CALCIUM DOBESILATE - A NEW THERAPEUTIC AGENT FOR TREATMENT OF NAVICULAR DISEASE IN HORSES

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Magnetic Resonance Imaging (MRI) has improved the diagnosis of foot pain in horses originating from the area of the navicular bone because this imaging technique enables the clinician to differentiate soft tissue from bony lesions. Pathological lesions of the navicular bone can be identified in absence of radiographic changes and with no detectable abnormalities of the flexor fibrocartilage or cortex, but with diffuse abnormalities of the medulla charaterised by increased signal in fat suppressed images. This may reflect a variety of pathological processes including fibrosis, necrosis, bone oedema or abnormal trabecular modelling.

It has been hypothesised that impaired venous drainage causes venous hypertension in the navicular bone marrow resulting in intraosseous hypertension and bone edema (Pleasant *et al.* 1993; Svalastoga and Smith 1983). Alternatively, the accumulation of osmotically active proteins in the subchondral tissue cause leads to a compartment syndrome within the navicular bone, which is characterised by increased tissue pressure, acidosis, pain and a vicious cycle of progressive pathological changes. The degenerative processes within the compartment are triggered by a switch from aerobic to anaerobic metabolism locally. Surgical procedures have been explored to decompress the medullary cavity of the navicular bone in sound horses (Jenner and Kirker-Head 2011). An experimental study revealed that drilling the bone reduced excessive intraosseous hydrostatic pressure due to lowered perfusion resistance and improved local blood circulation. However the direct decompression effects are short-lived due to the rapid healing of the drill channels.

Effective and specific medical treatment methods for lameness due to navicular disease are currently not available because the aetiopathogenesis of bone oedema in the navicular bone is poorly understood.

Tiludronate is widely used for similar bone pathologies in horses. The most important mechanism of action of bisphosphonates is to regulate bone metabolism through inhibition of bone resorption Tiludronate had a significant effect on reduction of bone resorption in horses that were immobilized in a full limb fiberglass cast during eight weeks (Delguste *et al.* 2007). In a double-blind, placebo-controlled study there was improvement in lameness scores of horses with navicular disease given tiludronate and horses returned to normal level of activity 2 to 6 months after administration (Denoix *et al.* 2003). Anecdotally, there may be benefit from use of tiludronate in horses with subchondral bone injury. Biphosphonates may help to normalize metabolism in bone injuries characterized by abnormal absorption and formation, but it has probably no detectable effect on pressure dynamics in bone oedema.

Calcium dobesilate* (Calcium 2,5-dihydroxybenzene sulfonate) has been used to treat high protein edema in humans and there are anecdotal reports of clinical effects using the drug in navicular disease in horses. The suggested mode of action is a macrophage-driven removal of osmotically active proteins, which has been described in models of lymphoedema in rats. Calcium dobesilate is a synthetic venoactive drug with a variety of biochemical functions such as inhibition of serotonin, bradykinin, free radicals and histamine induced capillary permeability, inhibition of prostaglandin and thromboxane synthesis, reduction of experimental lymphoedema and intralymphatic pressure, increased lymphatic flow, decreased angiogenesis, it also reduced albumin leakage.

In a recent experimental study on an osteoarthritis model in rabbit knees the intramedullary pressure dynamics and joint characteristics were investigated. In this model calcium dobesilate has a detectable effect on pressure dynamics in the subchondral bone of osteoarthritic joints (Miles *et al.* 2011).

There are anecdotal reports of positive clinical effects of calcium dobesilate on horses affected by navicular disease in the absence of adverse effects of the drug. Benzopyrone, a chemically very similar and similarly acting substance to calcium dobesilate (without a pyrone ring) has been used to treat subchondral cyst-like lesions in horses. Twelve of 19 horses with subchondral cyst-like lesions returned to full athletic function after oral administration of benzopyrone for 4 months. No side effects were reported (Jackson *et al.* 2008).

Advances in MRI diagnosis in the foot suggest different aetiopathogenesis for navicular disease, but there is a lack of targeted treatment options for specific pathological processes affecting the navicular bone. In a pilot study is 12 horses with lameness due to increased signal intensity in fat suppressed images in the medulla of the navicular bone were treated with Calcium Dobesilate and lameness and signal intensity in the navicular bone was monitored two and four months after diagnosis. All but one horse improved clinically and significant reduction of the signal intensity in the fat suppressed images in the navicular bone occurred. Further research is required to confirm these promising results.

**Manufacturers` address: Dobavet GmbH, Schlyffistrasse 10, 8806 Bäch, Swiss*

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