The effect of the Thai “Eye Drop Guide” on success rate of eye drop self-instillation by glaucoma patients

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Background: Noncompliance can mislead clinicians regarding the efficacy of therapy and result in more aggressive, but inappropriate treatment. Improper techniques used for eye drop instillation frequently occurs in chronic glaucoma patients. The Thai Eye Drop Guide (EDG) device has been developed to ensure precise instillation. However, whether the EDG is more effective than the traditional technique when careful instructions for both techniques are given is still unknown.

Objective: To compare success rates of eye drop self-instillation by chronic glaucoma patients using a traditional technique and the EDG when careful instructions for both are given.

Methods: Fifty-nine chronic glaucoma patients were instructed to instill eye drops using the EDG or a traditional technique in a randomized sequence. A two week practice period was assigned before groups were crossed-over. The instillation performance was VDO recorded after each practice period. Three criteria of success: time taken to instill an eye drop into the eye; instillation of only one drop; and without the bottle tip touching lids, lashes, periocular tissues, or the other hand, were scored by three independent readers from video-records. The readers were blinded to the sequence to which the patients were randomized.

Results: There were no significant differences in success rates between the EDG and traditional technique (61.0% and 66.1% respectively, \(p = 0.607\)) and the number of drops dispensed per application (median of 1 drop in both groups, \(p = 0.89\)). The time taken to instill eye drops with the EDG was significantly longer than using the traditional technique (median of 19 and 9 s respectively, \(p < 0.001\)). Older age (\(p = 0.049\), OR 4.23) and more education (\(p = 0.025\), OR 0.19) were found to be significantly associated with failure of the EDG.

Conclusion: EDG is not more effective than a traditional technique in terms of improving dispensing accuracy and decreasing the drops dispensed per application even when careful instructions are given. The results suggest that, if good instructions are provided, experienced glaucoma patients can improve their eye drop instillation performance.

Keywords: Compliance, drop administration, eye drop guide, glaucoma, self-instillation

The purpose of glaucoma treatment, most commonly with antiglaucoma eye drops, is to lower the intraocular pressure to retard or stop further vision loss. The intentional or accidental failure to take drops (noncompliance) is a major problem in glaucoma treatment. Noncompliance can be confused with lack of efficacy and lead to more aggressive treatment that will increase health care costs [1, 2]. For eye drops, noncompliance can be in the form of failure to take medication, improper timing of medication, taking the wrong medication, or taking excessive medication, in addition to improper techniques of administration. The common mistakes in eye drop administration observed in glaucoma patients includes an inability to instill a drop into the eye, instilling more than one drop, and touching the bottle tip to the eye or periocular tissues [3-8]. Incorrect techniques may increase health care costs and harm the eyes, e.g. by contamination, conjunctival congestion, conjunctival erosion, and episcleritis [9].

Various forms of aligning devices to improve accuracy of eye drop instillation have been developed [10-13]. None has been tested objectively for accuracy or efficacy. The Eye Drop Guide (EDG) is the first device developed in Thailand (Patent number 6555,
Mahidol University, 2 Sep 2011). Its purpose is to ensure precise instillation and prevent the bottle tip from touching the eye. It was made of lightweight plastic (chemically inert thermoplastic polystyrene) in a shape and size of a regular eye wash cup. The rim is curved to fit the orbit. One of the disadvantages of the EDG is that it was designed to fit the largest eye drop bottle available (15 ml). However, most glaucoma eye drop bottles are 2.5, 3, or 5 ml and may not closely fit the device. If the patients’ hands are not steady, the tips may sway when applying the eye drops. Another disadvantage it is available in only one size and may not fit properly in the orbit of some patients. Furthermore the EDG also requires skill and practice in order for patients to self-instill eye drops successfully.

Although instillation problems are well documented, clinicians often neglect these problems and assume that chronic glaucoma patients understand how to self-instill eye drops correctly. Whether the EDG is more effective than the traditional technique (without a device) remains hitherto unknown. In this study we compared success rates of eye drop self-instillation using the EDG and a traditional technique in patients with chronic glaucoma.

Materials and methods
A randomized cross-over design was used to eliminate the carry over effect (practice effect). Participants perform better over time because of practice and perform best with the most recently used technique. The study was conducted at the Faculty of Medicine, Siriraj Hospital, Mahidol University. The study was approved by the institutional review board [SI 487/2012 (EC4)] and is registered by Clinical Trials.gov (NCT01704248). Written informed consent was obtained from all participants.

Inclusion and exclusion criteria
Patients were enrolled from the out-patient clinic by the primary investigator who did not attend any of the participants. The patients were eligible for the study when they met all 3 criteria: age ≥18 years; diagnosed with chronic glaucoma ≥3 months; and regularly self-administering antiglaucoma eye drops. Criteria for exclusion were unwillingness to participate; allergy to artificial tears; perioperative status; visual loss from diseases other than glaucoma; ophthalmic conditions that affect the eye drop instillation e.g. nystagmus, ptosis, exophthalmos, and general conditions that affect the patient’s adherence to the protocol, e.g. dementia, psychosis, rheumatoid arthritis, neurological conditions resulting in tremor or paralysis.

Baseline evaluation and video-record setting
Baseline characteristics were collected from medical records and interviews. Two digital cameras (Canon EOS 550D) were set to record the performance of participants in 2 different angles at 0.5–1 meter from the eyes. It started when participants received the uncapped bottle in their dominant hands. The 3 ml bottle of artificial tears contained, 0.5% carboxymethyl cellulose Na (Cellufresh MD, Allergan, Irvine, USA). It was used for the study. The participants were asked to instill the artificial tears into the eye using their usual technique, as they would normally do at home. The study eye was the eye with worst sight based on best corrected visual acuity (BCVA). If the BCVA in both eyes was equal the mean deviation score (MD) from the latest visual field test was used to define the eye with worst sight. This was done to make the participants familiar with the process and atmosphere of being recorded. In the study room, there was an examination bed, 3 different sizes of chairs, a table, mirror, a small standing surgical lamp, and a hand wash sink.

Randomization
The list of random numbers was computer-generated by a statistician not involved in other parts of the study. The opaque, sealed envelope containing the assigned treatment sequence was drawn by a primary investigator after baseline video recording.

Procedures
All participants received training with both techniques and were randomly assigned to start with either the EDG (group 1) or the traditional technique (group 2). Each technique was carefully considered following the same instruction manual by the primary investigator, but allowing adjustments in details to serve each participant better. The participants would practice until confident in the techniques, to which they were randomized. The participants then were assigned to practice instilling eye drops in both eyes with the assigned technique at home for 2 weeks and keep the diary of date, time, and number of bottles used with the technique used in each eye. The participants were assigned to practice with the study eye drops and then their own medications. The evaluation session was
scheduled after 2 weeks of practice. On the evaluation visit, we video-recorded the instillation performance and collected the patient diary. After VDO recording the groups were crossed over.

To be able to see the eye drops when instilling with the EDG a 1.5 × 3 cm. window was made on the device (Figure 1). The video photographers recorded the participants’ performance with the device through this window (Figure 2).

**Primary and secondary outcomes**

Primary outcome was between group comparison of success rates, defined by the three criteria: time taken to instill an eye drop into the eye; instillation of only one drop; and without the bottle tip touching lids, lashes, periocular tissues, or the other hand.

Secondary outcomes included (1) comparison of the number of drops dispensed per application, (2) comparison of time needed to successfully instill eye drops (measured in seconds from the point when the participants had an uncapped bottle in hand until they believe one drop is successfully instilled into the eye), and (3) factors associated with failure of self-instillation with the EDG.

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**Sample size estimation**

The sample size was calculated based on success rates of eye drop self-instillation; 33.8%–80% in previous studies [3-8]. We estimated success rates of the traditional technique and the EDG to be 60% and 80% respectively. A sample size of 52 pairs will have 80% power to detect a difference in proportion of 0.200 when the proportion of discordant pairs is expected to be 0.300 using McNemar’s test of equality of paired proportions with a 0.050 two-sided significance level. We increased the sample size to 64 pairs to compensate for 20% drop-out and possible video tape retrieval problems.

**Statistical analysis**

The VDO records of both techniques were presented to the readers together after all the recordings were done. The readers scored the participants’ performance independently and without knowing the names, the disease status, or the randomized sequence of the participants.

All analyses were performed using PASW Statistics 18 (SPSS Inc, Chicago, IL, USA). The continuous data were summarized by the mean (± standard deviation) or median (interquartile range) where appropriate. The categorical data were summarized by the percentage of individuals falling into each category.

Success rates comparison between 2 techniques was analyzed following this order: (a) carry-over effect was analyzed by the Pearson’s chi-square test. (b) Success rate comparison was analyzed using McNemar’s test. If there was no carry-over effect, data from 2 sequences were combined and analyzed using McNemar’s test. In case of a carry-over effect, analysis was performed separately for each treatment sequence.

Wilcoxon signed-rank tests were used to compare the “drops dispensed per application” and “time to instill drops” between techniques. Binary logistic regression was used to analyze the factors associated with failure of eye drop instillation.

**Results**

**Baseline characteristics**

Sixty-four patients with various forms of glaucoma were recruited. By our definition of success; 26 of 64 participants succeeded in eye drop instillation using their usual techniques with a mean (SD) of 1.38 (0.67) drops per application. Five participants (2 from group
I and 3 from group II) withdrew from the study before the first evaluation visit at week 2. One participant was scheduled for glaucoma surgery, three withdrew because of travelling inconvenience, and one because of allergic reaction to the artificial tears used in the study. A total of 59 participants completed the entire study; their baseline characteristics were summarized in Table 1. There were no differences in baseline characteristics between the 2 randomized groups. Most of the participants had good visual function. The overall median MD was \(-5.14\) (mild visual field defect) and median BCVA was around 20/40 (near normal vision) in the study eyes. None had visual acuity in a better eye of less than 20/200 (severe vision loss) regardless of etiology of visual impairment. Seven participants (4 from group I and 3 from group II) had severe visual impairment (LogMAR VA \(\geq 1\)) and 14 participants (8 from group I and 6 from group II) had profound visual field loss (MD \(\leq -15\)) in the study eyes. More than 85% (51/59) had used glaucoma medications for \(>1\) year. Almost half of the participants (26/59) had recently been using only 1 medication to control their disease.

**Effect of the Eye Drop Guide**

The success rates of each technique in each group are summarized in Table 2. A carry over effect with either technique was not found (Fisher’s exact \(P = 0.717\)). The success rates for eye drops instillation for EDG technique and the traditional technique were 61% (36/59) and 66.1% (39/59) respectively. There was no significant difference in success rates between the two techniques (McNemar’s \(P = 0.607\)). The number of participants that could not instill the first drop into the eye was almost double with the EDG (23 versus 12). A portion of participants were eventually unable to instill one whole drop into the eye; 9 (15%) and 5 (8%) with the EDG and the traditional technique respectively. Thirteen participants contaminated the bottle tips with the eyes or periocular tissues when instilling with the traditional technique. Although the EDG prevented the bottle tip from touching the eye, in 7 participants the drops were instilled into the device before dropped onto the eye. The number of drops dispensed per application was not significantly different between two groups, \(P = 0.89\). The time used to instill eye drops with the EDG was significantly longer than with the traditional technique, \(p < 0.001\) (Table 3).

**Risk factors analysis**

Univariate and multivariate analyses of risk factors associated with failure of instillation with EDG are summarized in Table 4. The variables included in multivariate analysis were variables that were statistically significant in univariate analysis with \(P \leq 0.2\) and variables that were found to be significant in the previous studies i.e. female sex, age \(\geq 70\) years, less than high school education, lower level of visual acuity, and lower visual field score.

### Table 1. Baseline characteristics

<table>
<thead>
<tr>
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<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of participants</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>70.23(±7.76)</td>
<td>66.69(±10.83)</td>
</tr>
<tr>
<td>Female gender</td>
<td>14(46.67%)</td>
<td>16(55.17%)</td>
</tr>
<tr>
<td>LogMAR BCVA*</td>
<td>0.3(IQR 0.6)</td>
<td>0.3(IQR 0.3)</td>
</tr>
<tr>
<td>MD scores*</td>
<td>-4.90(IQR 15.56)</td>
<td>-5.14(IQR 8.41)</td>
</tr>
<tr>
<td>&lt;High school education</td>
<td>14(46.67%)</td>
<td>12(41.38%)</td>
</tr>
<tr>
<td>Duration of glaucoma (y)*</td>
<td>6.1(±5.96)</td>
<td>6.34(±4.19)</td>
</tr>
<tr>
<td>Mean no. of medications*</td>
<td>1.63(±0.66)</td>
<td>1.89(±0.84)</td>
</tr>
<tr>
<td>Sitting or standing position</td>
<td>19(63.33%)</td>
<td>18(62.07%)</td>
</tr>
<tr>
<td>Same eye-hand</td>
<td>22(73.3%)</td>
<td>18(62.1%)</td>
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</tbody>
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* = Characteristics of the study eye, LogMAR = logarithm of the minimum angle of resolution, BCVA = best corrected visual acuity, MD = perimetric mean deviation, Same eye-hand = same side of the study eye and the hand holding the bottle.
In multivariate analysis, female sex and older age were found to be significantly associated with failure of the traditional technique \((P = 0.030 \text{ and } 0.035\) respectively). For the EDG, older age \((P = 0.049, \text{ OR } 4.23)\) and more education \((P = 0.025, \text{ OR } 0.19)\) were found to be significantly associated with failure. The practice frequency of \(\leq 28\) times was significantly associated with failure in univariate analysis \((P = 0.018)\). However, in multivariate analysis, it was not significant \((P = 0.071)\). No association of the frequency of practice with age or education level was observed.

**Discussion**

Various types of aligning devices have been developed to aid the eye drop self-instillation. This is the first study that objectively assessed the efficacy of the aligning device using video-records. Previous studies that video-recorded the performance of experienced glaucoma patients, evaluated their usual instillation technique. They have reported a success rate of 31% and 39% with the 2.5 ml and 5 ml bottle respectively [5-14]. Using the same triple criteria of success, the success rate of patient’s usual technique of 41% in our study was consistent with previous studies. Although the EDG could improve the success
rates to 61% it is not more effective than the traditional
technique. When careful instruction regarding the
instillation techniques was given and adapted to be
suitable for each individual, the success rates were
not different between the two techniques. The success
rates for the EDG were substantially lower than we
had expected. We had expected that the EDG would
help in aligning the bottle directly above the eye, but a
number of patients could not handle the device
properly. As a result, 23 patients could not instill
the first drop into the eye with the EDG and 17 of
23 patients administered multiple eye drops. The
difficulties with the EDG that we observed were that
participants could not position it properly over the eye
or did not tilt their heads far back enough to allow
the eye drops to enter the orbit. A few participants
compressed the eye and forced the lids closed. We
also observed difficulty in handling the bottle and
device simultaneously; especially in older participants.
The 3 ml artificial tears used in the study was not a
close fit to the EDG so that the bottles were not aligned
in some cases. As a consequence, 7 participants
contaminated the eye drops by instilling them directly
into the devices. Another consequence was that
the first drop was not instilled into the eye or the
participants administered multiple eye drops. We
believe that if the bottle was tightly fitted to the device
the difficulties in handling and misalignment would be
eliminated and the success rate of EDG would be
improved.

The numbers of drops dispensed per application
were not different between the two groups. Although
the number of participants that instilled multiple drops
was almost double with the EDG, the participants
whose first drop missed the eye used more drops
when they were instilled with the traditional technique
(23 participants instilled 2–3 drops with EDG and 12
participants instilled 2–10 drops with the traditional
technique). This was probably because the EDG
forced the drops to fall close to, if not into, the eye
and the participants did not have to move the bottle
around to get eye drops into the eye.

The time to instill drops until the participants
believed one drop was successfully instilled into the
eye, was significantly longer using the EDG. If more
than one medication was prescribed, the difference
in time to instill all drops is expected to be even greater.
Therefore, if the device is not considerably more
effective than the traditional technique it is unlikely
that the participants will prefer to use the device.

Our results suggested that participants of female
sex and older age were less likely to succeed with the
traditional technique. Older age and more education
were found to be a predictor of failure with the EDG.
Older age and female sex was found to be associated
with failure of eye drop instillation in previous studies
[5, 14, 15]. By contrast, different results associated
with educational level was observed in a multicenter
study [3]. No association of instillation performance
was observed with visual impairment or severe visual
field loss, although an association has been suggested
in previous study [16]. Our contrasting results may
be the result of the greater number of participants
with good visual function participating in our study.

Conclusion

The limitations of our study included that we had
expected a higher success rate for the EDG technique,
which lead to decreased power and increased
possibility of a type II error (false negative) for the
study. The use of a single session VDO recording
at each step may not have reflected the actual
performance. Moreover, the presence of cameras and
investigators may have influenced the performance
(improved or worsened) of the participants.

In summary, the EDG is not more effective than
the traditional technique given careful instruction, in
terms of improving dispensing accuracy and decreasing
drops per application. Moreover the EDG increases
the time needed for eye drop administration. The
medications which are not a close fit with the EDG
may increase the difficultly of instillation using the
device. Older patients and those with more education
are less likely to succeed with the EDG. The results
also suggest that if participants received better
instructions, the experienced glaucoma patients can
improve eye drop instillation performance. Clinicians
should regularly check to determine whether their
patients need more advice regarding eye drop
instillation.

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