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Short Communication

Field use of N-butylscopolammonium bromide to facilitate thorough ophthalmic examination in horses



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ABSTRACT

N-butylscopolammonium bromide (NBB), an anticholinergic muscarinic antagonist, was assessed as a mydriatic agent for field examination of equine eyes. Six adult horses were randomly assigned to four treatments with 2 weeks washout between treatments: (1) topical saline/IV saline (negative control); (2) topical tropicamide/IV saline (positive control); (3) topical NBB/IV saline; or (4) topical saline/IV NBB. Horizontal and vertical pupil diameters, temperature, pulse, respiration, pupillary light reflexes (PLRs) and mydriasis sufficient to perform complete fundic examination were recorded. Tropicamide induced mydriasis in all horses. Topical NBB induced mydriasis in one horse, and IV NBB enabled thorough fundic examination in two horses, delayed PLRs without allowing thorough examination in two horses and had no effect in two horses.

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A horse's vision has a direct impact on its ability to perform desired functions, making thorough ophthalmic examination critical, especially during pre-purchase evaluations. For thorough examination, pupillary dilation is indicated, but often is omitted due to time constraints or concerns of adverse or long-acting effects of mydriatic agents (Steinmann et al., 1987). This omission may lead to inadequate lenticular and fundic visualization and subsequent failure to detect current or predict future performance limiting abnormalities in eyes that appear otherwise normal (Hurn and Turner, 2006).

N-butylscopolammonium bromide (NBB), an anticholinergic muscarinic antagonist used IV to treat equine spasmodic colic, competitively inhibits parasympathetic activation and may cause transient antispasmosis, tachycardia and mydriasis (FDA, 2004). Similar compounds routinely used in human medicine to achieve antispasmosis also result in mydriasis (Sissons et al., 1991). Tropicamide, the topical anticholinergic agent most commonly used for dilation of equine eyes, produces mydriasis for 4–6 h (Gelatt et al., 1995), which is much longer than is required for examination; therefore, a shorter-acting mydriatic agent may be desirable. Experimental evaluation of NBB as a temporary mydriatic agent in horses to facilitate fundic examination is thus warranted, but has not yet been attempted.

The study was approved by the University of California-Davis Institutional Animal Care and Use Committee (protocol number 16393, date of approval: 10 March 2011). Six adult horses were included, comprising three mares (Quarter horses) and three geldings (two

Thoroughbreds, one Quarter horse) aged 4–12 years, all of which were determined to have normal eyes by a board certified veterinary ophthalmologist. Horse 1 had one brown and one blue iris. Horses 2–5 had brown irides. Horse 6 had one brown and one heterochromic iris. Each horse was housed in a barn in the same stall with similar natural ambient light for each trial.

Horses were sedated with 0.01 mg/kg detomidine IV and randomly received four treatments with 2 weeks' washout between treatments. Treatment 1 (negative control) was 1.0 mL of 0.9% saline topically per eye and 0.9% saline IV (volume identical to calculated NBB dose). Treatment 2 (positive control) was 1.0 mL of 1% tropicamide topically per eye and 0.9% saline IV (volume identical to calculated NBB dose). Treatment 3 was 1.0 mL 2% NBB topically per eye and 0.9% saline IV (volume identical to calculated NBB dose). Treatment 4 was 1.0 mL 0.9% saline topically per eye and 2% NBB 0.3 mg/kg IV.

Horses were examined at 0, 10, 20, 30, 40, 60, 120, 180, 240, 300, 360 min and 24 h following treatment. Horizontal and vertical pupil diameters measured with manual calipers (Davis et al., 2003), temperature, pulse, respiration, PLRs, whether dilation occurred, time to dilation, and an ophthalmologist's ability to perform a thorough fundic examination were recorded. The ophthalmologist was masked to the horse's treatment.

Data were evaluated using a mixed effects linear regression model, with the horse treated as a random effect, and with treatment, time and their interaction as fixed effects. Post-hoc pairwise comparisons at individual times when the interaction was significant were performed using a Bonferroni multiple comparison adjustment. Results were considered to be significant if $P < 0.05$.

Following topical/IV saline, PLRs remained normal and fundic examination was not possible. Topical tropicamide/IV saline produced

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Table 1

Significant differences in pupil diameter of horses between treatments at different time points post-treatment.

Time post-treatment (min)	0	10	20	30	40	60
Horizontal diameter right eye	NS	2/1, 2/3	2/1, 2/3	2/1, 2/3	2/1, 2/3, 2/4	2/1, 2/3, 2/4
Horizontal diameter left eye	NS	2/1	2/1, 2/3, 2/4	2/1	2/1, 2/4	2/1, 2/4
Vertical diameter right eye	NS	4/3	3/2, 4/3	2/1	2/1, 2/3	2/1, 2/3, 2/4
Vertical diameter left eye	NS	4/3	NS	NS	2/1, 4/1, 2/3, 2/4	2/1, 2/3, 2/4

Treatment 1, topical saline/IV saline; Treatment 2, topical tropicamide/IV saline; Treatment 3, topical NBB/IV saline; Treatment 4, topical saline/IV NBB; NS, no significant difference.

Significance declared at $P < 0.05$; treatments that significantly differ are separated by a '/'; the first number refers to the treatment with the larger diameter.

consistent complete mydriasis and allowed thorough fundic examination in all horses. Mean time to maximal dilation was 36.7 min (minimum 30 min, maximum 40 min) and lasted for 350 min (minimum 300 min, maximum 360 min). Topical NBB/IV saline caused transient partial mydriasis in the blue iris of horse 1 by 60 min and lasted for 30 min. All horses had immediate squinting and tearing, with scleral hyperemia lasting up to 24 h.

Topical saline/IV NBB delayed PLRs sufficiently to enable thorough fundic examination in two horses (horse 2 from 10 to 40 min and horse 6 at 60 min), delayed PLRs in two horses (horses 1 and 3) but did not allow thorough fundic examination, and did not have an effect in two horses (horses 4 and 5). The mean time to maximal dilation was 25 min (minimum 10 min, maximum 60 min), lasting 30 min. Significant differences in pupil diameter are summarized in Table 1. No significant differences occurred in temperature or respiration between any treatments. For topical saline/IV NBB, heart rate was significantly higher than the other three treatments from 10 to 40 min ($P < 0.05$).

An unexpected finding was variable pupillary response to NBB between horses and between different colored eyes of the same horse. The cause may be related to enzymatic or structural differences in light versus dark irides or to breed, sex or color differences. DOPA-oxidase, which may be increased in dark irides, results in less pupillary dilation (Angenent and Koelle, 1953). Dark irides are more compact than light irides, making pupillary reactivity slower, since the tissue does not expand and contract as readily (Emiru, 1971). In one study, Arabian and female horses had greater average vertical pupil diameter following administration of atropine (Davis et al., 2003).

Variable pupillary dilation following IV NBB could result from a dose-dependent effect or individual variation in response to the drug. In a tolerance study, four horses administered 10 times the recommended NBB dose had fixed dilated pupils at 10 min. PLRs returned in two horses at 4 h and in two horses at 24 h (FDA, 2004).

Limitations of this study include the small sample size, which may have contributed to the absence of statistically significant differences in pupillary dilation following IV NBB. Additionally, the combined effect of detomidine and NBB on dilation is uncertain. Dose related mydriasis and bradycardia can follow α_2 agonist administration (Kemerling et al., 1988), but anticholinergic agents may override these effects (Pimenta et al., 2011). Since statistically significant heart rate increases followed IV NBB in all horses, despite sedation, it is likely that systemic NBB effects occurred. Similarly, significant increases in pupil diameter were not found following sedation alone. Further studies are warranted to determine an appropriate IV NBB dose that produces consistent, safe mydriasis in a majority of horses, to account for age, breed, sex or color differences, and to assess response variations in brown, blue and heterochromic irides.

Although tropicamide produced more consistent mydriatic results in this study, standard dose IV NBB represents an alternative to achieve more rapid, less sustained pupillary dilation for thorough fundic examination in some horses.

Conflict of interest statement

The study medication was provided by Boehringer Ingelheim upon request of the authors. None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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