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Journal

American Journal of Veterinary Research, 48(2)

ISSN

0002-9645

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Publication Date

1987-02-01

Peer reviewed

Reprinted from the AMERICAN JOURNAL OF VETERINARY RESEARCH, Vol. 48, No. 2, Pages 320-322.

A-652

Effect of topical phenylephrine on the equine pupil

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SUMMARY

The mydriatic effect of 10% phenylephrine was evaluated in 9 horses. Base-line pupillary size in mesopic conditions and during light stimulation was ascertained before application of pharmacologic agents. In study 1, 10% phenylephrine was applied to each eye (n = 5 horses). After 15 minutes, the pupillary size was determined in both lighting conditions. Phenylephrine was again applied to each eye, and after an additional 15 minutes, the pupillary size was determined. In study 2, 1% tropicamide was applied to each eye (n = 4 horses), and after 30 minutes, the pupillary size was determined in both lighting conditions. Tropicamide and phenylephrine were applied to each eye immediately after determination of pupillary size, and after an additional 30 minutes, the pupillary size was determined. There was no significant change ($P > 0.9$) in pupillary size when phenylephrine was used alone or when phenylephrine was used in an eye that had been dilated with tropicamide.

Phenylephrine has been advocated to assist dilatation of the equine pupil when atropine alone is ineffective[1] or when posterior synechiae are present.[2] Phenylephrine also has been recommended for use in the horse before cataract extraction to help maintain mydriasis.[3] The purpose of the present report was to study effects of phenylephrine on the equine pupil.

Materials and Methods

Horses—Five adult, neutered male horses were used in the study 1 and 4 in study 2. All horses were free of ocular disease.

Illumination—Horses for each study were kept in an outdoor corral with normal ambient illumination. After horses were brought into the examination room, they were positioned in stocks and were allowed approximately 2 minutes to adjust to the mesopic conditions. The right eye received 175 lux (16-foot candles [ft-c]) and the left eye received 11 lux (1 ft-c). Stimulation of the pupil was accomplished, using a transilluminator[a] with a fresh nickel-cadmium rechargeable battery. The light was directed along the visual axis of each eye with the tip of the transilluminator held approximately 30 cm from the cornea. The battery hand-piece was charged for 24 hours before the initiation of the studies and was kept continuously charged between each additional stimulation. The transilluminator provided 700 lux (65 ft-c) to the corneal surface from the distance of 30 cm.

Pupillary size—To measure pupillary width and height, a self-adhesive millimeter ruler was applied to the skin beneath the lower eyelid. Each eye of each horse was photographed[4,5] at a distance of 1 m, using a camera with an f = 3.5 lens.[b] Briefly, the flash was provided through a fiberoptic-light cable connected to a camera flash unit. The light cable passed through a lens ring and was centered in the lens aperture and aligned with the camera lens axis by the use of a light guide. To obtain camera settings, 1 horse not in the studies was photographed in light conditions similar to, but not the same as, those in the studies (Fig 1). Photographs were taken during mesopic and light-stimulated conditions initially and at various intervals after application of the pharmacologic agents and included the pupil and the millimeter rule. The film was routinely developed, and resultant transparencies were projected, using a standard slide projector[c] to a screen 5 m away. Using the millimeter rule as a scale to determine pupillary size, the width and height of the pupil were determined to within 0.5 mm.

Studies—Chemical restraint was not used. In study 1, the mydriatic effect of phenylephrine[d] when used alone was assessed. After base-line data concerning pupillary size during mesopic and light-stimulated conditions were gathered, 0.25 ml of phenylephrine was administered to the conjunctival cul-de-sac of each eye. The pupillary size was evaluated after 15 minutes during mesopic and light-stimulated conditions. Phenylephrine was again applied, and after an additional 15 minutes, pupils were evaluated.

In study 2, the effect of topical phenylephrine was assessed when used in conjunction with a pharmacologic agent (tropicamide) that would paralyze the pupil sphincter muscle. After base-line data on pupillary size during mesopic and light-stimulated conditions were gathered, 0.25 ml of 1% tropicamide,[e] a parasympathetic-blocking agent, was applied to the conjunctival cul-de-sac of each eye. The pupillary size under mesopic and light-stimulated conditions was recorded after 30 minutes. Phenylephrine (0.25 ml) and then a 2nd application of tropicamide (0.25 ml) were applied topically to the cul-de-sac of each eye. After an additional 30 minutes, the pupillary size during mesopic conditions and after light stimulation was recorded.

Statistical analysis—The pupillary size of each eye at each interval was treated as an independent variable. Data were

Received for publication July 11, 1986.

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The authors thank Dr. C. J. Murphy for suggestions concerning experimental design and Dr. H. C. Howland for use of the photographic lens.

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[a] Welch Allyn, Skaneateles Falls, NY.

[b] Nikkormat, 55 mm, f = 3.5 MicroNikkor lens, Nippon Kogaku KK, Tokyo, Japan.

[c] Ektagraphic, model B-2, Eastman Kodak, Rochester, NY.

[d] Neosynephrine 10% ophthalmic solution, Winthrop Laboratories, New York, NY.

[e] Mydriacyl, Alcon Laboratories, Fort Worth, Tex.

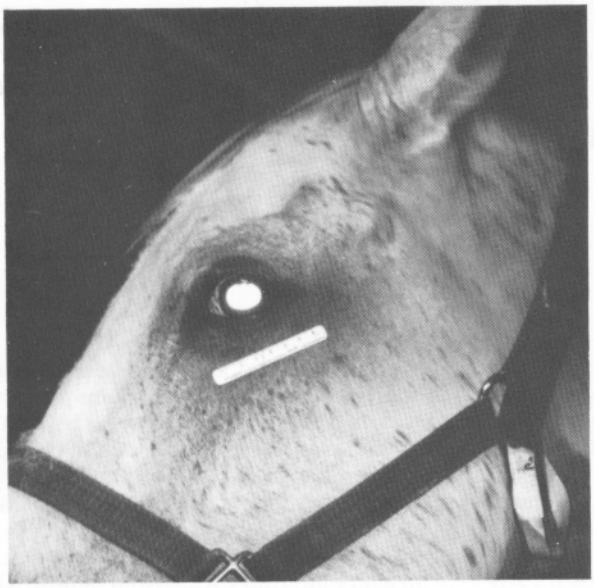

Fig 1—The pupil of a horse and the milimeter scale are seen in this photograph. When projected via a slide projector, the size of the pupil can be measured.

TABLE 1—Effect of topically applied phenylephrine on the pupillary size of horses (study 1)

	Initial pupil size		15 Min after phenylephrine		30 Min after phenylephrine	
Conditions	OD	OS	OD	OS	OD	OS
Horse 1						
MC	18×13	19×13	19×13	18×12	19×13	20×13
LS	18× 9	18× 9	18× 9	18×10	19×10	18× 8
Horse 2						
MC	22×15	22×15	22×18	21×16	21×16	21×16
LS	20×15	20×15	22×16	22×14	19×15	20×14
Horse 3						
MC	21×16	22×14	21×16	20×15	21×15	19×15
LS	19×16	19×14	19×16	19×15	20×13	20×12
Horse 4						
MC	20×12	19×10	23×16	20×13	20×14	20×12
LS	18×10	19×10	18× 9	ND	20×10	19×10
Horse 5						
MC	19×13	21×14	19×11	21×13	20×14	19×13
LS	17× 9	19×12	17× 9	19×12	19× 9	18× 9
Mean ± SD (W × H)						
OD-MC	20±1.6×13.8±1.6		20.8±1.8×14.8±2.×8		20.2±0.8×14.4±1.1	
OD-LS	18.4±1.1×11.8±3.4		18.8±1.9×11.8±3.8		19.4±0.6×11.4±2.5	
OS-MC	20.6±1.5×13.2±1.9		20±1.2×13.8±1.6		19.8±0.8×13.8±1.6	
OS-LS	19±0.7×12 ±2.5		19.5±1.7×12.7±2.2		19±1.0×10.6±2.4	

OD = Right eye; OS = Left eye. Pupil size (width [W] × height [H]) is given in millimeters.

ND = Horse 4 blinked during photography, and pupil size could not be determined. MC = mesopic conditions. LS = light-stimulated conditions.

analyzed, using the paired-comparison test.[6] Extreme values were analyzed, using the Student's t test.[6] A significance level was established before analysis at $\alpha = 0.05$ (and a confidence level of 95%).

Results

In study 1, horse 4 had a pupil that was increased in size at 15 minutes, but by 30 minutes, the pupil had returned to approximately the size during the initial, mesopic conditions (Table 1). This horse appeared slightly excited when brought into the examination room for the 15-minute evaluation. Average changes irrespective of increase or decrease in pupillary size for the eyes of all horses were not significant ($P > 0.9$).

TABLE 2—Effect of topically applied tropicamide and phenylephrine on the pupillary size of horses (study 2)

	Initial pupil size		30 Min after tropicamide alone		30 Min after tropicamide and phenylephrine	
Conditions	OD	OS	OD	OS	OD	OS
Horse 6						
MC	22×16	22×16	22×16	22×16	22×17	22×16
LS	ND	20×10	ND	22×16	ND	ND
Horse 7						
MC	21×16	22×16	22×17	22×18	22.5×18	23×19
LS	22×16*	19×13	22×17	22×17.5	22.5×17.5	22.5×17
Horse 8						
MC	22×15	21.5×16.5	22×17	21.5×16.5	21.5×20	22×17
LS	18×13	19×12	21×15	21.5×16.5	22×18	22×17
Horse 9						
MC	20×16	21×16	22×16	21×17	22.5×17	21×18
LS	18×13	19×11	ND	21×16.5	22×18	21×17.5
Mean ± SD (W × H)						
OD-MC	21.2±1×15.8±0.5		22±0.0×16.5±0.6		22.1±0.5×18.0±1.4	
OD-LS	19.3±2.3×14±1.7		21.5±0.7×16±1.4		22.2±0.3×17.8±0.3	
OS-MC	21.6±0.5×16.1±0.3		21.6±0.5×16.9±0.9		22±0.8×17.5±1.3	
OS-LS	19.2±0.5×11.5±1.3		21.6±0.5×16.6±0.6		21.8±0.8×17.2±0.3	

* Stimulation light did not align along visual axis.

OD = right eye; OS = left eye. Pupil size (width [W] × height [H]) is given in millimeters.

ND = Eye blinked during photography and pupil size could not be determined. MC = mesopic conditions. LS = light-stimulated conditions.

During study 2, resting pupillary size in neither eye 30 minutes after the 1st application of tropicamide was significantly different from the pupillary size in mesopic, nonstimulated conditions ($P > 0.5$; Table 2). Similar findings were evident after application of phenylephrine and a 2nd application of tropicamide. As expected, tropicamide alone prevented the pupillary response to light. The average pupillary size of nontreated eyes (base line) was significantly smaller than that of eyes given tropicamide or a combination of tropicamide and phenylephrine ($P < 0.01$). However, no significant change was found in average pupillary size when phenylephrine was added to eyes previously treated with tropicamide ($P > 0.9$).

Discussion

The iris of the horse has a pupillary sphincter and a pupillary dilator muscle that are composed of smooth muscle.[7,8] The pupillary dilator muscle is more pronounced in the vertical and oblique meridians and incomplete adjacent to the horizontal axis of the pupil.[7,8] The sphincter muscle is oriented radially along the horizontal axis.[7,8] It is assumed that the pupillary sphincter muscle is under cholinergic control and that the pupillary dilator muscle is under adrenergic control because this is the case in all mammals.[9]

The use of phenylephrine is somewhat contradictory in species other than the horse. Phenylephrine is effective[10,11] and ineffective[12] in causing dilatation in the dog, and effective[13] and ineffective[12] in causing dilatation in cats. Phenylephrine has been empirically recommended in the horse to augment pupillary dilatation when topical atropine sulfate is ineffective in attaining dilation[2,3,14-18] or as a preoperative medication, such as before cataract extraction, when increased pupillary dilatation is desired.[3] In these studies, topically applied phenylephrine did not cause mydriasis within 30 minutes when used alone. When tropicamide, a parasympathetic blocking agent, was used, the addition of phenylephrine did not significantly increase the pupillary size.

In human beings and some animals, dilatation of the pupil is dependent on contraction of the dilator muscle and relaxation of the sphincter muscle.[9] Inhibition of the occulomotor nerve input to the sphincter muscle by central inhibition or peripheral blockade, using parasympathetic blocking drugs such as atropine or tropicamide produces dilatation of the pupil. This dilatation is enhanced by sympathetic stimulation or by the use of sympathomimetic drugs such as 10% phenylephrine.[9] Seemingly, the aforementioned mechanism may be different in the horse. Further research is warranted in this regard.

In the horse, the pupillary dilator muscle may be under adrenergic control but may be weak. This would explain why phenylephrine was ineffective in preventing miosis during light stimulation. Alternately, the dilator muscle may not be under adrenergic control. Either of these possibilities would explain why phenylephrine did not add to the effects of a parasympathetic-blocking agent.

If there are few dilator muscle fibers along the horizontal axis,[7,8] we would expect the horizontal pupillary dimension to decrease as the dorsoventral aligned dilator muscle fibers contract and enlarge the pupil vertically. In contrast, we found that this dimension did not change significantly. This may indicate the presence of radially arranged elastic fibers that contract with relaxation of the sphincter muscle.

In human beings, the use of phenylephrine soaked pledgets is advocated to obtain effective dilatation that is unresponsive to light.[19] Although the effect of phenylephrine on the pupil is maximal at 1 hour, at 30 minutes, the pupil has dilated an average of 2 mm.[19] This effect was not seen in study-1 horses, in which 2 applications of phenylephrine given 15 minutes apart did not prevent miosis with light stimulation and did not significantly change the pupil size in mesopic conditions. In the horse, phenylephrine may be concentrated in melanin-containing cells. This mechanism, which is recognized for other drugs,[19] would cause phenylephrine to be concentrated in pigmented cells and a delayed onset and prolonged effect could occur. However, we used a regimen that is more frequent than generally advocated for clinical use in the horse. In cases in which a dose regimen is given, the recommendation is an unspecified quantity to be applied 1 hour and 45 minutes before cataract surgery[3] and 3 to 4 times daily to supplement atropine dilatation. It seems unlikely that the usual therapy regimen recommended for phenylephrine would have any effect in horses with uveitis during which there is pronounced miosis secondary to active sphincter muscle contraction. The present study does not rule out the possibility that a greater amount of phenylephrine or the application of phenylephrine over several hours may be required to prevent pupillary response to light or cause dilatation in the horse.

Seemingly, there appears to be no reason for applying phenylephrine topically to the eye of a horse if a parasympathetic blocking agent, such as atropine, fails to dilate the pupil. The use of phenylephrine before surgery also appears to be ineffective in augmenting pupillary dilatation.

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