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Description
This study was designed to evaluate the mydriatic effects of patients being dilated under differing illumination conditions. Twenty subjects, 10 females and 10 males, had their pupils dilated under darkened conditions and under normal illumination to determine if there would be a difference in the rate of mydriasis or overall pupil size at the point of maximum dilation. Iris colour and gender were separately evaluated factors in dilation results. Subjects were dilated using one drop each of 1% tetracaine, 2.5% phenylephrine HCl and 1% tropicamide. Pupil diameter was periodically measured using a Cogan pupillometer starting 6 minutes after drop instillation. Measurements with the pupillometer were taken at two-minute intervals throughout the 3 a-minute test period. The final measurement 33 minutes after instillation of the dilating drops was taken with a biomicroscope reticule; both horizontal and vertical diameters were measured. No Significant differences were seen between gender, iris colour and illumination type on the rate of maximum mydriasis. However, the relative pupil area was significantly greater following dilation under normal illumination conditions.

Disciplines
Optometry

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The effect of illumination on the time to, and pupil area of, maximum mydriasis

Rachel I Rushforth, Rodney I White, Kathleen R Solum, Hannu RV Laukkanen

Abstract: This study was designed to evaluate the mydriatic effects of patients being dilated under differing illumination conditions. Twenty subjects, 10 females and 10 males, had their pupils dilated under darkened conditions and under normal illumination to determine if there would be a difference in the rate of mydriasis or overall pupil size at the point of maximum dilation. Iris colour and gender were separately evaluated factors in dilation results. Subjects were dilated using one drop each of 1% tetracaine, 2.5% phenylephrine HCl and 1% tropicamide. Pupil diameter was periodically measured using a Cogan pupillometer starting 6 minutes after drop instillation. Measurements with the pupillometer were taken at two-minute intervals throughout the 30-minute test period. The final measurement 33 minutes after instillation of the dilating drops was taken with a biomicroscope reticle; both horizontal and vertical diameters were measured. No significant differences were seen between gender, iris colour and illumination type on the rate of maximum mydriasis. However, the relative pupil area was significantly greater following dilation under normal illumination conditions.

Résumé : Cette étude avait pour but d'évaluer les effets mydriatiques de différentes conditions d'éclairement de l'oeil. Vingt sujets, c'est-à-dire dix femmes et dix hommes, ont été soumis à des conditions d'assombrissement et d'éclairement normal afin de déterminer si le taux de dilatation pupillaire ou la taille globale des pupilles serait différente à leur dilatation maximale. On a évalué séparément la couleur de l'iris et le sexe des sujets dans les résultats. On a instillé aux sujets une goutte chacun de tétacaine 1%, de phényléphrine HCl 2.5% et de tropicamide 1% et mesuré à intervalles périodiques le diamètre des pupilles à l'aide d'un pupillomètre de Cogan, 6 minutes après l'instillation. Les relevés au pupillomètre ont eu lieu toutes les deux minutes pendant la période d'essai de 30 minutes. La dernière mesure, survenue 33 minutes après l'instillation des gouttes mydriatiques, a été faite à l'aide d'un biomicroscope à réticule, permettant ainsi de mesurer les diamètres horizontal et vertical. On n'a dégagé aucun écart pertinent du taux de dilatation pupillaire maximale selon le sexe, la couleur de l'iris ou le type d'éclairement. Toutefois, la superficie de la pupille était beaucoup plus grande après dilatation que sous un éclairage normal.

You have just finished placing mydriatic agents in the eyes of your patient: Do you now seat them in a dark or a well-lit room? Several studies have explored how drop size, patient age or iris colour affects dilation rate and final pupil size. However, few studies have considered the effect of room illumination upon pharmaceutical-induced mydriasis.

Despite patient inconvenience and increased examination time, dilated fundus exams are becoming more routine in today's optometric practice. To reach an acceptable mydriastic state of optimal retinal viewing requires a 20- to 30-minute wait after the instillation of the mydriatic drops; yet, the procedure for a thorough evaluation of the retina may only require a few minutes. In today's fast-paced world, time spent waiting for the patient to dilate is a valuable commodity to both the patient and the optometrist. Therefore, any factor that could provide a faster or more complete mydriasis should be investigated, especially an option as simple as placing the patient in either a light or a dark environment while the drug takes effect.

Several pharmaceuticals, in varying concentrations, are available for use in dilating patients. The clinical drug combination of choice continues to be 2.5% phenylephrine HCl and 1% tropicamide. For this reason, we chose to use this drug combination to evaluate the effect of illumination on the dilation process.

Drug characteristics of phenylephrine HCl

 Phenylephrine is a direct-acting alpha-adrenergic agent that provides mydriasis without cycloplegic effects. It may also be used as an ocular decongestant or to break or prevent posterior synechia in uveitis. Phenylephrine 2.5% is the recommended concentration for routine fundus examinations. At this concentration, maximum mydriasis should occur 15 to 60 minutes post-drop. Recovery to pre-drop pupil size will most likely occur in 3 hours.

Clinically, topical use of 2.5% phenylephrine in conjunction with punctal occlusion induces few serious side effects, but there may be mild ocular reactions. These mild ocular reactions include transient stinging on instillation, irritation, headache, brow ache, blurred vision, transient epithelial keratitis, allergic reactions and reactive hyperemia. Repeated doses of phenylephrine may cause rebound miosis or reduce the mydriatic effect needed for ophthalmic surgery. Therefore, excessive or repeated use with elderly patients should be avoided.
Drug characteristics of tropicamide

Tropicamide is an anticholinergic agent that is primarily used to dilate the pupil for fundus examinations and to prevent posterior synechiae during uveitis or trauma. The cycloplegic effect of tropicamide is also beneficial in determining refractive errors when a relaxed accommodative system is needed. Although it is classified as a cycloplegic agent, tropicamide is considered the drug of choice for mydriasis due to its quick onset and short duration of action. As a mydriatic agent, tropicamide provides maximum dilation 20 to 40 minutes post-drop. The pupil usually recovers to the pre-dilation state within 6 hours of instillation.

When tropicamide is used in conjunction with punctal occlusion, systemic side effects are lessened. However, the patient should be educated about the potential for ocular and systemic effects. Ocular reactions may include increased punctate keratitis and possible allergic reactions. Systemic side effects include CNS disturbances, flushing and dryness of the mouth and skin, headache, a rapid irregular pulse, irritability, bladder distention, hallucinations, drowsiness, decreased gastrointestinal motility, coma, medullary paralysis and, in very rare instances, death.

Cycloplegic mydriatics should not be used with patients who are pregnant or hypersensitive to the formulation, or who have posterior synechiae, primary open-angle glaucoma or a potential for angle-closure glaucoma.

Pharmacological mechanism of mydriasis

There are two separately innervated muscles involved in pupil mydriasis: the iris sphincter and the iris dilator. Tropicamide blocks cholinergic stimulation to the sphincter muscle of the iris and the ciliary body causing both pupil dilation and accommodative paralysis. In contrast, phenylephrine acts as an alpha receptor agonist, causing contraction of the iris dilator muscle acting on the radial fibres. Other nonmydriatic effects that occur simultaneously with the use of phenylephrine include constriction of the arteriole smooth muscle (causing "blanching" of the conjunctiva) and the widening of the palpebral fissure by stimulation of Mueller's muscle. The combined use of both a parasympatholytic (tropicamide) and a sympathomimetic (phenylephrine) provides maximal dilation that is resistant to intense light stimulation.

Physiological and anatomical influences on drug absorption

One of the most important aspects of pharmacokinetics is the absorption phase. Without adequate absorption, drug distribution and metabolism are altered and the intended effect does not occur. Absorption depends on the molecular properties of the drug, the penetrating factor of the tissue, the patient's age, iris pigmentation and tear flow.

The major topical drug-absorbing tissue of the eye is the avascular cornea. The corneal epithelium acts as a reservoir for lipophilic drugs, and the stroma stores hydrophilic drugs. Any disruption of the corneal epithelium can affect drug absorption. The use of topical anaesthetic, or any abrasion to the cornea, can cause an increase in corneal penetration of mydriatic drugs. Phenylephrine has characteristics that may lead to corneal epithelium disruption. This change in corneal integrity may lead to an increase in both the effect and the duration of the phenylephrine- and tropicamide-induced mydriasis.

Other ocular tissues and structures have limited effects on drug absorption. The sclera and conjunctiva account for less than one-fifth of all drug absorption into the iris and ciliary body because they are so highly vascularized. Pigment granules within the iris absorb drugs with lipophilic properties and slowly release that drug over a period of time.

Anecdotal clinical evidence has suggested that dark irides take longer to dilate than light-coloured irides, but this has not been supported by studies comparing the dilation rate in light versus dark irides using 0.5% tropicamide. Furthermore, the ciliary body is involved with drug detoxification and elimination and is the major drug-metabolizing tissue of the anterior segment.

Tears play a major role in the process of drug absorption. Only 30 μL can be held by the palpebral conjunctiva and fornix at one time, which includes the 8 to 10 μL of normal tear volume. Therefore, too large a volume or too many drops will simply roll off the cheek or pass through the puncta, resulting in no increase in the desired pharmacological effects of the drug. Similarly, ocular pharmaceutical agents may become diluted from reflex tearing if the drugs sting upon instillation, which would further increase tear volume. Increasing drop size has no effect in increased drug absorption.

Increased absorption of a drug may occur with people who have a decreased tear flow rate such as elderly patients, patients with rheumatoid arthritis or keratoconjunctivitis sicca, or postmenopausal women.
Concerns about dilation

When compared to an undilated pupil, a dilated pupil facilitates locating and identifying posterior segment anomalies and abnormalities by providing an increased viewing area. However, there are drawbacks with pupil dilation. Increased examination time, patient inconvenience and the fear of systemic and ocular side effects are commonly cited reasons why some practitioners do not routinely dilate and why some patients refuse dilation.4

Most patient objections can be overcome with proper education. Most patients want the assurance that their optometrist is providing them with the best possible care. Benefits of dilation include an increased viewing area for accurate peripheral fundus assessment and clear stereo views to assist diagnosis. By simply explaining the benefits of dilation, the optometrist can make the patient feel more comfortable and assured that they are getting proper care. Also, patient comfort after the dilation can be enhanced by reducing the photophobic effects through use of mydriatic glasses or Rev-Eyes, a drug that reverses mydriasis by blocking the alpha-adrenergic receptors in the iris dilator.13 Patient risk associated with potential side effects can be minimized if the administrating doctor is pharmacologically current, well educated and prudent.

Most topically applied pharmaceuticals used for pupil dilations are relatively safe. Mydriatics and cycloplegics, according to Rengstorff and Dougherty, "have a history of extensive use in ophthalmic practice and ... serious complications are rare. When they do occur, they are often related to dosage, use with other drugs, surgery, trauma and very ill patients."2 Bartlett and Jaanus also suggest that the avascularity of the cornea provides a direct route for drug penetration without absorption by systemic circulation, thus minimizing systemic side effects.4 Applebaum and Jaanus presented a study demonstrating the safety of diagnostic pharmaceutical application (DPA) by using data collected by the Southern California College of Optometry and 20 other private practices.14 Of the 12,493 DPA cases, only 6 patients showed minor side effects with the use of tropicamide or phenylephrine. The best way to prevent harmful side effects is to avoid circumstances where known characteristics and conditions are expected to trigger unwanted reactions. The optometrist should know the properties, recommended uses, and precautions and contraindications of every drug he or she administers.

Project goals

The intent of this study was to investigate whether the time needed for maximum mydriasis could be decreased or whether the amount of mydriasis could be increased by altering room illumination during dilation. Based on our understanding of the pharmaceutical properties of tropicamide and phenylephrine, and the physiology involved in pupil mydriasis, we predict that pupil dilation will occur faster if patients are placed in a darkened room rather than a well-lit room following instillation of the topical dilation drops. In a dark room, the iris sphincter will relax with natural pupil dilation, and the parasympatholytic drug will not be opposed by light-induced antagonistic muscle constriction. Likewise, the sympathomimetic drug will be acting as an agonist in the natural direction with pupil dilation during darkness. Therefore, pharmaceutical dilation in darkness should put the system in harmony to achieve faster and more complete mydriasis.

Subjects and methods

Subjects

Twenty subjects—10 females and 10 males between the ages of 19 and 37 years—participated in this study. All subjects reported themselves to be in good health and free of significant systemic, neurologic and ocular diseases. Only subjects who had not experienced allergies or adverse reactions to anaesthetics or dilating agents in the past were included in this study. All participants had vision correctable to 20/20, unremarkable slit lamp findings and anterior chamber angles greater than 3 via Van Herick technique. Before participation in the study, informed consent was obtained from each subject.

Methods

The initial examination of the subjects included a thorough biomicroscopy evaluation to assess the general ocular health of each eye and Goldmann tonometry to measure intraocular pressures. One drop of 1% tetracaine was instilled into each lower fornix just before performing tonometry. Care was taken to minimize any systemic absorption by occluding the puncta and having subjects close their eyes for 15 seconds. Anterior chamber angles were determined by using Van Herick and shadow methods. In addition, eye colour was classified as either light or dark.

Subjects were then randomly placed in either a dark or a well-illuminated room. By using a photometer in the illuminated rooms, light levels were controlled at 22 footcandles. A baseline horizontal pupil diameter was measured using the Cogan pupillometer.

The Cogan pupillometer is a hand-held card that has a series of paired pinholes. The horizontal separation between the paired pinholes increases by 0.5 mm with each pair down the card. The vertical spacing is uniform between the paired pinholes. When the card is held at a common vertex distance from the eye, the subject can see through a pair of two tiny holes simultaneously. While viewing a distant light target, the subject subjectively moves the card up and down until the two holes appear to just touch without overlap or separation. From this "ideal" pinhole separation distance, a pupil diameter can be determined.15 When the procedure was performed in a light room, subjects viewed a white wall at 6 metres under ambient room illumination as previously described;
when the procedure was performed in a dark room, subjects viewed a UV “black light” positioned 6 metres in front of them.

After each subject was trained in the proper use of the Cogan pupillometer, a baseline pupil diameter measurement was obtained for each eye in normal room illumination. One drop of 2.5% phenylephrine HCl was then instilled into the lower fornix of each eye and the timer was started. After 15 seconds, one drop of 1% tropicamide was instilled into each eye. Room lights were extinguished immediately during dark dilation. In each instance, precautions were taken to minimize systemic absorption through the use of punctal occlusion. Subjects were encouraged to keep their eyes open and to look into the distance for the duration of the experiment. Six minutes after instillation of the first drop, subjects were asked to measure their horizontal pupil diameter with the Cogan pupillometer. After the subjects identified the pinhole pair that yielded touch without overlap or separation, the examiner then noted the pupil size equivalent from the front of the card. Subjects were unaware of which pupil sizes corresponded to the pinhole pairs. Following this pupil size determination, measurements were taken every 2 minutes until 30 minutes had elapsed. At 30 minutes, normal room illumination (22 foot-candles) was resumed for those subjects who were dilated under dark illumination conditions. After a further 3 minutes in the light (i.e., 33 minutes after the instillation of the drops), a final horizontal and vertical pupil diameter was measured using the slit lamp reticule. Tonometry was then repeated to check for any significant intraocular pressure (IOP) changes. The subjects then returned in one week to complete the protocol with the alternate illumination condition. A minimum of one week was required between dilations to prevent any possibility of an additive effect of the dilation pharmaceuticals.

In the remainder of this paper, subjects dilated in a well-lit room may be referred to as “light dilation” and those subjects dilated in a dark room may be referred to as “dark dilation.”

Statistical analysis

The time to maximum mydriasis was arbitrarily classified as the time after which subjects chose the same pinhole pair for five consecutive readings, thus indicating a pupil size fluctuation of no more than 0.5 mm. Readings were recorded for both eyes and then a mean time was determined for each subject.

Paired t-tests were used to compare the time required in the dark to the time required in the light for maximum mydriasis to occur. Unpaired t-tests were used to analyse the effects of iris colour. The mean times to maximum dilation with dark irides were compared to those with light irides in the illuminated room. Then the same computations were made with the results obtained in the darkened room. Unpaired t-tests were used in a similar fashion to compare times to maximum dilation of males to females under the same illumination conditions.

An average horizontal pupil measurement was calculated from both the eyes using the slit lamp reticule. Similarly, an average vertical pupil measurement was calculated. Paired t-tests were used to compare mean horizontal and mean vertical pupil diameters in a light room. The same comparison was made for data obtained from the dark-room condition. The relative pupil area was determined by considering the pupil as an ellipse rather than a circle. Thus, a relative pupil area was calculated using the formula \( \frac{\pi v h}{4} \), where “v” is the maximum vertical pupil diameter and “h” is the maximum horizontal pupil diameter. A paired t-test was then used to compare dark dilation versus light dilation relative to pupil area for each subject at 33 minutes post drug instillation. In addition, a paired t-test was used to compare mean horizontal and mean vertical pupil measurements that were taken under the same lighting conditions. The gender versus pupil size comparison was made using an unpaired t-test to compare the mean relative pupil area for males versus females who were dilated under the same lighting conditions. Similarly, an unpaired t-test was used to determine if iris colour had any effect on the size of the dilated pupil area.

Results

Time to maximum mydriasis

Table 1 presents the mean time to maximum mydriasis, as measured by Cogan pupillometer, for the 20 subjects who experienced light dilation and dark dilation. Although the subjects dilated faster in a dark room with a mean time of 18.1 minutes compared to the mean of 19.7 minutes for dilation in a well-lit room, the one-tailed paired t-test indicated that there was no significant difference (p > 0.05) between light and dark colour irides. That is, in a light room there was no difference in the time required for subjects with dark irides to dilate compared to those subjects with light irides. Similarly, when the dilation process was completed in a dark room, there was no significant difference in the time to maximum dilation.

Relative area of pupil dilation

Table 2 presents the slit lamp pupil measurements obtained from the 20 subjects at 33 minutes post instillation of the mydriatic drops. When comparing the relative pupil area of subjects dilated in dark conditions versus

<table>
<thead>
<tr>
<th>Illumination level</th>
<th>Number of subjects</th>
<th>Males/Females</th>
<th>Mean time to mydriasis in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>light</td>
<td>20</td>
<td>1/1</td>
<td>19.7 (4.5)</td>
</tr>
<tr>
<td>dark</td>
<td>20</td>
<td>1/1</td>
<td>18.1 (4.4)</td>
</tr>
</tbody>
</table>

Table 1. Time to maximum mydriasis (with standard deviations)
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Table 2. Mean pupil measurements at 33 minutes after tropicamide 1% and phenylephrine HCl 2.5% were instilled (with standard deviations)

<table>
<thead>
<tr>
<th>Illumination condition</th>
<th>Mean horizontal pupil diameter in mm</th>
<th>Mean vertical pupil diameter in mm</th>
<th>Mean relative pupil area in mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>light</td>
<td>8.12 (0.65)</td>
<td>8.07 (0.64)</td>
<td>51.73 (7.60)</td>
</tr>
<tr>
<td>dark</td>
<td>7.94 (0.55)</td>
<td>7.91 (0.62)</td>
<td>49.55 (7.01)</td>
</tr>
<tr>
<td>mean difference</td>
<td>0.18 mm</td>
<td>0.16 mm</td>
<td>2.18 mm²</td>
</tr>
</tbody>
</table>

Light conditions using a paired t-test, there was a significant difference (p < 0.05). Subjects dilated in a well-lit room had a significantly increased relative pupil area compared to dark dilation.

When considering only the mean horizontal diameter of the pupil, dilation during light conditions yielded a significantly (p < 0.05) larger horizontal diameter than dark dilation. However, the vertical pupil diameter differences fell just short of significance (p > 0.05). This surprising finding indicates that more of the increased relative area obtained from light dilation is derived from the horizontal measure. Within the same lighting conditions, there was not a significant difference between the horizontal and vertical pupil diameter measurements (p > 0.05).

There was no significant pupil size relationship between males and females or between light and dark iris colours within the same set of illumination conditions using unpaired t-tests (p > 0.05).

Subjective response

During the dark dilation procedure, when the lights were turned on 30 minutes after drop instillation, many subjects complained of discomfort due to the bright lights. The same subjects in the light dilation procedure did not report this discomfort.

Discussion

The goals of this project were to determine whether the speed or size of maximum dilation would be different if the patient were dilated in a darkened room versus a well-lit room. In other words, do illumination conditions after drop instillation affect pupil dilation? Also, we were interested whether gender differences or iris colour would influence dilation results.

Contrary to our original prediction, this study showed that placing a patient in a dark room does not result in a significantly faster dilation than dilating the patient in a well-lit room. Although dilation rate indicated a trend toward a slightly faster dilation in the dark, it is conceivable that our measurements were influenced by differences in chromatic aberration between light and dark conditions. Allowing the patient to dilate in a dark room did improve overall comfort. However, this initial comfort is short-lived because the patient will soon be subjected to the bright lights of an indirect ophthalmoscope. Perhaps waiting for this procedure in a well-lit room will lessen the discomfort of the bright lights to come.

Based on slit lamp measurements 33 minutes after dilation, there was a significant difference (p < 0.05) in the relative pupil area when patients dilated in a dark room compared to a light room. Unexpectedly, the relative pupil area obtained from light dilation produced a greater mean pupil area by 2.18 mm² than that from dark dilation. Although we do not know exactly why, one possible explanation may be that in the light, the iris is constricted and thus more area of iris and ciliary body is exposed and available for absorption of mydriatic agents. Surprisingly, it was the horizontal pupil diameter that was statistically larger, whereas the vertical pupil measurement was not. This may be explained by the natural pooling of the mydriatic in the palpebral fissure in the horizontal meridian. With the eyes open, fluid will tend to accumulate in the horizontal meridian along the lower lid margin and the blinking action may push fluid toward the fissure. In a well-lit room, we believe that the lids may tend to assume a more squinted posture than in the dark, thus narrowing the palpebral fissure and decreasing the vertical width of the drug reservoir in contact with the front surface of the eye. Increased drug concentration along the fissure could conceivably increase the drug availability to the cornea and might explain the greater horizontal mydriasis obtained from a light dilation. We call this our "serendipitous sectorial mydriasis explanation".

Neither gender nor iris colour was a factor in either the rate to maximum mydriasis or the difference of relative pupil area. Our finding that gender has no impact on dilation results was expected, since there are no anatomical differences between healthy male and female eyes that would increase or decrease drug absorption. Our finding that iris colour has no significant effect is consistent with past research, which has shown that iris colour (categorized as light or dark) has no significant effect in the amount or rate of dilation.³¹

The ambient illumination during patient dilation is usually determined by the doctor rather than the patient. For patient comfort one may recommend low illumination during dilation. However, our results demonstrate that dilation with low light levels is not significantly faster and may yield a pupil area that is slightly smaller, although this difference is probably not clinically significant. The bottom line is that although patient comfort may be slightly enhanced with dark dilation, the patient is not going to be ready for the fundus examination any faster. One might argue that is preferable to have the patient sit in the reception area and enjoy the company of friends or other patients. The additional benefits of undergoing dilation in a well-lit room include not only the increased final dilation area, but also, as the dilation progresses, the gradual adaptation of the eyes to the increased light reaching the retina. After all, it seems paradoxical during the dilation to place the patients in a dark room for comfort when, moments later, very bright lights will be aimed directly through their...
fully dilated pupils. In the future, after instillation of the mydriatic drops, we will seat our patients in a well-lit room while the drops take effect.

We would like to thank all those individuals who took part in our thesis and volunteered to be dilated. We express much appreciation to Dr Robert Yolton for all his help with the statistics and valuable advice. In addition, we thank Dr Bradley Coffey for his help in obtaining information on the Cogan pupillometer.

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key words: mydrias, illumination, phenylephrine, tropicamide, rate time, light, dark, pupil, dilation, dilation rate

mots clés : dilatation pupillaire, éclairement, phényléphrine, tropicamide, temps de dérivation, lumière, obscurité, pupille, dilatation, taux de dilatation