

The Corticosteroid Laminitis Story: What Do We Know?

Marian R. Graves, DVM, Technical Services Veterinarian, American Regent, Inc.

Pain and inflammation associated with development of osteoarthritis (OA) can be career-limiting for athletic horses required to perform at a high level. In routine management of OA by equine practitioners, intra-articular corticosteroids are considered a cornerstone of therapy to reduce inflammation. However, because horses have developed laminitis following systemic corticosteroid administration, practitioners remain concerned about the potential risk of inducing laminitis. The following information is provided as a summary of the basis for, and evidence of, an association between corticosteroids and laminitis, along with clinical recommendations amidst this concern.

The general theories on the pathogenesis of laminitis currently focus on:

- **A primary disturbance of perfusion of the laminae followed by secondary events that lead to laminar injury;**¹
- **A disturbance in the structure and strength of the epidermal and dermal laminae by toxic or metabolic substances;**¹
- **Increased matrix metalloproteinase (MMP) activity (that can be induced, for example, by endotoxins or streptococcal exotoxins);**¹
- **Endocrinopathies primarily relating to pituitary pars intermedia dysfunction (PPID), equine metabolic syndrome (EMS) and insulin resistance (IR)**¹
 - **Insulin resistance (IR) is associated with a predisposition to laminitis**²
 - Glucocorticoids inhibit the actions of insulin by disrupting post-receptor signaling pathways and administration of dexamethasone has been shown to induce IR in horses³
 - Glucocorticoid-induced decrease in insulin sensitivity may increase the risk for development of laminitis²

Current understanding of the molecular mechanisms of glucocorticoid action can be implicated in most of the above theories.¹

Summary of the Evidence:²

The data reflects the overall lack of information on iatrogenic laminitis and the small risk of inducing laminitis in healthy horses following systemic administration of corticosteroids. In a 2016 review, no studies currently investigating a causal association between corticosteroid administration and laminitis were identified, and insufficient evidence exists to support a direct link between corticosteroids and laminitis in healthy horses. However, there is evidence of an association between administration of multiple doses of systemic corticosteroids and onset of laminitis in horses with underlying endocrine disorders, as well as severe systemic disease, or SIRS [systemic inflammatory response syndrome].

Data:

- In vitro research demonstrated corticosteroid potentiation of the vasoconstrictor actions of catecholamines and serotonin, suggesting that resulting venous obstruction in the hoof may cause laminitis

[Data continued]

- Skin perfusion was decreased in a study using six days of daily dexamethasone and the authors suggested perfusion to the hoof may also be reduced, increasing risk of laminitis
- Following a standard overnight dexamethasone suppression test, non-obese ponies with a history of prior laminitis showed elevated insulin concentration and exaggerated production of insulin in response to corticosteroids compared to control ponies
- After a single administration of triamcinolone, one study reported a prolonged period [3 - 4 days] of hyperglycemia, hyperinsulinemia and hypertriglyceridemia. Additionally, four of the five horses in this study developed laminar rings without clinical laminitis
- Healthy horses demonstrated marked insulin resistance following alternate day dexamethasone administration for three weeks
- An observational study investigating iatrogenic laminitis following treatment with triamcinolone reported a prevalence of 0.8% [n=1/132; 95% confidence interval 0 - 2.2%]. In the same study, three other cases of laminitis were reported, of which two were diagnosed with laminitis prior to triamcinolone but did not develop laminitis subsequent to its use. Therefore, laminitis following triamcinolone administration was observed in 33% of horses with a previous history of laminitis [n=1/3]. The third horse developed laminitis 18 months after triamcinolone therapy as a result of post-foaling toxemic metritis
- Of 106 laminitis cases reported to Center for Veterinary Medicine (CVM) as adverse drug events over a 26 year period, 18% [n=19] were attributed to corticosteroid treatment, whereas 35% of cases [n=37] were attributed to administration of anthelmintics and 32% [n=34] were reported following treatment with antibiotics or antiprotozoals

Take Home and Additional Sources of Information:

- **Practitioners are encouraged to take appropriate steps to assess *any* underlying systemic disease that could potentially predispose horses to laminitis (including insulin dysregulation or resistance, EMS, PPID, SIRS, etc.). Assessment should be conducted prior to administration of corticosteroids within the scope of treatment of OA, particularly where repeated doses are indicated. Horse age, breed, body condition, and history are important factors to consider. For the complete summary of the data and risk factors described above, please visit:**

<https://veterinaryevidence.org/index.php/ve/article/view/12/17>, No Evidence That Therapeutic Systemic Corticosteroid Administration is Associated With Laminitis in Adult Horses Without Underlying Endocrine or Severe Systemic Disease.

For clinical evaluation of potential endocrine disease and current diagnostic protocols, practitioners are referred to:

<http://sites.tufts.edu/equineendogroup>⁴

References:

1. Cornelisse, CJ, Robinson NE. Glucocorticoid therapy and the risk of equine laminitis. *Equine Vet Edu*. 2013; 25(1): 39-46
2. McGowan, C. No evidence that therapeutic systemic corticosteroid administration is associated with laminitis in adult horses without underlying endocrine or severe systemic disease. *Vet Evi Online*. 2016; 1(1): 1-17 Accessed October 24, 2018.
3. Tadros EM, Frank N. Endocrine Disorders and Laminitis. *Equine Vet Educ*. 2013; 25(3): 152-162. doi:10.1111/j.2042-3292.2011.00327
4. Equine Endocrinology Group website. <http://sites.tufts.edu/equineendogroup/> Accessed June 10, 2019