Equine degenerative joint disease – medical treatment and management

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DAVID BOLT reviews the various available options for treating this commonly-encountered disease in horses, including their advantages and disadvantages

Summary

Treatment of degenerative joint disease (DJD) in the horse is one of the most commonly performed tasks in equine practice. It requires knowledge of the anatomy of synovial joints and understanding of the basic pathophysiology of the disease process. The equine practitioner is faced with many options for treating and managing DJD. Each of these treatments has advantages and disadvantages and the efficacy of some is not well established yet. This brief review presents a summary of the most commonly used treatments.

DEGENERATIVE joint disease (DJD) is the single most common cause of lameness in the horse[1,2]. Advanced knowledge of the structure, biochemistry and metabolism of the articular cartilage and soft tissues of the joint, as well as improved understanding of the pathophysiology of DJD, has resulted in a multitude of available treatment modalities[3].

In addition to relieving inflammatory pain, medical treatments for DJD should arrest, or at least slow, progression of cartilage degeneration – a concept referred to as chondroprotection or disease modification[4]. Decisions for the treatment of DJD in horses are usually based on the following

factors[3]:

• the actual joint involved;

• the stage of DJD;

• current and intended use of the horse;

• age of the animal;

• drug use regulations in competitions;

• treatment cost; and

• observed or projected response to therapy.

Despite the enhanced understanding of the pathophysiology and availability of new treatment options, established DJD is incurable and often limits the future performance of equine patients[4]. The following sections will provide a brief overview of the most commonly used drugs for the treatment of equine DJD.

Non-steroidal antiinflammatory drugs

NSAIDs remain the most frequently used drugs to manage equine DJD. Advantages of NSAIDs include the relatively low cost and effectiveness in reducing lameness in many horses. NSAIDs mainly decrease joint inflammation by suppressing prostaglandin and thromboxane synthesis via inhibition of the cyclooxygenase (COX) pathway[5].

Dose-dependent toxicity effects, consisting of gastrointestinal ulceration and renal papillary necrosis, have been described for many compounds. However, they are infrequently observed clinically when used in otherwise healthy horses[3]. Furthermore, right dorsal colitis can be a serious complication affecting individual horses independent of dose used or duration of administration.

The existence of several COX isoenzymes and the discovery that most toxicity effects can be attributed to COX-1 inhibition[6] has resulted in development of new NSAIDs with more selective COX-2 inhibition[3]. Non-COX-mediated antiinflammatory effects have been described for some NSAIDs used in horses[7].

Corticosteroids

Corticosteroids represent the most potent anti-inflammatory agents and are frequently used to treat DJD. Injected directly into affected joints, they suppress multiple inflammatory pathways including

capillary dilation, leukocyte margination, migration and accumulation, as well as liberation of enzymes, cytokines and inflammatory mediators[4].

Corticosteroids also inhibit prostaglandin, leukotriene and thromboxane synthesis by sequentially suppressing phospholipase A2 (PLP A_2) and COX-2 activity, but their main effects can be attributed to inhibition of transcription of pro-inflammatory mediators[8].

Despite their beneficial effects on joint inflammation, certain corticosteroids at high concentrations have been shown to induce degradation of articular cartilage by inhibiting proteoglycan synthesis and unfavourably influence structural organisation of collagens[9]. Conversely, chondroprotective properties have been attributed to other steroids at lower dosages[10],[11].

A risk of septic arthritis exists with any form of intra-articular injection. However, clinical signs of joint infection can be delayed after intra-articular corticosteroid injection[12]. One of the most serious perceived risks associated with glucocorticosteroid use in horses is acute laminitis. Although a direct causal association between corticosteroid use and laminitis has yet to be scientifically proven, circumstantial evidence suggests very high dosages and differences in individual susceptibility between horses may be responsible for this rare complication[13].

Hyaluronan

Hyaluronic acid (HA) is a linear glycosaminoglycan composed of D-glucuronic acid and N-acetyl-D-glucosamine. HA is an integral component of both synovial fluid and articular cartilage[14].

The benefits of intra-articularly injected HA in the management of DJD have been demonstrated in numerous studies in horses and other species, making this an attractive therapeutic option[4]. HA confers viscoelasticity to synovial fluid and is responsible for boundary lubrication of both synovial membrane and articular cartilage[3].

HA has further been shown to have anti-inflammatory properties and may influence the composition of synovial fluid through steric hindrance of active plasma components and leukocytes entering the joint cavity[14]. However, the exact mechanism by which exogenous HA has been hypothesised to benefit diseased joints remains unknown.

Therapeutic effects may result from supplementation of depleted or depolymerised endogenous HA or, alternatively, result from other properties that have been ascribed to the compound on the basis of experimental work. Beneficial effects of HA on cartilage metabolism have been demonstrated in horses after both intra-articular and intravenous administration[3].

Polysulphated glycosaminoglycans and pentosan polysulphate

Polysulphated glycosaminoglycans (PSGAGs) have been shown to alter progression of DJD by

sustaining or promoting metabolic activity of chondrocytes and inhibiting degrading effects of cytokines or prostaglandins on cartilage[3].

While there has been convincing evidence of their beneficial effects, the exact mechanism of their action is also unknown. It has been theorised that PSGAGs form complexes with fibronectin and collagen fibres and are deposited in articular cartilage[15]. In vitro work further suggests they inhibit multiple degradative enzymes involved in DJD[3]. Weak anti-inflammatory activity has been described, based on observation of inhibitory effects on leukocyte migration[16] and interleukin levels[17].

PSGAGs consist primarily of chondroitin sulphate and are extracted from animal cartilage (such as bovine trachea) subjected to sulphate esterification[18]. Although originally approved for both intramuscular and intra-articular administration, most equine practitioners prefer to administer PSGAGs intramuscularly because severe joint infections and inflammations have been observed following intra-articular use[19]. However, there appears to be little hard evidence for the actual efficacy of intramuscular PSGAGs in horses with DJD[20].

Pentosan polysulphate sodium (PPS) is a heparinoid compound derived from beech wood hemicellulose that has been shown to have similar effects to PSGAGs[4]. Both, PSGAGs and PPS have only weak anti-inflammatory properties. Their use has therefore been recommended in cases where addressing cartilage damage is considered more important than treatment for acute synovitis[21].

Glucosamine, chondroitin sulphate and other joint supplements

Glucosamine and chondroitin sulphate are compounds extracted from animal products that have been used to treat and prevent DJD in animals and people for a long time[4]. These oral supplements supposedly also possess antiinflammatory and diseasemodifying effects. Evidence based on rigid in vitro and in vivo studies is lacking, but available data imply some beneficial effects[4]. Glucosamine salts are well absorbed after oral administration[22],[23].

In vitro studies suggest glucosamine increases proteoglycan synthesis by chondrocytes and that it has some antiinflammatory activity[4]. However, the efficacy of the enteral absorption of chondroitin sulphate in its biologically active (long-chain) form remains a topic of debate.

In monogastric species, the oral bioavailability of chondroitin sulphate has been shown to be less than 20 per cent[24]. In the horse, the actual gastrointestinal absorption and bioavailability of chondroitin sulphate are still largely unknown. Chondroitin sulphate is less sulphated, but essentially resembles PSGAGs in its structure and mechanism of action[4].

Other substances commercially available include methyl sulphonyl methane, fatty acids, collagen hydrolysate, as well as various vitamins, minerals, trace elements and herbs[23]. In vitro data have

shown lyophilised products of the green-lipped mussel (*Perna canaliculus*) have a range of anti-inflammatory activities in animals and people.

In a recent experimental study, horses with fetlock lameness treated with green-lipped mussel extract were shown to be less lame than control animals treated with placebo[25].

IL-1 receptor antagonist protein

Interleukin-1 (IL-1) has been identified as one of the major cytokine mediators involved in the pathogenesis of osteoarthritis (OA)[4]. More recently, inhibitors of inflammatory cytokines have been evaluated for the treatment of OA in horses.

Interleukin-1 receptor antagonist (IL-1Ra) protein has been used successfully for many years in the management of OA, rheumatoid arthritis, spinal disorders and muscle injuries in people[26,27]. IL-1Ra can be produced in high concentrations in autologous conditioned serum (ACS), which is prepared by culturing patient blood with medical grade borosilicate glass beads to stimulate up-regulation IL-1Ra and other anti-inflammatory mediators[28].

Kits for preparation of equine ACS are commercially available and the preparation is administered intra-articularly. Anecdotal reports for the use of this product have been favourable, even for cases that had been refractory to intra-articular corticosteroid medication[3]. A controlled in vivo study, performed at Colorado State University using an experimentally induced equine OA model, confirmed the safety of intra-articular ACS administration in horses.

Results from this study further indicated significant clinical and histological improvement in OA-affected joints, following treatment with ACS, compared to joints receiving placebo treatment[28]. However, results of large-scale controlled clinical trials in horses are still not available. Interestingly, in a recent study using an equine chondrocyte culture model, the benefits of ACS compared to unprocessed autologous equine serum were found to be minimal[29].

Tiludronate

Tiludronate is a non-nitrogenous bisphosphonate licensed in several European countries for the treatment of navicular disease and bone spavin in horses[30,31]. Bisphosphonates inhibit bone resorption by inducing osteoclast apoptosis via blocking of the mevalonate pathway.

The resulting slowing down of bone remodelling is supposedly beneficial and reestablishes a normal balance between bone resorption and formation[32]. Evidence of inhibitory action on bone resorption and bone mineral density in the horse has been demonstrated in a disuse osteoporosis model with limb casts[33].

Tiludronate has further been shown to have anti-inflammatory properties by decreasing the amount

of nitric oxide and cytokines released from activated macrophages[34]. Several studies investigating the clinical use of tiludronate in horse have been conducted, but different standards of research of these publications have so far failed to provide a strong evidence base.

Administration of tiludronate has occasionally been associated with abdominal discomfort, therefore some practitioners opt to treat horses simultaneously with NSAIDs.

Conclusions

The equine practitioner has many options for medical treatment of horses with DJD. However, knowledge of the limitations, as well as the advantages and disadvantages of the different drugs, is important. An individual treatment plan based on the affected joint, disease stage, intended use and age of the animal and cost should be formulated for every patient.

• Please note some of the drugs mentioned within this article are not licensed for use in the UK.

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Factors such as excessive training can impact on direct joint trauma leading to degenerative joint disease, meaning a horse could no longer be able to perform to its full potential.

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Inherent problems such as poor nutrition can also play a part in the development of equine degenerative joint disease.

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