OPEN

# A Comparison of Patient Acceptance of 3 Eye Drop Instillation Aids

*Catherine Q. Zhu, MD,* Natalie Sadlak, BS,† Marissa G. Fiorello, BS,‡ Deborah Lee, OD,* and Manishi Desai, MD**

**Precis:** Patients can be quite amenable to using eye drop instillation aids. We should consider recommending these devices to patients who otherwise struggle with drop instillation and medication adherence.

**Purpose:** The purpose of this study was to compare patient acceptance of 3 commercially available eye drop instillation aids in a diverse tertiary care population.

**Methods:** In this prospective, randomized controlled study, 39 patients being treated with topical antihypertensives were assigned to Arm A (no intervention) or Arm B (AutoDrop, AutoSqueeze, or SimplyTouch). Subjects in Arm B were instructed to administer their eye drop with the assigned drop aid at every use for ~6 weeks. Satisfaction surveys were administered at 3 and 6 weeks, where patients also reported the number of drops missed.

**Results:** Thirty-two of 39 subjects completed study participation and full data analysis. Within this total group, 24 subjects were randomized to drop aids (AutoDrop N = 10, AutoSqueeze N = 8, SimplyTouch N = 6), and 8 were randomized to no drop aid. At the 3 and 6-week timepoints, patients found instillation easier with AutoDrop (70.0%, 60.0%) followed by the AutoSqueeze (62.5%, 75.0%), and lastly SimplyTouch (33.3%, 33.3%). For the AutoSqueeze, the mean number of drops missed with and without the drop aid were significantly different ($P = 0.015$ at 3 wk, $P = 0.008$ at 6 wk). There was no difference in the mean number of drops missed with the AutoDrop and SimplyTouch at either timepoint.

**Conclusions:** For the AutoDrop and AutoSqueeze groups, over 60% of the patients found the devices helpful and would consider using them long-term. Our results suggest that patients would be amenable to using eye drop instillation aids, although more objective data is needed to determine whether these devices would improve medication compliance and clinical outcomes.

**Key Words:** glaucoma, eye drops, drug instillation, medication adherence

(*J Glaucoma* 2021;30:725–731)

Glaucoma affects ~64.3 million people worldwide and is a leading cause of irreversible visual impairment.[1] Progression of the disease can be stopped with adequate lowering of the intraocular pressure (IOP). Daily administration of ocular hypotensive medications is the current mainstay of treatment. Poor eye drop instillation may cause patients to miss doses of their medications, resulting in under treatment and disease progression and or need for other more invasive treatment options.[2–4]

Patient adherence to topical ocular medications involves the successful interplay of several factors. Davies et al[5] describe the 4 major steps in eye drop adherence: obtaining the medication, instilling the eye drops into the eye successfully, instilling the eye drops at the appropriate time, and following this routine daily as prescribed. Several studies have demonstrated that patients frequently have difficulty with successful instillation of eye drops.[6–15] Successful instillation requires the patient to grip the bottle and squeeze with the adequate force to precisely dispense a single drop onto the ocular surface. Poor aim can result in medication wastage and early bottle exhaustion from repeated attempts to administer drops, leading to a need for early refills and increased medication costs.[16–18] Patients also have to take great care in trying to avoid touching the bottle tip, to reduce risk of infection from contaminated bottle tips,[19] corneal abrasions and ulceration,[20] and contact dermatitis.[21] Patient education, through verbal, written, or video feedback, plays a key role to have all these steps converge successfully.[22–24] Other factors that may contribute to poor compliance include poor vision[9,10,13,25,26] and limited formal education,[12,26] both of which are characteristics of our patient population.

Several eye drop instillation aids have been developed to improve patients' ability to properly instill their eye drops. The various designs of these aids attempt to address 1 or more of the physical barriers noted above to self-administer the drop.[5] Patient utilization of these instillation aids is currently unknown. These devices are typically available at local pharmacies or available through online platforms for purchase, but are not commonly recommended as they can be costly, and their usefulness has not yet been proven.[27] As many as 78% of patients welcome the possibility of using an aid, but actual use of the devices was not evaluated and this finding was more hypothetical.[28] Given this reported positive perception, the goal of this study was to compare patient acceptance of 3 commercially available eye drop instillation aids in a diverse patient population at an academic urban safety-net hospital.

## METHODS

### Design

This was a prospective, randomized controlled study at Boston Medical Center (BMC), located in Boston, MA. BMC is a single nonprofit, safety-net, academic medical center which serves a diverse patient population from across the New England area. This study was internally funded by Boston Medical Center's Patient Safety Grant. This research

Received for publication January 24, 2021; accepted May 13, 2021.
From the *Boston Medical Center, Boston University School of Medicine; †Harvard Medical School; and ‡Boston Medical Center, Boston, MA.
Disclosure: The authors declare no conflict of interest.
Reprints: Manishi Desai, MD, Boston Medical Center, Boston University School of Medicine, 85 East Concord Street, 8th Floor, Boston, MA 02118 (e-mails: manishi.desai@bmc.org; madesai@bu.edu).

DOI: 10.1097/IJG.0000000000001891

protocol followed the tenants of the Declaration of Declaration of Helsinki; was approved by the Boston Medical Center and Boston University Medical Campus Institutional Review Board, Boston, MA; and adhered to the Health Insurance Portability and Accountability Act.

Subjects were recruited from the glaucoma services within the ophthalmology department at BMC. Those eligible for participation were individuals who were 18 years or older and were on the same topical medication for glaucoma treatment for a minimum of 2 months. Patients were excluded if they underwent recent surgical intervention.

Patients who were deemed eligible based on review of their medical chart by the investigator and designated study team members were approached for participation. Only those who agreed to integrate their designated randomization group into their daily treatment regimen, as determined by their glaucoma specialist, were allowed to continue with participation. All patients were consented into the study by an investigator or designated study team member in a private examination or consult room once all questions were answered.

Following consent, the subject was told if they were enrolled into Arm A (no intervention) or Arm B (AutoDrop, AutoSqueeze, or SimplyTouch). Those enrolled into Arm A were instructed to make no changes to their treatment regimen explained by their glaucoma specialists. Those randomized into Arm B were dispensed their designated drop aid: AutoDrop, AutoSqueeze, or SimplyTouch. These drop aids were chosen due to their accessibility (both in drug stores and online) and relatively low cost. An educational session was conducted with a study team member to ensure the subject was comfortable using the drop aid with their medication regimen at home. A description of each drop aid is as follows (a photo of each drop aid can be seen in Fig. 1):

- AutoDrop eye guide (Owen Mumford, Georgia) is a plastic device that can be attached to most eye drop bottles. It claims an "anti-blinking" design intended to guide the user's gaze away from the dropper. The dropper also has a lower lip that gently holds the lower lid in place. This helps to ensure that the nozzle is positioned directly over the eye so that drops are successfully delivered on the first attempt. The device is reusable and can be used in conjunction with AutoSqueeze bottle aid.
- AutoSqueeze bottle aid (Owen Mumford) is a plastic device with arms that clip around the bottle to provide an ergonomic grip and extra leverage for easy bottle squeezing. This was designed to make eye drop treatment easier for patients with dexterity issues. The device is reusable and can be used in conjunction with AutoDrop Eye Guide.
- SimplyTouch eye drop applicator (SimplyTouch LLC, Florida) is a plastic device in the shape of a small paddle. An eye drop is placed on the round edge of the applicator, which securely holds the drop. When brought to the eye, the drop slides off onto the surface of the eye. This allows for better control of the amount and placement of drops. It also allows patients to instill drops without tilting their heads back and can be applied with or without glasses on.

Subjects were also sent home with an instruction guide and a contact number for the study team if they had any questions regarding installation instructions. On the day of enrollment, the patient's IOP and visual acuity (VA) were measured and recorded as part of the standard of care examination. Lastly, subjects were sent home with a study diary which they would record the start and stop dates of their medications.

After ~3 weeks, the study team followed up over the phone with the subjects. During this phone call, the study team conducted a satisfaction survey to receive cohesive feedback about their randomization group. The study team also answered any questions the subject may have regarding their randomization group and treatment regimen.

Subjects were seen by their glaucoma specialist for a standard of care appointment after ~6 weeks of enrollment. As done per standard of care, the subject's IOP and VA were measured and recorded. The study team conducted a second satisfaction survey with all subjects and collected their study diary. Medication dispensing dates were confirmed with the subject's pharmacy, as needed.

Patients were terminated early from the study if there was a change in eye medication as determined by their standard of care provider. Patients could also be withdrawn from the study if they demonstrated noncompliance with study procedures.

## Statistical Analysis

### Preference

Preference was determined via a survey of yes or no questions designed to assess likability, utility, and acceptance of the drop aid devices. The questions were as follows: "(1) Do you like using the drop aid?"; "(2) Do you find it easier to instill drops with the drop aid?"; and "(3) Would you use a drop aid long term?." Answers to these questions were reported as a percentage of affirmative answers at the 3 and 6-week timepoints. In addition, a *z*-test was used to determine


**FIGURE 1.** Pictures of the eye drop instillation aids used: AutoDrop eye guide (Owen Mumford) (A), AutoSqueeze bottle aid (Owen Mumford) (B), SimplyTouch eye drop applicator (SimplyTouch LLC) (C). Figure 1 can be viewed in color online at www.glaucomajournal.com.

whether there was a significant change in the proportion of affirmative answers over time.

### Performance

For this analysis, performance was defined to be the mean number of drops missed at each timepoint both with and without the assigned drop aids. Only patients who at least attempted to use their assigned drop aid throughout all 6 weeks were included for analysis. Mean number of drops missed was reported for each of the 3 drop aid groups as well as for the no drop aid control group. For the drop aid groups, 2 different values were reported to account for participants' inconsistent usage of their assigned drop aids.

Differences in mean number of drops missed with and without the assigned drop aid within each group were tested for significance via *t* test. In addition, differences between mean number of drops missed with each drop aid and mean number of drops missed in the no drop aid control group were assessed for significance using a *t* test. A Bonferroni correction was used to account for multiple comparisons. All the above reported numbers and statistical tests were performed using the data from the 3-week timepoint and the 6-week timepoint. Finally, a *t* test was used to determine if there were a significant difference in mean number of drops missed with the drop aid for each randomized group between the 3 and 6-week timepoints.

### Effect of Preference on Performance

Fisher exact test was used to determine if performance was independent of preference at the 6-week endpoint. Since all preference questions were found to be dependent on one another by Fisher exact test even with a Bonferroni correction, the first question, "Do you like using the drop aid?", was selected to represent overall preference of a drop aid for the purpose of this analysis. In this setting, performance was defined to be mean number of drops missed while using a drop aid.

Statistical analysis was performed using RStudio version 1.2.5019.

## RESULTS

Thirty-nine patients were enrolled in this study, with 32 completing full study participation. Of the 7 patients who did not complete full study participation, 4 patients were unreachable at the 3-week timepoint, one was unreachable at the 6-week timepoint, one withdrew, and one was lost to follow-up. Twenty-four of the remaining 32 subjects were randomized to 1 of 3 drop aids: AutoDrop (n = 10), AutoSqueeze (n = 8), and SimplyTouch (n = 6). The other 8 subjects were randomized to the no drop aid control group. Of the 24 subjects randomized to drop aids, only 19 utilized their drop aids throughout the entire 6-week period: AutoDrop (n = 9), AutoSqueeze (n = 7), and SimplyTouch (n = 3).

Table 1 demonstrates the characteristics of the 32 patients enrolled in the study, as well as for each of the arms in the study. The mean age of the study population was 66.9 ± 10.3 (range, 38 to 83 y). There were 15 females (47%) and 17 males (53%). Sixty-three percent of patients were of Black or African American race. The majority (81%) of the patients had baseline VA of 20/40 or better in the study eye. The baseline IOP of the study eye was 16.9 ± 4.3 mm Hg. Ten (31%) of patients were on 1 glaucoma eye drop, 10 (31%) were on 2 eye drops, 11 (34%) were on 3 eye drops, and 1 (3%) patient was on 4 eye drops.

### Preference

As seen in Table 2, between the 3 and 6-week timepoints, there were no significant changes in proportions of affirmative versus negative responses regarding whether participants liked using the drop aid ($P = 1.00$), found it easier to instill drops with a drop aid ($P = 1.00$), or would use their assigned drop aid long term ($P = 0.760$).

### Performance

As seen in Table 3 and Figure 2, at the 3-week timepoint, the mean number of drops missed when using the drop aid as compared with when the assigned drop aid was not used was not significantly different for the AutoDrop and SimplyTouch ($P = 0.088$ and 0.215, respectively). However, for the AutoSqueeze, the mean number of drops missed was significantly

**TABLE 1.** Demographics and Clinical Characteristics of the Study Population

| | Total (N = 32) | AutoDrop (N = 10) | AutoSqueeze (N = 8) | SimplyTouch (N = 6) | No Drop Aid (N = 8) |
|---|---|---|---|---|---|
| Age [mean (SD)] (y) | 66.9 ± 10.3 | 68.1 ± 8.3 | 59.8 ± 12.3 | 69.2 ± 10.3 | 70.8 ± 8.5 |
| Sex [n (%)] | | | | | |
| Female | 15 (47) | 6 (60) | 4 (50) | 3 (50) | 2 (25) |
| Male | 17 (53) | 4 (40) | 4 (50) | 3 (50) | 6 (75) |
| Race [n (%)] | | | | | |
| Black or African American | 20 (63) | 7 (70) | 5 (63) | 4 (67) | 4 (50) |
| White | 6 (19) | 1 (10) | 2 (25) | 2 (33) | 1 (13) |
| Asian | 1 (03) | 0 (0) | 0 (0) | 0 (0) | 1 (13) |
| Unknown | 5 (16) | 2 (20) | 1 (13) | 0 (0) | 2 (25) |
| No. glaucoma eye drops [n (%)] | | | | | |
| 1 | 10 (31) | 4 (40) | 0 (0) | 3 (50) | 3 (38) |
| 2 | 10 (31) | 1 (10) | 5 (63) | 1 (17) | 3 (38) |
| 3 | 11 (34) | 5 (50) | 3 (38) | 1 (17) | 2 (25) |
| 4 | 1 (3) | 0 (0) | 0 (0) | 1 (17) | 0 (0) |
| Baseline visual acuity of study eye [n (%)] | | | | | |
| 20/40 or better | 26 (81) | 6 (60) | 7 (88) | 6 (100) | 7 (88) |
| 20/50 to 20/150 | 3 (9) | 2 (20) | 0 (0) | 0 (0) | 1 (13) |
| Worse than 20/200 | 3 (9) | 2 (20) | 1 (13) | 0 (0) | 0 (0) |
| Baseline intraocular pressure of study eye [mean (SD)] (mm Hg) | 16.9 ± 4.3 | 15.2 ± 4.1 | 19.0 ± 2.2 | 14.2 ± 3.3 | 18.9 ± 5.1 |

**TABLE 2.** Patient Preference Regarding Drop Aids

| | Overall (AutoDrop N = 10, AutoSqueeze N = 8, SimplyTouch N = 6) | | | |
|---|---|---|---|---|
| | Yes | % of Cohort | No | % of Cohort |
| Week 3 | | | | |
| Do you like using the drop aid? | | | | |
| AutoDrop | 7 | 70.0 | 3 | 30.0 |
| AutoSqueeze | 6 | 75.0 | 2 | 25.0 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |
| Do you find it easier to instill drops with the drop aid? | | | | |
| AutoDrop | 7 | 70.0 | 3 | 30.0 |
| AutoSqueeze | 5 | 62.5 | 3 | 37.5 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |
| Would you use a drop aid long term? | | | | |
| AutoDrop | 7 | 70.0 | 3 | 30.0 |
| AutoSqueeze | 6 | 75.0 | 2 | 25.0 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |
| Week 6 | | | | |
| Do you like using the drop aid? | | | | |
| AutoDrop | 6 | 60.0 | 4 | 40.0 |
| AutoSqueeze | 6 | 75.0 | 2 | 25.0 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |
| Do you find it easier to instill drops with the drop aid? | | | | |
| AutoDrop | 6 | 60.0 | 4 | 40.0 |
| AutoSqueeze | 6 | 75.0 | 2 | 25.0 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |
| Would you use a drop aid long term? | | | | |
| AutoDrop | 9 | 90.0 | 1 | 10.0 |
| AutoSqueeze | 6 | 75.0 | 2 | 25.0 |
| SimplyTouch | 2 | 33.3 | 4 | 66.7 |

different when participants used the AutoSqueeze as compared with when they did not, even with a Bonferroni correction (0.43 drops with device, 1.5 drops without device, $P = 0.015$). When compared with the control group assigned no drop aid, the use of a drop aid did not result in a significant difference in mean number of drops missed in any of the 3 drop aid groups (AutoDrop: $P = 0.519$, AutoSqueeze: $P = 0.167$, SimplyTouch: $P = 0.129$).

**TABLE 3.** Performance of Drop Aids

| | Overall (AutoDrop N = 9, AutoSqueeze N = 7, SimplyTouch N = 3, No Drop Aid N = 8) |
|---|---|
| Week 3 | |
| Mean number of drops missed with drop aid | |
| AutoDrop | 1.33 |
| AutoSqueeze | 0.43 |
| SimplyTouch | 0.33 |
| Mean number of drops missed without drop aid | |
| AutoDrop | 2.11 |
| AutoSqueeze | 1.50 |
| SimplyTouch | 1.00 |
| Control (no drop aid) | 1.00 |
| Week 6 | |
| Mean number of drops missed with drop aid | |
| AutoDrop | 1.33 |
| AutoSqueeze | 0.43 |
| SimplyTouch | 0.00 |
| Mean number of drops missed without drop aid | |
| AutoDrop | 1.89 |
| AutoSqueeze | 1.86 |
| SimplyTouch | 0.75 |
| Control (no drop aid) | 0.88 |

Similarly, at the 6-week timepoint, only the AutoSqueeze group demonstrated a significant difference in average number of drops missed when participants used their assigned drop aid (0.43 drops with device, 1.86 drops without device) as compared with when they did not (AutoSqueeze: $P = 0.008$; AutoDrop: $P = 0.139$, SimplyTouch: $P = 0.293$). This difference was found to be significant even with a Bonferroni correction. When compared with the control group, there was no significant difference in mean number of drops missed between each drop aid group and the control with a Bonferroni correction (AutoDrop: $P = 0.384$, AutoSqueeze: $P = 0.293$, SimplyTouch: $P = 0.041$).

Finally, between the 3 and 6-week timepoints, there was no significant change in mean number of drops missed over time among any of the drop aid groups (AutoDrop: $P = 1.00$, AutoSqueeze: $P = 1.00$, SimplyTouch: $P = 0.43$).

### Effect of Preference on Performance

At the 6-week timepoint, final performance, in terms of mean number of drops missed, was found to be independent of preference, as indicated by whether a participant liked the assigned drop aid, for all types of drop aids (AutoDrop: $P = 0.524$, AutoSqueeze: $P = 1.00$, SimplyTouch: $P = 1.00$).

## DISCUSSION

Medication adherence is a complex, multifactorial behavior that is influenced by a variety of barriers including medication regimen, patient factors, provider factors, and situational or environmental factors.[29] Poor eye drop instillation technique negatively impacts the patient's ability to achieve good IOP control. In our study, we examine the medication administration aspect of adherence by observing patient experience with 3 eye drop instillation aids. Over 60% of the patients randomized to the AutoDrop and AutoSqueeze liked using the devices, found drop instillation easier, and would use them long-term at both the 3 and 6-week marks. Compared with the other devices, there was a less positive response from patients who were randomized to the SimplyTouch device. Taken together, over half the patients who tried a drop aid received it positively.

Our study design enabled patients to take their assigned device home and use them for a period of 6 weeks. This allowed patients a reasonable amount of time to be acquainted with the device and trial it as part of their daily medication regimen, providing a more accurate assessment of patient satisfaction. Notably, the SimplyTouch yielded the lowest compliance out of the 3 devices, which may be in part attributable to the small size of the applicator, allowing it to be easily misplaced. Patients may also have been uncomfortable with the device directly contacting their eye. The AutoDrop and AutoSqueeze devices, on the other hand, are attached to the eye drop bottle itself.

This is the first study to compare the use of 3 eye drop aids in a randomized clinical trial. To date, there is no study data using the AutoDrop eye guide, the AutoSqueeze bottle aid, or the SimplyTouch eye drop applicator. On a review of current literature, the most comprehensively studied device is the XAL-Ease delivery system (Pfizer Ophthalmics, New York, NY), made for use with Xalatan and Xalacom eye drops. Nordmann and colleagues reported over 70% patient satisfaction after 1 month, without significant adverse effects. Use of this device significantly decreased the need for additional help in eye drop instillation and risk of the tip of the bottle touching the eye, as compared with

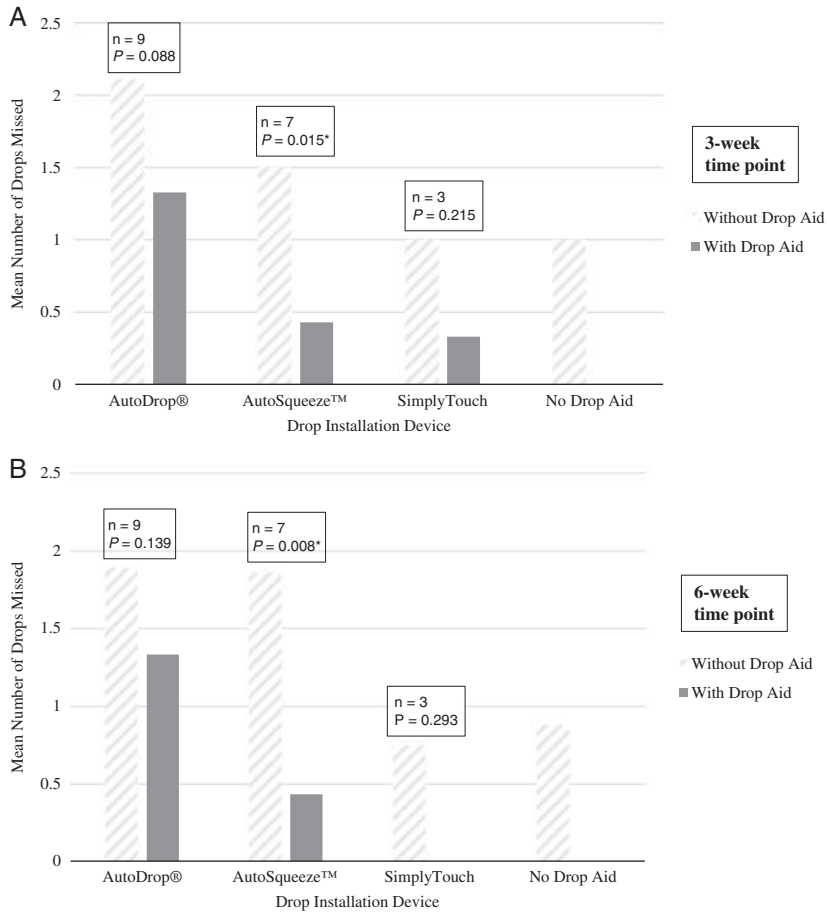


**FIGURE 2.** Self-reported mean number of eye drops missed with each instillation attempt at week 3 (A) and week 6 (B). Note: SimplyTouch users reported zero drops missed with use of the device at 6 weeks, hence no bar. *$P < 0.05$.

conventional use.[30] Other devices do exist and have demonstrated varying success rates in improving drop instillation,[31–33] but they are not widely available, and the XAL-Ease has been discontinued in the United States.

The limited health literacy in our population reminds us that our patients may require different approaches, more time, and their health conditions explained in simple terms to ensure understanding and compliance. Sleath et al[34] showed that a short glaucoma medication questionnaire can help identify patients who may need further education and or help with eye drop instillation. Level of vision may also help detect at risk patients as noted previously.[9,10,13,25,26] Education by a provider can play a role in helping patients improve their technique,[22–24] however, sometimes this alone is not successful and can require additional intervention by a caregiver.[24] If these options are limited, an eye drop instillation aid could be a potential solution to help the patients improve their chances of successful self-administration.

Poor eye drop administration techniques may also result in wasting of the drops and increased medication costs, leading to financial implications for the patients, their insurance companies, and government healthcare spending.[18] These cost considerations are particularly significant in patients with lower socioeconomic status and those dependent on federal government health insurance programs, as are many of the patients in our clinic population. An eye drop instillation aid could potentially save costs in multiple areas if compliance is improved.

A number of new ocular drug-delivery systems (injectables and drug eluting implants) are being evaluated in clinical trials and potentially coming to market to replace conventional drop therapy.[35–41] However, presently, topical drops remain the gold standard in clinical practice. Most glaucoma patients appear to be amenable to sustained drug-delivery modalities as an alternative, but only if these were more effective than eye drops or eliminated the need for surgical intervention.[42] A survey by Wang et al[43] demonstrated overall limited acceptance of these alternatives among glaucoma patients, with rates ranging from 30% to 54%, as the majority patients prefer less invasive routes. In addition, until these newer formulations are widely accepted by insurance companies, the out-of-pocket costs may be prohibitive for many patients.

There are several limitations to this pilot study that should be considered when interpreting its results. The study had a relatively small sample size at a single academic center, and our results may not be generalizable to other populations. Response bias may impact the survey responses, though we took care to word our questions clearly and precisely. Because we wanted to keep the surveys short and manageable for our participants, we did not interrogate the details regarding the advantages and disadvantages of the devices. We were not always able to elicit specific feedback regarding the positives and negatives of the device. Our study relied on self-report, which is less reliable than direct observation, or a video recording that would allow for a

 

masked observer and multiple raters. Another consideration is that our participants were randomized to 1 of the 3 drop aids investigated, rather than being assigned specifically to the one that may be the most beneficial for their needs. For example, some may help by providing additional leverage for the grip and force requirements, while others eliminate the need for neck extension. It may also be useful to examine the utility in specific populations, such as Parkinson for example, as these patients have unique challenges with mobility. Further investigation of this topic may include a larger sample size, more specific questions regarding the pros and cons of each device and matching the patient's specific physical barriers in eye drop administration with the appropriate device. Incorporating objective measures to evaluate for an improved instillation technique may also be beneficial.

In summary, our results suggest that patients can be quite amenable to using eye drop instillation aids and we should consider recommending them to patients who otherwise struggle with drop instillation and medication adherence. As to the clinical impact on IOP and progression, more objective data is needed to determine whether these devices translate to improved clinical outcomes and drop compliance long term.

## ACKNOWLEDGMENT

*The authors acknowledged Avni Badami, MD, Nina Tamashunas, BS, Merit Gorgy, BS, Priyanka Patel, BS.*

## REFERENCES

1. Jonas JB, Aung T, Bourne RR, et al. Glaucoma. *Lancet*. 2017;390:2183–2193.
2. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120:701–713; discussion 829–830.
3. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. *Am J Ophthalmol*. 2000;130:429–440.
4. Sleath B, Blalock S, Covert D, et al. The relationship between glaucoma medication adherence, eye drop technique, and visual field defect severity. *Ophthalmology*. 2011;118:2398–2402.
5. Davies I, Williams AM, Muir KW. Aids for eye drop administration. *Surv Ophthalmol*. 2017;62:332–345.
6. Davis SA, Sleath B, Carpenter DM, et al. Drop instillation and glaucoma. *Curr Opin Ophthalmol*. 2018;29:171–177.
7. Schwartz GF, Hollander DA, Williams JM. Evaluation of eye drop administration technique in patients with glaucoma or ocular hypertension. *Curr Med Res Opin*. 2013;29:1515–1522.
8. Gupta R, Patil B, Shah BM, et al. Evaluating eye drop instillation technique in glaucoma patients. *J Glaucoma*. 2012;21:189–192.
9. Hennessy AL, Katz J, Covert D, et al. A video study of drop instillation in both glaucoma and retina patients with visual impairment. *Am J Ophthalmol*. 2011;152:982–988.
10. Hennessy AL, Katz J, Covert D, et al. Videotaped evaluation of eyedrop instillation in glaucoma patients with visual impairment or moderate to severe visual field loss. *Ophthalmology*. 2010;117:2345–2352.
11. Stone JL, Robin AL, Novack GD, et al. An objective evaluation of eyedrop instillation in patients with glaucoma. *Arch Ophthalmol*. 2009;127:732–736.
12. Kholdebarin R, Campbell RJ, Jin Y-P, et al. Multicenter study of compliance and drop administration in glaucoma. *Can J Ophthalmol*. 2008;43:454–461.
13. Dietlein TS, Jordan JF, Lüke C, et al. Self-application of single-use eyedrop containers in an elderly population: comparisons with standard eyedrop bottle and with younger patients. *Acta Ophthalmol (Copenh)*. 2008;86:856–859.
14. Hosoda M, Yamabayashi S, Furuta M, et al. Do glaucoma patients use eye drops correctly? *J Glaucoma*. 1995;4:202–206.
15. Brown MM, Brown GC, Spaeth GL. Improper topical self-administration of ocular medication among patients with glaucoma. *Can J Ophthalmol*. 1984;19:2–5.
16. Moore DB, Walton C, Moeller KL, et al. Prevalence of self-reported early glaucoma eye drop bottle exhaustion and associated risk factors: a patient survey. *BMC Ophthalmol*. 2014;14:79.
17. Kawai-Tsuboi N, Kawai M, Minami Y, et al. A study of the association between patterns of eye drop prescription and medication usage in glaucoma subjects. *J Glaucoma*. 2015;24:202–206.
18. Schmier JK, Halpern MT, Jones ML. The economic implications of glaucoma: a literature review. *Pharmacoeconomics*. 2007;25:287–308.
19. Geyer O, Bottone EJ, Podos SM, et al. Microbial contamination of medications used to treat glaucoma. *Br J Ophthalmol*. 1995;79:376–379.
20. Solomon A, Chowers I, Raiskup F, et al. Inadvertent conjunctival trauma related to contact with drug container tips: a masquerade syndrome. *Ophthalmology*. 2003;110:796–800.
21. Holdiness MR. Contact dermatitis to topical drugs for glaucoma. *Am J Contact Dermat*. 2001;12:217–219.
22. Davis SA, Carpenter DM, Blalock SJ, et al. A randomized controlled trial of an online educational video intervention to improve glaucoma eye drop technique. *Patient Educ Couns*. 2019;102:937–943.
23. Friedman DS, Hahn SR, Gelb L, et al. Doctor-patient communication, health-related beliefs, and adherence in glaucoma results from the Glaucoma Adherence and Persistency Study. *Ophthalmology*. 2008;115:1320–1327.
24. Lampert A, Bruckner T, Haefeli WE, et al. Improving eye-drop administration skills of patients - A multicenter parallel-group cluster-randomized controlled trial. *PLoS One*. 2019;14:e0212007.
25. Aptel F, Masset H, Burillon C, et al. The influence of disease severity on quality of eye-drop administration in patients with glaucoma or ocular hypertension. *Br J Ophthalmol*. 2009;93:700–701.
26. Sayner R, Carpenter DM, Robin AL, et al. How glaucoma patient characteristics, self-efficacy and patient-provider communication are associated with eye drop technique. *Int J Pharm Pract*. 2016;24:78–85.
27. Ghate D, Edelhauser HF. Barriers to glaucoma drug delivery. *J Glaucoma*. 2008;17:147–156.
28. Winfield AJ, Jessiman D, Williams A, et al. A study of the causes of non-compliance by patients prescribed eyedrops. *Br J Ophthalmol*. 1990;74:477–480.
29. Tsai JC. A comprehensive perspective on patient adherence to topical glaucoma therapy. *Ophthalmology*. 2009;116(suppl):S30–S36.
30. Nordmann J-P, Baudouin C, Bron A, et al. Xal-Ease: impact of an ocular hypotensive delivery device on ease of eyedrop administration, patient compliance, and satisfaction. *Eur J Ophthalmol*. 2009;19:949–956.
31. Strungaru MH, Peck J, Compeau EC, et al. Mirror-hat device as a drop delivery aid: a pilot study. *Can J Ophthalmol*. 2014;49:333–338.
32. Salyani A, Birt C. Evaluation of an eye drop guide to aid self-administration by patients experienced with topical use of glaucoma medication. *Can J Ophthalmol*. 2005;40:170–174.
33. Junqueira DM, Lopes FS, de Souza FC, et al. Evaluation of the efficacy and safety of a new device for eye drops instillation in patients with glaucoma. *Clin Ophthalmol*. 2015;9:367–371.
34. Sleath B, Blalock SJ, Stone JL, et al. Validation of a short version of the glaucoma medication self-efficacy questionnaire. *Br J Ophthalmol*. 2012;96:258–262.
35. Pasquale LR, Lin S, Weinreb RN, et al. Latanoprost with high precision, piezo-print microdose delivery for IOP lowering: clinical results of the PG21 study of 0.4 μg daily microdose. *Clin Ophthalmol*. 2018;12:2451–2457.
36. Zhang X, Cao X, Qi P. Therapeutic contact lenses for ophthalmic drug delivery: major challenges. *J Biomater Sci Polym Ed*. 2020;31:549–560.

 

37. Ciolino JB, Ross AE, Tulsan R, et al. Latanoprost-eluting contact lenses in glaucomatous monkeys. *Ophthalmology*. 2016;123: 2085–2092.
38. Brandt JD, Sall K, DuBiner H, et al. Six-month intraocular pressure reduction with a topical bimatoprost ocular insert: results of a phase ii randomized controlled study. *Ophthalmology*. 2016;123:1685–1694.
39. Wong TT, Novack GD, Natarajan JV, et al. Nanomedicine for glaucoma: sustained release latanoprost offers a new therapeutic option with substantial benefits over eyedrops. *Drug Deliv Transl Res*. 2014;4:303–309.
40. Lewis RA, Christie WC, Day DG, et al. Bimatoprost sustained-release implants for glaucoma therapy: 6-month results from a phase I/II clinical trial. *Am J Ophthalmol*. 2017;175:137–147.
41. Aref AA. Sustained drug delivery for glaucoma: current data and future trends. *Curr Opin Ophthalmol*. 2017;28:169–174.
42. Varadaraj V, Kahook MY, Ramulu PY, et al. Patient acceptance of sustained glaucoma treatment strategies. *J Glaucoma*. 2018; 27:328–335.
43. Wang BB, Lin MM, Nguyen T, et al. Patient attitudes toward novel glaucoma drug delivery approaches. *Digit J Ophthalmol*. 2018;24:16–23.

 