AN EVALUATION OF HOW GLAUCOMA PATIENTS USE TOPICAL MEDICATIONS: A PILOT STUDY

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ABSTRACT

Purpose: Multiple factors can influence patients' adherence to topical ophthalmic intraocular pressure–lowering medications. An important factor that is often overlooked is the method of eye drop administration, including the handling, storing, and actual administering of eye drops. These aspects of patients' eye drop administration, which may be strongly related to the success of prescribed therapies, are evaluated.

Methods: A 2-page questionnaire was distributed to 253 sequential glaucoma patients at the time of their regular clinical visit with one of two geographically distinct glaucoma specialists. In addition to providing demographic data, the patients were asked to complete a 2-page questionnaire about their current use of eye drops.

Results: The study participants had a mean age of 71.5 years (SD, 15.1 years) and were predominantly female (59.8%) and white (72.6%). Approximately 17% of them relied on others for the administration of drops and most commonly cited inadequate vision and trouble with manual dexterity leading to this dependency. Of those who self-administered drops, only 16.3% used a mirror. The most common location for administration was the bedroom (46.8%), followed by the bathroom (23.4%) and kitchen (16.1%). Almost 16% reported "rarely" or "never" washing their hands.

Conclusions: Although most individuals may have little difficulty with the use, storage, and handling of eye drops, this study demonstrates that broad variation in reported practices exists. This finding suggests a need for better instruction in eye drop administration and illuminates some of the methodological problems that could be overcome to reduce patients' frustration, improve compliance, and increase efficacy.

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INTRODUCTION

The medical management of glaucoma relies primarily on the administration of topical ocular medications. Noncompliance with prescribed treatments has proven to be a significant obstacle to effective glaucoma management. Kass and associates[1,2] found that most patients overestimate their compliance and that physicians are unable to determine which patients adhere to prescribed therapy. Lack of compliance may be confused with a therapy's lack of efficacy. This confusion could lead to a change in therapy or the application of more aggressive therapeutic measures, such as laser or incisional surgery.

A medication's cost, the complexity of a medical regimen, and the side effects of medications are all factors that may contribute to noncompliance. One factor that is often overlooked is the method of each patient's eye drop administration. Eye care providers often neglect the importance of instruction on how to handle, store, and administer eye drops. They do not ask patients how the medications are stored, whether patients rely on others for administration, and how patients actually place the medication on the eye. These issues may be related to the relative success or failure of new eye drop bottle designs as well as the success of currently prescribed therapies.

There have been few attempts to describe the practical aspects of patients' eye drop administration and to identify potential problems that may adversely affect effective therapy. A better understanding of the settings, circumstances, and methods adopted by patients when they administer eye drops may be the first step toward improving patient education, compliance, and therapeutic efficacy. This study attempts to address this issue.

METHODS

A 2-page questionnaire was distributed to 253 consecutive patients with various forms of glaucoma who had at least 6 months of experience with topical glaucoma medications. The questionnaire was given at the time of their regularly scheduled clinical visit with one of two geographically distinct glaucoma specialists. Before the regularly scheduled ophthalmic examinations, trained technicians asked both demographic information and a combination of 10 multiple-choice and open-ended questions about patients' use of eye drops. Institutional review board approval was obtained, and all participants gave informed consent. This study followed the tenets of the Declaration of Helsinki. The study was performed and analyzed before HIPAA approval was required.

RESULTS

Demographic data for the surveyed patients are summarized in Table 1. The majority were older, white, and women.

Survey results for selected questions are summarized in Table 2. The majority (20, 82.6%) of the 253 participants reported

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administering their own eye drops. Forty-four (17.4%) admitted to being dependent on others for eye drop administration. The reasons for this dependency were inadequate vision (25%), problems with manual dexterity (25%), and trouble getting only 1 drop out of the bottle (25%).

TABLE 1. DEMOGRAPHIC DATA FOR 253 GLAUCOMA PATIENTS WHO COMPLETED QUESTIONNAIRE ON EYE DROP USE

AGE	
Mean 71.5 ± 15.1 years	
SEX	
Female 59.8%	
Male 40.2%	
SELF-REPORTED ETHNICITY	
White	76.2%
Black	20%
Other	3.5%

In those patients who self-administered drops, most took drops while either sitting (37.8%) or standing (36.4%). Of the 66 (31.6%) who lay down, most used the bed (57 of 66; 86.4%). Most patients administered their drops in either the bedroom or the bathroom and did not use a mirror.

Some patients may have a problem with eye drop bottle contamination. Only 36.4% of survey participants reported "always" washing their hands before administering eye drops, and 15.8% reported "rarely" or "never" doing so. Furthermore**,** almost 5% reported "always" or "usually" having the dropper tip touch the eye during administration.

Most patients used both hands to apply an eye drop. By far, the most common practice was to use the right hand to hold the dropper bottle and the left index finger to hold the eyelid open.

Most patients did not keep their medication in a refrigerated area. The most common storage locations for glaucoma medications were the bedroom (45.4%) and bathroom (23.9%). Twenty-five patients (12.2%) kept medications in the refrigerator, and half of these reported doing so at the instruction of a provider or the package.

In response to the open-ended question "What do you not like about administering your glaucoma medications?" many patients described no problems, but common responses also included frustration with difficult-to-handle bottles (14.1%), problems getting the proper dosage into the eye (12.9%), and general dislike of putting eye drops in their eyes (11.2%).

TABLE 2. RESULTS OF QUESTIONNAIRE ON EYE DROP USE BY 253 GLAUCOMA PATIENTS

Are the eye drops self-administered?	
Yes	82.6%
No	17.4%
In what position are you when the drops are administered?	
Standing	36.4%
Sitting	37.8%
Lying down	31.6%
Varies	8.1%
Is a mirror used for drop administration?	
Yes	16.3%
No	83.7%
At home, what room is generally used for drop administration?	
Bedroom	46.8%
Bathroom	23.4%
Kitchen	16.1%
Living room	12.7%
Den	3.4%
Other	5.4%

TABLE 2. (CONTINUED) RESULTS OF QUESTIONNAIRE ON EYE DROP USE BY 253 GLAUCOMA PATIENTS

Do you wash your hands before drop administration?	
Always	36.4%
Usually	28.7%
Sometimes	19.1%
Rarely or never	15.8%
Does the dropper tip touch your eye?	
Always or usually	4.8%
Sometimes	20.6%
Rarely or never	74.6%
In which hand do you hold the dropper?	
Right	87.4%
Left	12.6%
Do you use fingers to hold open the lids?	
Yes	79.7%
No	20.3%
Which lids are held?	
Both upper and lower	20.0%
Upper only	9.7%
Lower only	64.2%
No answer	6.1%
Where do you keep glaucoma medications in the home?	
Bedroom	45.4%
Bathroom	23.9%
Kitchen	19.0%
Refrigerator	12.2%

DISCUSSION

There can be little doubt that noncompliance with prescribed medical management is a major factor in glaucoma treatment failure. Studies have repeatedly shown that missed doses are commonplace.[1-6] Kass and associates[1] demonstrated with an electronic medication monitor built into an eye drop bottle that 62% of patients surveyed omitted 10% of prescribed doses and 15% of patients omitted 50% of prescribed doses. A commonly overlooked component contributing to noncompliance with eye drop therapy is the method of patients' eye drop administration. The current study begins to address the paucity of data in the literature regarding many of the practical aspects of eye drop administration. Although most participants in this study reported little difficulty with the use, storage, and handling of eye drops, the survey results demonstrate that broad variations in reported practices appear to exist.

Preferred techniques for applying eye drops have been described in the literature.[7,8] Fraunfelder[7] has confirmed that variations in technique can have a significant impact on the ocular contact time of a topically applied medication. Contact time is related to a medication's efficacy and potentially to its systemic absorption and adverse events.

Maximizing ocular contact time is easily achieved by directing patients to follow these simple instructions: First, grasp the lower eyelid near the margin with the thumb and index finger and pull outward to create a pouch in the lower cul-de-sac. Then, without touching the dropper tip to any ocular structures, position it above the eye by direct visualization. Just before releasing a drop, look upward. Allow the drop to settle by gravity into the lower cul-de-sac before releasing the eyelid. With the drop in place, close the eyelids and apply pressure to the nasolacrimal duct or forced eyelid closure for at least 2 minutes to minimize drainage and systemic absorption.[8]

The results of this survey study highlight multiple avenues eye care providers can use to improve patients' eye drop administration. First, the variability in patient practices suggests that eye care providers need to first ask patients how they administer medications. In fact, it may be helpful to directly observe patients administering medications. Eye care providers should give better instructions about optimal eye drop administration techniques. For example, several questions in this survey indirectly addressed whether or not patients

followed the recommended eye drop procedure. Most seemed to follow something similar to the recommended best practice by holding the lower lid with the index finger of the left hand. It is concerning, however, that 25.4% of participants reported contaminating the dropper tip by touching it to the eye at least sometimes. Similarly worrisome is the admission by 15.8% of participants that they rarely or never wash their hands prior to eye drop administration. The reported practices illustrate deficiencies in patients' understanding of optimal methods of safe and effective eye drop administration. These results are consistent with those of other investigators who find a high rate of eye drop contamination.[9,10] Many nations address this problem by prohibiting eye drop bottles to contain more than approximately a 1-month supply.

The results of this survey may better inform both physicians and eye drop manufacturers about ways to better accommodate patient individuality, thereby making eye drop administration easier to remember and eyedroppers easier to use. The frequency of dropper contamination and infrequency of hand washing may argue that eyedroppers should be constructed to better protect the tip from contamination. Alternatively, it may be preferable for eye drops to be supplied in smaller, disposable bottles to prevent prolonged use of a contaminated bottle.

We found that many patients lack the manual dexterity to administer their own eye drops. Many reported "difficulty getting one drop out" as the reason they preferred having an assistant, a response supported by previously published observations that over 37% of patients instill 2 or more drops per eye treatment.[11] The volume of the conjunctival sac is smaller than a drop from most commercial droppers.[12] Therefore, the administration of multiple drops per treatment is, at best, an unnecessary waste and, at worst, a potentially harmful practice, because the risk of side effects increases when excess drug drains into the nasolacrimal system and is systemically absorbed. Some medications, such as prostaglandin analogues, may be less effective if given more than once daily.[13] This problem might be addressed by better eyedropper technology.

We found variations in eye drop storage. While most patients stored eye drops in the bedroom (45.4%), significant numbers also stored them in the bathroom or kitchen, where there may be inadequate temperature control. Commercial eye drop preparations currently come with a broad range of storage requirements.[14] Most specify an upper range for temperature exposure during storage, not uncommonly 25ºC (77ºF)—a temperature that could easily be exceeded in locations such as the kitchen or bathroom. Even the bedroom can exceed these temperatures in warm climates without constantly maintained air conditioning. Some medications have express warnings against freezing, whereas others do not recommend storage temperatures in the near-freezing or refrigerator range. This may be especially problematic for the 12.2% who store medications in the refrigerator, if instructions are not well understood or if the temperature in the refrigerator is not held constant. Certainly, these results welcome the development of eye drops that are stable in a broader range of conditions to better accommodate the actual storage conditions adopted by patients.

Caution is needed when interpreting these results. First, this is a pilot study and as such relies upon patients' self-report. Patients are known to overestimate their ability to comply with therapy.[1,2] Second, enrollment in the study was limited to patients in glaucoma practices in either Baltimore, Maryland (A.L.R.), or Fort Worth, Texas (J.P.S.). Greater geographic diversity may yield different results. Furthermore, results may not be applicable to all forms of prescription or nonprescription eye drop therapy or to practices not specializing in glaucoma. Patients were asked about their use of topical glaucoma therapy only.

Nevertheless, the results of this survey add to a growing body of literature that addresses many of the problems contributing to noncompliance with topical glaucoma therapy.[15] This survey study confirms that eye drop practices can vary considerably from one patient to the next. Some patients even report practicing behaviors, such as contamination of the dropper tip and administering more than 1 drop per treatment, that are potentially harmful. These results agree with other studies in the literature that suggest a need for better instruction in the use of topical eye medications.

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PEER DISCUSSION

DR RONALD L. GROSS: Adherence is one of the most important factors that must be considered in the therapy of every medically treated patient in ophthalmology. Whether the scenario is glaucoma, a postoperative cataract patient, one with microbial keratitis, or cystoid macular edema, successful therapy depends upon the actual appropriate administration of the medication. The challenge of adherence is increased in the treatment of a chronic, usually asymptomatic disease for which the therapy has no perceived immediate benefit, such as glaucoma. In one study,[1] 77% of glaucoma patients stated they were compliant with their medication; only 52% of these patients could correctly identify the medication and its frequency of use. Even when the disease is symptomatic or there is immediate benefit, adherence is often surprisingly poor.

In order to meet the challenge of improving adherence by our patients, we must first understand the factors that lead to suboptimal patient use of medications. Studies attempting to address this subject specifically in glaucoma have shown that patient forgetfulness, unavailability of the medication, and the timing or frequency of drop administration are identified by patients as barriers.[2] However, the actual instillation of a drop is a barrier as well.[3] The authors should be congratulated for their attempt to begin to decipher this important question with this pilot study exploring the method of topical ophthalmic medication instillation as it may impact adherence.

Given all the factors that stand in the way of our patients actually using their medications appropriately, it is particularly frustrating if the final hurdle of actually putting the drop in is the fatal flaw that prevents success. However, given the paucity of information on this subject, this study represents a very reasonable first step. The use of a questionnaire presents many challenges, including the method of administration and the validation of the instrument. As this is a pilot project, the plan for validation should be addressed. Additionally, technicians administering the questionnaire in the clinic setting could influence patient responses, the validity of which is already questionable.

An unfortunate reality is the current unavailability of a method to determine the actual successful use of eye drops. Even with the best information to date, the measure was removing the cap and inverting the bottle, not an actual drop in the eye.[4] As the authors point out, if we cannot believe patient reporting of compliance, is the information going to be better concerning the method of administration? Additionally, it would be interesting to know if the use of multiple bottles of medication or the duration of use of eye drops has an effect on patients' behaviors in instilling medications.

However, the results are informative. The relatively high frequencies of needing assistance with instillation and contamination of the bottle are factors that can be identified and addressed. The concern with the temperature of storage needs more clarification. Is this a real concern? Are FDA guidelines for temperature stability inadequate?

Given the results of this study, the authors' conclusions are important messages to the practitioner: Increased education as to how to instill a drop into the eye with follow-up to evaluate technique is a valuable step in addressing this important, although often underestimated, factor in all forms of topical ophthalmic therapy.

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DR. DAN B. JONES: I am a consultant with Bausch & Lomb and am trying to help them figure out how "MoistureLoc" became "Fusarium Lock", and they do not know how that happened yet. I just would urge paying attention to what the patient does after they instill the drops. Peter Watson back in the 1960's, in effort to improve therapeutic outcomes in treating scleritis, did a study in which he basically used a radioisotope labeled drop and showed, indeed, you get more drop concentration to the ocular surface and retained if you put the drop in, close the eyelids, and put the head down for 15 to 30 seconds. With the splash and blink technique or by putting a tissue to the side and wiping away excess tears, you are probably are taking drug away from the ocular surface. I think there should be more uniformity in attention paid to how patients manage once the drop hits the ocular surface.

DR. GARY C. BROWN: I would like to congratulate both speakers on superb talks. When my wife was a resident at Wills Eye Hospital in the glaucoma clinic with George Spaeth, she observed patients in the resident glaucoma clinic and then George's private patients using their eye drops. She actually watched every one of them instill their glaucoma drops. All of George's 50 patients got the drops in correctly, but in the resident clinic, 20% of people who thought they were putting them in correctly never got them near the eye. They let the drops roll down their finger or they put them on their face. Twenty per cent of patients who are not instructed on how to put in drops actually miss the eye.

DR. THOMAS D. FRANCE: No business aspects. It is an interesting discussion about drops in glaucoma. I am a pediatric ophthalmologist and that makes for a compound problem in these patients. Because the child usually does not want to get whatever medication we are instilling, this means that they require assistance. I wonder how often the parents actually want to put it in the drops. My concern over the years has been that drops are perhaps harder to instill in children and that compounds the problem. I have therefore recommended ointments whenever I could. Nowadays, with the use of atropine for amblyopia treatment, the question is: do you use a drop or an ointment? I am wondering when you are looking at this problem, if you have any feeling about whether ointments are useful. How well do they work compared to drops and will ointments be a better answer for the pediatric ophthalmologist?

DR. DOUGLAS R. ANDERSON: Probably every drug company has given me or my department some consideration at one time or another, but none has anything to do with the subject at hand. I am wondering whether or not we can learn how patients put their drops in and whether they do it in an effective manner by asking them to instill the dilating drops before we examine the fundus. We can ask them put the drops into their eyes and we can observe whether they are successful in doing it. That is something I might suggest. Secondly, I learned when I started to need artificial tears for myself that it was not so easy to put drops in the eye. Although I thought I knew all kinds of ways to do it, I had to wait until Paul Palmberg showed me how to instill them in a very effective manner. I wish I had been prepared to show you a slide of how this is done. I might demonstrate how he tells them to hold the bottle upside down, because the dropper is going to be upside down, to tilt the head backward, to use the little finger to pull the lower lid down to expose the conjunctival sac, and to look upward so they can see the drop directly above them over the ceiling. When the bottle is squeezed the drop goes smack right on the cornea. It is a good method. I am sure there are also some other good methods, but the speaker did not mention any particular one that was helpful. I think that it might be helpful sometime to have a discussion about what is easiest for the patient to do and to improve the likelihood of actually getting the drop in the eye. I found the technique that Paul Palmberg taught me to be, for me, the easiest of all that I have tried. However, it is not easy for some people with arthritic hands or poor eyesight.

DR. ROBERT RITCH: No financial interest. This is such an important topic and I want to congratulate Alan, not only for presenting it, but for doing such a good job. Drop installation and the ability of a patient to get the drop in the eye is the first part. The second part is performing nasolacrimal occlusion after instilling the drops. This technique was described by Thom Zimmerman originally 25 years ago. With punctal occlusion one gets 50% more drop into the eye, 50% longer duration of action of the drops, less fluctuation, less systemic absorption, and less side effects. I have all of my patients to watch a video we made that demonstrates how to take the drops properly. A number of years ago, we noted that some patients spaced their drops about a minute apart. I tell the patients that this is like having 3 people getting into the bathtub at once and having the water overflow. I instruct patients to space their drops by ten minutes and to use nasolacrimal occlusion. In our video, we also demonstrate a technique developed for patients who have lost fixation. This method guarantees that the drop gets in the center of the cornea and the bottle top never touches the eye. We published it in American Journal of Ophthalmology. I show this video to every new patient and it really makes a big difference. It is available on our website at http://www.glaucoma.net . If anybody would like to show to it in their offices, email me and I will send you a copy of the DVD .

DR. GEORGE O. WARING, III: No money from drug companies. We have heard over the years about sustained release devices, but nothing recently. I wonder if you could comment on the current state of sustained release mechanisms that could obviate eye drop use.

DR. ALAN L. ROBIN: Thank you for your comments and for your appreciation of this issue. You may think of it simply as taking an eye drop, but obviously, as Doug Anderson so aptly put it, this is not as easy as we think it is. How do we go about achieving better instillation of eye drops? Well, I think we should investigate what our patients really do. The concept of using tropicamide or phenylephrine to dilate the pupils and then watching the patients instill these drops is very important. I think education, as Bob Ritch points out, is crucial. I have worked in India and we, as physicians, do not need to waste much of our valuable time doing the majority of this teaching. We all have paramedical personnel working with us who may play video games in between patients or shop on the web, so perhaps it might be better to utilize their time in helping patients learn how to use their drops and to determine if the patients know how to take their eye drops correctly. The question regarding the various delivery systems is very important. Most of you are aware that I am working with anecortave acetate for glaucoma treatment. At least preliminarily this is given as an anterior juxtascleral injection with effects lasting for six months in many individuals. Shouldn't we be looking for different delivery systems that can help us obviate the need for drops in patients? When I was a resident we admitted patients for six days after cataract surgery because everybody else did. Now we realize that perhaps this was not the best way to do things, and we usually do not do admit these patients anymore. Perhaps eye drops are not the best mode of delivery and there are better ways of giving ocular medications.