptomyces spp.

Another cross-sectional study was done in India, regarding assess microbial contamination of the eye drop solution after use for one month. Only eye drop solution was examined. None of the eye drops had any qualitative or quantitative evidence of growth after 14 days of incubation on various culture media. The absence of microbial growth was not related to the type of content ($p >0.9$), presence of preservative ($p >0.9$) or external appearance of the bottle ($p >0.9$). (Shalini Virani1 et al., 2015). Another cross-sectional study was conducted in Kenya, at the Kenyatta National Hospital regarding determine the magnitude and pattern of microbial contamination of multi-dose ocular solutions. Six (6%) of the 101 vials were contaminated. Isolated bacteria were micrococci ($n = 2$), Staphylococcus epidermidis, Haemophilus spp, Bacillus spp and a Gram-negative rod. The dropper tip was more often contaminated ($n = 6$) than the residual solution ($n =1$), and only one vial showed a contamination of both the drop and the tip (M.M Nentwich et al., 2007).

A cross sectional study was conducted in Iraq at Baghdad national hospital regarding the magnitude and pattern of microbial contamination of eye drops in out –patients. Out of 54 analyzed vials, eight (15%) were contaminated, and isolated contaminants were Staphylococcus auereus, Micrococcus, Neisseria catarrhalis, Gram negative Rods, Candida albicans, and Staph epidermidus. The dropper tip was more contaminated ($n=5$) than the residual solution ($n=2$) and only one vial showed a contamination of both the drop and tip (Raghad A. Razooki et al., 2011).

Improper handling of eye drops

A cross-sectional, open-ended questionnaire-based study was done by Chirayu Mohindroo et al., (2015) on the knowledge, attitude regarding eye drop instillation and self-care practices among glaucoma patients who were attended urban tertiary care hospital of North India. Only 61.4% subjects knew that the eye drops should be stored in a cool and dry place. 71.3% of them did not use the eye drops beyond 40 days after opening the vial. 57.4% of the participants washed their hands before instilling the eye drops. There were no statistically significant differences in the mean domain and total scores between males and females and between urban and rural patients. Another cross-sectional observational study was done by AJ Tatham et al., (2013) to evaluate the technique of eye drop instillation in patients with glaucoma and to assess the factors associated with a good technique in the Department of Ophthalmology, University Leicestershire, UK. 54.1% of patients had poor drop technique, 81.2% could not recall that how to instill eye drops.

METHODOLOGY

Study design

This study was conducted as a Laboratory based descriptive cross-sectional study conducted in Eye – clinic at Teaching Hospital, Jaffna, Sri Lanka

from November 2016 to September 2017. Patients who were from Jaffna and Nallur divisions and received ophthalmic solutions for glaucoma were included in the study. Data were collected for one month and the sample size was minimized to 35 because of the limited time and resources.

Equipment and apparatus

Light microscope
Incubator
Autoclave
Biochemical reagents
Blood agar
Mac Conkey agar
KIA agar
Gram – staining reagents
Normal saline
95% ethyl alcohol
1% solution of oxidase reagent
Hydrogen peroxide
Urease agar
Blood plasma
Peptone water

QUESTIONNAIRE

The interviewer-administered questionnaire was used. The questionnaire contained two parts, such as part – A contained socio demographic factors, part – B contained safety usage techniques. Part – B was prepared according to WHO guidelines.

DATA AND SAMPLE COLLECTION

Data and sample collection procedure

Before interviewing patients, informed consent was obtained from them. After interviewed the patients, their address was obtained and travel to their homes to collect the used eye drops.

Collection procedure and transport of the sample

Used empty eye drops were collected from patients. Samples were labeled and packed in air proof bag and transported to the Microbiology Laboratory at Faculty of Medicine, University of Jaffna.

Laboratory analysis

Swabs were taken from the dropper tip by using sterile absorbent cotton wool, moistened into sterile normal saline. 95% ethyl alcohol will be used to clean the dropper tip, after that 0.1ml residual solution was taken from the bottle by using 25-gauge sterile needle. The samples were inoculated on the Mac Conkey agar, Blood agar and incubated overnight without delay at 37℃ aerobically according to the Laboratory Manual in Microbiology by Sri Lanka College of Microbiologist.

Isolation of bacteria

Further microscopic tests and biochemical assays were conducted on the isolates to identify organisms accordingly to the Laboratory Manual in Microbiology by the Sri Lanka College of microbiologist.

Gram-staining and biochemical examination

Gram staining and all biochemical tests were done according to the Laboratory Manual in Microbiology, (2nd edition, Sri Lankan College of Microbiologists)

Data Analysis

Data were analyzed by using SPSS 21 software (Statistical Package for Social Sciences). The questionnaire B part contained 5 questions, among those, two questions got ‘1’ point for yes response and ‘0’ point for no response . 03 questions got ‘0’ points for yes response and ‘1’ point for no response. Levels of knowledge on safety usage of eye drops were good, average and poor. Good knowledge was considered for 5 points,

average knowledge was considered for 3 to 5 points, poor knowledge was considered for below 3 points.

Ethical consideration

Ethical clearance for the study was obtained from the ethical review committee, Faculty of Medicine, University of Jaffna.

RESULTS

Evaluation of bacterial contamination in eye drops

Table: 4.1 Frequency of bacterial contamination in the dropper tip of the bottle and remaining residual solution.

Contamination of eye drops	No of contaminated samples (n)	Percentage (%)
Dropper tip only	4	11.4%
Contamination in both (tip and residual solution)	4	11.4%
Over all contamination	8	22.8%

Table 4.1 depicted the frequency of bacterial contamination. Among the whole samples, overall contamination rate was 22.8% (n=8). Among those contaminated samples, 11.4% (n=4) of the eye drops were contaminated on their dropper tip only, 11.4% (n=4) of the eye drops were contaminated on both tip of the bottles and remaining residual solutions.

Identification of contaminated bacteria from the used eye drops

Table: 4.2 Details of contaminated bacteria

Gram staining	Number of bacteria (n)	Percentage (%)
Gram-negative bacilli	7	87.5%
Gram-positive cocci	1	12.5%

Table: 4.2 depicted details of contaminated bacteria. According to their gram reaction 20.0% (n=7) of samples contaminated by gram-negative bacilli and 2.9% (n=1) of samples contaminated by gram-positive cocci. None of them were contaminated with gram-positive bacilli and gram-negative cocci.

Table: 4.3 Distribution of isolated organism.

Isolated organism	Frequency (n)	Percentage (%)
E.coli	2	25.0%
Proteus spp.	1	12.5%
Klebsiella spp.	2	25.0%
Staphylococcus aureus	1	12.5%
Pseudomonas spp.	2	25.0%

Table 4.3 depicted, five types of bacteria that were isolated from the samples and categorized by using morphological characteristics of them in the culture media and biochemical test. Among the contaminated eye drops, 25.0% (n=2) of the eye drops contaminated by E.coli, 12.5% (n=1) of eye drop contaminated by Proteus spp, 25.0% (n=2) of the eye drops contaminated by Klebsiella spp, 12.5% (n=1) of the eye drop contaminated by Staphylococcus aureus, and 25.0% (n=2) of the eye drops contaminated by Pseudomonas spp.

Knowledge on Safety usage techniques of eye drops

Table 4.4 depicted knowledge on safety usage techniques of eye drops. All patients who were participated in this study, were recapped their eye drop bottles very tightly. 74.3% (n=26) of the patients were not washed their hands before instilling their drops. When instilling their drops, 17.1% (n=6) of the patients were touched their eye drop tips against their eye, face and hands. If the bottle contains residual solution over 30 days, 31.4% (n=11) of the patients were used it until finished.

Table: 4.4 Description of knowledge on Safety usage techniques of eye drops

	Response	Frequency (n)	Percentage (%)
Do you wash your hands thoroughly before instilling your eye drops by using soap with water?	Yes	9	25.7%
	No	26	74.3%
When you administer your eye drops do you touch the dropper tip against your eye, face, hand or anything else?	Yes	6	17.1%
	No	29	82.9%
If your eye drops have remained solution until the end of one month from the first opening; Do you use that eye drops over 30 days?	Yes	11	31.4%
	No	24	68.6%
Do you position the tip of the bottle, that it does not come closer than away from the eye at adequate distance (approximately 2cm) of your lower lid?	Yes	16	45.7%
	No	19	54.3%
Do you close the bottle cap tightly after using your eye drops immediately?	Yes	35	100.0%
	No	0	0.0%

The influence of safety usage techniques on bacterial contamination of eye drops

Table 4.5 depicted the influence of safety usage techniques on contamination in the used eye drops. Among the usage techniques, touching of dropper tip showed a statistically significant association (p=0.001) with the contamination of eye drops.

Table: 4.5 Association between safety usage techniques and bacterial contamination of eye – drops.

Safety usage techniques	Contamination of the bottles				Significant
	Present		Absent		
	n	%	n	%	
Q1: Do you wash your hands thoroughly before instilling your eye drops by using soap with water?					X^2 value 3.202
					df 1
Yes	4	50.0%	22	81.5%	p value 0.074
No	4	50.0%	5	18.5%	After Fisher's exact test
					p value 0.162
Q2: When you administer your eye drops do you touch the dropper tip against your eye, face, hand or anything else?					X^2 value 15.020
					df 1
					p value 0.000
Yes	5	62.5%	1	3.70%	After Fisher's exact test
No	3	37.5%	26	96.3%	p value 0.001*
Q3: If your eye drops have remained solution until the end of one month from the first opening; Do you use that eye drops over 30 days?					X^2 value 0.177
					df 1
					p value 0.674
Yes	3	37.5%	8	29.6%	After Fisher's exact test
No	5	62.5%	19	70.4%	p value 0.685
Q4: Do you position the tip of the bottle, that it does not come closer than away from the eye at adequate distance (approximately 2cm) of your lower lid?					X^2 value 3.584
					df 1
					p value 0.058
Yes	6	45.7%	10	37.0%	after getting Fisher's
No	19	54.3%	17	63.0%	exact test
					p value 0.105
Q5: Do you close the bottle cap tightly after using your eye drops immediately?					
Yes	8	100.0%	27	100.0%	
No	0	0.0%	0	0.0%	

n- Number, % - percentage, (*) statistically significant at P < 0.05

Overall knowledge of safety usage techniques on bacterial contamination

The overall knowledge score on Safety usage techniques of eye drops varies from one to five. The mean value was 3.80 ±1.106. Table 4.6 depicted the overall knowledge level of patients on safety usage techniques of eye drops. In this study, 34.3% of (n=12) patients had good knowledge, 54.3% (n=19) of patients had average knowledge and 11.4% (n=4) of patients had poor knowledge on Safety usage of eye drops. Majority of patient had average knowledge on safety usage of eye drops.

Table 4.6: Distribution of knowledge level on Safety usage techniques of eye drops

Knowledge level	Frequency (n)	Percentage (%)
Good	12	34.3%
Average	19	54.3%
Poor	4	11.4%

Influence of overall knowledge of safety usage techniques on bacterial contamination

Table 4.7 depicted the influence of overall knowledge of safety usage techniques on bacterial contamination in the used eye drops. The level of nowledge showed statistical significant)=0.044) with contaminated eye drops.

Table: 4.7 Association between the overall knowledge level and safety usage techniques on the contamination of eye – drops.

Over all knowledge level about Safety usage techniques	Contamination of the bottles				Significant
	Present		Absent (%)		
	n	%	n	%	
Poor	3	37.5%	1	3.7%	X^2 value 7.638
Average	4	50.0%	15	55.6%	*df* 2
Good	1	12.5%	11	40.7%	p value 0.022
					After getting Fisher's exact test
					p value 0.044*

n- Number, % - percentage, (*) statistically significant at P < 0.05

The influence of socio-demographic factors on bacterial contamination of eye – drops

Table 4.8 depicted the influence of socio-demographic factors on contamination of the used eye drops. There was no statistical significant between contaminated eye drops and sex, age, living place, education level and occupations.

Table: 4.8 Association between socio-demographic factors and contamination of eye drops

Socio demographic factors	Contamination				Significant
	Present (%)		Absent (%)		
	n	%	n	%	
Age (years)					
40 – 49	1	12.5%	2	7.4%	X^2 value 3.953
50 – 59	1	12.5%	5	18.5)%	*df* 4
60 – 69	2	25.0%	10	37.0%	p value 0.412
70 – 79	3	37.5%	10	37.0%	after Fisher's exact test
80 – 89	1	12.5%	0	0.0%	p value 0.493
Gender					
Male	3	37.5%	13	48.1%	X^2 value 0.282
Female	5	62.5%	14	51.9%	*df* 1
					p value 0.595
					after Fisher's exact test
					p value 0.700
Education					X^2 value 0.233
Grade 1 to 11	5	63.0%	17	62.5%	*df* 2
G.C.E. O/L	2	25.0%	8	29.6%	p value 0.890
G.C.E. A/L	1	33.3%	2	66.7%	after Fisher's exact test
					p value 1.000
Occupation					X^2 value 0.365
Self-employment	1	12.5%	6	22.2%	*df* 1
					p value 0.546
No job	7	87.5%	21	77.8%	after Fisher's exact test
					p value 1.000

n- Number, % - percentage

DISCUSSION

Bacterial contamination was found in both the dropper tip and residual solution of the used eye drops. The contamination rates of dropper tip (22.9%, n=8) were higher than the residual solution (11.4%,n=4). It may be due to the bottles touching the conjunctiva, eyelids, eyelashes and hands of the persons while they were instilling the drops.

In this study, five type of bacteria were isolated, such as E.coli, Proteus spp, Klebsiella spp, Staphylococcus aureus, and Pseudomonas spp. In contrast to the study conducted in Iran on fungal and bacterial contamination of in-use eye drop products, similar to this study and Staphylococcus epidermidis and one type of Bacilli were isolated. According to another cross-sectional study conducted in Leicester, regarding the microbial status of part – used eye drops from a hospital eye clinic, similar results were obtained. However, microbial load was different. And also Serratia marcescens, Staphylococcus epidermidis, Pseudomonas aeruginosa, C. albicans were isolated. A cross-sectional study conducted in Iraq on magnitude and pattern of microbial contamination of eye drops in out –patient, which revealed that the dropper tip was more often contaminated than the residual solution and only one vial showed a contamination of both the drop and tip (Raghad A. et al., 2011). This results were consistent with our study.

Another cross-sectional study was conducted in New York, on the microbial contamination of eye drops used to treat glaucoma and it revealed that the bottle tip was more frequently contaminated than the drops (Orna Geyer et al., 1992). Another cross-sectional study was conducted in Austria on the microbial contamination of eye - drops used by glaucoma patients in the hospital outpatient department, which revealed that the tip was more frequently contaminated (20.2%) than the drops (8.4%) and

residual internal fluid (5%), (Barbara Teuchner et al., 2014). The findings of these studies is consistent with our study.

Another study was conducted in Iran on microbial contamination of preserved ophthalmic drops in outpatient departments and possibility of an extended period of use, which revealed that contrastingly the most contaminated part of the ophthalmic drops was residual contents (50%), whereas a lower contamination rate (31.5%) was obtained in eye drop caps.(Mohammad reza fazelid et al., 2004). Another cross- sectional study was conducted in India, regarding assess microbial contamination of the eye drop solution after use for one month, which revealed that none of the eye drop had any qualitative or quantitative evidence of growth after 14 days of incubation on various culture media. (Shalini Virani1 et al., 2015). These results were inconsistent with this study. A cross-sectional study was conducted in London, regarding the bacterial contamination of multi - dose eye drops used in the outpatient area, which revealed that Staphylococcus epidermidis and Staphylococcus aureus were isolated (J.D Stevens et al., 1992). Another cross-sectional study was conducted in Kenya, regarding the magnitude and pattern of microbial contamination of multi-dose ocular solutions that revealed that the isolated contaminants were micrococci (n = 2), Staphylococcus epidermidis, Haemophilus spp, Bacillus spp and a gram-negative rod (M.M Nentwich et al., 2007).

A cross-sectional study was done in Brighton, which revealed that isolated contaminants were Serratia marcescens, Staphylococcus epidermidis, Pseudomonas aeruginosa, staphylococcus aureus, micrococcus spp.bacillus spp, proteus mirabilis, gladosporium sp. and Penicillium spp (D.J Livingstone et al., 1998). Another cross- sectional study was done in UK, regarding the microbial contamination of preservative free eye drops in multiple application containers, which revealed that the isolated contaminants were Staphylococcus aureus, coagulase-negative staphylococcus, Bacillus spp, Serattia spp, Klebsiella oxytoca, Enterobacter cloacae, and alpha streptococcus (Rahman et al.,2005). Cross sectional study was conducted in Israel, which revealed that isolated contaminants were Pseudomonas aeruginosa, three Staphylococcus epidermidis, one Streptococcus viridans, and one Klebsiella (Yair porges et al., 2001). This study showed that there is no statistically significant association between the duration of usage and contamination rate. Previous study in Iran revealed that the significant difference between usage duration and contamination rate from the first day to seven day was obtained. However, they did not find a significant relationship between usage duration and contamination rate. Ochiogu et al., revealed that there was no statistically significant relationship between the duration of usage of the eye drops and the percentage of bacterial contamination. This study showed that there was a statistically significant association between getting help from others to administering the drops.

Limited published studies only assessed the impact of the patients' knowledge on the safety usage techniques with contamination of eye drops. Even though in the current study, one of the participant had good knowledge on safety usage, his eye drop was contaminated. The reason behind this could be that they were not followed good practice of safety techniques.

CONCLUSION

Bacterial contamination was found in the used eye drops of glaucoma patients. Knowledge on safety usage of eye drops need to be improved. Practical base

continuous education on safe usage of eye drops should be conducted among patients to improve their safety usage of eye drops.

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