

CURRENT APPROACHES TO TREATMENT AND PREVENTION OF LAMINITIS

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There has been very little variation in our approach to the treatment of acute and chronic laminitis over the course of recorded history, mostly due to the fact that the normal function of the lamellae in suspending the distal phalanx within the hoof is largely unrecoverable once disrupted. Therapeutic efforts in laminitis should be focused on prevention and early intervention in acute cases. We now recognize that there are important differences in the mechanisms that lead to laminitis depending on the inciting cause, and laminitis may be classified as being sepsis-associated, endocrinopathic or supporting limb laminitis, with the preventative/therapeutic strategies and priorities being different for each.

Sepsis-associated laminitis

Once established, laminitis causes derangements of lamellar structure that are largely irreversible; therefore efforts should be aimed at prevention and this begins with identification of the “at risk” horse. Conditions associated with a high risk of laminitis development include colitis, enteritis, complicated gastrointestinal obstructions, metritis, pneumonia and alimentary carbohydrate overload. Therapeutic efforts to control the primary disease and systemic inflammation in cases of equine sepsis are paramount. Intravenous fluids for circulatory support, binding of circulating endotoxin using polymixin B and hyperimmune plasma and the use of NSAIDs to control downstream inflammation are reasonable treatment strategies particularly in cases of gut-derived sepsis. Prophylactic continuous cooling of the feet has been demonstrated in several experimental studies and one clinical study of naturally occurring colitis to be protective and this is the only therapy to have withstood scientific rigor in human or veterinary research for the prevention of end-organ damage in sepsis.

Digital hypothermia (cryotherapy)

The protective effect of prophylactic continuous cooling of the feet has been demonstrated in several experimental studies of sepsis-associated laminitis and it remains the only therapy to repeatedly withstand scientific rigor. Supporting its clinical application, a recent retrospective study of hospitalized equine colitis cases showed that survival was 98% in horses that did not develop laminitis, compared with only 48% in those that did, and that horses treated with digital hypothermia were 10 times less likely

to develop laminitis. There are several potential mechanisms by which hypothermia might protect against sepsis-related laminitis. When applied before the onset of clinical lameness in an experimental model, continuous digital hypothermia dramatically inhibited transcription of inflammatory mediators including cytokines, chemokines and cyclooxygenase in lamellar tissue. In addition, hypothermia had an inhibitory effect on lamellar matrix metalloproteinase expression, a finding consistent with experimental studies of hypothermia in brain trauma and cardiac arrest. Interestingly, despite a marked therapeutic effect in preventing lesion progression when applied after the onset of lameness in an experimental laminitis model, inhibition of inflammation did not appear to be a therapeutic mechanism based on the lack of a detectable effect on inflammatory mediator expression. In other animal models of sepsis, preservation of cellular energy metabolism and mitochondrial function, reduced inflammation and inhibition of apoptotic pathways are effects of hypothermia that protect against end-organ damage in the liver, lung and heart. The contribution of cellular energy failure (non-ischemic) to the different forms of laminitis is unclear, but hypothermia of the equine digit may exert protective effects on lamellar tissue by modulating mitochondrial function and reducing metabolic demands.

Any horse that is at immediate risk of developing acute laminitis is an appropriate candidate for the application of continuous distal limb hypothermia. Although prophylactic application is ideal, there is experimental evidence supporting digital hypothermia application in horses with acute sepsis-related laminitis (i.e., with pre-existing lameness). There is currently no scientific evidence to guide the duration of therapeutic hypothermia nor the temperature specifically in the clinical setting; however, continuous cooling of all four feet until after the abatement of clinical signs/clinical laboratory evidence of sepsis is generally recommended, which may be several days in some cases. Based on experimental data, digital hypothermia should be aimed at achieving hoof wall surface temperatures that are (at least) consistently below 10°C, and it appears that cooling from the mid-cannon region distally (including the hoof and sole) is required to effectively cool incoming arterial blood as well as prevent heat transfer from the environment to the lamellae via the hoof itself. A water interface against the limb overcomes the conduction barrier of the hair coat and negates the difficulty in getting consistent contact of a heat exchanger with the uneven surface of the equine distal limb. Immersion of the limb from the mid-upper metacarpus/metatarsus distally in an ice and water mixture effectively achieves this, although constant ice replenishment is labor intensive. A practical and effective solution particularly for field application is still lacking.

There are anecdotal reports of complications in horses being treated with digital hypothermia: dermatitis of the pastern and maceration of the coronary band can occur

particularly when cooling for more than 5 days, but in most cases this resolves with no or minimal treatment once the cooling is ceased. On rare occasions, more extensive and severe necrosis of superficial distal limb tissue that is consistent with true frostbite is reported – this appears to be more commonly associated with the application of ice typically directly from a freezer (between -20°C and -30°C) directly to the limb without a water interface, which should be avoided.

Endocrinopathic laminitis

The key to prevention of endocrinopathic laminitis is early identification of horses at risk. Testing for evidence of insulin dysregulation (including insulin resistance as well as the propensity for post-prandial hyperinsulinemia) using insulin testing pre and post oral sugar challenge is the most effective way to identify horses and ponies at risk of laminitis development early. Management to reduce the laminitis risk in these cases can then include a combination of dietary control, pasture access management, weight loss and exercise, which can dramatically reduce the risk of laminitis development or progression. Cases that have a profound hyperinsulinemic response to oral sugar ingestion may benefit from medications such as metformin that blunt this insulin response. Since the systemic effects of metformin on insulin sensitivity appear inconsistent, the use of targeted administration (prior to meal/turnout) appears most effective and rational in order to reduce postprandial hyperinsulinemia in these cases. Testing for pituitary pars intermedia dysfunction (PPID) in appropriately aged horses (at least >5 years) can help to identify this condition before the development of irreversible laminitis pathology. It is important to recognize that although laminitis may be the only important clinical manifestation of PPID in some horses, the recognition of clinical signs of laminitis (lameness) often only occurs after the development of irreversible laminitis pathology, which can be insidious and gradual. Treatment of PPID with pergolide can be quite effective in preventing laminitis development (or its progression) however dosage adjustment guided by frequent monitoring of ACTH is required for adequate control in most cases. It is impossible to adequately control chronic laminitis in cases where there is inadequate control of an underlying endocrinopathy.

Supporting-limb laminitis

It appears that cyclic loading and unloading of the feet plays an essential role in digital homeostasis. In a horse that is preferentially weight bearing on one limb, it is currently not clear whether static or dynamic manipulations of the supporting limb (using orthotics or other devices) are sufficient to improve lamellar perfusion and energy balance without intermittent complete unweighting of the limb, however studies specifically evaluating this are underway. The key to supporting limb laminitis prevention is likely to be the development of strategies to monitor and then regulate load cycling frequency in

the supporting limb of patients at risk. Monitoring should include some form of serial assessment of limb load cycling – human pedometer devices and fitness tracking devices that incorporate accelerometers can track limb load cycling over time and may be of use clinically. In horses at risk, regular encouragement to walk may be beneficial, however there is insufficient data to support specific recommendations at this stage and the logistics of this may depend on the nature and severity of the primary condition. Strategies to reduce weight on the supporting limb may include partial sling support and periodic forced or encouraged recumbency. Although sedation may help to encourage recumbency, it also reduces voluntary exercise and limb load cycling in stabled patients and therefore may be contraindicated. Effective analgesia to control pain in the primarily affected limb will help to encourage more normal weight-bearing patterns in the supporting limb. The use of NSAIDs, opioids and multimodal or regional analgesic techniques have been reviewed in detail elsewhere.

Treatment of the acute laminitis case

There is experimental evidence that the application of digital hypothermia during the acute phase of sepsis-related laminitis (after lameness develops) can help to limit progression. We have new (unpublished) data indicating that digital hypothermia is also effective in ameliorating laminitis due to hyperinsulinemia in an experimental model, supporting its use as a first aid measure in horses and ponies with an acute bout of laminitis associated with insulin dysregulation/pasture consumption. Although there is no evidence to guide the duration of therapeutic cooling in acute laminitis cases, the therapeutic effect is likely to diminish past seven days after the onset of lameness, particularly if the sepsis has resolved. The analgesic effects of digital hypothermia can also be useful in acute cases in conjunction with traditional pharmacological analgesia (including NSAIDs).

Restricting ambulation is paramount in the early stages of acute laminitis regardless of the cause. Horses should be confined to a stall and encouraged to lie down by providing deep comfortable bedding. Tranquilizers and sedatives may encourage recumbency and reduce voluntary weight-bearing and ambulation in horses with acute laminitis. Providing support to the caudal sole and frog using either orthotic support material attached to the feet (silicone impression material, foam or similar) and/or bedding material that conforms to the foot and yields both under the toe to minimize break over and also while pivoting (ideally sand) can help to reduce mechanical distractive forces on the lamellae and often rapidly improves lameness in acute cases. Careful serial radiographic assessment is essential to track progress in the early stages of acute laminitis.