What is the basis for hyaluronic acid therapy?

Hyaluronate sodium (hyaluronic acid) is a nonsulfated glycosaminoglycan. It has anti-inflammatory effects that may be physical (steric hindrance), or pharmacologic (inhibition of inflammatory cells and mediators). There is in vitro evidence for protection against interleukin-1-driven prostaglandin synthesis, as well as inhibition of free radicals. More recently, hyaluronate sodium has been used as a therapy to treat synovitis in people, and it appears to have a slow, but long-term positive response.

What are the ideal indications?

It has been my clinical impression that hyaluronate sodium alone is useful for mild to moderate synovitis; and for the treatment of more severe synovitis a corticosteroid may be necessary. However, based on clinical evidence in people, while there may not be an obvious immediate clinical response to hyaluronate sodium alone, the long-term disease-modifying activity is accumulating and with further evaluation of clinical cases later, the benefit could be more obvious. Recent work from our laboratory at Colorado State University (CSU) testing intra-articular hyaluronate sodium with the CSU equine osteoarthritis model showed significantly less articular cartilage fibrillation compared with controls, but minimal reduction in synovial membrane vascularity and subintimal fibrosis. The conclusion was that hyaluronate sodium had disease-modifying effects given intra-articularly and was a viable therapeutic option in equine osteoarthritis (but there may not be obvious immediate clinical evidence regarding its ability to inhibit synovitis).

What about corticosteroid therapy?

As mentioned previously, the use of a corticosteroid is commonly practiced and is rational. Methylprednisolone acetate has been shown to have degradative effects on the articular cartilage in joints. The other commonly used corticosteroids—triamcinolone acetonide and betamethasone esters—do not. The negative effect of methylprednisolone acetate on articular cartilage has been published by the team at CSU and by others as well. The use of an intra-articular corticosteroid, other than methylprednisolone acetate or betamethasone esters, is appropriate therapy.

What about intravenous use?

Our previous work with horses demonstrated that intravenous hyaluronate sodium (Legend® [hyaluronate sodium] Injectable Solution) provided considerable beneficial effects, particularly with regard to synovitis. The mechanism of action is presumed to be related to access via the vascular synovial membrane; and in addition to anti-inflammatory effects, possibly upregulation of endogenous hyaluronate sodium production into the joint.

Legend® Multi Dose is approved only for intravenous use. Legend® Multi Dose is approved only for intravenous use. Legend® (4ml) and Legend Multi Dose (20ml) are approved only for intravenous use. Legend® (2ml) is approved for intravenous and intra-articular use. Legend® Multi Dose is approved only for intravenous use. Legend® (4ml) and Legend Multi Dose (20ml) are approved only for intravenous use. Legend® (2ml) is approved for intravenous and intra-articular use.

For use only in horses. Do not use in horses intended for human consumption.
Hyaluronic acid (hyaluronic acid) is a joint fluid component. It decreases production of the mediators of inflammation within the joint. Hyaluronic acid also lubricates and protects the joint cartilage and synovial membrane. Legend (hyaluronate sodium) Injectable Solution (Bayr Animal Health) is produced by a bio-fermentation process and purified through a 12-step microfiltration system. It is produced by a bio-fermentation process and purified through a 12-step microfiltration system. The horses were graded on a scale of 0 to 5 for severity according to the American Association of Equine Practitioners (AAEP) guidelines. Synovial fluid samples were evaluated from each middle carpal joint, measuring total protein, inflammatory cell, hyaluronate, glycosaminoglycan, and glycosaminoglycan concentrations. Synovial membrane and articular cartilage were evaluated histologically.

Results
Because of its purity, Legend can be administered intra-
ovously or intra-articularly, the only FDA-approved joint therapy product labeled for both routes. Intra-articular administration
is preferred for repeated intra-articular injections in horses and the associated complications of joint infection, trauma, and reaction. It also ensures a rapid onset of action in multiple joints.

Efficacy
Is Legend effective? In field studies, clinical improvement was judged to be excellent or good in 90 percent of horses with lameness that were treated
with intra-articular Legend. In addition, clinical improvement was judged to be excellent or good in 96 percent of horses treated with intra-articular Legend. Additional studies have corroborated these results as well. Researchers at Colorado State University evaluated the use of intraarticular hyal
uronate (Legend) on carpal joints in exercising horses after arthroscopic surgery and osteochondral fragmen
tation. In this study, 12 clinically normal horses underwent osteochondral fragmentation of the distal aspect of one radiocarpal joint, creating a naturally occurring osteochondral fragmen
tation. Six of the horses were treated with 40 mg hyaluronate intravenously and the other six with saline injections. The horses were followed for 40 days and hyaluronate intravenously and the other six with saline injections. The horses were followed for 40 days and
had fewer flares with Legend than with anything else, and I like that,” he says. “Also, I personally feel that every time you inject something directly into a joint you have risk. By delivering the treat
ment intra-articularly, you’re not only treating the joint with the ongoing issue, you’re also getting therapy in the secondary joints so that you can produce their own synovial fluid, and any horse that is working hard can only benefit from that.

Other hyaluronic acid products
What about similar products used for equine arthritis? Currently there are other FDA-approved hyaluronic acid products on the market (Figure 3), significantly better synovial membrane histologic scores (signifi
cantly less inflammatory cell infiltration and inflammation), and significantly lower concentrations of total protein and prosta
glandin E_2 within synovial fluid 72 days after therapy than placebo-treated horses. Researchers concluded that intrarticular hyaluronate alleviates lameness by interacting with synovio
cyes and decreasing inflammatory mediator pro
duction and release. They believe that the results of their study indicate a pro
longed beneficial effect after intraarticular treatment with hyaluronate.

Safety
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