Joint Supplements

Frequently Asked Questions

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DOES INFORMATION FROM HUMAN STUDIES REALLY APPLY TO HORSES?

*The following information includes studies on humans and horses**, both in the laboratory or the results of actual clinical testing.*

The simple answer is we don't know for sure, but a great deal of it could be relevant. Much that we have learned about nutrition, drug treatment, and disease has come from animal studies. So applying human information to horses makes sense – as long as one is cautious-particular about safety. Compared to human studies, there is less scientific information about joint problems available from studies actually done on horses, but what is available is very promising.

**If you would like more technical information about studies on joint therapies specifically in horses, I refer you to the excellent reviews by DV Richardson (1) or JE Decant (2)

A. GLUOSAMINE

WHY USE GLUCOSAMINE?

There is more information available about glucosamine (G) than any other supplement used for joint health. This is primarily because – in the sulfate form - it seems to be effective for human use (3, 4), as well as for animals (primarily horses and dogs) (5, 6). Arthritis is a major illness in people, and pharmaceutical companies compete intensely for market share in this area. As a result, we have many "arthritis drugs." Aspirin was the first truly effective remedy in the NSAID group developed for human arthritis. But now there are many others (Ibuprofen, Naprosyn, Celebrex, to name just a few). Glucosamine may have some of the same anti-inflammatory and pain relieving effects of NSAIDS, with the added benefit of fewer side effects, and it may actually help restore the integrity of cartilage in the joints, (which NSAIDS do not appear to be able to accomplish).

HOW DOES GLUCOSAMINE WORK?

There is considerable confusion and debate about this. Originally, it was suggested that the glucosamine molecule may actually be incorporated into the cartilage structure itself – making it stronger. Some studies suggest that the actual amounts of glucosamine absorbed into the blood and joint fluid may be too low to actually form building blocks in cartilage, but may stimulate growth of cartilage in other ways. In addition glucosamine may activate (or inhibit) other chemical reactions that slow the breakdown of cartilage (7-11). Cartilage, like other tissues in the body, is always simultaneously growing and breaking down. It is the balance between the two that is important. For example, if bone growth is faster than break down, then bones will heal and grow stronger. But if breakdown is faster than growth, then bones get thinner and osteoporosis results. Glucosamine may also work to reduce production of substances which cause inflammation in tissues (12, 13), whereas chondroitin does not have this anti-inflammatory benefit (14)

WHY GLUCOSAMINE SULFATE?

The glucosamine molecule is available commercially in several forms. The usual types found in commercial supplements is glucosamine attached to sulfate (GS) or to hydrochloric acid (GHCL). Most of the many human studies on glucosamine have been done with GS. Relatively few studies have been done with GHCL. Many have been sponsored by Rotta, a major European pharmaceutical company that brought GS to market and therefore to the attention of the nutraceutical and medical communities. Glucosamine sulfate (GS) seems to be more effective than GHCL (15). The sulfate part of GS contains a sulfur atom, and sulfur is an important part of the chemical structure of cartilage. Many experts feel that the sulfur is just as important as the glucosamine, and together they work effectively (4, 16). (Note – sulfur may also be provided by MSM or chondroitin sulfate (CS) in some supplements). Other researchers feel this is not clear, and that more information is needed (17, 18).

WHY NOT USE GLUCOSAMINE HCL?

Glucosamine HCL (GHCL) used alone is probably not effective. A recent review of all human G studies concluded that some studies showed benefit for joint disease, and other studies did not show any benefit. Interestingly, most of

the studies that showed a benefit used GS, while most of those with no benefit used GHCL(19). A recent study conducted by the National Institutes of Health concluded that moderate or minimal benefit resulted from use of GHCL combined with CS (20), whereas either ingredient alone had no benefit. A similar result was found in a laboratory study of equine joint cartilage (21). This makes sense if you realize that you need both the glucosamine and the sulfur together to have maximal benefit. In addition, a recent study in horses found that no GHCL was detectable in the blood after oral feeding (22).

Even more convincing, was a study conducted at Michigan State University, looking at the ability of GHCL to prevent joint damage (23). Standardbreds just beginning race training were divided into two groups. One group received glucosamine HCL at the dosage recommended on the label of a commercial product (4 grams twice a day). The placebo group was given glucose (sugar) at the same dosage. Horses were put on a training regimen for 48 weeks, with periodic blood sampling. The authors concluded that GHCL had no recognizable effect on cartilage protection at the dosage administered. This conclusion was supported by the fact that there was no difference in the changes of concentration of the three biochemical markers of osteoarthritis between the treatment and placebo groups.

Glucosamine Sulfate has better absorption than GHCL. In horses, following oral administration of a clinically recommended dose of GS, higher levels were found in plasma and in synovial (joint) fluid, compared to an equivalent dose of GHCL (5).

This new information has been summarized by Dr. David Davenport (DVM, MS), a Certified Nutritional Specialist (24):

> *"…. new studies have proven that only Glucosamine SULPHATE 2KCl (Potassium Salt) and Glucosamine Sulphate NACl (Sodium Salt) actually get to the joint tissues. Recent studies have shown that very little Glucosamine HCl gets into the joint tissue, yet many of the Glucosamine supplements that you find in national chain stores contain this form of Glucosamine rather than Glucosamine Sulphate. Glucosamine HCl does not contain a sulphur source and, therefore, has NO EFFECT on the body in that form. It is necessary for it to undergo changes before it can be used in connective tissues. The HCl must be removed and a sulphate added. Because*

of this, Glucosamine HCl is not sold by itself, but, rather, with other ingredients that provide the sulphur. One of the most popular ingredients added to supplements that use Glucosamine HCl is Chondroitin Sulfate. The problem with Chondroitin Sulfate is that it has larger molecules, which affects how well it gets into the joints. Even with the best Chondroitin Sulfate on the market, as much as 70% ends up in the urine and feces."

WHY NOT USE CHONDROITIN SULFATE AND GLUCOSAMINE HCL

This is certainly an option. In fact, most joint supplements (for humans or for horses) contain these ingredients. But, as described above, this combination may be less well absorbed than pure glucosamine sulfate, and may not be as effective. Further, GHCL alone is probably not effective alone. (25). There is also strong evidence that the chondroitin part of the CS molecule is just not well absorbed from the horse's intestine (22) However, several human clinical trials show benefit from CS alone (26) (possibly due to the presence of the sulfate)

WHY NOT USE INJECTABLE TREATMENTS SUCH AS ADEQUAN, LEGEND, HA (HYALURONIC ACID)?

These injectables have a chemical structure similar to glucosamine, and can be loosely described as a long chain of glucosamine-like molecules, strung together to form a viscous liquid. If these compounds are injected directly into the horse (into muscle or IV), or directly into the joints, they can be very effective in relieving arthritis and/or overall joint stiffness. But such treatments are obviously much more expensive than oral supplements, and do require repeated injections. (Injections always carry some risk of infection or tissue trauma).

WHAT ABOUT ORAL HA (HYALURONIC ACID)?

HA can be very effective when injected directly into the joint (both in horses and humans) (1, 27). But the evidence that it works well as an oral supplement is still very weak. There have been only 2 published studies that actually look at oral dosing in horses. The first study shows oral HA may speed post-operative healing in young thoroughbreds, but no evidence it works in general arthritis in horses, or is good for prevention (28). A second found that oral HA did not improve joint swelling caused by osteochondrosis in young horses.

Unfortunately, many supplement manufacturers are still promoting it, using poor scientific evidence. For example, in 2010, the Hyaluronex web site cites “research” studies done on mice, not horses!!

Another problem with oral HA is the actual molecular size of the HA can vary, and some sizes may be better absorbed that others (1). It is difficult to know the actual size of the HA in the supplement you buy. And finally, HA is very expensive, and would add at least a dollar a day to the cost of the supplement. So when you see someone trying to sell you HA in an oral supplement, ask them to show you the study IN HORSES that proves it really works, and at doses that are affordable, and that you are actually getting exactly the same HA molecule that was used in the studies.

If and when oral HA is clearly shown to be effective for horses, it would be important to know whether or not it is actually more effective than less expensive supplements containing glucosamine sulfate. Interestingly, glucosamine is actually a precursor of HA, and is used by the body to manufacture naturally-occurring HA.

IS GLUCOSAMINE SAFE?

Glucosamine in all forms has no known toxicity, and is very safe. This has been confirmed repeatedly in horse and human studies (2, 29). In a recent study on absorption, horses were given 10 times the usually dose, and still had no adverse effects (30)

DOES GLUCOSAMINE INCREASE THE SUGARS IN YOUR HORSE’S DIET?

Glucosamine, given at standard doses, cannot add enough sugar to the diet to cause a problem for Insulin Resistant (IR) horses. There is a growing awareness among horse owners that many horses may develop insulin resistance, a metabolic condition where horses have a problem processing carbohydrate/sugar rich feeds. These horses are more susceptible to developing laminitis, loss of muscle mass, abnormal coat, and easily become obese (31, 32). Since glucosamine contains a glucose molecule, it could theoretically contribute to sugar in the horse’s diet. However, a simple calculation shows that it could only increase the total dietary carbohydrate by a few percent, even with a low carbohydrate diet. (So if your horse is now on a 10.0% carbohydrate diet, addition of glucosamine would change this to only 10.3%). The same concern

has been raised about diet in people with diabetes (which also causes insulin resistance). Several studies have shown that this is not likely to be a problem for humans either; addition of G to the diet of diabetic patients does *not* increase their average blood sugar levels (33, 34).

WILL GLUCOSAMINE HELP PREVENT FUTURE ARTHRITIS PROBLEMS?

GS may actually help restore damaged cartilage. That is, it may have preventive effects that could actually provide long term protection for the joint. Most of this information comes from human studies. A recent study showed significant cartilage repair in knee joints after 3 years of GS use (20).

WHAT IS THE CORRECT DOSE?

The usual dose recommended for humans is probably about 1500 mg daily. Doses for horses in commercial supplements cover a wide range. But if one extrapolates from human doses to equine, based on body weight, then an equivalent dose for horses is about 8 to10 gms daily (8,000 to 10,000 mg). This is similar to doses used in horse studies that show improvement with use of joint supplements (35, 36)

ARE THERE ANY CLINICAL STUDIES ON HORSES TAKING GLUCOSAMINE?

Many of the equine studies described above have either been laboratory studies or have looked at various measures of absorption, or biochemical markers in the blood, etc. Very few studies have actually evaluated the ability of these supplements to improve lameness in horses in clinical trials.

In 2006, results of a long term study on working show hunter/jumpers was reported. This was a crossover study (not double blind or placebo controlled) that evaluated 10 horses over 8 years. Before given supplementation with GCHL and CS, they needed 1.7 joint injections per year. About 6 months after beginning the supplement, fewer joint injections (0.85 per year) were needed to maintain the same level of performance (37).

Two additional clinical studies in horses used Cosequin® powder (glucosamine HCL, chondroitin sulfate, and a small amount of Vitamin C) for treatment of lameness caused by osteoarthritis or navicular disease (35, 36). In both studies, lameness scores and clinical scores improved as a result of treatment. The osteoarthritis study used the recommended label dose of

Cosequin®, but was not blinded or controlled. The second study on navicular lameness was double-blinded and placebo controlled, with significant improvement in investigator scores at 8 weeks, but less improvement in owner scores during the same period. This study was well designed, but used doses of Cosequin© that were twice the label dosage recommendations. This was the first randomized, double-blind placebo-controlled clinical trial in the horse.

Another important study was carried out by Dr, Hilary Clayton at University of Michigan (38). She conducted a double blind study comparing use of Cortaflex® to placebo in working horses with some degree of stiffness and asymmetric gait. She used pressure plates for gait evaluation, and found some improvement in range of motion and smoothness of gait after only 2 weeks of supplement use. (Cortaflex® contains precursors of glucosamine and chondroitin.)

B. METHYLSULFONYLMETHANE (MSM)

In spite of its widespread use, MSM really hasn't been studied all that much. In humans, MSM has been evaluated mainly as a treatment for allergy - to help reduce inflammation. In theory, MSM, which is closely related to DMSO chemically, may reduce muscle pain and spasm. It is also helpful for arthritis pain in the knee and spine (39-42).

There have been two studies in horses that have demonstrated some benefit. The aim of the first study was to determine if supplementation with MSM and Vitamin C could alleviate exercise-induced oxidative stress in horses undergoing jumping competition. This stressful exercise caused significant changes in the blood levels of substances associated with stress and injury. Twenty-four horses were divided into 2 groups, and each group given a different treatment diet: control (without supplementation), or MSM (about 4 grams a day), or combined supplements (MSM 4 grams + Vitamin C 21/2 grams daily). MSM administration significantly ameliorated all these exercise-related changes in the blood. This effect was potentiated by Vitamin C so that these substances returned to levels similar to those found before competition. The authors of this study concluded:

"These results suggest that jumping exercise induces harmful

effects on horses, probably due to an increase in oxidative damage and proinflammatory molecules. In addition, we have demonstrated that MSM could exert some protective effect on oxidative and inflammatory exercise-induced injury. The addition of Vitamin C was even more beneficial. (43)."

An earlier uncontrolled study evaluated training times in racing standardbred horses. MSM supplementation appeared to significantly improve training times (44). Because MSM has a high content of sulfur, it may help with cartilage structure (similar to the sulfur in GS). Toxicity and safety profile are good.

In summary, MSM may have significant benefit for horses, even though the scientific evidence is scanty (3).

C. VITAMIN C

Vitamin C has been studied extensively -- both in the laboratory and in human and animal studies. It is well know as an "antioxidant." This is a molecule that may inactivate harmful substances in the body called "free radicals" which can cause various types of cellular damage. Vitamin C is also commonly used as an antioxidant preservative in foods and many animal feeds, since it helps prevent deterioration In humans, Vitamin C is used for treatment and/or prevention of various ailments including the common cold. There continues to be considerable scientific controversy about uses of Vitamin C since some studies showing benefit, others not. The dose is one of the critical factors. Unfortunately, many human clinical studies have used very low doses (less than 100 mg daily) even though many experts believe higher doses are necessary to show any benefit (2000 to 10000 mg daily). But it is generally agreed that vitamin C supports synthesis of collagen (important component of elastic and muscle tissues), stimulates activity of certain white blood cells, and speeds healing of wounds. It is an antioxidant as well.

In horses, studies on racing thoroughbreds (45) and endurance horses (19) who were given Vitamin C orally, demonstrated that higher levels of Vitamin C reach the blood during exercise, which may prevent cellular damage. Vitamin C is also used as an effective treatment for recurrent airway obstruction in horses,

also called “heaves” (46). This is very similar to asthma in humans. More importantly for our purposes, vitamin C may protect cartilage from degeneration. One long term (uncontrolled) study on lame horses showed significant improvement in 9 of 10 animals (47). Even in very high doses, vitamin C doesn’t have any adverse effects. Doses should probably be at least several grams daily to be effective.

This is still a young field, and we will know much more ten years from now. In the meantime, using joint supplements for your horse has no known real risk, and often has a great deal of benefit!

RECOMMENDED READING -- MEDICAL AND VETERINARY LITERATURE

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