Microbial contamination in eyedrops of patients in glaucoma treatment

Contaminação microbiana em colírios de pacientes em tratamento de glaucoma

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ABSTRACT

Objetives: To assess the degree of fungal and bacterial contamination of hypotensive eye drops and the way these are preserved by the patients at the Glaucoma outpatient clinic of Santa Casa Hospital in Ribeirão Preto. Methods: Fifty-five patients were randomly assigned to follow-up in the outpatient clinic, and, after their consent, an eye drop was collected per patient and later sent by mail for analysis by microbiologist and pathologist in up to 72 hours. Approximately 0.5ml of the medications were analyzed and the patients were asked to answer a simple questionnaire on the method of drug conservation and whether they considered it adequate. Results: Of the 55 analysed eye drops, five (9.01%) had their liquid contents contaminated. Among the microorganisms isolated there were 4 Gram negative bacteria, 1 (1.8%) by Serratia marcescens, 1 (1.8%) Pseudomonas aeruginosa and 2 (3.6%) Stenotrophomas maltophilia. An eye drop was contaminated by the fungus Candida ssp. All the patients in the study judged their methods of storage and instillation appropriate. The patients who had the positive coliria were summoned for clinical examination and passed through a new questionnaire by the investigator. Conclusion: The time and methods of preservation influence the contamination of medicinal products. All the eye drops that presented growth of microorganisms in the present study were open between 30 and 90 days. The fact that most patients take their eye drops on daily tasks increases the exposure of the bottles and can be a relevant fact to determine the contamination of these medications. Keywords: Eye drops; Ophthalmic solutions; Bacterial contamination; Remedy expiration

RESUMO

Objetivos: Avaliar o grau de contaminação por fungos e bactérias e o modo de conservação destes colírios hipotensores por parte dos pacientes no ambulatório de Glaucoma da Santa Casa de Ribeirão Preto. Métodos: Foram selecionados aleatoriamente cinquenta e cinco pacientes, em seguimento no ambulatório, e após consentimento dos mesmos os colírios eram coletados e enviados via correio para análise por microbiologista e patologista em até 72 horas. Foi analisado 0,5ml aproximadamente das medicações e os pacientes respondiam a um questionário simples sobre o método de armazenamento e instilação adequado. Resultados: Dos 55 colírios analisados, cinco (9.01%) tinham seu conteúdo líquido contaminado. Entre os microrganismos isolados haviam 4 bactérias Gram negativas, sendo 1 (1.8%) por Serratia marcescens, 1 (1.8%) Pseudomonas aeruginosa e 2 (3.6%) Stenotrophomas maltophilia. Um colírio estava contaminado pelo fungo Candida ssp. Todos os pacientes no estudo julgaram seus métodos de armazenamento e instilação adequado. Os pacientes que tiveram os colírios positivados foram convocados para exame clínico e passaram por novo questionário pelo investigador. Conclusão: O tempo de abertura dos frascos e os métodos de conservação influenciam na contaminação dos medicamentos, todos os colírios com crescimento de microrganismos no presente estudo estavam abertos entre 30 e 90 dias. O fato de que a maioria dos pacientes levam seus colírios em tarefas cotidianas, aumenta a exposição dos frascos e podem ser um fator relevante para determinar a contaminação destas medicações. Descritores: Colírio; Soluções oftálmicas; Contaminação bacteriana; Conservação de medicamentos

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INTRODUCTION

Eyedrops used in ophthalmic treatments should be aseptically prepared, sterile, and containing the appropriate preservative compatible with the medication used, and be in a dosage that is nontoxic or irritant to the patient. Benzalkonium chloride (BAK) is a common preservative widely used for the preservation of ophthalmic products, mainly in hypotensives increasing the penetration of the active ingredient of the medication and inhibiting the growth of microorganisms.

Since most eyedrops used in the treatment of glaucoma should be instilled more than once a day, it is natural for patients with good adherence to treatment to take their medication with them during daily tasks, increasing the risk of contaminating the vial or the medication itself. The association between the number of instillations per day and the increased risk of infections has been demonstrated in several studies. In addition, glaucoma medications are more often contaminated than antibiotic or anesthetic eyedrops.

The most frequently isolated pathogens in these studies in eyedrops are of bacterial origin on the surface of the bulb or the skin, and the environment. In a study carried out from the analysis of 119 samples of eyedrops instilled by the patient, 24.4% were contaminated. Among the isolated agents, 1.5% were from pathogenic bacteria (Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter Iwoffii, Stenotrophomonas maltophilia and Staphylococcus Aureus). In another study with eyedrops of patients with glaucoma, 28% were contaminated, with gram positive agents being more frequently found (91% of positive cultures). Some authors have found fungal isolates in some samples of eyedrops.

Besides, most studies have shown that the tip of the eyelid container was the most frequently contaminated site, which may result in an increased risk of eye infections, especially if corneal integrity is compromised.

Since glaucoma is a chronic disease and its treatment, the instillation of these medications occurs more than once a day, so that the patient adhering to the treatment ends up taking the medication vials to the different environments of their daily lives. Caring for contamination should become a habit and be strict.

Thus, the objective of the present study was to evaluate contamination in topical medication eyedrops of patients from the glaucoma ambulatory of a university hospital, and use a questionnaire to analyze the storage and method of instillation of the eyedrops collected.

METHODS

A cross-sectional study in which 55 hypotensive eyedrops used in the treatment of glaucoma were randomly collected. The patients provided the eyedrops during the visits to the glaucoma department of Hospital de Ensino Santa Casa de Misericórdia of Ribeirão Preto, SP, Brazil.

After the patients consent, the eyedrops were sealed in a disposable plastic bag hermetically closed and sent by mail to the laboratory Saúde Instituto de Análises Clínicas in Goiânia - GO, where a microbiologist and a pathologist had them analysed within seventy-two hours.

Regarding the possible contamination of the eyedrops, the study and the technical analysis were carried out with the analysis of 0.5 ml of the product, thus not being evaluated the contamination of the product vial and of the conjunctival sac fundus. The content of the eyedrops was analysed in slides stained by the Gram Technique for bacterial and fungal research. The material was placed in blood agar and Brain Heart Infusion broth (B.H.I.) for bacterial culture, and in Agar Saboraud and Mycosel for fungal culture.

Bacterial cultures that did not grow were incubated for forty-eight hours and released. However, the ones that grew went to isolation in MacConkey Agar and mannitol, and later the identification of the bacterium was carried out with biochemical tests and the manual antibiogram by Kirby-Bauer method in Müller Hinton plate to analyze their sensitivity profile. The fungi were incubated for 30 days and released after this period.

In addition, after accepting to participate in the study and signing the informed consent form, the patients answered a questionnaire with epidemiological data (age, gender), methods and places to store eyedrops, and answered if they considered it adequate care. Patients with contaminated eyedrops were invited for a clinical examination and a new interview.

Among the 55 patients who participated in the study, 27 (49.1%) were females and 28 (50.9%) were males, and the average age was 65.1 years.

One eye drop was collected from each participant, and among the eyedrops evaluated 22 (40.0%) were timolol maleate 0.5%, 10 (18.2%) travoprost, 9 (16.4%) brimonidine, 4 (7.3%) dorzolamide, 4 (7.3%) bimatoprost, 4 (7.3%) eyedrops in association, and 2 (3.6%) brinzolamide. Only 1 (1.8%) of the total sample had expired (travoprost).

When asked about the storage location of the eyedrops, 22 (40.0%) patients stored in the room, 15 (27.3%) in the living room of their homes, 10 (18.2%) in the bathroom cabinet, 4 (7.3%) in the refrigerator, and 4 (7.3%) in the purse. All patients in the present study reported considering the methods of storage and instillation of their medications adequate.

Regarding the microbiological analysis, contamination by microorganisms was observed in 5 (9.1%) eyedrops. Among the microorganisms isolated, there was one contamination by Candida spp and four bacterial contaminations, all of them being gram-negative, 1 (1.8%) Serratia marcescens, 1 (1.8%) Pseudomonas aeruginosa, and 2 (3.6%) Stenotrophomas maltophilia.

Of these contaminated eyedrops, 3 (5.5%) were timolol maleate 0.5%, 1 (1.8%) dorzolamide, and 1 (1.8%) brinzolamide. All patients with contaminated eyedrops were older than 60 years, the eyedrops were within the validity, and opened between thirty and ninety days. In the biomicroscopic analysis, no alterations were found in these patients, and one patient who presented with eyedrops contamination was not found to be examined.

Contamination of ophthalmological topical medications should be a reason for concern on the part of ophthalmologists, in order to guide adequately the patient regarding the proper handling and storage of these medications. Inappropriate care with eyedrops, especially those used daily, can lead to contamination of medications and cause from minor symptomatic alterations to more severe cases of bacterial and fungal keratitis. In pharmacological preparation of medications for ocular use, the sterile solutions are mandatory, and the BAK preservative is present in numerous ophthalmic solutions. BAK is a quaternary ammonia with detergent properties to prevent bacterial contamination. On the ocular surface, BAK acts on the lipid layer of the tear film, and promotes a direct cytotoxic effect on the cells of the corneal epithelium. Exposure for prolonged periods of medications containing this preservative may lead to the perpetuation of immune-inflammatory processes, and generate a number of adverse effects to patients because of their cumulative potential on the ocular surface.

The incidence of microbial contamination in the present study was 9.1%, and is similar to other studies in the literature reporting 6.1% to 11.7%. And the longer opening time of the vials may justify the greater risk of contamination of these medications as all positive exams in our sample were in eyedrops opened for more than thirty days.

The ocular solutions used for the treatment of Glaucoma are subject to contamination, and this is also related to the time of use of that medication, that is, the longer the exposure time after opening the drug seal the greater the risk of microbial contamination of the product, and several studies point to this. In our study, among the contaminated eyedrops the opening time of the seals ranged from one to three months, and all eyedrops were instilled more than once a day which may increase the risk of contamination of the medications due to increased exposure and handling, which is also reported in other publications.

The microorganisms found in the drugs were Candida ssp. (diploid fungus) in an eye drop (20%), Serratia marcescens in one eye drop (20%), Pseudomonas aeruginosa in one eye drop (20%), and Stenotrophomas maltophilia bacteria present in two eyedrops solutions (40%). All bacteria isolated in the study were gram negative, both Pseudomonas aeruginosa and Stenotrophomas maltophilia are aerobic germs related to hospital infections, and the strains are resistant to traditional antibiotics. Infections by these microorganisms are more common in immunocompromised patients. The bacterium Serratia marcescens is a facultative anaerobic germ, and usually causes nosocomial infections, being found in food, water and plants, and in hospital environments, and may colonize the respiratory and urinary tracts of adults.

In a study carried out on this topic with 95 eyedrops, eight (8.4%) had bacterial contamination, and among the most frequent germs in the samples were Staphylococcus aureus, followed by Bacillus ssp and Serratia ssp. In another survey evaluating the contamination in 42 drops of borric acid solution, only 1 (2.4%) presented contamination of the solution by Staphylococcus aureus, but the analysis of the vials increased it to 17 (40.5%) eyedrops contaminated by the same bacteria. Our sample did not have a microbiological analysis of the patients' conjunctival sac fundus secretion nor the medication vial, which may explain why Staphylococcus aureus did not appear in the cultures.

After identifying the eyedrops, the researcher invited the five respective patients who provided them for an interview. The patient whose eyedrops were contaminated with the fungus Candida ssp was not found. In this second moment, these patients were asked about the eyedrops storage place, and all repeated their first answer: 2 patients reported keeping the eyedrops in the living room, 2 stored it in the bedroom. All took the eyedrops with them in different daily activities, and the 4 stated again that they store their medications adequately.

An important point observed was that in Pseudomonas aeruginosa contamination the patient had other chronic-degenerative comorbidities, having to go to the hospital every week for administration of medication, appointments and routine exams taking the glaucoma eyedrops with them. The other 3 patients had not gone to the hospital during the last 30 days.

Constant handling and prolonged use of ophthalmologic topical medications has proven to be a risk factor for the contamination of these medications by microorganisms present in the various environments we go to. The risk of contamination is also directly related to the patients' care in storage and in the proper instillation, being it clear in other studies showing the contamination of most of the vials analyzed by germs found on human skin, suggesting that the lid of the patient's eyedrops may be touched. In the present study, at the second time of evaluation, patients with contaminated eyedrops were asked to instill a dose of their medications in the presence of the researcher, and all did so incorrectly by touching the lid of the vial (two touched the eyelids, and two touched the region of the caruncle). In addition, more than one drop of the solution was instilled in all situations. It has been widely proven that this incorrect way of using these medications implies an increased incidence of exogenous contamination and side effects.

Conclusion

After the completion of the present study, it is evident that relying solely on the preservative of eyedrops for the treatment of glaucoma is wrong thinking. Guidance on the handling and storage of these medications is a key topic in the guidelines for patients with glaucoma.
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The lack of basic hygiene care from patients with their eyedrops associated with poor instillation and poor medical guidance on this subject are risk factors for exogenous contaminations and ocular infections, which can generate from a light to a severe case of acute endophthalmitis.

REFERENCES


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