

### Furosemide (Salix® or Lasix®) Use in Racehorses: A Nutritional Perspective

A 2005 study estimated that approximately 90% of Thoroughbreds and 70% of Standardbreds are treated with furosemide before racing in the United States to prevent exercise-induced pulmonary hemorrhage (EIPH) (Hinchcliff et al., 2005). It is likely that the percentage of racehorses regularly administered furosemide is even greater today.

Strong evidence supports the efficacy of furosemide to reduce the incidence of EIPH. In a study by Hinchcliff et al. (2009), 167 Thoroughbred racehorses in South Africa were allocated into race fields of 9-16 horses each and raced twice. Both of the races consisted of the same race field each time. Horses were randomly treated with either furosemide (500 mg, IV; 10 cc) or placebo (saline solution) before each race. Therefore, each horse raced under the same conditions each time except with or without furosemide administration. Severity of EIPH was scored on a scale of 0 (no bleeding) to 4 (large amount of blood in the trachea) after each race using endoscopy (Figure 1).

Researchers found that horses were substantially less likely to develop EIPH following administration of furosemide than placebo. In addition, 81 of the 120 horses (67.5%) that had EIPH after placebo treatment had a reduction in EIPH severity score of at least one grade when treated with furosemide. In sum, results indicated that pre-race administration of furosemide decreased the incidence and severity of EIPH in Thoroughbreds racing under typical conditions in South Africa.



Figure 1. Pre-race administration of furosemide decreased the incidence and severity of EIPH in Thoroughbreds racing under typical conditions in South Africa. Scores range from 0 (no sign of EIPH) to 4 (significant degree of EIPH) (Hinchcliff et al., 2009).

Besides affecting EIPH, does furosemide administration have other effects? Kentucky Equine Research (KER) has conducted multiple studies to help answer the following questions:

- How does furosemide affect body weight and performance?
- What are the effects of different furosemide doses?
- How does furosemide affect water intake?
- How long does it take the horse to recover from furosemide administration?
- How does furosemide affect electrolyte and mineral balance?
- Can recovery be influenced through dietary supplementation?

#### How does furosemide affect body weight and performance?

Furosemide has long been considered a performance-enhancing drug because it has been reported that horses treated with it ran faster, earned more money, and were more likely to finish first, second, or third than horses that did not receive furosemide before racing (Gross et al., 1999).

One potential explanation for furosemide's effect on performance is related to its effect on the horse's body weight after administration. A lighter horse would expend less energy and therefore fatigue less quickly than if it carried greater weight. This is a similar rationale to using jockey weight as a handicapping tool.

To determine energy expenditure in Thoroughbreds administered furosemide, KER conducted a study using six Thoroughbreds (Pagan et al., 2013). The horses performed a standardized exercise test (SET) on a high-speed treadmill 4 hours after receiving either 250 mg (5 cc) of furosemide or a placebo. Horses were weighed prior to treatment and at intervals for 72 hours after exercise. During the exercise test,  $VO_2$ ,  $VCO_2$ , and plasma lactate were measured, which indicate oxygen uptake, carbon dioxide production, and anaerobic work.

Body weight loss during the 4 hours prior to the SET was higher in the furosemide group ( $26.4 \pm$ 3.3 lb) compared to the control group  $(14.7 \pm 2.6 \text{ lb})$  (Figures 2 and 3).



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Figure 3. Body weight change over 72 hours following 250 mg furosemide and SET.

Based on  $VO_2$  and lactate measurements, horses given furosemide expended less energy when exercised at the same speed than horses given a placebo. At racing speed, this translates to a reduction in lactate production, resulting in delayed fatigue.

Multiple studies have demonstrated that furosemide improves performance by reducing the amount of weight the horse carries during a race. In a study by Hinchcliff and coworkers (1996), furosemide decreased the accumulated oxygen deficit and rate of increase in blood lactate concentration of Standardbred horses during brief high-intensity exertion. Further, in a study that questioned the performance-enhancing effects of furosemide (Zawadzkas et al., 2006), researchers concluded that improved performance was due more to the weight-loss effects of the drug rather than its apparent alleviation of EIPH.

## What are the effects of different furosemide doses?

Researchers at KER investigated body weight loss of nine Thoroughbreds given either 150 mg (3 cc), 250 mg (5 cc), or 500 mg (10 cc) of furosemide. Feed, hay, and water were withheld for 4 hours after administration. Body weight was measured 4 hours after administration, and surprisingly, there was no significant difference in weight loss between treatments (Figure 4). Urinary output was higher in the 500-mg treatment group, but its effect on body weight was offset by a reduction in fecal output during the 4-hour period post administration. This reduction in fecal output was likely due to fluid shifts from the gastrointestinal tract resulting in a lower volume of fecal material.



Figure 4. Body weight loss is not greatly affected by furosemide dose. No significant difference in weight loss between 150 mg, 250 mg, and 500 mg.

Withholding water 4 hours after administration of 500 mg of furosemide significantly affects body

weight loss. When water was withheld, horses lost an average of 32 lb, whereas in a separate study horses given free-choice access to water during the same time frame only lost an average of 14 lb.

### How does furosemide affect water intake?

A series of studies was performed at KER to determine how furosemide affects 24-hour water intake in exercised and unexercised horses. Surprisingly, these studies showed that furosemide did not affect 24-hour water intake, regardless of dose amount, in either the exercised or unexercised group. All of the exercised horses did, however, drink more water than the unexercised group (Figures 5 and 6).



Figure 5. Furosemide alone does not affect water intake.

Figure 6. Furosemide dose does not affect water intake independent of exercise. Exercise increases water intake, but the dose of furosemide does not.

These findings are important because they showed that when water is withheld from horses for 4 hours after furosemide administration they do not drink additional water during the next 20 hours even though their 24-hour urinary output is significantly increased. The net result of this mismatch between fluid intake and loss is that there is a dose-dependent 24-hour weight loss in horses receiving furosemide.

### How long does it take the horse to recover from furosemide administration?

KER measured the length of time required for six Thoroughbred racehorses administered 250 mg (5 cc) of furosemide to regain body weight losses following racing in Florida during the winter. The horses' body weights averaged 35 lb lighter 24 hours post-race, and it took three days for horses to return to their pre-race weights (Figure 7).



Furosemide is a diuretic that decreases sodium absorption in the kidney. This results in increased production of dilute urine and fluid loss. Further, furosemide interferes with transport of calcium and magnesium in the kidney.

In KER-conducted furosemide dose-response studies, furosemide caused a massive increase in urinary sodium and chloride excretion during the first 4 hours after administration, with excretion equaling as much as 40-50 times that of untreated horses (Figure 8). Potassium excretion during the first 4 hours post-dosing was unaffected by furosemide regardless of dose amount.

In a series of longer balance trials, researchers at KER used six fit Thoroughbreds to determine the effect of furosemide on urinary and fecal mineral excretion for 24 hours before and at 24, 48, and 72 hours after furosemide administration both with and without exercise (Pagan et al., 2014). Calcium excretion increased following a 250-mg dose of furosemide and remained elevated for 72 hours after treatment, and overall calcium balance remained low for at least 72 hours after administration (Figure 9).

# Can recovery be influenced through dietary supplementation?

Fortunately, the minerals that are lost as a result of furosemide administration can easily be replaced

through proper supplementation. To improve weight recovery and replace these mineral losses, KER developed a two-stage electrolyte program called Race Recovery<sup>™</sup>. Race Recovery Paste is used immediately after racing and serves to stimulate thirst and hasten body-weight recovery. KER studies have shown that horses had a 17% increase in 24-hour water intake and a 30% improvement in body-weight rebound when given Race Recovery Paste compared to control horses.

Race Recovery Powder is fortified with highly bioavailable sources of electrolytes and minerals. KER balance trials have shown that Race Recovery Powder is effective in replacing electrolytes, including calcium and magnesium, lost in sweat and urine in exercised horses treated with furosemide.



Figure 7. Horses require 72 hours post-racing to return to preadministration body weight when treated with furosemide.



Figure 8. Urinary sodium and chloride excretion during the first 4 hours after furosemide administration was as much as 40-50 times that of controls.



Figure 9. Urinary calcium excretion increased after furosemide was given and remained elevated for 72 hours. Calcium balance was lower after dosing with furosemide and remained so for at least 72 hours.

### Take-home message

Though furosemide is an effective preventive for EIPH, it causes substantial loss of body weight regardless of dose amount (3 cc to 10 cc). Furosemide reduces the energy cost of exercise, which has given it a reputation as a performance-enhancer. One disadvantage of furosemide is a delayed return to pre-administration body weight, with horses requiring 3 days to fully recover from lost weight. Further, furosemide causes a substantial loss of minerals, including a 40- to 50-fold increase in 4-hour urinary sodium and chloride loss and a sustained calcium loss over several days. With Race Recovery, mineral losses are entirely reversible. Race Recovery stimulates thirst and replaces body weight quickly. Race Recovery Powder is suitable for use as a daily electrolyte supplement.

### References

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