LASIX REVISITED: THE AMERICAN HORSEMEN'S STORY

Medication Forum

Saturday, January 14, 2012

9:00 am – 11:00 am
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By

THOMAS TOBIN MVB, MRCVS, PhD, DABT

The Maxwell H. Gluck Equine Research Center University of Kentucky Lexington, Kentucky, 40546-0099

and

KIMBERLY BREWER, DVM

Phoenix Rising Veterinary 1711 Lakefield North Court Wellington FLA, 33414



SUMMARY

Revisit mechanism of action of Furosemide Connect some Furosemide dots.

Horsemen have long withdrawn water prerace.

Furosemide allowed standardization of this pre-race "fluid reduction" procedure.

"Fluid reduction" reduces the susceptibility of lung tissue to shock wave damage.

→ <u>reduces EIPH.</u>

TAKE HOME MESSAGE

1/ FUROSEMIDE VERY EFFECTIVELY REDUCES EIPH

2/ AMERICAN HORSEMEN WERE THE FIRST TO IDENTIFY THE NOVEL AND UNIQUE ANTI-EPISTAXIS EFFECTS OF FUROSEMIDE

WATER WITHHOLDING

- 1/ Horsemen for many years have withheld water pre-race.
- 2/ Furosemide administration apparently started in the late 1960s as an extension of this pre-race water withholding.
- 3/ Horsemen noted that it reduced EIPH.

REGULATORY ACCEPTANCE

Based on its perceived efficacy in the prevention of EIPH, horsemen sought regulatory approval for Furosemide.

In the early 80s Illinois sought to ban Furosemide: Illinois horsemen went on strike: Furosemide was very rapidly approved in Illinois.

EFFECTS ON DRUG DETECTION

A possible problem with Furosemide was its diluting effect on certain drugs/drug metabolites in urine.

This effect can be marked [20 fold] but is also brief.

Research from Kentucky showed that the diluting effect was over within 4 hours after a 250 mg IV dose.

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EFFECTS ON DRUG DETECTION

This work was confirmed by other researchers, which helped with approval of Furosemide.

→The four hour rule for Furosemide.

→ Research supported by the Kentucky HBPA gave rise to the 100ng/ml 4 hour regulatory threshold [1983].

FURODSEMIDE AND DRUG DETECTION

THE POSITION OF MOST ANALYSTS [Maylin, Sams, TT] IS THAT UNDER CURRENT RULES AND WITH CURRENT TESTING TECHNOLOGY THERE IS NO SIGNIFICANT INTERFERENCE WITH DRUG TESTING PROCEDURES BY FUROSMIDE

REGULATORY ACCEPTANCE

In September 1995, New York became the last major racing state to approve Furosemide.

REVISIT THE MECHANISM OF THE ANTI-EPISTAXIS **EFFECT OF FUROSEMIDE**

THE BLOOD PRESSURE THEORY OF EIPH

One suggestion is that EIPH is due to the unusually high blood pressures in the equine pulmonary system during intense exercise ["Capillary stress failure" theory].

Furosemide acts to reduce pulmonary blood pressure and in this way is thought to reduce EIPH.

THE SHOCK WAVE THEORY OF EIPH

Schroeter et al, EVJ, 1998: In the running horse intense shock waves are transmitted up the [lead] foreleg.

These shock waves reach the lung and travel "north" through the lung tissue.

THE SHOCK WAVE THEORY OF EIPH

When these shock waves hit the interface between the lung and the thorax they are reflected back into the lung.

Reflected waves double the intensity of half of the incoming waves.

→ Local capillary rupture → EIPH.

SHOCK WAVE THEORY

THE SHOCK WAVE THEORY EXPLAINS:

1/ The unusual location of EIPH lesions in the dorso-caudal lobes.

2/ Why EIPH damage occurs preferentially on the lead forelimb side.

3/ Why EIPH has never been recorded in swimming horses [Hong Kong data].

SHOCK WAVE THEORY

4/ Explains how furosemide acts; reduces shock wave damage by reducing the mass [water content] of the delicate alveolar tissues.

5/ Explains why EIPH is more likely to occur on hard fast tracks [more intense shock waves] and in Steeplechase horses.

SHOCK WAVE THEORY

6/ Why Furosemide reduces EIPH even though the drug is largely eliminated at four hours after administration.

7/ Furosemide is still effective at 4 hours after administration because the effect is action is due to water volume reduction rather than to a direct pharmacological effect of Furosemide.

8/ Explains why the original water withholding approach served to reduce EIPH/ improve performance.

9/ If reducing lung hydration reduces EIPH, what effects does increasing lung hydration have on lung physiology?

1/ The normal horse running at top speed is unable to fully oxygenate his blood.

2/ If you over-hydrate a horse this inability to fully oxygenate his/her blood is accentuated, which has the potential to reduce performance.

8/ There are reports that EIPH is also accentuated by over-hydration, consistent with the effects of water withholding and furosemide on EIPH.

9/ It appears that hydration of the lung decreases its ability to oxygenate blood and reduced hydration reduces EIPH.

HYDRATION AND RACING

For racing purposes, a water withheld lung is a more efficient lung.

A hydrated horse is likely to perform suboptimally.

A water withheld horse will perform better.

In the absence of furosemide, the hydration status of a horse is unknown.

9/ POSSILE OUTCOMES FOR RACING:

Absent Furosemide, the lung hydration status of a horse is unknown.

A hydrated horse is likely to perform suboptimally.

A water withheld horse will perform better.

I am not aware of any in place test that can distinguish these situations.

9/ I am not aware of any in place test that can define the lung hydration status of a horse.

10/ However, a horse on Furosemide is clearly water withdrawn and its status as such is clearly communicated to the bettor.

SUMMARY

1/ I believe that EIPH is not EXERCISE Induced Pulmonary Hemorrhage.

2/ The correct title would be SHOCK WAVE Induced Pulmonary Hemorrhage.

3/ Furosemide appears to act by reducing the water content of the lung, making the lung more resistant to EIPH.

SUMMARY

This action of furosemide is entirely consistent with and explains the traditional approach of withholding water before a race.

Treating a horse with furosemide prerace immediately communicates that the horse is being pointed for and is capable of an optimal performance.

TAKE HOME MESSAGE

AMERICAN HORSEMEN WERE THE FIRST TO IDENTIFY THIS UNIQUE AND NOVEL ANTI-EPISTAXIS EFFECT OF FUROSEMIDE

Thank You

This and other ongoing research in 2011 and work on the HBPA World Rules Book has been made possible by generous support from the Florida HBPA, the Indiana HBPA, the Pennsylvania HBPA, the National HBPA, the Kentucky HBPA, the Minnesota HBPA, the Ontario HBPA, the Nebraska HBPA and the Washington HBPA, as well as ongoing support over the years from many other HBPAs, and which support is gratefully acknowledged.

Acknowledgements

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gratefully acknowledged.

EFFICACY OF LASIX

- FACT: LASIX HAS BEEN SHOWN, CLINICALLY & EXPERIMENTALLY, TO REDUCE EIPH/EPISTAXIS

- FACT: EXPERIMENTALLY, LASIX WAS MOST EFFECTIVE AGAINST HIGH SCORE EIPH [Morley, colleagues]

- FACT :IN NEW YORK, LASIX APPROVAL REDUCED EPISTAXIS ALMOST 80%

EFFICACY OF LASIX

EXPERIMENTAL WORK

LASIX WAS MOST EFFECTIVE AGAINST HIGH SCORE EIPH

[Hinchcliff, Morley, Guthrie, JAVMA Vol 235, No 1 July 1, 2009]

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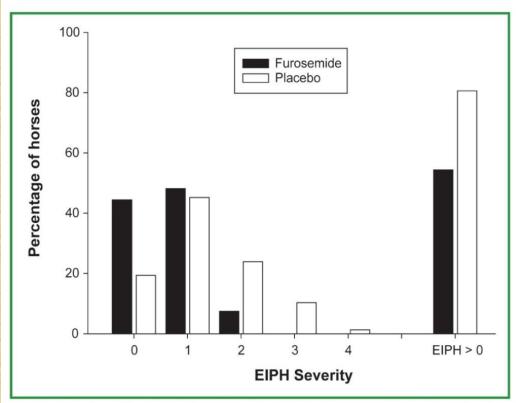


Figure 1—Distribution of scores for endoscopic severity of EIPH in Thoroughbred horses that raced following administration of furo-semide (500 mg, IV; n = 161) or a placebo (saline solution; 156).

NOTE THE MARKED EFFECT OF FUROSEMIDE IN PREVENTING GRADE 2, 3 AND 4 EIPH SCORES

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EFFICACY OF LASIX ON RACETRACK

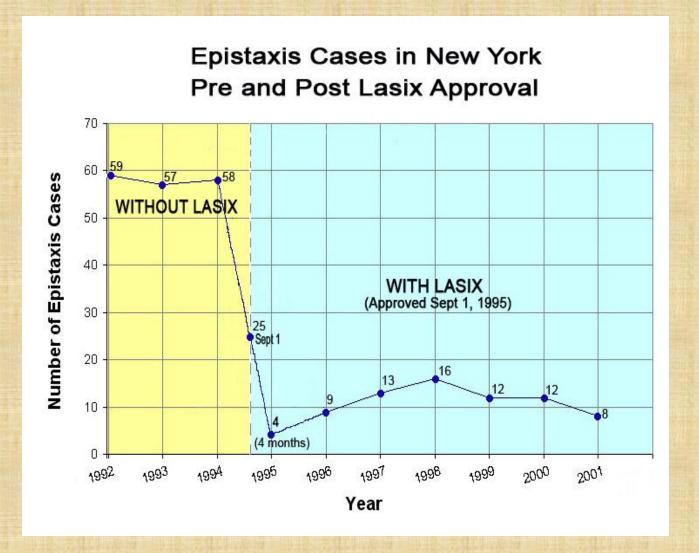
IN NEW YORK RACING, LASIX REDUCED EIPH ALMOST 80%

[Data from Heller, "Run Baby Run" page 112, published 1992]

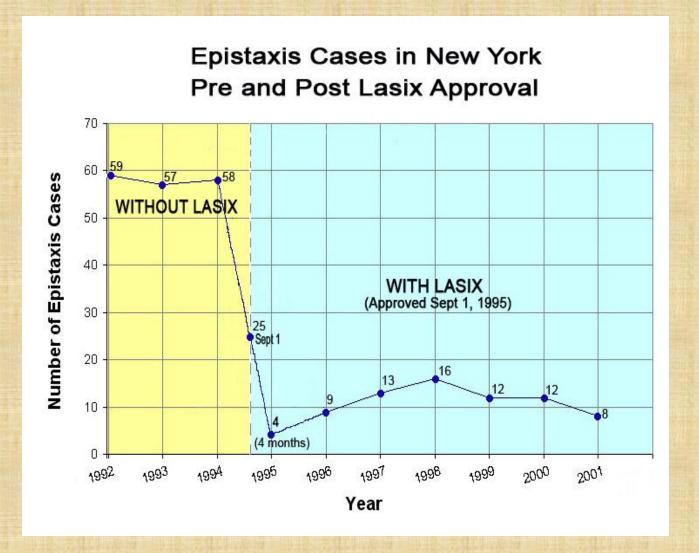
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