



ORIGINAL RESEARCH PAPER

Pharmacology

DROP SIZE OF COMMONLY USED ANTI-GLAUCOMA EYE DROPS

KEY WORDS: glaucoma, drop size.

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ABSTRACT
Introduction: Many factors affect the adherence to therapy in glaucoma patients. One of these factors being size of the drop administered. Big drop size not only leads to early exhaustion of medication but also causes unwanted adverse effects. This study was done to find out the drop size of commonly used anti-glaucoma eye drops. **Material and methods:** Four commonly used eye drops were included in the study: Timolol 0.5%, Brinzolamide 1%, Brimonidine 0.2% and Bimatoprost 0.03% eye drops. Three bottles of each drug was taken. The bottles were emptied in a 10 ml graduated cylinder drop by drop. The total volume and number of drops were noted, and drop size was calculated. **Result:** The drop size for Timolol, Brinzolamide, Brimonidine and Bimatoprost was 38.62 µl, 43.09 µl, 45.87 µl and 39.19 µl respectively. **Conclusion:** The drop size of anti-glaucoma medications can further be reduced and this may lead to improved patient compliance and reduce the adverse effects.

INTRODUCTION

Glaucoma, a chronic debilitating disease of eye, is leading cause of irreversible blindness.^{1,2} Glaucoma requires long term drug treatment which may lead to low adherence to the drug therapy.³

One of the factor responsible for low adherence to therapy is difficulty instilling eye drops.⁴ One factor related to eye drop bottle responsible for low compliance is early exhaustion of the bottle which according to some patients is because of either of the two reasons: more than one drop coming out while administering the eye drops or the size of the drop being too large.⁵ A problem with large drop size is that some medication overflows to the surrounding area or gets absorbed in systemic circulation and cause unwanted adverse effects.⁶ This may further decrease the adherence to therapy.

The drop size depends on various factors. Manufacturer controlled factors are design of bottle tip and properties of the contained solution. Patient related factors are angle at which the drops are administered.⁵ Force required to squeeze the bottle is another determinant of drop size. In fact many patients may struggle to extract a drop from the bottle.⁷

This study was undertaken to find out the drop size of commonly used anti-glaucoma medications in tertiary health care center in Andaman and Nicobar Islands.

MATERIAL AND METHODS

Four commonly used drugs used in glaucoma were included in the study: Timolol 0.5% eye drops, Brinzolamide 1% eye drops, Brimonidine 0.2% eye drops and Bimatoprost 0.03% eye drops. Three bottles each of the eye drops used in the study were taken.

To calculate the drop size, first the total drops and total volume of the bottle had to be measured. The method used for this measurement had to be accurate and reproducible.

The actual volume of each bottle was measured by emptying each bottle in a 10 ml graduated cylinder with 0.1 ml gradations.

While emptying, the bottles were held at approximately 45° and the drops were counted. The pressure was applied on the plastic body of the bottle with the index finger and the thumb. As soon as a drop fell in the cylinder, the pressure on the body of the bottle was released. The method used for counting the drops was tally marks method.

While noting the actual volume from the cylinder, the cylinder was kept on a flat surface at eye level and reading was noted from the center of the lower meniscus.

Like this the actual volume and number of drops were counted for each bottle. Now the drop size was calculated.

Drop size = actual volume measured / total number of drops counted

The same graduated cylinder was used to measure volume and count drops of all the bottles. After each measurement, the cylinder was washed with distilled water, dried with cloth and was left for sufficient time to air dry completely. It was made sure that no residual liquid was left attached to the walls of container.

RESULTS

Table 1

Eye drop name	Labeled volume (ml)	Actual volume (ml)	Total drops (avg)	Drop size (µl)
Timolol 0.5%	5	5.6	145	38.62
Brinzolamide 1%	5	5.3	123	43.09
Bimatoprost 0.03%	3	2.9	74	39.19
Brimonidine 0.2%	5	5	109	45.87

The mean actual volume of two drugs was more than the labeled volume. For one drugs, bimatoprost, it was marginally less than the labeled volume and for brimonidine was equal to the labeled volume.

Total drops for 5 ml bottles (timolol, brinzolamide and brimonidine) were 145, 123 and 109 respectively. For 3 ml bimatoprost bottle, there were 74 drops.

The drop size ranged from 38.62 µl to 45.87 µl. The change in

drop size for different bottles of the drugs was insignificant.

DISCUSSION

Glaucoma is a chronic disease and requires treatment for years. The eye drops taken by patients to treat this disease must not have any systemic side effects. Along with minimum side effects, patients also require that the cost of medication is not bothersome for them.

One important parameter of drug therapy for glaucoma with eye drops is the size of drop. If the drop size can be reduced from existing size without reducing the therapeutic effect, it will have both economic and therapeutic advantages for the patients. Smaller size drop means that more drops can be extracted from a bottle and wastage will also be reduced.

In a study done by German EJ et al, drop volume of multi-dose eye drop bottles varied significantly between drug manufacturers, ranging from 33.8 µl to 63.4 µl. The angle at which drops were instilled also determined the drop size, with angles less than 60° giving smaller drops.⁸ A study by Lederer CM et al shows the drop size of timolol 0.5% (5 ml bottle) was 30.8 µl. The average drop size for various bottles varied between 25.1 µl and 56.4 µl. The average drop size was 39.0 µl.⁹ In another study the drop size varied significantly among the studied formulations, ranging from 0.024 to 0.221 mL.¹⁰

The amount of volume that can be held in cul-de-sac (formed by cornea and conjunctiva with eyelid) is 7-9 µl. This volume can be transiently increased by pulling the lower eyelid down to accommodate 30 µl but reflex blinking reduces the volume to 10 ml which remains in contact with eye for few seconds.¹¹ The excess medication either overflows or gets drained by lacrimal apparatus and is absorbed. This excess medication will either show local effects or systemic effects. For example, the prostaglandin analog eye drops causes lengthening, thickening and hyperpigmentation of eyelashes and hyperpigmentation of surrounding skin when the excess medication overflows.⁷ Other example is of timolol associated cardiovascular, central nervous system, pulmonary and gastrointestinal tract side effects of β-blockage.¹²

A smaller drop volume can also produce the same therapeutic effect. This claim was supported with a study by Chrai et al. 10 µl of 2% epinephrine and 50 µl of 1% epinephrine when administered in rabbit eyes, produced same pupillary response. In the study it was suggested that drop size should be reduced to 5 or 10 µl for maximum efficiency.¹³

In a study it was shown that by reducing the drop size (by inserting a glass capillary tube into the dropper tip and by changing the physical properties of the formulation), each bottle lasted longer and the yearly cost of medication also reduces.¹⁴ In another study Propine 0.1% eye drops available as 15 ml bottle (actual volume 15.5 ml), contained 389 eye drops with a drop size of 39.8 µl and provided 13.9 weeks of therapy. If the same drop size can be reduced to 15 µl, then the same bottle can give 1033 drops and provide 36.9 weeks of therapy with 265% savings.⁹ In a study comparing angles of instillation (45 vs. 90), it was suggested that administration at 45° would result in up to \$1.93 savings per bottle compared to 90°.¹⁵

CONCLUSION

The drop size of commonly used eye drops for treatment of glaucoma in present study was between 38.62 µl and 45.87 µl. The manufacturing companies should lay more emphasis on producing bottles which produce smaller drop size as this will have economic as well as therapeutic advantage for the patients.

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