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Mydriatics: Drop the dose

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Mydriatics: Drop the dose

Abstract

This study investigated the difference in pupillary dilation between a normal dose and a substandard dose of a topical ophthalmic mydriatic agent, the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% (Paremyd™ solution). The manufacturer's recommended dosage is 1-2 drops per eye. A typical opthalmic drop ranges in volume from 30 - 75. We hypothesized that a small, substandard dose of 10 will create a pupillary dilation clinically and statistically equivalent to that of the larger, standard dose of 30 in part due to the reflex tear response and increased lacrimal drainage. Our research found that the smaller dose of the mydriatic does indeed provide a clinically and statistically equivalent pupillary dilation to the larger dose. Clinically, the use of a reduced dose of a topical mydriatic will reduce the inherent risks and side effects to the patient (especially to the high-risk patient), while still allowing the eye care practitioner ample pupillary dilation to provide a quality dilated fundus examination.

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MYDRIATICS: DROP THE DOSE

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A thesis submitted to the faculty of the
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BIOGRAPHIES:

Jerry A. Hendricks:
Born and raised in Colorado Springs, Colorado, Jerry attended both the University of Colorado (UCCS) and Colorado State University (CSU) for his undergraduate studies. He graduated from CSU in 1989 with a Bachelor of Science degree in Physical Science, with minors in Physics and Mathematics. Upon graduation, Jerry worked as a systems engineer for an aerospace firm for five years. He was married in 1992 to Kelley Saville. He entered the optometry program at Pacific University in 1994, and will receive the Doctorate of Optometry degree in 1998. Notable achievements and activities in graduate school were: Student Optometric Association (SOA) Executive Board, SOA Speaker Series Chairman, Class President, Dean's Council, MS Walk PUCO Team Captain, VOSH International, Amigos Eye Care, and Pacific University Standards & Appeals Board. Future plans include owning an optometric practice in Colorado, raising a family, and traveling the globe.

Tracy E. Dodd:
Born and raised in the Pacific Northwest, Tracy attended Pacific University, Forest Grove, Oregon for her undergraduate as well as her optometric education. Tracy has earned a Bachelor of Arts degree in French (1993) and Doctor of Optometry degree (1997). A few of the most memorable activities and organizations in which Tracy has participated include: Amigos Eye Care, Campus Crusade for Christ, Pacific Study Abroad Program and Fellowship of Christian Optometrists. Tracy has been awarded the King County Optometric Association Scholarship, the Western Interstate Commission for Higher Education Grant, the Optometry Deans Award Scholarship, and the honor of being a 1996 Who's Who Among Students in American Universities and Colleges. Future goals include practicing with the Indian Health Service and serving the underserved both overseas and at home.

Craig F. Rouse:
Born in Rivas, Nicaragua, Centro America, Craig's first language is Spanish. He resided and attended school in Nicaragua until the age of twelve. He and his family later moved to Long Beach, California. Craig attended the University of Montana for his undergraduate endeavors and earned a Bachelor of Science degree in secondary education. Also while attending college Craig played on the varsity basketball team. His professional education was attained at Pacific University College of Optometry earning a Doctor of Optometry degree in May of 1997. Future goals include practicing full-scope optometry while providing care to an under-served population.

ABSTRACT:

This study investigated the difference in pupillary dilation between a normal dose and a substandard dose of a topical ophthalmic mydriatic agent, the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% (Paremyd™ solution). The manufacturer's recommended dosage is 1-2 drops per eye. A typical opthalmic drop ranges in volume from 30 - 75 μL. We hypothesized that a small, substandard dose of 10 μL will create a pupillary dilation clinically and statistically equivalent to that of the larger, standard dose of 30 μL, in part due to the reflex tear response and increased lacrimal drainage. Our research found that the smaller dose of the mydriatic does indeed provide a clinically and statistically equivalent pupillary dilation to the larger dose. Clinically, the use of a reduced dose of a topical mydriatic will reduce the inherent risks and side effects to the patient (especially to the high-risk patient), while still allowing the eye care practitioner ample pupillary dilation to provide a quality dilated fundus examination.

KEY WORDS:

mydriasis; mydriatic; dilation; drop size; dose; pupil; eyedropper; Paremyd; hydroxyamphetamine hydrobromide; tropicamide

INTRODUCTION:

Routine pupillary dilation has become a standard procedure in optometric practice, and is necessary for a thorough evaluation of the posterior segment of the eye.[1-6] Topical mydriatic medications play a critical role in any eye care practitioner's practice. Several risks and side effects must be considered when using these medications. Systemic absorption risks may include the following: increased ocular pressure, dryness of mouth, blurred vision, CNS disturbances, sweating, tachycardia, headache, hypertension, myocardial infarction, allergic reactions, nausea, vomiting, palor, subarachnoid hemorrhage, cardiac arrhythmias, muscle rigidity, gastric secretory dysfunction, necrotizing entercolitis, and death.[5,7-11] Patient discomfort (e.g., transient stinging and photophobia) resulting from the use of these drops is a factor as well.[8,12] One way of decreasing these risks and side effects is to decrease the drop volume instilled into the patients' eyes.

Normal fluid holding capacity of the tear film is approximately 7 to 10 μL with a maximum expandable volume of 30 μL before blinking.[13-16] Any excess fluid (tears and/or drops) is quickly blinked out onto the cheek or into the nasolacrimal drainage system to restore the tears to its normal volume. Systemic absorption takes place via the vascularized mucous membrane of the nasolacrimal system. A smaller drop volume would reduce the amount of fluid forced into the nasolacrimal ducts, thereby reducing the systemic uptake of medications into the circulatory system. This systemic uptake reduction inherently reduces the possibility and magnitude of adverse systemic side effects and toxicities.

Another aspect of concern is the reflex tearing associated with instillation of ophthalmic drops. Irritating or hypertonic solutions instilled into the eye result in a more rapid tear dilution (due to hypersecretion of tears) and thus a lower concentration and quantity of drug remains in the tear film.[14] A smaller drop size will potentially produce less ocular irritation to the patient, thus resulting in decreased reflex tearing, less lacrimal washout, increased drug-corneal contact time, and improved patient comfort.

A number of researchers have previously investigated the effects of reducing mydriatic drop volumes. Gray found that equivalent mydriasis was achieved with 5 μL of tropicamide 1% as compared to a 26 μL dose.[12] Brown *et al.* found that a better dilation was achieved with an 8 μL drop of phenylephrine 10% than with a 32 μL drop of phenylephrine hydrochloride 2.5%.[10] Lynch *et al.* showed that 8 μL of phenylephrine 2.5% dilates as well as 30 μL, while systemic absorption dropped by 50%.[9] Wheatcroft *et al.* found that 5 μL of cyclopentolate 0.5% and phenylephrine 2.5% produced equivalent dilation in premature infants compared to a 26 μL dose.[17] Craig and Griffiths demonstrated a 10 μL drop of phenylephrine 10% dilates just as well as a standard 30 μL drop.[11]

Our study investigated the difference in pupillary dilation between a 30 μL dose (a typical mydriatic drop volume)[14,15,18] and a 10 μL dose of a common mydriatic agent. Note that some researchers state that standard commercial eyedroppers produce drops ranging in volume from 50-75 μL.[13,15,19,20] We chose the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% (Paremyd) as our test mydriatic due to its clinical efficacy and convenience of a single-bottle administration system. Hydroxyamphetamine is an indirect-acting sympathomimetic agent which

causes the release of norepinephrine from the intact post-ganglionic adrenergic nerve terminals, which in turn stimulate the dilator, producing mydriasis. Tropicamide is a parasympatholytic agent which blocks the sphincter receptor sites, thus producing mydriasis. Because these two agents act on different effector sites, their combined application produces an additive mydriatic effect greater than either of the singular effects.[8] As stated in the *PDR for Ophthalmology*, the recommended dosage of Paremyd for routine pupillary dilation is one to two drops per eye; it also states that the onset of action with Paremyd occurs within 15 minutes, followed by maximum effect within one hour.[8]

As shown in Table 1, due to the variation in drop size and number of drops administered, the amount of drug actually delivered for a routine bilateral dilation can be quite variable. This is a considerable difference in drug dosage, and is a critical issue when considering systemic absorption.

Table 1: Potential Drug Quantities Delivered for Bilateral Dilation

Dosage (Paremyd)	Hydroxyamphetamine Hydrobromide	Tropicamide
One 10 μL drop X 2 eyes	0.2 mg	0.05 mg
One 30 μL drop X 2 eyes	0.6 mg	0.15 mg
Two 75 μL drops X 2 eyes	3.0 mg	0.75 mg

A dilated pupil of at least 7 mm diameter is sufficient to permit a thorough examination of the fundus, including the peripheral retina.[21] Therefore, for the purpose of this experiment, we have defined a "clinically significant

pupillary dilation" as one which achieves at least a 7 mm diameter within 30 minutes post-administration.

We hypothesized that a substandard dose of a topical mydriatic agent would create a pupillary dilation clinically and statistically equivalent to that of the larger, standard dose. Clinically, the use of a reduced dose of a topical mydriatic will reduce the inherent risks and side effects to the patient while still providing a clinically significant pupillary dilation.

METHODS:

Subjects:

The study compared the mydriatic response of 24 subjects (15 females, 9 males). Of the selected subject pool, 8 had light-colored irides, 10 had medium-colored irides, and 6 had dark irides (these findings based upon subjective determination by the researchers). The criterion for selection of the subject pool was as follows:

- Age: 19 - 50 years old (mean = 27 years, S.D. = 3.8 years);
- No known allergies to Paremyd (hydroxyamphetamine hydrobromide 1% + tropicamide 0.25%)
- No history of anterior segment eye disease which permanently affected the actions of the iris or ciliary body;
- No history of hypertension, hyperthyroidism, diabetes, or cardiac disease;
- No history of retinal disease;
- No history of anisocoria, Horner's Syndrome, Adie's Pupil, Adie's Syndrome, Marcus Gunn afferent pupillary defect, third nerve palsy, or other pupillary disorder;
- Not currently taking any drugs which can cause mydriasis, including anticholinergics, CNS stimulants (amphetamines, methylphenidate, cocaine), CNS depressants (barbiturates, anti-anxiety agents), antihistamines (including over-the-counter), or phenothiazines;
- Not currently taking any drugs which can cause miosis, including opiates, heroin, codeine, morphine, anticholiesterates (neostigmine);
- No difficulties in maintaining a steady gaze;
- No current anisocoria of greater than 1 mm difference (under illuminance of 90 ± 5 lux)
- No history of any neurological disorders or seizures;

- No history of glaucoma (including angle-closure glaucoma);
- No history of subluxated crystalline lens;
- No history of permanent eye damage due to trauma, disease, or congenital conditions;
- No history of eye surgery;
- Not currently pregnant or nursing;
- Non-heterochromia iridium;
- Anterior chamber angles of grade 3 or 4, as determined by the van Herick slit-lamp technique;[22]
- Current IOP's of > 8 and < 21 mm Hg OU (as determined by non-contact tonometry);
- Habitual distance Snellen visual acuities of 20/40 or better (OD, OS).

Apparatus:

Pupil measurements were obtained using an Essilor corneal reflection digital pupillometer. Illiminance levels were measured using a Tektronix J-16 photometer. An adjustable Oxford 3000 micropipette (capacity: 10-50 μL) with sterile, disposable tips was used to accurately administer the topical ophthalmic pharmaceutical agent. The mydriatic agent used was the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% (Allergan's Paremyd™ Solution).

Preliminary Examination Procedures:

Every subject was asked to complete an informed consent form and a qualification questionnaire before any testing occurred. Each testing session started with a preliminary examination consisting of distance visual acuities (habitual), non-contact tonometry, pupils evaluation, and a

slit-lamp examination (including van Herick assessment of the medial and lateral anterior chamber angles). If the subject was a contact lens wearer, s/he would be instructed to remove their lenses immediately following the determination of their habitual visual acuities. The sessions were held in an examination lane with controlled lighting conditions; the room illuminance levels were maintained at 90 ± 5 lux,[23] using the light meter and a rheostat as control devices.

Testing Sessions:

Before the mydriatic solution was administered, the subject's baseline pupil diameters was measured using the pupillometer. To accomplish this, the subject would be instructed to look at the target inside the pupillometer. The researcher would line up the measuring line inside the pupillometer with the temporal limit of the right pupil margin, another researcher would read and document the digital readout from the meter (in millimeters). Next, without having moved the pupillometer since the original reading (i.e., it was still on the subject's face), the first researcher would realign the mark with the nasal limit of the right pupil margin, and again the data would be read and documented. The difference between the two readings was recorded as the pupil diameter in millimeters. This process was repeated for the left eye.

Next, the subject would be instructed to tilt their head back slightly and to look up and back. A researcher would gently pull the lower right lid out slightly so that a trough is formed by the inferior cul-de-sac. The researcher would administer 30 μL of the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% to the exposed cul-de-sac via the micropipette. Another researcher would start the

stopwatch at the moment the right eye was administered the drop. The subject was instructed to keep their eyes closed for one minute and the researcher would occlude the subject's upper and lower right puncta by gently pinching the medial canthal area during the course of that minute (thereby minimizing lacrimal drainage). After one minute, 10 μL of the mydriatic solution would be administered to the left eye, the subject was instructed to keep both eyes closed for an additional two minutes, and the researcher would occlude the subject's upper and lower left puncta in the same manner (for the first minute). Note that the right eyes (herein referred to as the "30 μL eyes") always received the 30 μL drops, whereas the left eyes (herein referred to as the "10 μL eyes") always received the 10 μL drops.

After 6 minutes (following application of the mydriatic to the right eye), the right pupil diameter was measured and recorded following the same methods used previously. One minute later (6 minutes post-left eye mydriatic instillation), the left pupil diameter was measured and recorded. Subsequent pupil diameter measurements were taken and recorded again every 6 minutes up to the 30 minute mark, for a total of five post-instillation recordings per eye (i.e., at 6, 12, 18, 24, and 30 minutes post-instillation per eye).

RESULTS:

Four different methods of analysis were used:

- whether or not the dilation was "clinically significant",
- maximum pupil diameter increase ("*Δ Diameter*"),
- maximum pupil area increase ("*Δ Area*"),
- time to maximum dilation.

Note that all measurements were taken within a 30 minute time frame.

Reference Table 2.

Table 2: Summary of Dilation Responses

Criterion (within 30 minutes)	**10 μL eye (OS)**	**30 μL eye (OD)**
% of eyes tested achieving mydriasis of ≥7 mm diameter	100%	100%
Δ ***Diameter*** (mm)	Mean = 1.81 S.D. = 0.94	Mean = 1.94 S.D. = 0.79
Δ ***Area*** (mm^2)	Mean = 19.48 S.D. = 9.76	Mean = 20.84 S.D. = 7.71
Time to maximum dilation (minutes)	Mean = 24.00 S.D. = 7.30	Mean = 23.25 S.D. = 6.46

Within the 30 minute time frame, all of our subjects achieved a dilation of at least a 7 mm diameter in <u>both</u> the 10 μL eyes and the 30 μL eyes. Therefore, based upon the pre-established criterion defining a "clinically significant dilation" as ≥7 mm overall pupil diameter, 100% of all eyes tested successfully obtained a clinically significant dilation within 30 minutes.

The mean *Δ Diameter* for the 30 μL eyes was 1.94 mm, whereas the mean *Δ Diameter* for the 10 μL eyes was 1.81 mm. Probability was 35.4%, showing there is no statistically significant difference between these means (using a repeated measures two-tailed t-test with rejection critical value of 5%).

Assuming that the pupils measures were perfectly circular before and after dilation, the mean *Δ Area* for the 30 μL eyes was 20.84 mm^2, whereas the mean *Δ Area* for the 10 μL eyes was 19.48 mm^2. Probability was 36.9%, showing there is no statistically significant difference between these means (using a repeated measures two-tailed t-test with rejection critical value of 5%).

Mean time to maximum dilation within 30 minutes for the 30 μL eyes was 23.25 minutes, whereas the mean time for the 10 μL eyes was 24.00 minutes. Once again, these means show no statistically significant difference.

As shown in Table 3, there was little variation between the 10 μL and the 30 μL eyes within any given irides darkness category (i.e., light, medium, dark) for either Δ Diameter, Δ Area, or time to maximum dilation. However, there was (dosage independent) variation in Δ Diameter and Δ Area due to irides darkness, presumably due to pigment absorption of the drug.

Table 3: Means of Dilation Responses by Irides Darkness

	Irides Darkness	10 μL eye (OS)	30 μL eye (OD)
Δ Diameter (mm)	Overall	Mean=1.81 S.D. = 0.94	Mean=1.94 S.D. = 0.79
	Light	Mean=2.19 S.D. = 0.92	Mean=2.38 S.D. = 0.83
	Medium	Mean=1.70 S.D. = 1.01	Mean=1.85 S.D. = 0.71
	Dark	Mean=1.50 S.D. = 0.84	Mean=1.50 S.D. = 0.63
Δ Area (mm^2)	Overall	Mean=19.48 S.D. = 9.76	Mean=20.84 S.D. = 7.71
	Light	Mean=22.46 S.D. = 9.15	Mean=24.45 S.D. = 8.21
	Medium	Mean=19.40 S.D. = 10.99	Mean=20.91 S.D. = 7.08
	Dark	Mean=15.68 S.D. = 8.48	Mean=15.91 S.D. = 6.21
Time to Maximum Dilation (minutes)	Overall	Mean=24.00 S.D. = 7.30	Mean=23.25 S.D. = 6.46
	Light	Mean=26.25 S.D. = 5.50	Mean=24.00 S.D. = 5.55
	Medium	Mean=21.60 S.D. = 8.10	Mean=24.00 S.D. = 6.32
	Dark	Mean=25.00 S.D. = 7.97	Mean=21.00 S.D. = 8.27

DISCUSSION:

We hypothesized that a substandard dose of a topical mydriatic agent would create a pupillary dilation equivalent to that of a larger, standard-sized dose. This study found no statistically significant difference in pupillary dilation when a topically-administered quantity of the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% was administered in a 10 μL versus a 30 μL dosage. When comparing the increase in mean pupil area, the increase in mean pupil diameter, and mean time to maximum dilation within 30 minutes, we found no statistically significant difference between a 10 μL and a 30 μL dosage of the mydriatic.

It is clear that the goal of dilation should be a rapid and maximally-dilated pupil.[24] Minimally-dilated pupils pose a risk of pupillary-block glaucoma that is not present with maximally-dilated pupils.[5] A pupillary diameter of 7 mm is usually adequate to permit thorough examination of the fundus, including the peripheral retina.[21] Our research found that a 10 μL drop of mydriatic did indeed provide a pupillary dilation of ≥7 mm diameter for 100% of our subjects within 30 minutes, thus achieving a clinically significant dilation in all eyes tested. Our results indicate that a properly-administered 10 μL dose of the combination of hydroxyamphetamine hydrobromide 1% and tropicamide 0.25% is equally efficacious for pupillary dilation when compared to a 30 μL dose.

It should be noted that although we only recorded and analyzed the time to maximum dilation within the 30 minute time frame, it is possible, and even likely, that an even greater pupillary dilation was achieved beyond the 30 minute window. The *PDR for Ophthalmology* states that maximum dilation

will be achieved within 60 minutes with Paremyd.[8] However, we believe it is often unrealistic for the patient and doctor to wait longer than 30 minutes for dilation to occur before proceeding with a dilated fundus examination. Therefore, we believe the data we obtained in the 30 minutes post-drug instillation should be considered to be more clinically applicable than if we had used a one hour time frame.

The human lacrimal fluid volume in the lower eyelid sac is normally between 7 and 10 μL, and can expand momentarily and variably to 30 μL without overflow.[13-16] Therefore, a normal tear volume of 7-10 μL plus a single 30 μL drop already exceeds holding capacity. Two drops instilled concurrently produce a total volume greater than 67 μL, severely exceeding maximum capacity, thus producing spillage and increased lacrimal drainage.

The lacrimal fluid is itself normally being turned over at a rate estimated to be 16% per minute.[16] Blinking will considerably increase the rate at which the tear volume (i.e., tears plus eye drops) is drained into the nasolacrimal apparatus. Topical application to the lower cul-de-sac, accompanied with nasolacrimal occlusion, is the standard method of administering eye drops in order to increase bioavailability and therapeutic index; thus, this method was utilized for this study.[22] Zimmerman *et al.* have found that nasolacrimal occlusion in conjunction with post-instillation eyelid closure reduces systemic absorption of the drug by more than 60%.[25]

Once instilled, topical ocular pharmaceutical agents gain access to the nasolacrimal drainage system; the loss of drug decreases topical efficacy and increases the potential for systemic absorption. In addition, drug dilution and loss will increase as drop size increases because instillation of

a greater drop volume causes an increased potential for ocular irritation and reflex blinking, eliciting reflex lacrimation which dilutes the drug and increases the drainage rate to the nasolacrimal canal. An excess of tear/drug volume beyond maximum holding capacity of the lower eyelid sac will also cause increased nasolacrimal drainage and spillage onto the cheeks and eyelashes.[14,19] We did not measure systemic absorption, but it is clear that the potential for systemic toxicity may be increased by the large size of commercial eye drops.[9,10,13,19,26] A small eye drop volume improves bioavailability in many ways;[13,14,19] it provokes less reflex tearing, causing less drug dilution on contact with lacrimal fluid. Reduced tear volume also decreases drug loss through lacrimal drainage. Therefore, eye drops administered in smaller volumes should achieve a greater tear-film concentration and longer contact time, thus improving corneal penetration.

Application of multiple drops at one time is not recommended. While one may initially believe that ocular bioavailability is increased, in reality over-capacity spillage and lacrimal washout occur, resulting in increased lacrimal drainage, increased systemic uptake, and possible side effects or toxicity.[15] If two drugs must be given, it is recommended that they be instilled at least five minutes apart so that the first drop can be sufficiently diluted and absorbed prior to application of the second drop.[13,27]

It should be noted that we are not recommending mydriatic drops be produced in higher concentrations; rather, we are suggesting drug manufacturers make the mydriatics available in eyedroppers which produce lower volume droplets. Theoretically, the therapeutic index of most topical drugs may be improved by increasing drug concentration and decreasing volume.[14] To maintain patient safety, however, this approach depends on a

delivery system capable of insuring that only a single drop is delivered per dose; this is currently not possible with commonly-available eyedroppers. Ophthalmic solutions and suspensions are generally administered by means of a squeeze bottle with an attached dropper tip, and one of the criteria the drop size is influenced by is the outer diameter of this dropper tip surface. Several eyedroppers with small outer tip diameters have been proposed which produce drops smaller than 30 µl.[11,12,20,28,29] In addition to tip diameter, drop size is influenced by the density and the dynamic surface tension of the solution. Therefore, no standard dropper can be used for all solutions or suspensions.[14] However, Hurst *et al.* claim that dropping angle, drug type, and drop number were the only factors influencing drop size; their study showed that a reduction in dropping angle of the eyedropper to less than 60° from the horizontal provided a smaller drop volume.[30]

Without a single-drop delivery system, safety considerations may limit the application of the high concentration/small volume approach. For instance, delivering a topical mydriatic or cycloplegic drug as a highly concentrated, small volume droplet may improve the therapeutic index if only a single drop is administered. However, the practitioner or assistant may inadvertently instill multiple drops with each delivery, and a highly concentrated drug could lead to an increased risk of systemic toxicity.

It is often believed that eyes with less pigmentation (i.e., lighter irides) more readily respond to mydriatics as compared to eyes with more pigmentation.[31-33] Opposing that viewpoint, other research claims equal mydriasis occurs between light and dark irides.[34-38] Our research shows the eyes with lighter colored irides generally achieved an overall larger dilation as compared to those with darker irides (dosage independent); but within any

given irides darkness category, there is no significant statistical difference between the dilation of the 10 μL eyes and the 30 μL eyes. This indicates that a smaller mydriatic droplet is equally effective as a larger drop regardless of iris color. (However, it should be noted that our data using irides darkness as an analysis criterion has limited foundation due to the small population size tested within each darkness category).

One other expected benefit to the patient for the utilization of smaller ophthalmic droplets is greater comfort during instillation. Many of our subjects were not aware of the 10 μL droplet being instilled, yet they usually felt the larger 30 μL drop. This too was noted by other researches during similar investigations.[11,12]

This and other studies[9-12,17,18,26] make it clear and plausible that mydriatic drop volumes well below those currently utilized by standard delivery systems can and should be used to dilate the pupils with adequate clinical efficacy in a timely manner. This, in turn, will decrease systemic absorption, thereby reducing the inherent risks of mydriatic-induced side effects.

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