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CLINICAL STUDY

Force requirements in topical medicine use—the squeezability factor

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Abstract

Introduction **Patient compliance is essential to ensure efficacious treatment. The ease of topical drop delivery is of paramount importance. At least 50% of patients report difficulty in self-administration of topical ocular medicine. The two most frequently reported causes of difficulty include aiming the bottle and squeezing the bottle.**
Purpose **The aims of this study were to identify (I) the force required to deliver a single drop from a bottle (the squeezability factor), (II) are some bottle designs easier to use than others? (III) Do compliance aids reduce the finger strength required to deliver an eye drop?**
Method **We measured the force required to deliver a single drop from a variety of commonly used ophthalmic preparations. Force was slowly applied at the midpoint along the bottle until a drop fell from the tip. Compliance aids were also tested with this technique.**
Results **We report a wide variation in the force requirements needed to use topical medicines. Three of the four compliance aids tested increased force requirements but may have had other beneficial effects by altering the grip on the medicine bottle.**
Conclusion **This study highlights the large variability in force required to deliver a single drop using the ophthalmic preparations and compliance aids tested. We feel our results will be of interest and relevant to prescribing physicians and manufactures alike.**
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Introduction

Patient compliance is essential to ensure efficacious treatment. There are many psychological, educational, and social factors implicated in non-compliance. Non-compliance in glaucoma and ocular hypertension is common.[1–3] The insidious nature of disease progression and necessity for long-term therapy are key issues. In these conditions the ease of topical drop delivery is of paramount importance.

At least 50% of patients report difficulty in self-administration of topical ocular medicine.[4] The two most frequently reported causes of difficulty include aiming the bottle and squeezing the bottle.

Purpose

The aims of this study was to identify (I) the force required to deliver a single drop from a bottle (the Squeezability Factor), (II) are some bottle designs easier to use than others? (III) Do compliance aids reduce the finger strength required to deliver an eye drop?

Materials and methods

We measured the force required to deliver a single drop from a variety of commonly used ophthalmic preparations. Force was slowly applied at the midpoint along the bottle until a drop fell from the tip. The force was applied from either side of the bottle with the points of contact being 5 mm diameter (Figure 1). The force was measured using a static pressure transducer. (Weigh-tronix Force gauge, Salter Brecknell Ltd, Tonbridge, UK).

Five measurements were taken for each of the following criteria; full, $\frac{1}{2}$ empty, $\frac{1}{4}$ empty, held at 45° and held at 90°. No statistically significant differences were found between each of these measurements (except single dose medicines, reported separately). Therefore, the remaining bottles were subjected to a shortened testing regime of five measurements when full and held at 90° only.

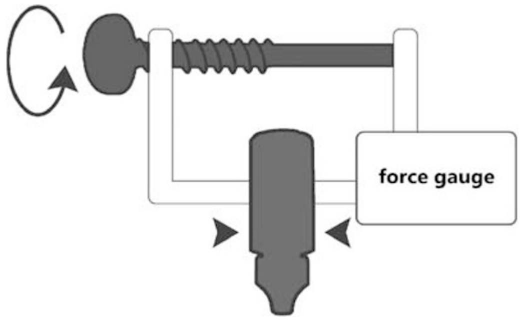

Figure 1 Experiment design.

All compatible compliance aids were identified and tested as above. All aids were tested with their appropriate medication. Any compliance aids, which did not have an action to press on the bottle were excluded.

Two bottles had a pump action built into the bottle and these required a modification to the testing technique. These bottles had force manually applied to the pump as the force was measured with the force gauge.

Means were calculated. These are reported with confidence intervals calculated for $P = 0.05$.

Results

The results for glaucoma medications are reported in Table 1. The results for all other medications are reported in Table 2. The differences between the force requirements of the first drop and subsequent drops in some single dose bottles are reported in Table 3. The results for compliance aids and the resultant change in force requirements are shown in Table 4.

Discussion

Our study highlights the large variability in force requirements between different topical medicines. Although we have not directly observed patient difficulty in using these medicines, we are aware of the impact this has on patient compliance. Winfield's study[4] found over half of the patients report some difficulty in using drops. A total of 21% of patients never administer their own eye drops and 13% could not expel a drop from a hypromellose bottle. Beckmans study[5] of medicine compliance in the elderly found that cognitive problems were the most common cause of difficulty. In all, 9.4% of patients were unable to read instructions on a medicine container and 14.6% had difficulty opening a plastic flip-top medicine bottle. A study of geriatric admissions by Atkin *et al*.[6] showed that over 40% of patients were unable to perform one or more tasks necessary to gain access to their own medications. More importantly they

Table 1 Force requirements in glaucoma medications

Medicine	*Force*
Xalacom (Pfizer, New York, NY, USA)	3.1 N ± 0.2
Xalatan (Pfizer)	3.8 N ± 0.2
Cosopt (Merck, Whitehouse Station, NJ, USA)	5.0 N ± 0.4
Trusopt (Merck)	7.6 N ± 0.6
Alphagan (Allergan, Irvine, CA, USA)	9.1 N ± 0.3
Travatan (Alcon, Hünenberg, Switzerland)	9.3 N ± 0.5
Lumigan (Allergan)[a]	9.9 N ± 1.4
Teoptic (Novartis, Basel, Switzerland)[a]	10.0 N ± 0.5
Betagan (Allergan)	11.1 N ± 0.8
Azopt (Alcon)	11.7 N ± 0.4
Ganfort (Allergan)	12.1 N ± 0.9
Azarga (Alcon)[a]	12.2 N ± 0.9
Betoptic (Alcon)[a]	13.8 N ± 1.0
Timoptol PF (MSD, Hoddesdon, UK)	15.4 N ± 0.9
Iopidine (Alcon)	17.2 N ± 0.8

[a]Shortened testing technique.

Table 2 Force requirements in all other medications

Medicine	*Force*
Mydrilate (Intrapharm Labs, Maidenhead, UK)[a]	5.5 N ± 0.9
Tears naturale (Alcon)[a]	6.1 N ± 0.8
Betnesol (UCB Pharma, Brussels, Belgium)[a]	6.3 N ± 0.7
Predsol (UCB Pharma)[a]	7.1 N ± 0.3
Oculotect (Novartis)[a]	7.2 N ± 1.5
Betnesol N (UCB Pharma)[a]	7.5 N ± 0.5
Maxidex (Alcon)[a]	7.5 N ± 0.9
Systane (Alcon)[a]	8.1 N ± 1.6
Voltarol PF (Novartis)[a]	8.3 N ± 2.0
Acular (Allergan)[a]	8.5 N ± 0.8
Predforte (Allergan)[a]	9.1 N ± 0.7
Hypromellose PF (Pharma Global, Chennai, India)	9.3 N ± 1.5
Celluvisc 0.5% (Allergan)[a]	10.0 N ± 1.5
Exocin (Allergan)[a]	10.0 N ± 0.9
Blink (Abbott Medical, Chicago, IL, USA)[a]	10.1 N ± 1.3
Hyabak (Spectrum thea pharma, Macclesfield, UK)[a]	10.5 N ± 0.5
Liquifilm tears (Allergan)[a]	10.8 N ± 0.6
Viscotears preservative free (Novartis)	11.0 N ± 1.3
FML (Allergan)[a]	11.2 N ± 1.4
Hypromellose 10 ml (Tubilux pharma, Rome, Italy)	11.6 N ± 0.4
Genticin (Amdipharm, St Helier, Jersey)[a]	13.7 N ± 1.1
Ciloxan (Alcon)[a]	15.0 N ± 2.0
Optive (Allergan)	15.4 N ± 1.3
Chloramphenical (Martindale Pharma, Romford, UK)[a]	17.6 N ± 1.4
Atropine minim (Bausch and Lomb, Madison, NJ, USA)[a]	23.8 N ± 1.0
Saline minim (Bausch and Lomb)	26.4 N ± 1.1
Artificial tear minim (Bausch and Lomb)	27.0 N ± 1.8
Hylo-forte (Scope Ophthalmics, Manchester, UK)[a,b]	36.4 N ± 4.0
Hylo-tear (Scope Ophthalmics)[a,b]	41.1 N ± 2.2

[a]Shortened testing technique.
[b]Modified technique with manual force application.

Table 3 Force requirements in first and subsequent drops in single dose unit bottles

Medicine	*First drop*	*Second drop*	*Third drop*	*Fourth drop*
Timoptol, 0.5%, preservative free (MSD)	11.3 N ± 1.0	14.5 N ± 1.4	16.5 N ± 1.9	17.1 N ± 1.3
Iopidine, 1%, single dose unit (Alcon)	12.9 N ± 0.5	17 N ± 0.4	19.3 N ± 0.4	19.4 N ± 2.0
Viscotears PF (Novartis)	9.7 N ± 1.4	10.7 N ± 0.5	11.2 N ± 1.7	12.3 N ± 1.7
Artificial tear minim (Bausch and Lomb)	23.9 N ± 1.8	26.1 N ± 1.3	29.5 N ± 2.6	28.3 N ± 1.3
Saline minim (Bausch and Lomb)	24.5N ± 0.5	25.9N ± 3.4	27.6N ± 0.1	27.7N ± 0.5

Table 4 Force requirements in compliance aids

Device	*Force*	*Change*
Xalaease and xalatan (Pfizer)	6.4 N ± 0.2	3.3 N +ve
Eyot (Geert Kerssies, Vianen, The Netherlands) and optive	21.6 N ± 1.3	6.2 N +ve
Opticare (Cameron Graham, Huddersfield, UK) and optive	17.1 N ± 1.0	1.7 N +ve
Opticare artho (Cameron Graham) and optive	1.9 N ± 0.1	13.5 N −ve

showed that poor medicine compliance was associated with poorer cognitive function and poorer visual acuity.

Mathiowetz *et al.*[7] carried out a study of over 600 health volunteer's grip strength and their data is accepted as the normative range. They found that of the three types of grip that are used in day to day activities pinch grip (between finger and thumb) had lower force generating capacity than key grip (between thumb and clench fingers), which had lower than palmar grip (between palm and fingers). In addition they found that increasing age, female sex and non-dominant hand were associated with lower strengths. Pinch grip, the force generated when squeezing a dropper bottle, in normal individuals ranges from 17.8 N to 160 N.[5] As expected, the majority of healthy volunteers in that study would produce enough pinch force to use the bottles we have tested. However, the range of finger strengths does fall below some of the force requirements of the bottles we tested. The implications of this being some patients would be unable to use these medicines.

The limitations of making comparisons between our study and normative finger strengths are the exclusion of anyone with musculoskeletal or neurological disease. Rheumatoid arthritis,[8] osteoarthritis,[9] carpal tunnel disease[10] and stroke[11] have all been reported as having lower finger strengths. In addition to neurological disease causing lower strengths these can also cause deficits in control and direction of force application,[11] which are also required to co-ordinate functional tasks such as squeezing a bottle.

Other limiting factors in the instillation of an eye drop is the ability to lift a hand to the face, maintain aim, coordination and fine motor control as the bottle is directed close to the eye. These factors in themselves are barriers to compliance. Doing these things at the same time as generating a pinch grip may have an effect on the maximum force generating capacity of the fingers. Although we know that poorer visual acuity is associated with inability to read instructions and open medicines,[5] aiming a medicine bottle toward the eye is a task that requires a greater level of vision.

The bottles tested in our study came in a variety of designs. Some bottles had flexible areas or a pump action to facilitate the action of dispensing a drop. Other factors which influence design is the amount of medicine contained within the bottle. This is influenced by degradability of the medicine and whether this contains preservatives. In recent years there has been a move to produce preservative free medicines, which are available as small single dose units. These single dose units in general have higher force requirements. Factors which were thought to influence the force requirements were the rigidity of the plastic of the bottle, the ratio of bottle height to width, viscosity of the medication and length of nib. The diameter of the opening of the bottle and the surface tension of the medication also has an effect by influencing how big the drop has to be before it falls.

Three out of the four compliance aids tested increased the force requirement. However, this individual measurement can be misleading. The xalaease device exploits the ability of the hand to produce a higher force with a key grip hold on the device. Whereas the opticare and eyot can either be held with force produced with a key grip or a palmar grip.

Although we highlight the difficulty some patients encounter using drops, it is important to remember the consequences of failure. Medicine which is difficult to administer will clearly result in poor compliance. The most important adverse outcome of poor compliance is disease progression, which could lead to increased rates of blind registration. This may have important social and economic effects. Patients are more likely to struggle with activities of daily living, which will lead to the need for nursing and home care as well as a poorer quality of life.

Conclusions

This study highlights the large variability in force required to deliver a single drop using the ophthalmic preparations and compliance aids tested. We feel our results will be of interest and relevant to prescribing physicians and manufactures alike.

Conflict of interest

The authors declare no conflict of interest.

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