Medical management of acute laminitis

Laminitis is a medical emergency. It encompasses three distinct forms: sepsis-related laminitis, supporting limb laminitis and endocrinopathic laminitis. The latter is most commonly encountered in equine practice and is associated with hyperinsulinaemia. Regardless of the underlying cause, management of acute laminitis involves treatment of the underlying cause, and providision of analgesia and biomechanical support of the foot.

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Laminitis is a painful and severely debilitating condition commonly encountered in equine practice (*Figure 1*). Three distinct forms of laminitis have been identified; inflammatory or sepsis-related laminitis, supporting limb laminitis and 'endocrinopathic' laminitis (van Eps and Burns, 2019), but endocrinopathic laminitis accounts for the vast majority of cases seen in practice and likely parallels the rise of obesity in equids (Donaldson et al, 2004; Potter et al, 2016; Patterson-Kane et al, 2018). The acute phase of laminitis begins at the onset of clinical signs which may include varying degrees of lameness, increased digital pulses, stiff gait, weight shifting, reluctance to move or sensitivity to hoof testers over the sole, particularly towards the toe (van Eps, 2010a). Laminitis should always be considered a medical emergency and treatment should be instituted immediately at the onset of clinical signs. Irrespective of the primary mechanism, medical management of acute laminitis focuses on treating the underlying cause, providing analgesia and supporting the foot. Regular assessment of the patient is imperative to gauge clinical response, adjust treatment and minimise suffering.

Figure 1. 10-year-old Welsh pony, shifting weight caudally in the typical laminitic stance.

Endocrinopathic laminitis

Equine metabolic syndrome (EMS) and pituitary pars intermedia dysfunction (PPID) are the two endocrinopathic disorders associated with laminitis (Patterson-Kane et al, 2018).

The central features of EMS (*Figure 2*) are insulin dysregulation, obesity (regional or general) and a predisposition to laminitis (Durham et al, 2019). Research studies were pivotal in demonstrating that protracted increases in levels of insulin led to the development of laminitis (Asplin et al, 2007; de Laat et al, 2010) and reduction in hyperinsulinaemia has therefore become fundamental to both the prevention and management of laminitis in horses with EMS.

Dietary management is critical in limiting hyperinsulinemia and thus preventing and managing endocrinopathic laminitis. At the onset of clinical signs, the patient should be removed from pasture and placed on a diet low in non-structural carbohydrates (NSC) with the aim of preventing elevations in insulin levels in response to high levels of dietary sugars. This may be achieved by feeding a forage-based ration (ideally forage with <10% NSC) at approximately 1.5% of body weight (Durham et al, 2019). A ration balancer should also be fed to ensure adequate intake of protein, vitamins and minerals (Durham et al, 2019).

In addition to dietary management, medical interventions may also hasten the recovery from laminitis in selected cases (*Table 1*). Metformin has historically been used to limit hyperinsulinemia but oral bioavailability in horses is poor and studies showing its effectiveness at improving insulin sensitivity have yielded inconsistent results (Durham et al, 2008; Hustace et al, 2009; Tinworth et al, 2012). Studies have demonstrated that the administration of levothyroxine (0.1mg/kg per os once a day) to obese horses with a his-

Figure 2. 12-year-old Quarter horse mare displaying the typical obese equine metabolic syndrome phenotype.

tory of laminitis results in both weight loss and improvements in insulin sensitivity compared to controls (Sommardahl et al, 2005; Frank et al, 2008a). A number of reports have also shown that levothyroxine is safe and well tolerated even when used for very long periods or at high doses (Sommardahl et al, 2005; Frank et al, 2008b; Bertin et al, 2019). Levothyroxine tablets and liquids are registered for use in canines but these products have limitations in horses and extemporaneous preparations are generally considered more suitable. In other species, the bioavailability of levothyroxine is reduced markedly by concurrent feeding, therefore administration of oral paste into the mouth on an empty stomach is recommended.

While not registered for use in horses, sodium-glucose cotransporter 2 inhibitors (SGLT2i) offer a novel treatment option for hyperinsulinemia. SGLT2i promote urinary glucose excretion, thereby lowering blood glucose levels and reducing the stimulus for insulin secretion from the pancreas (Nauck, 2014; Kalra et al, 2016). Experimental studies have demonstrated the effectiveness of the SGLT2i in the treatment of hyperinsulinemia (Frank, 2018; Meier et al, 2018, 2019). Ertugliflozin is the newest SGLT2i developed for human medicine and it is being used with increasing frequency in horses. However, as pharmacokinetic and long-term safety data are lacking, the potential for adverse effects should be considered, and horses should be closely monitored throughout treatment. A recent case series demonstrated that ertugliflozin significantly reduced insulin concentrations and improved laminitis scores in 51 horses and ponies with laminitis within 30 days (Sundra et al, 2022). This study suggests that ertugliflozin may be an effective pharmacological aid for the treatment of hyperinsulinemia and endocrinopathic laminitis in horses that fail to improve following diet and management changes.

PPID is a condition affecting aged horses and results from loss of dopaminergic inhibition at the pars intermedia (Durham, 2016; *Figure 3*). The link between PPID and laminitis remains to be elucidated; studies suggest that insulin dysregulation occurs in approximately 30–60% of PPID cases (Horn et al, 2019; McFarlane, 2022), and those with concurrent PPID and hyperinsulinemia may be at a higher risk of developing laminitis (Johnson et al, 2004). Whether the two conditions are linked has not yet been determined and it has been proposed that EMS and PPID may simply occur concurrently without any causal association (McFarlane, 2011). Insulin dysregulation should be investigated and managed in all cases of PPID-associated laminitis (McFarlane et al, 2016).

Pergolide, a dopamine agonist, has been the mainstay of PPID treatment for over two decades (*Table 2*). While pergolide use is associated with improvement in many of the clinical signs of PPID, there is currently no evidence to suggest pergolide reduces the incidence of laminitis or improves insulin dynamics (Valencia et al, 2018). A study in Australia demonstrated that the administration of pergolide was strongly associated with survival (Horn et al, 2019), but this may reflect commitment of owners rather than the effect of pergolide per se. Compliance associated with daily, oral administration of pergolide (and many other medications) can be poor. A report highlighted that more than 50% of horses did not receive the recommended dose of pergolide with compliance rates dropping to 25% among owners of Shetland ponies and geriatric horses (Hague et al, 2021). Cabergoline is another dopamine agonist that is an increasingly used as an alternative to pergolide. The mechanism of action is the same but cabergoline can be administered by owners once per week as a long-acting intramuscular injection. Cabergoline has been used in the USA for a number of years with good anecdotal responses to treatment reported. The results from a small number of horses with PPID treated with the long-acting cabergoline injection demonstrated that it is effective in suppressing pars intermedia output and improving clinical signs of PPID for an extended period of time (author's unpublished data). Further studies assessing the pharmacokinetics and long-term safety of cabergoline in horses are warranted.

Inflammatory or sepsis-related laminitis

Ingestion of excessive amounts of carbohydrate (such as grain overload; Potter et al, 2016) leads to a drop in pH in the large colon which causes the lining of the hindgut to deteriorate and absorption of toxins into the systemic circulation occurs (Katz and Bailey, 2012). These toxins and subsequent systemic inflammatory response may be important factors in lamellar injury and the development of laminitis (Skrzypczak et al, 2022). If inadvertent grain overload is recognised early enough, gastric lavage to prevent ingested contents from reaching the large colon may prevent clinical progression. Mineral oil administered by nasogastric tube may encourage intestinal transit of grain, although evidence to support its use is lacking.

Laminitis may also develop as a consequence of diseases which cause a systemic inflammatory response syndrome such as colitis or pneumonia. One study also suggested that insulin resistance will be exacerbated in horses or ponies that develop endotoxaemia, with the administration of levothyroxine for 15 days beforehand, being protective against endotoxin-induced insulin resistance (Tóth et al, 2010). Theoretically reduction in insulin resistance may reduce the risk of laminitis.

Horses exhibiting clinical signs of endotoxaemia should be considered high risk for developing laminitis and preventive measures

Table 1. Treatment options for equine hyperinsulinaemia

Drug	Formulation	Dosage	Mode of action	Considerations
Ertugliflozin*	Tablets/paste	0.05mg/kg per os once daily	SGLT2 inhibitor. Promotes urinary glucose excretion, thereby lowering blood glucose and insulin levels	• Rapidly reduces insulin concentrations and may hasten recovery from laminitis • May be used in both obese and lean equine metabolic syndrome horses • Potential to develop hypertriglyceridaemia and polyuria/polydipsia • Should be used in conjunction with appropriate dietary management
Levothyroxine*	Tablets/paste/powder	0.1mg/kg per os once daily	Synthetic thyroid hormone. Increases metabolic rate, promotes weight loss and improves insulin sensitivity	• Typically used in obese horse to accelerate weight loss and increase insulin sensitivity • Should be used in conjunction with dietary restriction • Anecdotal reports that it helps recovery from laminitis • Absorption affected by feeding, administer on an empty stomach
Metformin*	Tablet/powder	30mg/kg per os twice/three times a day	Blunts glucose absorption and reduces insulin responses	• Poor oral bioavailability in horses • Used to reduce insulin responses to feeding • Administer around 30 minutes before feeding or turnout • Efficacy is widely questioned

*Not registered for use in horses, use in accordance with medicines regulation

such as foot supports and digital cryotherapy (see below) should be considered as pro-active measures that may prevent or limit laminar damage (McFarlane et al, 2016).

Supporting limb laminitis

Supporting limb laminitis develops because of increased loading on a single limb as a result of reduced loading of the contralateral lame limb. In horses, cyclic loading and unloading plays a role in promoting blood flow through the foot, so if there is a prolonged mechanical overload on one digit without sufficient periods of unloading, inadequate perfusion and ischaemia may develop (van Eps et al, 2010). Horses with poor hoof quality and those with a long-toe and low-heel are considered to be at increased risk (Redden, 2004).

Therapy should be aimed at increasing the level of the comfort in the lame limb while supporting the contralateral, weightbearing limb. This can be achieved by raising the heels and loading the palmar aspect of the foot to decrease tension on the deep digital flexor tendon. This support should ideally be initiated early in treatment, before the development of laminitis in the supporting limb.

Figure 3. A 24-year-old miniature pony mare displaying hypertrichosis associated with pituitary pars intermedia dysfunction.

Pain management

Failure to adequately control pain is one of the primary reasons laminitic horses are subjected to euthanasia (Hopster and van Eps, 2019). Pharmacological intervention should provide analgesia without encouraging excessive movement. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used, first-line analgesics for horses with laminitis (Hopsters and van Eps, 2019). Phenylbutazone (2.2mg/kg) or flunixin (0.5–1mg/kg) will provide effective analgesia in most cases of acute laminitis. COX-2 selective NSAIDs (firocoxib, meloxicam) may also be used, although anecdotally their effectiveness for controlling pain associated with acute laminitis is inferior to the non-COX selective NSAIDs. Experimental evidence also suggests that non-selective cyclooxygenase inhibition produces superior analgesia than inhibition of either alone (Martinez et al, 2002).

Paracetamol is a commonly used analgesic in humans and anecdotally appears to be effective in horses with laminitis that require additional pain relief. Although evidence is lacking for its use in horses, the use of paracetamol in one laminitic pony has

Table 2. Treatment options for equine pituitary pars intermedia dysfunction

Drug	Formulation	Dosage	Mode of action	Considerations
Pergolide	Tablets/paste*	2g/kg per os once daily	Dopamine agonist	• Good efficacy and evidence to support its use • Once daily oral administration may be associated with poor medication compliance • Potential to develop transient inappetence and lethargy
Cabergoline*	Long-acting intramuscular injection	0.005mg/kg intramuscularly once weekly	Dopamine agonist	• Once weekly injection may overcome compliance issues • Limited evidence to support its use in horses with pituitary pars intermedia dysfunction • Potential to develop transient inappetence and lethargy for up to 24 hours following injection.

*Not registered for use in horses, use in accordance with medicines regulations.

been described (West et al, 2011) and one report suggests it may be beneficial in the treatment of mechanical lameness (Mercer et al, 2022).

Opioids are typically used as an adjunct to NSAIDs in horses with severe pain (Hopster and van Eps, 2019). The use of morphine, methadone, buprenorphine and tramadol have all been documented in horses (Hopster and van Eps, 2019). A study also demonstrated that fentanyl, applied as transdermal patches, was rapidly absorbed and no adverse effects were noted (Skrzypczak et al, 2022). Side effects associated with opioids include increased locomotion, excitation and impaction colic (Price et al, 2002). However, used appropriately the risk of adverse effects is low and opioids provide potent analgesia and alleviate considerable suffering in acute laminitis. Constant rate infusions of ketamine, lidocaine, acepromazine, xylazine and combinations thereof (Hopster and van Eps, 2019) provide further options for analgesia; however, their use necessitates hospitalisation which may pose practical challenges in some cases.

Strict confinement in deep bedding or provision of alternative solar support is essential to minimise stress placed on the dorsal lamellae during ambulation and to prevent further pain associated with progressive laminar pathology. Turning further increases shearing forces between the lamellae and the consequences of excessive movement should be emphasised to owners. Stabling or confinement to a small fenced-off section of the paddock is required and if this is not available, then hospitalisation of the patient during the acute phase may be necessary and allows for close monitoring and improved case management. The importance of confinement should be emphasised to owners of horses receiving SGLT2 inhibitors as reduction in lameness can be dramatic.

Frequent assessment of the horse is important to monitor progression of disease and response to therapy. A new laminitis grading scale has been developed by researchers in Australia (Meier et al, 2021). The modified-Obel scale provides veterinarians with a more reliable and consistent method to quantify the degree of lameness associated with laminitis and is a useful tool to monitor the clinical status of the patient.

Cryotherapy

Digital hypothermia initiated during the developmental phase of laminitis has been shown to be an effective preventive measure in experimentally induced laminitis (van Eps, 2010b). Ideally, cryotherapy should be initiated early and continuously in the case of carbohydrate overload and sepsis-related laminitis. Some anecdotal reports also suggest that, in the case of colitis, cryotherapy may be beneficial after signs of endotoxaemia develop. To be effective, the entire distal limb should be submerged in a slurry of water and ice which may present practical challenges in a hospital and field setting. However, given the proven benefits of cryotherapy in both endotoxaemia-driven laminitis, clinicians should commence cryotherapy before the onset of laminitic signs. In the author's opinion, cryotherapy should be seen as a preventative rather than curative measure and it therefore has limited application in insidious endocrinopathic laminitis cases.

Foot support

Remedial farriery of the laminitic patient focuses on improving comfort and providing mechanical support to prevent or limit displacement of the third phalanx (Pollitt, 2004). Typically the dorsal laminae are the most severely compromised so it is necessary to redistribute load to the caudal half of the foot and reduce lever forces on the toe and tension from the deep digital flexor tendon (Pollitt, 2004; Reilly et al, 2010).

Farriery 'first-aid' should include the application of a supporting material such as dental impression material, foam pads or urethane pads held in place with gaffa tape or casting material. Standard shoes tend to distribute loading around the periphery of the foot which may potentiate laminar damage. Some controversy exists surrounding shoe removal in acute laminitis, and the decision should be made on a case-by-case basis. If the shoe is removed, care should be taken and shoe removal should be performed as atraumatically as possible to prevent inadvertent damage to the hoof capsule.

Peer-reviewed data documenting the efficacy of different farriery interventions are also lacking (Bamford, 2019). The greatest chance of a successful outcome relies on a cohesive team-based approach between the owner, the veterinarian and the farrier. The farriery plan has to be adaptable and a degree of trial and error is often required, depending on each patient's comfort levels.

Conclusions

Acute laminitis is a medical emergency and while three distinct forms have been identified, endocrinopathic laminitis associated with hyperinsulinemia is most frequently encountered in general

practice. New medications such as ertugliflozin offer promising alternatives to specifically target hyperinsulinemia and may hasten recovery in acute cases. The treatment of laminitis can be challenging but strategies should be aimed at providing pain relief and halting the progression of the disease. In addition to medical management, a team-oriented approach between the owner, veterinarian and farrier is imperative to limit further lamellar damage and provide biomechanical support. Horses suffering from acute laminitis should be closely monitored and response to therapy should be frequently assessed and adjusted based on clinical response. EQ

Conflicts of interest

The author has no conflicts of interest to declare.

KEY POINTS

- Acute laminitis is a medical emergency.
- Frequent assessment of the patient is critical to determine response to pain-relief and therapeutic farriery.
- Endocrinopathic laminitis associated with hyperinsulinemia is most commonly encountered form of laminitis in equine practice.
- Dietary management is critical in the treatment of endocrinopathic laminitis.
- SGLT2 inhibitors may provide a new therapeutic option in cases which fail to respond to dietary management.

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