THE ROLE OF NSAIDS AND THE EQUINE INTESTINE

Nonsteroidal anti-inflammatory drugs (NSAIDS) are commonly used for horses. Amongst the most common are phenylbutazone (bute), flunixin meglumine (banamine), or firocoxib (Equioxx). NSAIDS are administered when a horse has a sprain, colic, generally not feeling well, arthritis, or laminitis. They are also administered after surgery, or during an illness, such as influenza. We use the NSAIDS for horses, much as we use aspirin for ourselves.

We know from research in humans that NSAIDS usage is closely associated with gastrointestinal irritation. Studies in the horse have indicated the same thing. A review article written by Marshall et al, (2011) has investigated the research and summarized the effects of NSAIDS on the equine intestinal tract. (Marshall and Blikslager, 2011)

Before reviewing the contents of the article, let’s quickly review the parts to the equine digestive system. The following is a small review of the digestive system.

The Mouth:
Digestion begins in the mouth, also known as the oral cavity.

The Esophagus:
The esophagus connects the mouth to the stomach. It is about four feet in length. The cardiac sphincter at the caudal end of the esophagus (between the esophagus and the stomach), is very muscular. This sphincter is the main reason why horses are unable to vomit.

The Stomach:
The horse has a small stomach. It does not perform all of the digestive tasks and has a relatively short transit time of two to four hours. There are two sections to the horse’s stomach, the non-glandular proximal region and the glandular distal region. The non-glandular region is smooth, whilst the glandular region is rough.

Acid and digestive enzymes break down the food in the stomach so that the constituents can be absorbed.

The Small Intestine:
The horse’s small intestine is responsible for most of the absorption. The transit time in the small intestine is 0.5 to 1.5 hours. There are three parts to the small intestine, the
duodenum, jejunum and ileum. Some of the enzymatic breakdown occurs in the duodenum. These enzymes originate in the stomach, the liver, or the pancreas. The horse does not have a gall bladder. The majority of absorption occurs in the jejunum.

### The Large Intestine:

The large intestine is made up of the cecum and colon. The transit time through the large intestine is about 35 to 50 hours, or more! About 50% of the caloric yield is absorbed in the large intestine. This includes fermentation of fibers, as well as sugars that have not been absorbed by the small intestine.

#### Cecum:

The cecum is a blind pouch at the head of the large intestine. It is fairly large, holding about seven to eight U.S. gallons of ingesta. It contains bacteria to break down plant fiber through fermentation. In humans, the cecum is very small, without the significance of that in the horse.

#### Colon:

The large colon, small colon, and rectum make up the remainder of the large intestine.

The large colon holds about 20 gallons of ingesta and is about 10 to 12 feet long.

The parts to the large colon are important. I have listed them below, in order.

- Right ventral (lower) colon
  - Sternal flexure
- Left ventral (lower) colon
  - Pelvic flexure
- Left dorsal (upper) colon
  - Diaphragmatic flexure
- Right dorsal (upper) colon
- Transverse colon

The main purpose of the large colon is the fermentation of fiber and the absorption of volatile fatty acids. If you follow carefully the path of the large colon, you see that it crosses back and forth across the abdomen. The flexures are narrowed bends in the
large colon, where the colon changes direction. These flexures are common places for an impaction colic.

The transverse colon attaches to the small colon where water is absorbed and fecal balls are formed. The small colon is about 10 to 12 feet in length, which is why a horse can still have fecal matter in the stall when it has an impaction colic. The last areas are the rectum and the anus.

Role of Prostaglandins:
Prostaglandins are necessary for normal tissue repair. There are two main types of enzymes that make the prostaglandins, COX-1 and COX-2. COX-1 is necessary for normal tissue functioning. COX-2 is up-regulated in response to injury. We want to reduce the up-regulation of COX-2, but we do not want to inhibit the response to COX-1. The problem with most NSAIDS is that they inhibit both.

Barrier Function:
The intestines have a unique function that they absorb nutrients, but also need to prevent the absorption or entry of particles that are damaging to the body.

During some types of colic, the barrier of the intestines is damaged because of lack of blood supply (ischemia). This occurs in the jejunum with a twist in the intestines or from a strangulating lipoma.

Effects of NSAIDS on Restoration of Barrier Function of The Jejunum:
The effects of NSAIDS on the cells of the jejunum depend upon which NSAID is used. Banamine retards the recovery of the barrier function in the jejunum in three different important tests. Interestingly, neither Equioxx nor meloxicam retarded the recovery of the barrier function in any of the tests. When lidocaine was added to the administration of banamine, the results were quite different in that the slowing of recovery of the barrier function was not present.

This should not be a surprise. NSAIDS also slow healing of other body systems. In humans, after knee ACL surgery, it is no longer recommended to take NSAIDS for pain nor swelling because of the delay in healing.

Effects of NSAIDS on The Large Intestine:
Barrier Function. Interestingly, the mechanisms of action in the large intestine barrier function are different than in the small intestine. In the large intestine, the barrier function takes longer to re-establish than in the small intestine. Because of this difference in the healing process, banamine has not been shown to slow the recovery of the barrier function further because it is a different mechanism of action.
**Right Dorsal Colitis.** It has been shown that 21 days of bute causes a decrease in volatile fatty acid production and a decrease in mucosal blood flow. Right dorsal colitis can cause death in a horse. Other NSAIDS have not been studied.

**Effects of NSAIDS on Intestinal Motility of Both Large And Small Intestines:**
NSAIDS reduce the intestinal motility of both the large and small intestines. The following NSAIDS have been shown to reduce the intestinal motility:

- Banamine
- Bute
- Ketoprofen
- Indomethacin

This should be kept in mind when stabling horses. A new study out showed that intestinal motility was reduced in stabled horses compared to pasture horses. (Williams et al., 2011) Although the effect of stabling plus NSAIDS has not been studied, it may be important when stabling horses.

**Take Home Message:**
- NSAIDS affect both the large and small intestines
- NSAIDS slow the healing of the small intestines (as well as other body systems)
- Prolonged use of NSAIDS can result in right dorsal colitis, which can be deadly
- NSAIDS reduce the motility of the intestines
- NSAIDS should be used for short-term use only

**Note:**
I have used the term banamine in the article for ease of readability. My intent is any drug that is flunixin meglumine, not just the brand name banamine. I have used the term bute in the article for ease of readability. My intent is any drug that is phenylbutazone.
References:

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Stomach: http://etc.usf.edu/clipart/58600/58622/58622_stomach.htm
Digestive tract: http://ukpmc.ac.uk/articles/PMC2769846?figure=fig2/

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This article originally appeared in Dr. Eleanor Kellon's ezine, The Horse's Mouth. For subscription information, please go to www.drkellon.com