

# Therapeutics & Medicine

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## Flunixin Meglumine: More or Less?

Foot pain can be difficult to control, so Jonathan Foreman, DVM, MS, Dipl. ACVIM, of the University of Illinois at Urbana-Champaign, and his colleagues recently examined the possibility that higher-than-standard doses of non-steroidal anti-inflammatory drugs (NSAIDs) might better alleviate foot pain.

They used a reversible model of equine foot lameness to test this idea—a reversible heart bar shoe can make sound horses lame temporarily, and when researchers loosen the screw in the shoe to relieve foot pressure, the pain abates. This allowed them to study the same horses weekly for four weeks so each served as its own control. The tighter the screw, the higher the pain level as reflected by rising heart rates. They confirmed the tightened shoe's effects in each horse with palmar digital (heel) nerve blocks. Heart rates dropped from 60 to 40 beats per minute (bpm) following this regional anesthesia application.

Foreman also wanted to see if the half-strength dose of flunixin commonly used as an anti-endotoxin dose in colic treatment could provide sufficient foot pain relief. In a previous study he compared varying doses of phenylbutazone (Bute) and found no difference between the effects of a normal, single dose (1x), and those of twice the normal dose (2x), but the effects of one-half dose were not as long-lived as those seen with a 1x dose.

“More is not better, and less is less effective.”

DR. JONATHAN FOREMAN

In this study the scientists compared the effects of varying intravenous (IV) doses (half-dose, 1x, 2x) of flunixin meglumine; they used saline as a control. Ten sound horses wore a reversible heart bar shoe on the left front foot. Following treatment, the 1x and 2x doses improved heart rates for

the 12-hour duration, whereas heart rates remained elevated in the control horses. Heart rates in the horses given half-doses of flunixin did not decrease as much as those in the 1x and 2x horses, and they didn't remain low for as long. “They responded intermittently and not as obviously,” Foreman said. There was no difference in heart rate results between the horses receiving 1x or 2x flunixin meglumine.

Plasma concentrations of flunixin meglumine increased in a dose-dependent manner, but by Hour 8, there was no difference among concentrations at half-dose, 1x, and 2x doses. This indicates that horses rapidly metabolize and excrete the drug.

In conclusion, Foreman noted that the double dose was no more effective than the single dose and presents a higher toxicity risk. The half-dose was less effective than the single dose; so one can't rely on an anti-endotoxin half-dose to provide complete pain control for painful hoof conditions such as laminitis. This is significant when treating colicking horses with flunixin meglumine to alleviate intestinal pain and combat endotoxemia. Since



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laminitis can be a sequel to colic, never rely on smaller-than-usual doses of flunixin meglumine to alleviate musculoskeletal pain. He summed up by saying, "More is not better, and less is less effective."

### Oral vs. IV Bute and Drug Testing

The FEI (Fédération Internationale Equestre) has a drug-free policy for all equine disciplines. Recently, there was talk of allowing veterinarian-administered half-doses of flunixin meglumine or of Bute. After examining the legal implications and the ethics of fairness, FEI officials abandoned this modification, but the discussion caused Foreman to question whether alternate dosing approaches would help ensure testing compliance.

He wondered if half-doses of an NSAID could result in different blood plasma concentrations than full doses. He and colleagues studied this approach using Bute in nine healthy horses. They administered five consecutive once-daily half-doses of IV or oral Bute, taking blood samples 12 and 24 hours post-administration. After a week off, in the third week the administration methods were swapped.

The team compared oral vs. IV dosing and noticed Bute plasma concentrations accumulated, with concentrations higher on Day 5 than Day 1. They didn't note this with IV dosing. Foreman suggested that even at half-doses, oral Bute is not 100% bioavailable and accumulates in plasma. After stopping oral dosing, concentrations decreased to levels a test will not detect within 12 hours of dosing; horses on an IV dose tested close to a positive level but levels declined quickly after dosing stopped.

The potential for a positive test is a function of dose, administration route, time administered relative to testing, individual horse variability, and the regulatory threshold. Foreman said, "Even at lower doses than the single dose of Bute, oral phenylbutazone can accumulate in plasma over time and therefore may trigger a positive drug test particularly if given within 12 hours of the test. But at 24 hours, or even better would be 48 hours, the horse will likely be safe from testing positive."

### GI Drug for Equine Eye Exams?

Sometimes veterinarians stumble across a drug side effect that's more useful than

detrimental. As it turns out, the antispasmodic N-butylscopolammonium bromide (NBB), marketed as Buscopan (Boehringer Ingelheim) to treat colic, could help practitioners examine horses' eyes.

"One side effect of NBB is mydriasis—dilation of the pupil of the eye," explained Joanie Palmero, DVM, Dipl. ACVIM, formerly of the University of California, Davis (UC Davis), Veterinary Medical Teaching Hospital. She and UC Davis colleagues examined NBB's potential for eye exam use.

They administered the following treatments (interspersed by a two-week wash-out period) to six healthy adult horses: topical tropicamide (positive control; the gold standard for ocular exams), topical NBB, intravenous NBB, and topical or IV saline (negative controls). They measured pupil diameter, pupillary light reflex, and other parameters from time of administration and at least 60 minutes after administration. They observed:

- No changes in horses treated with either topical or IV saline, as expected;
- Topical tropicamide resulted in dilation, allowing a complete exam in all horses (mean time to dilation was 36.7 minutes; dilation lasted an average of 360 minutes);
- Topical NBB caused the pupillary dilation of one blue iris in one horse;
- IV NBB allowed for dilation and complete exam in two horses (mean time to dilation was 25 minutes; dilation lasted an average of 30 minutes);



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An antispasmodic drug called N-butylscopolammonium bromide can be used to dilate the pupil, but more research on this application is needed.



### Convention Tweet

**Mike Pownall, DVM**

@McKeePownall

**Don't keep too many controlled drugs in your vehicle. Supposed to have only enough for what you might use on 1 day.**

- NBB also caused partial dilation and incomplete exams in two horses, and caused no effect in two horses; and

- A transient heart rate increase was evident in all horses after IV NBB.

Palmero, now at Alamo Pintado Equine Medical Center, in Los Olivos, Calif., also noted that eye color can influence how the eye responds to mydriatics—a phenomenon well-documented in human medicine.

"Interestingly, the mydriatic effect of NBB seemed to be more profound in the horses with blue or heterochromatic irises than in horses with uniformly brown irises," Palmero noted.

She added, "These findings suggest that NBB can result in ocular dilation in some horses; however, further studies are warranted to account for breed, gender, and color differences and to determine a safe, yet reliable, NBB dose that results in dilation in a majority of horses." 🐾