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TREATMENT PERSPECTIVES FOR EQUINE LAMINITIS: A LITERATURE REVIEW

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Abstract: Laminitis is classified as one of the pathologies that most affect horses, and is classified as inflammation of the laminar tissues. Its cause is multifactorial, in which the following conditions stand out: metabolic syndrome, physical exercise and systemic infections. Laminitis can vary from mild to severe, and the signs can be acute, chronic, refractory and subacute. The aim of this literature review study is to address equine anatomy and pathophysiology, as well as the predisposition and risk factors for laminitis, the types of this disease, diagnostic methods and the pharmacology associated with treatment. The prognosis depends on the speed of diagnosis and the appropriate treatment plan according to the stage of laminitis.
Keywords: laminitis, horses, foot disease, insulin dysregulation, lameness.

INTRODUCTION

According to the IBGE (2022), Brazil has the fourth largest equine herd in the world, with approximately 5 million animals. Because of the great importance of horses to the Brazilian economy, owners and veterinarians should pay attention to cases of laminitis, which is responsible for affecting 15 to 20% of horses, according to the Council of Veterinary Medicine (IBGE, 2022; SYNTEC, 2021).

Laminitis can be defined as a failure in the connection between the distal phalanx and the inside of the hoof, and is the most serious disease affecting the equine hoof (Rosa; Vieira; Edler, 2022). It is popularly referred to as watering and technically described as aseptic pododermatitis (Luz *et al*., 2021).

Laminitis usually affects the thoracic limbs, as they support a large part of the animal's body weight. However, this does not rule out the possibility of it affecting all four limbs. It should be noted that ponies are the most susceptible, with an incidence four times higher than other equines (Luz *et al*., 2021).

Some theories seek to explain the pathophysiology of laminitis, among the main ones: the vascular, traumatic, enzymatic and glucose deprivation theories (Rosa; Vieira; Edler, 2022).

This disease is classified into three variables, with different symptoms and severity. In the initial stage, the animal presents sudden and intense lameness, along with heat, hoof pain, restlessness and sweating. In the second stage, also called acute, in some cases the pain may subside, but there is still obvious lameness, making the hoof wall more sensitive and fragile. In the third stage, the pain may disappear almost completely, but the equine may still have mild lameness, which can evolve into permanent deformation of the hoof, making it difficult for the animal to move (Oliveira; Costa, 2023).

Laminitis is a recurring problem in equine medicine. This raises the question: what treatments are used to treat equine laminitis? This work is justified by the fact that equine laminitis affects around 20% of horses, according to the Federal Council of Veterinary Medicine, with pathogenesis difficult to determine, including predispositions and risk factors, so diagnosis and treatment can be compromised by being late, causing the retirement of athletic animals, or even death.

The aim of this paper is to carry out a literature review on the best prospects for treating equine laminitis, covering equine anatomy and pathophysiology, as well as predisposition and risk factors for laminitis, the types of this disease, diagnostic methods and the pharmacology associated with treatment. The qualitative research was carried out using the *Scientific Electronic Library Online* (Scielo) and *National Library of Medicine* (PubMed) electronic databases, in Portuguese, English and Spanish.

LITERATURE REVIEW

EQUINE ANATOMY

Equines have their digital bones abbreviated into a single finger, the most distal portion of which is made up of two phalanges (second and third) and a distal sesamoid bone. The distal phalanx is completely internal to the hoof, as is the navicular bone (Luz et al., 2021).

The third phalanx is made up of a dorsoproximal process, where the common extensor tendon is inserted: by the lateral and medial extensor processes, which are continued by the ugual cartilages; by the palmar flexor face, for the insertion of the deep flexor tendon and by the articular face, which connects the distal phalanx to the distal portion of the second phalanx and to the navicular bone (Luz et al., 2021).

All of these structures are protected by the hull, produced by germ cells, which form the keratinocytes. Through keratinocytes, keratins are produced, which can be defined as the main structural proteins and are normally found in the cytoskeleton of epidermal cells.

For Yang and Lopez (2019) the amount and type of keratin within a tissue depends on age and pathology. Thus, there are differences in the amount of keratin within the unaffected hoof versus the laminitic hoof.

In endocrinopathic laminitis, there is a partial replacement of lamellar tissue with aberrant keratin, and hyperproliferation of keratinocytes has also been documented in insulin-induced laminitis. In cases of laminitis induced by carbohydrate overload, cytokeratins are seen clustered around the nucleus (Yang; Lopez, 2019).

The vascularization of the hoof is done through the branching of the palmar/plantar digital arteries, generating their anastomosis and thus forming the terminal arch. Laminar irrigation and nutrition are provided by these branched capillaries, which at the same time facilitate the entry of pro-inflammatory cells and are also responsible for laminitis.

Vascular alterations in the laminar dermis form the process of laminitis, where, in chronic cases, necrosis of this portion occurs, destabilizing the support of the third phalanx in relation to the hoof wall, thus causing it to rotate (Luz et al., 2021).

According to Luz et al. (2021) in laminitis, there is distortion of the lamellae and elongation, as well as reduction and detachment of the basal membrane, which is a critical component for lamellar fixation, leading to loss of integrity and detachment of the lamellae. The lamellae are compromised in order to maintain a tight connection between the third phalanx and the hoof capsule when this region is injured. There is an independent movement of the distal phalanx in the hoof capsule, causing the traction force of the digital flexor tendon to act intensely on it. In the clinic, the sole will appear flat or convex, and there may be perforation of the sole.

PATHOPHYSIOLOGY OF EQUINE LAMINITIS

The term laminitis is used to describe the clinical and pathological consequences of disturbances in the attachment between the inner hoof wall and the distal phalanx, which is usually provided by the digital lamellae (Van Eps; Burns, 2019).

It is important to note that, according to Van Eps and Burns (2019) the lamellae normally act to suspend the bone within the hoof capsule, and it is the largely irrecoverable loss of this suspending function that leads to lameness, dysfunction and morphological disorders characteristic of chronic laminitis.

The central role of inflammation in the pathogenesis of acute laminitis has been highlighted experimentally, with endothelial activation, up-regulation of cytokines and chemokines and emigration of leukocytes

into the lamellar tissue, occurring early during the development of experimentally induced laminitis (Van Eps; Burns, 2019).

In addition, Luz et al. (2021) point out that endocrine disorders such as hyperglycemia, hyperinsulinemia and insulin resistance occur in obese horses that are treated for long periods with high concentrations of glucocorticoids, or even those affected by Cushing's syndrome, which could be the cause of laminitis.

This is explained by the need of the basal cells of the laminae for glucose in their nutrition and, thus, the impediment of this increases the activation of the metalloproteinases present in the hoof. This leads to the separation of the desmosomes, explaining why diseases related to altered glucose metabolism are the cause of laminitis (Luz et al., 2021).

In addition, the ischemic theory suggests that there is a change in perfusion at the distal end of the limb, which triggers laminar metabolic and structural dysfunction. Initially, there is hypoperfusion due to vasoconstriction, laminar edema, opening of the arteriovenous anastomoses, generating ischemia and, subsequently, necrosis of the lamellar interdigitations and biomechanical failure (Luz et al., 2021).

Associated with this is an increase in the hydrostatic pressure of the capillaries and vascular resistance, migrating fluid from the capillaries and vascular resistance, migrating fluid from the capillaries to the interstitium and increasing interstitial pressure, causing capillary collapse and ischemia. This causes necrosis and separation of the sensitive and insensitive laminae, with rotation and/or sinking of the distal phalanx (Luz et al., 2021).

PREDISPOSITIONS AND RISK FACTORS FOR EQUINE LAMINITIS

Until the turn of the millennium, laminitis was considered a simple disease with a common pathophysiology, regardless of its cause. However, the conditions that trigger laminitis are extremely diverse, and in many cases it is difficult to attribute to just one compelling cause (Van Eps; Burns, 2019).

Some of the predisposing factors for the onset of laminitis are the ingestion of foods rich in rapidly fermentable carbohydrates, diseases that are capable of generating toxemia and/or septicemia, excessive and prolonged support in one of the limbs and mainly hormonal changes (Van Eps; Burns, 2019).

Metabolic syndrome

Endocrinopathic laminitis is reported to be the most common form of the disease, mainly affecting horses with an obesity phenotype and insulin dysregulation, especially when they are exposed to a diet containing a lot of non-structural carbohydrates. Insulin dysregulation is a central predictive risk factor for endocrinopathic laminitis, particularly related to persistent hyperinsulinemia (Van Eps; Burns, 2019).

Initial hypotheses generated on the basis of this risk postulated that insulin may be causing lamellar alterations through its affinity for the insulin-like growth factor-1 receptor (IGF-1R). The insulin receptor itself has limited distribution in the digital world of lamellae, including very little expression by keratinocytes; however, IGF-1R expression is more extensive and abundant than the insulin receptor in this tissue, which could perhaps be a mechanism by which insulin could directly signal lamellar keratinocytes and alter their phenotype (Van Eps; Burns, 2019).

It is also important to note that, according to Van Eps; Burns (2019), activation of the insulin receptor or IGF-1R can promote

signaling through the mammalian target of rapamycin (mTOR) pathway, directly linking energy metabolism and response to nutritional substrate with regulation of cytoskeletal elements and epithelial differentiation. This link may represent an attractive target for therapy and prevention of this disease, and further research is needed.

Physical exercise

Traumatic laminitis, according to Luz et al. (2021), is based on causes that generate direct trauma to the hoof blades, not due to systemic causes. The mechanical causes are: excessive work on hard flooring or after long training sessions or excessive support on the contralateral limb when a limb has severe lameness and is therefore considered to have supportive laminitis.

Luz et al. (2021) also point out that despite this, the mechanisms that lead to the structural failure of the blades are not well known, but there are hypotheses about how the excessive force applied to the limb and, consequently, to the dermal and epidermal interdigitations generates an exacerbated inflammatory response with vasospasm, increasing the hydrostatic pressure of the capillaries. This process causes edema and the compartmentalization system in the same way as is advocated in the ischemic theory and, associated with this, vasospasm and inflammatory reaction cause further injury to the lamellar interdigitations due to ischemia.

Systemic infections

Authors who defend this theory describe laminitis as a common consequence of diseases complicated by the systemic inflammatory response syndrome, particularly when there is gram-negative bacterial infection or bacterial products (including endotoxins) driving this inflammatory response (sepsis). Sepsis is differentiated from simple infection by the presence of an aberrant host or one with dysregulated responses (inflammatory, coagulopathic and metabolic disorders) and organs in dysfunction (Van Eps; Burns, 2019).

For Van Eps; Burns (2019) the development of target organ dysfunction has an important effect on survival in humans with sepsis and, similarly, laminitis appears to be a form of target organ dysfunction with critical importance for the survival of adult horses with sepsis. However, the pathophysiology of sepsis-associated laminitis is still poorly understood. Research has focused on mechanisms that could disturb cellular homeostasis in sepsis, including circulatory disorders, inflammatory processes, apoptosis and disturbances in cellular energy metabolism.

TYPES OF EQUINE LAMINITIS

Laminitis in horses has four main forms of morphophysiological presentation of the hoof, which are: subacute, acute, refractory and chronic (Luz et al., 2021).

Chronic laminitis

In the chronic phase of equine laminitis, ischemic necrosis has already occurred, followed by rotation and sinking of the third phalanx, which causes it to lose its parallel relationship with the hoof wall and move towards the sole. It is worth noting that if this process is too intense, it can even rupture the sole and lead to a septic process (Cassimeris *et al*., 2021).

In addition, Laskoski *et al*. (2016) say that the main clinical sign of this phase is pain, which causes lameness, a "treading on eggs" appearance and reluctance to move, the animal may also show increased sensitivity to hoof clamping. In addition, there may be an increase in the temperature of the coronary band and pulsation of the digital artery, as well as tremors, anxiety, increased respiratory and heart rates and congestion of the mucous

membranes. The chronic phase is considered an advanced stage of the disease, making treatment and interventions more difficult and time-consuming in order to restore the animal's health.

Other factors that can be observed in the chronic phase are the convexity of the sole, growth of the heels, formation of a transverse ring and concavity of the cranial face of the hoof wall, where these factors can further affect the animal's posture and locomotion, causing discomfort and continuous pain (Cassimeris *et al*., 2021).

It's worth noting that in the chronic phase of equine laminitis, treatments aim to relieve pain and restore the animal's health. The important thing is to prevent the disease from progressing so that hoof structures are preserved. It is worth mentioning the use of special horseshoes, which help distribute the animal's weight while maintaining pressure on the third phalanx (Cestari, 2022).

Figure 1- Photographic image of the patient in an antalgic posture, with the thoracic limbs extended cranially

Source: Carvalho, 2024.

Subacute laminitis

The mildest form of the disease is subacute laminitis, which occurs during the window of time between exposure to the causative agent and the first symptoms. During this phase, mild clinical signs are observed, especially in horses with short hooves. It is therefore difficult to diagnose during this period. A moderate increase in the digital pulse, relief of the weight of the limb by taking it off support for seconds, claudications in a circle, pain in clamps are all clinical signs present (Luz *et al*., 2021).

Acute laminitis

Acute laminitis is characterized by the intensification of the severity of the clinical picture, which does not respond quickly to treatment and is likely to progress to phalangeal rotation (Luz et al., 2021).

Laskoski et al. (2016) point out that the acute phase of equine laminitis is a critical period in which the horse can experience pain and significant damage to the internal structures of the hoof. In addition, during this phase, the horse may present a variety of clinical signs, including difficulty moving, reluctance to walk or trot, resistance to raising and lowering the head, as well as signs of pain, such as excessive sweating and motor acceleration, and separation of the hoof wall, which becomes more fragile and sensitive.

According to Oliveira and Costa (2023), the acute phase of equine laminitis lasts an average of 72 hours, or until the third phalanx rotates. It is usually during this period that treatment begins in order to limit the severity of the inflammation, trying to prevent the failure of the hoof structures, promoting the transition to the sub-acute phase. It is important that treatment is started as soon as possible to increase the chances of success and minimize damage to the horse.

Refractory laminitis

In refractory laminitis, there is no response or satisfactory evolution to treatment within the first 10 days, indicating degeneration and severe lamellar inflammation. It therefore has a poor prognosis (Luz *et al.*, 2021).

DIAGNOSTIC METHODS FOR EQUINE LAMINITIS

For Garcia (2013), the diagnosis of laminitis can be relatively obvious in acute cases, due to the clinical history, the characteristic station position and the digital examination. However, in chronic cases, clinical diagnosis is probably much more complicated, especially in older horses that may suffer from concomitant distal arthropathies that facilitate lameness.

Physical examination

Animals affected by acute laminitis show anxiety, muscle tremors, increased respiratory and heart rates, as well as blood pressure when there is a lot of pain (Guimarães, 2022). In general, the signs are serious, as they don't respond quickly to treatment and can develop into phalanx rotation, affecting the front or back limbs, so the animal will try to support its body weight on the back limbs or by extending its legs their back limbs so that the weight is shifted to the front limbs (Guimarães, 2022).

Furthermore, if it happens to affect only one of the horse's limbs, it will try to shift its weight to the collateral limb, which shows that the initial lameness of the other limb is less pronounced. In turn, when all four legs are affected by the disease, horses are inclined to continue lying down for long periods and when they get up, they push the hindquarters forward and the forelegs backwards, reducing their support (Guimarães, 2022).

According to Guimarães (2022), the animal shows the first signs of lameness, which persists for an average of 72 hours, or until the rotation of the third phalanx is analyzed. Generally, this is the initial time of treatment, which aims to determine the severity of the inflammation so that the horse enters the sub--acute phase, without the hoof structures failing.

COMPLEMENTARY TESTS

Radiographic examinations are the main imaging tests used in the diagnosis and treatment of laminitis. Good quality radiographs should be part of the follow-up work for each case of laminitis to document the change in position of the third phalanx (F3) within the hoof wall, providing important diagnostic and prognostic information (Garcia, 2013).

Radiographs should be taken with the horse on station, on a flat surface and on top of wooden blocks. A metal line should be placed at ground level. A radiopaque marker of pre-established length should be placed on the dorsal wall of the hoof, next to the coronary band. Beforehand, the hoof should be sanitized and the groove cut. The x-ray beam should be parallel to the ground and aimed at the center of F3 (Garcia, 2013).

According to Garcia (2013) radiographs should assess the distance between the radiopaque marker and the dorsal surface of F3 (hoof wall thickness), the distance from the coronary band to the extensor process of F3 and the degree of rotation of F3. The radiographic measurements of a normal horse are 16.3 ± 1.8 mm, 5.2 ± 2.0 mm and 47.6 ± 2.1˚ respectively (Garcia,2013). The The most common radiographic changes include rotation and/or sinking of F3, increased thickness of the dorsal hoof wall and the presence of radiolucent lines on the dorsal hoof, reflecting necrotic tissue, serum or gas caused by infection or separation of the hoof wall (Garcia, 2013).

The distance between the dorsal wall of the hoof and the dorsal surface of F3 never varies in normal horses, and if there is an increase

in this, laminitis is the likely cause, and it is extremely important to know the speed and magnitude of the increase (Garcia, 2013).

Contrast radiography (venography) can also be used, when a compound (contrast) is administered into a vein, with the region properly tourniqueted, then an X-ray examination is carried out and changes in blood flow in the region are observed.

Figure 2: Rotation of third phalanx in left forelimb and right forelimb

Source: Oliveira; Paes, 2024.

Other tests that can be used to diagnose laminitis are thermography, ultrasound and magnetic resonance imaging, but these can be expensive, so their use is limited.

TREATMENT

The treatment of equine laminitis can involve a variety of approaches, including nutritional management, pain control and anti-inflammatory therapy, acupuncture, chiropractic, physiotherapy, the use of stem cells and surgery (Carvalho, 2019).

Cryotherapy is a technique that consists of using low temperatures to reduce inflammation and discharge in the region, this therapy can be applied at different times of the treatment, from the acute phase to the chronic phase, being very effective in reducing pain and improving the animal's quality of life (Oliveira *et al.*, 2020).

It's worth noting that there are several ways of applying cryotherapy, including the use of ice packs, immersion in ice water and the application of specific devices, such as cooling boots. As well as being a very effective technique, cryotherapy should be used with caution and under the supervision of a veterinarian, since in more severe cases of laminitis, there is a need to associate cryotherapy with other treatments, such as administering medication and changing the animal's diet (Oliveira *et al.*, 2020).

In general, cryotherapy is a very promising technique for treating equine laminitis. However, it is worth noting that the success of the treatment depends on several factors, such as the stage of the disease, the severity of the symptoms and the individual response of each animal to the treatment (Oliveira *et al.*, 2020).

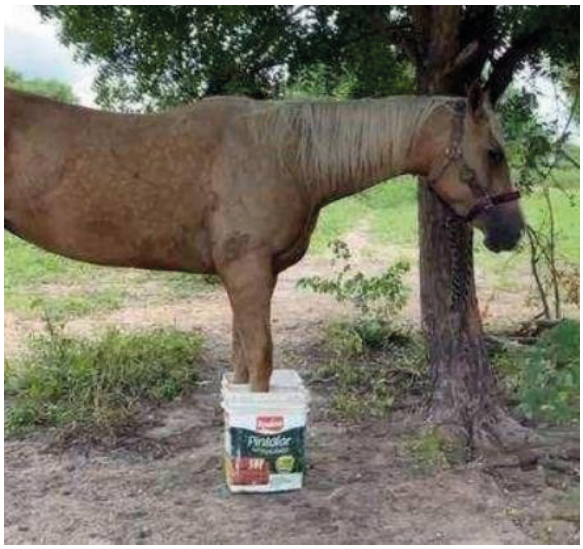

Figure 3- Cryotherapy.

Source: Maia, 2021.

A complementary treatment option for equine laminitis is acupuncture, a technique which involves placing needles at specific points on the animal's body, in order to stimulate and speed up the healing and re-establishment process. It can help relieve pain and reduce inflammation, as well as improving blood and lymph circulation, aiding tissue recovery (Freitas, 2020). However, it is important to note that acupuncture should not be used as the sole treatment for equine

laminitis. Veterinary monitoring and the use of other therapies are always recommended, depending on the degree and stage of the disease (Freitas, 2020).

According to Silva (2021), chiropractic is a joint and spinal manipulation technique that has been used in animals as a complementary therapy to treat various musculoskeletal problems, including equine laminitis. This technique is carried out by a professional called a chiropractor, who uses his hands to exert pressure on specific points on the spine and other joints, with the aim of promoting pain relief and re-establishing joint mobility, restoring the animal's biomechanical function.

In chronic equine laminitis, chiropractic helps improve blood circulation, reduces inflammation and releases endorphins, which are known to be a natural painkiller. It is also noted that the technique improves the animal's emotional state and reduces stress.

It is important to note that each individual case must be carefully assessed, as not all animals can be treated with chiropractic care, especially if the laminitis is very severe and the animal has significant joint deformities (Silva, 2021).

Mendes et al. (2021) point out that stem cell therapy has been increasingly studied as a potential treatment for equine laminitis. Stem cells are cells with the ability to transform into different types of cells in the body, and can come from the animal's own bone marrow or fat. Stem cell therapy can aid in the recovery of laminitis lesions, promoting healing and reducing pain and inflammation.

However, more research is needed to determine the effectiveness of stem cell therapy for equine laminitis and to establish appropriate treatment protocols (Mendes et al., 2021).

Stem cells are collected from the animal itself or from a donor and injected directly into the affected area. Stem cell treatments can be carried out in conjunction with other treatments, such as cryotherapy and pain control drugs (Mendes et al., 2021).

Carvalho (2019) says that physiotherapy has proven to be an effective treatment in the rehabilitation of horses with chronic laminitis, where the main objective of physiotherapy is to reduce pain, improve mobility and increase the function of the limbs of the community . The techniques used include stretching exercises, muscle strengthening, electrical stimulation and massages.

Stretching exercises are important for maintaining the flexibility of dependent limbs and preventing muscle contractures from forming, while massage helps to relax muscles and reduce tension, stimulating blood circulation and lymph flow, and joint manipulation is useful for correcting joint misalignments and improving joint mobility (Carvalho, 2019).

Carvalho (2019) also points out that muscle strengthening is an important component of physiotherapy for horses with chronic laminitis, as stronger muscles can help support the animal's weight and reduce the load on the affected limbs. In electrical stimulation, an electric current is applied to promote muscle contraction. It is important for recovering muscle strength in animals affected by laminitis.

It is necessary to adjust to a balanced and adequate diet in order to reduce the effects of equine laminitis and also to prevent it.

This diet should be high in fiber and low in carbohydrates, especially fermentable carbohydrates, as excessive intake of fermentable carbohydrates can lead to an increase in blood glucose levels, which can increase the risk of laminitis (Carvalho, 2019).

For horses that have already been diagnosed with laminitis, it is extremely important to limit the intake of feed rich in fermentable carbohydrates, such as grains and concentrated feed. On the other hand,

it is necessary to increase the intake of fiber-rich foods. Horses can also benefit from nutritional supplements, such as antioxidants and omega-3 fatty acids, which have anti-inflammatory properties and can help reduce pain and inflammation related to the disease (Carvalho, 2019).

Finally, Cestari (2022) emphasizes that surgery is generally considered an option of last resort for severe and refractory cases, when other nerve functions work to control pain and the progression of the disease. Furthermore, not all cases of laminitis are candidates for surgery.

It should be noted that the procedure may vary depending on the underlying cause of the laminitis and the individual characteristics of the horse. Therefore, surgery may be indicated in cases of chronic laminitis with projected hoof deformities, such as rotation of the third phalanx, sinking of the sole and excessive convexity of the hoof wall. In these cases, surgery may be necessary to correct the deformity and relieve chronic pain. While the techniques vary depending on the severity and location of the deformity, they usually involve removing part of the hoof or fixing metal plates to stabilize the third phalanx (Cestari, 2022).

FINAL CONSIDERATIONS

It can be concluded that laminitis is a multifactorial disease with a high prevalence in horses, but as the pathophysiology of the disease is still unclear, each treatment needs to be individualized and treated in isolation. A good prognosis is directly linked to early treatment, at the onset of lameness**.**

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