

## Evaluation of used eye drop containers for microbial contamination in outpatient department of tertiary care teaching hospital

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### ABSTRACT

**Background:** Contaminated eyedrops are considered as serious risk factor for many iatrogenic ocular infections. Apart from the risk of infection, microbial contamination may alter the pH of the solution thereby reducing the efficacy of drugs. Presently many preservatives are added to these eye drops preparations to extend the duration of use. Hence authors aimed this study to find the contamination rates in such eye drop preparations.

**Methods:** This was a prospective observational research conducted at Ophthalmology OPD, of tertiary care teaching hospital for the period of 2 months. Total fifty five used eyedrops were collected.

**Results:** Authors found that 25.45% of the collected eye drops were contaminated with various organisms, viz. *E. coli* (10.90%), *Staphylococcus aureus* (9.09%), *Pseudomonas aeruginosa* (1.81%), *Bacillus subtilis* (1.81%) and *Candida albicans* (1.81%). Among various eyedrops, mydriatic (60%) eyedrops had the highest rate of contamination. We also found that, different preservatives in the eye drops were presents with different level of microbial contamination.

**Conclusions:** The present study showed that there is a definite co-occurrence between eyedrop contamination and ocular infections irrespective of preservatives. This research raises a concern about questionable efficacy of preservatives.

**Keywords:** Eyedrops, Preservatives, Ocular infections

### INTRODUCTION

Contaminated eyedrops are considered as a serious risk factor for many iatrogenic ocular infections. The data from published researches found a variable contamination rate of 0.07 % to 35.8 %.<sup>1</sup> The wide range of complications with use of such eyedrops varies from conjunctivitis, endophthalmitis to keratitis. Generally in hospital set up around 5.6% of such samples collected from wards and outpatient departments (OPDs) were contaminated with various microorganisms.<sup>2</sup> The British Pharmaceutical Codex had given some standards about the use of eyedrops but these standards seem to be an arbitrary figure.

According to British Pharmaceutical Codex standards eyedrops should be discarded within one day after first opening.<sup>3,4</sup> However, in routine practice patients were advised to use it for about 28 days. Especially in government hospital set up this duration can extend further. As such there is no significant correlation between duration and amount of contamination but it increases with frequency of use increases. One of the study conducted by Livingstone DJ showed that the incidences of microbial contamination were 6.1% and 9.1% after 7 and 14 days use of eye drops respectively.<sup>5</sup> Apart from the risk of infection, microbial contamination may alter the pH of the solution thereby reducing the efficacy of drugs.<sup>6</sup>

Recently many preservatives were added to these eyedrops preparations to extend the duration of use. The aim was to prevent or inhibit the growth of microorganisms in order to prevent contamination of formulation and subsequent complications. Most preparations contain antimicrobial substances to prevent such contamination, unless it itself has an antimicrobial effect.<sup>7</sup> Commonly used preservatives are benzalkonium chloride, thiomers, chlorhexidin, chlorobutanol, benzylalcohol, phenylethyl alcohol, parahydroxy benzoate, phenylmercuric nitrate, EDTA, and parabens.<sup>8</sup>

Plastic bottles mainly contaminated near the bottle cap due to unavailability of preservative at this area.<sup>9</sup> However, most studies bottle tips found to be more often contaminated than the residual medicine.<sup>9,10</sup> Hence authors aimed their study to determine the magnitude and pattern of microbial contamination rate in multidose used eyedrop containers and residual medicine in presence/absence of preservatives.

**METHODS**

There were Fifty five used eyedrops and duration of the study was from 1<sup>st</sup> January to 28<sup>th</sup> February 2017.

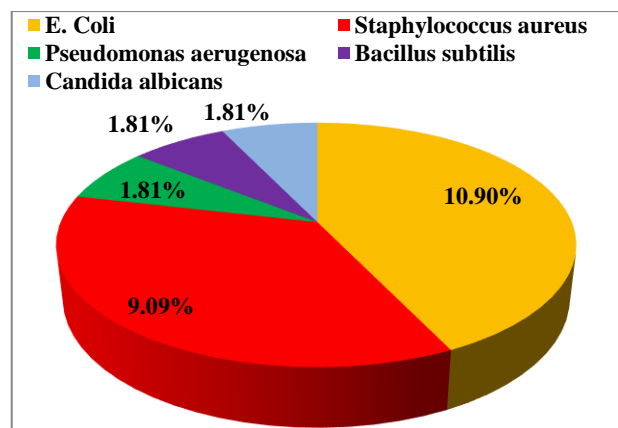
This was a prospective observational research conducted at Ophthalmology OPD, of tertiary care teaching hospital, only after approval from institutional ethics committee. Authors collected fifty five used eyedrop containers from patients attending Ophthalmology OPD.

After recording preliminary data in case record forms, samples were sent to microbiology department for further analysis. From each eyedrop, 0.5ml of the residual medicine was aseptically pipetted and then cultured in brain heart infusion broth for 4 hours at 35°C. It was also sub-cultured on blood agar, Sabauroids Dextrose agar and/or MacConkey agar to see microbial contamination. Microbial isolates were confirmed by conventional method.<sup>11</sup> Authors also used unopened eyedrop containers as control, for all the microbiological investigation.

**RESULTS**

In this study, authors found that 25.45% of the collected eyedrops were contaminated with various organisms, viz. *E. coli* (10.90%), *Staphylococcus aureus* (9.09%), *Pseudomonas aeruginosa* (1.81%), *Bacillus subtilis* (1.81%) and *Candida albicans* (1.81%) (Figure 1).

In this study, level of microbial contamination in eyedrops was varied according to its contents. Table 1, illustrates different content wise frequency of eyedrop contaminations and its percentage. Mydriatic (60%) eye drops had the highest rate of contamination followed by NSAIDs (40%) and lubricants (33.33%). Whereas antibiotic eyedrops (6.66%) showed lowest rate of microbial contamination because of their inherent antibacterial property (Table 1).



**Figure 1: Percentage of all eye drop contamination.**

**Table 1: Content wise frequency of eye drops contaminations.**

Contents of eye drop	No. of eye drops collected	No. of contaminated eye drops	Isolates found
Antimicrobial agent + Glucocorticoids	22	05 (22.72%)	<i>E. coli</i> (3) <i>S. aureus</i> (1) <i>C. albicans</i> (1)
Antimicrobial agents only	15	01 (6.66%)	<i>S. aureus</i> (1)
NSAIDs	10	04 (40%)	<i>E. coli</i> (3) <i>S. aureus</i> (1)
Lubricants	03	01 (33.33%)	<i>Bacillus subtilis</i> (1)
Mydriatics	05	03 (60%)	<i>S. aureus</i> (2) <i>Pseudomonas</i> (1)

Authors also found that, different preservatives in the eye drops were presents with different level of microbial contamination. Specifically, in this study, there was more microbial contamination seen in eyedrops containing chlorbutol (60%) as preservative (Table 2).

**Table 2: Preservative wise frequency of eye drops contamination.**

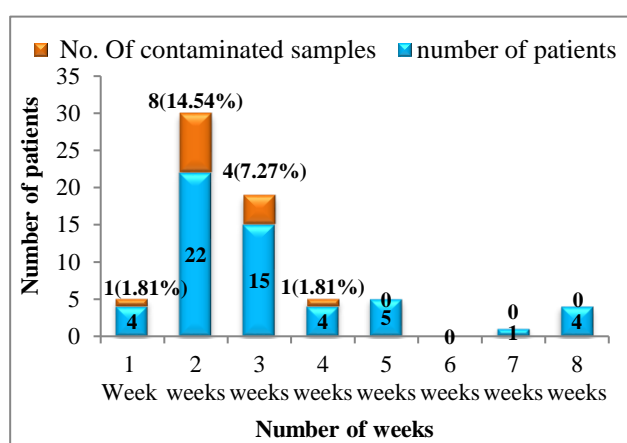
Preservative	No. of medication	Percentage of contamination
Benzalkonium chloride	41	8 (19.51%)
Chlorbutol	05	3 (60%)
Sorbic acid	01	0 (0%)
None	08	3 (37.50%)

Table 3 showed that there was no definitive correlation between instructions followed by the patients and level of contamination. In this study, all the contaminations (29.16%) were found in the eyedrops of the patients who followed the given instructions (Table 3).

**Table 3: Correlation of instructions followed and level of contamination.**

Instructions followed	No. of patients	Contamination found	No. of organisms found (%)
Yes	48	14	29.16
No	07	00	00.00

In this study, out of 55, maximum percentage of contamination (14.54%) was found in the patients who used the eyedrops for 2 weeks. However, percentage of contamination was 1.81%, 7.27% and 1.81% in the eyedrops used for 1, 3 and 4 weeks respectively. Whereas, no contamination was found in the eyedrops used for more than 4 weeks (Figure 2).



**Figure 2: Duration of eye drop use and level of contamination.**

## DISCUSSION

A contaminated eye drops presents a serious health risk for avoidable ocular infections. In this study, fifty five used eyedrops from ophthalmology OPD of Shri Vasantrao Naik Govt Medical College, Yavatmal were examined microbiologically with respect of its content and preservatives. None of the eyedrops was expired. Residual medicines as well as swabs from caps and/or nozzle portion of eyedrop taken as a specimen for microbial culture. Authors found that microbial contaminations were present maximally in the caps and the residual contents of the eyedrops. The rate of microbial contamination in used eye drops varies widely in the various published literature from 0.07% to 35.8%.<sup>12,13</sup>

However, microbial contamination in this study was 25.45%, which was higher than the similar study conducted by Razooki et al, i.e. 15% and lower than the study done by Fazeli et al, i.e. 34%.<sup>14,15</sup> Total 5 different organisms were isolated from culture. Out of five, two were gram positive and two were gram negative whereas last one was candida spp. Razooki et al, showed the similar

findings in his study conducted at, University of Baghdad, Iraq.<sup>14</sup>

One of the study conducted by Rahman et al, on preservative-free eyedrops found similar organisms as that of this study but in smaller proportion.<sup>16</sup> These microorganisms are potential risk of many ocular infections. This correlation of eyedrop contamination and ocular infection and also between preservatives and contamination was showed by Saisyo et al, in his study on Microbial contamination of in-use ophthalmic preparations and its prevention.<sup>17</sup> The risk is even more in case of compromised corneal epithelium as in ocular trauma, the use of topical steroids or extensive contact lens wear.

Eyedrops are generally contaminated by contact with eyelashes, conjunctiva, fingers or lids, and cornea even if instilled by healthcare professionals. Therefore antimicrobial activity is important to prevent contamination during the process of instillation.

Following are the possible cause of microbial contaminations:

- Failure of prescriber to inform the patient about proper use of eyedrop preparations. All the prescribers did explain the precautions to patients, but the older age of patients, lower educational status and the noisy ambience of government OPD made the work difficult.
- Failure of patients to follow the precautions of eyedrop use- when inquired authors found that many patients did not follow the precautions, but on analysis authors could not found any direct correlation between findings of contamination and not taking the aseptic precautions.
- Failure of preservative added to the eyedrop- the guidelines of using an eye drop up to four weeks after opening, is based on proper functioning of the preservative used.

In this study, authors did not find any direct correlation between duration of eyedrop usage and level of contamination. As shown in the fig. 4, no contamination was found in the eyedrops used for more than 4 weeks. Authors findings were consistent with the study done by Feghhi et al at Iraq, who did not find such correlation.<sup>18</sup>

The role of preservative to prevent contamination of eyedrops has been controversial.<sup>17</sup> Preservatives are added to eyedrops to prevent microbial contamination. Infact, the shelf-life of eye drops is decided by the preservatives themselves, rather than the principal ingredient. Expired eyedrop actually does not mean expired medicine, but it means loss of potency of preservative to protect it from microbial contamination.<sup>19</sup> Preservatives must meet certain criteria such as; it should be compatible with other ingredient, should be non toxic and should be efficient during the entire period of use.

Commonly used preservatives of ophthalmic solutions are benzalkonium chloride, chlorobutanol, thiomers, parahydroxy benzoate, chlorhexidine, phenylmercuric nitrate, phenylethyl alcohol, EDTA, benzylalcohol and parabens. Preservatives inhibit the growth of organism by interfering with their metabolism. It may have similar role on human cells which cannot be neglected. Benzalkonium chloride is the commonest preservative in this study. However neither benzalkonium nor chlorbutol could protect the preparations from being contaminated. These results were similar to that of study conducted by Saisyo et al.<sup>17</sup>

Authors found that contamination was occurring irrespective of use of preservative, and the principal content of the preparation. Only eyedrops containing antimicrobial agents, without any additional glucocorticoids were having the least incidence (6.66%) of contaminations. Saisyo et al in his showed that eyedrops without preservatives had zero risk of oculotoxic effects and lack of microbial contamination.<sup>17</sup>

These results raise the serious questions about role of preservatives in eyedrops.

Limitations of the study that it is still progressing to reach a larger sample size, so that authors can come to some statistically significant correlation and conclusions. The test samples from patient's conjunctiva need to be investigated to validate the results of microbial contamination.

## CONCLUSION

From this study, authors suggest that there is a definite co-occurrence between eyedrop contamination and ocular infections. Authors did not find direct correlation between duration of usage and level of contamination. Thus, authors research raises a concern about questionable efficacy of preservatives.

In presence of questionable efficacy of preservatives, authors chief concern is about the cut-off duration of four weeks about using an opened eyedrop. Further research focusing development of more competent preservatives is needed. This study supports the importance of the correct handling and application of eye medications during its use. Also, the importance of proper counselling at the time of prescribing eyedrops is vital.

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