CLINICAL TRIAL

Use of a nutraceutical supplement (**EXCEED 6 WAY™**) **Med Vet Pharmaceuticals (MVP)** for daily joint support in horses with osteoarthritis – Minimal risk field trial and survey.

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Introduction:

Osteoarthritis in athletic horses is a leading cause of poor performance. Arthritis in the performance horse results in decreased range of motion, pain, inflammation and increased effusive pressure within the affected joint(s). Advancements in the understanding of the molecular pathways involved in arthritis has allowed for more robust treatment options such as interleukin-1 receptor antagonist protein (IRAP) and other disease modifying agents, however, daily supplementation of joint protective and reparative molecules remains a cornerstone of modulating the arthritic response.

Exceed 6 Way™ provides a daily supplement containing oral joint support molecules (glucosamine sulfate, methylsulfonylmethane (MSM), chondroitin and hyaluronic acid). Each of these molecules have been shown to be available and measurable in the quality and quantities necessary to attain certification with the **National Animal Supplement Council (NASC)** for **Exceed 6 Way™** and manufactured under **FDA** required GMP guidelines.

Exceed 6 Way™ also provides several other ingredient molecules measurable in quality and quantity as nutritional support for gastric function, muscle, hoof health, skin/coat, and digestion.

The objective of this trial was to subjectively assess the potential benefits of **Exceed 6 Way™** in performance horses with established osteoarthritis during short term use (16 weeks).

Materials and Methods:

Ten Horses (4 thoroughbreds, 4 quarter horses and 2 warmblood) were selected. Inclusion criteria were horses with an age between 3 and 25 years with osteoarthritis confirmed by radiographs and clinical exam findings. All horses were in athletic work during the trail time period of 16 weeks. The horse's athletic disciplines included 2 thoroughbred race horses, 2 barrel racing horses, 2 western pleasure/AQHA trail horses, 1 cutting horse, 1 reining horse, 1 3-day eventing horse and 1 hunter/jumper horse. There were 7 geldings and 3 mares in the group.

All horses underwent lameness and clinical evaluation at 4 week intervals during the trial period in addition to an initial inclusion criteria exam. Each exam included evaluation of vital parameters (heart rate, respiratory rate and quality and temperature), assessment of gastrointestinal auscultation, skin and hair coat quality, weight, muscle/joint/bone palpation and lameness evaluation including joint range of motion, palpation, hoof tester exam, joint flexions and movement exam.

In addition, during the initial and final exam, radiographs were taken of the arthritic joint(s) based on the overall clinical exam. No perineural anesthesia or joint blocks were performed. Assessment of arthritis was based on previous perineural anesthesia and/or decreased range of motion, pain on joint flexion or effusion of the suspected joint(s) to localize the joint at issue. All lameness grades were based on the **American Association of Equine Practitioners (AAEP)** grading scale and all lameness exams were performed by the author **(Dr. Chris Bell, DVM)**.

Horse owners and/or trainers and/or barn managers in charge of the regular husbandry for each horse were given copy of the study protocols and asked to administer the supplement daily as well as record confirmation of daily administration and any adverse reactions or events surrounding the administration of the supplement.

The supplement administration protocol was as follows: administer 2 ounces orally twice a day with regular meal for 120 days. Additionally each caretaker was given a survey at the completion of the trial upon which they were to make comments regarding their perceptions on the effectiveness of the supplement.

Results:

Of the included horses, all had radiographically confirmed osteoarthritic changes within at least 1 joint and several horses in multiple joints prior to beginning the study. The joints radiographed included 12 tarsi, 6 stifles, 3 fetlocks and 1 carpus. Two horses had previous evidence of fractures involving the affected joint – one with a repaired lateral condylar fracture and one with a repaired third carpal bone frontal plane slab fracture. The radiographic changes seen in the tarsi included enthesiophytosis and osteophytosis lesions of the tarsometatarsal (TMT) and distal intertarsal joints (DIT), partial fusion of the TMT and DIT joints and soft tissue swelling of the periarticular joint structures. Radiographic changes seen in the stifles included osteophytosis and enthesiophytosis of the medial aspect of the distal femur and proximal tibia as well as periarticular soft tissue swelling most commonly associated with the medial collateral ligament or medial meniscal structures.

Radiographic changes seen in the fetlocks included enthesiophytosis and osteophytosis of the articular margins of proximal P1 and distal metacarpal/tarsal 3 (MC/T3) bones as well as flattening of the distal palmar/plantar aspect of MC/T3 and osteophytosis or exostosis of the articular margins of the sesamoids. One horse also had mild sesamoiditis changes seen. At conclusion of the trial, six horses showed no difference in degree of osteoarthritis seen

initially, 1 horse had radiographic improvement of the osteophytes seen initially and 3 horses had further degradation of the arthritic changes seen initially. In the three with degradation of their radiographic arthritis changes included; one had increased severity of changes in the fetlock, one of the carpus including a new osteochondral fragmentation within the affected joint and one had increased osteophytosis of the TMT/DIT joints.

All horses displayed lameness at initial exam. The lameness ranged from grade 1-4 with a mean grade of 1.85. The lameness distribution between forelimb: hindlimb was 3:7 respectively. The lameness grade scores improved overall throughout the trial with a final overall mean of 0.5 at conclusion of the trial (Table 1.)

Table 1: Lameness grade score per subject at time points 0, 30, 60, 90 and 120 days

Subject	0 days	30 days	60 days	90 days	120 days
1	3	1	2	1	0
2	1	0	0	0	0
3	2	1	0	1.5	0
4	1	1	2	0	0
5	3	2	2.5	3	2
6	1.5	0	0	2.5	1.5
7	1.5	0	0	0	0
8	1	1	1	0	0
9	2	1.5	2.5	1.5	1
10	2.5	0	0	0	0
Average	**1.85**	**0.75**	**0.8**	**0.95**	**0.5**

90% showed average decreased lameness score at the end of 30 days (1.85 down to .75 or <1), a reduction of 60%. 4 out of the 10 went to a 0 lameness score after 30 days (40% of the horses). The mean decreased lameness scores leveled out for 60-90 days and at 120 days dropped to an average of .5 (1.85 to .5 or <1) or73% improvement from start of the trial. 7 out of the 10 horses (70%) had a 0 lameness score at the end of 120 days.

The overall palatability of the supplement was good. No caregivers reported any palatability issues or refusal to consume the product. One horse was able to be taken off a concurrent gastrointestinal medication (omeprazole) with the addition of the supplement to the diet.

Owner survey results were positive for all but one horse. Of the 10 horses, 9 reported antidotal improvement in horse comfort and athletics (90%). Three owners reported improvement in hair coat quality and/or quantity. Four caregivers reported horses to be 'more playful' in their pasture and during interactions with herd mates. One caregiver reported requiring fewer joint injections compared to prior to beginning the supplement

with the horse at the same level of performance. One owner reported the horse had decreased susceptibility to exercise induced pulmonary hemorrhage since beginning the trial compared to the same level of athletic performance prior to the trial.

There were 3 horses that required additional intra-articular joint injections of corticosteroid and/or hyaluronic acid during the trial. Those horses developed an increased lameness during the trial which was attributed to the joints previously documented at initial exam (2 horses) or a new injury (1 horse). All three horses responded with a decreased in the grade of lameness following injection.

During the trial, one horse developed colitis that required intensive medical management. This horse was stabled with several horses that also developed colitis during a 4 day period following a change in feed management and quality of feed in their barn. The supplement was withheld during the course of medical management as a precaution. The horse recovered uneventfully and returned to supplement use for the remainder of the trail without incident.

Discussion

In the case of **Exceed 6 Way™**, quantity and quality of ingredient are not called into question as this supplement has taken the added step of attaining quality seal with the **National Animal Supplement Council (NASC)**. Further to that, this prospective clinical trial was undertaken and the findings show that **Exceed 6 Way™** has the potential to improve the subjective comfort and degree of lameness in horses with concurrent osteoarthritis.

The results show a marked decrease in the grade of lameness score from a mean of 1.85 over ten exams at the onset of the trial to a mean grade of 0.5 at conclusion. Of greater interest was the decrease in overall lameness grade after the initial 30 days (1.85 to 0.75). This suggests that the supplement had a rapid uptake into the horses systems and resulted in improvement in the overall comfort of the arthritic joints as well as concurrent gastrointestinal and/or other musculoskeletal related issues. Although these concurrent issues could not be accurately quantified, there was suggestive evidence that this supplement did improve the overall demeanor and comfort of the horses during the first 30 days and carrying through to 120 days.

There were three horses with degradation of their radiographic changes over the course of 120 days. The changes seen in the fetlock and carpus were most certainly related to heavy training and racing schedules associated with these two subjects. The arthritis would not be attributable to supplementation. To the contrary, the horse with development of distal radial carpal bone fragmentation within the carpus remained sound throughout the trial and although showed significant lameness in the days following fragmentation during her race, recovered to sound within 1 week which the trainer attributed to supplementation with the chondroprotective molecules and decreased inflammation resulting from feeding the **Exceed 6 Way™** supplement. The changes in the fetlock were minor and as will be

discussed, this horse developed comorbidity lameness issues. The final horse with degradation of his radiographs showed increased arthritic changes in the DIT and TMT joints consistent with the degree of exercise and use. The changes were not unexpected and did not prevent the horse from continuing in the trial.

In one horse, there was a failure of the horse to improve through 120 days. Although the horse was maintained on the supplement appropriately, arthritic damage within the fetlock joint and subsequent findings of a navicular bone cyst and lateral splint bone fracture resulted in the horse becoming increasingly lame during the trial. The joint that was subject to arthritis was injected and the horse showed improvement. The navicular bone cyst with treated with a bisphosphonate (Osphos) and responded well with decrease in lameness and arrest of the cystic structure radiographically. The horse was rested during the final weeks of the study and thus had come sound for the final exam but unfortunately this horse will not be continuing in his current career as a racehorse.

Some of the limitations with this trial were the low number of horses making valid and complete statistical analysis challenging as well as the issues in measures of a subjective nature. Both the subjective caregiver survey and the subjective observer bias in the grading scale make statistical analysis difficult. Even with multiple observers, then intra and inter observer repeatability of grade becomes an issue. No blood or synovial analysis was performed to confirm level of each ingredient within the blood or synovium to validate the therapeutic effect seen in many of the horses. Those types of measurements were outside the scope of this trial. A randomized, double blind, prospective clinical trial would be the next study suggested to complete a thorough assessment of efficacy.

Conclusion

Overall, this trial showed excellent results for a complete, comprehensive joint support supplement in **Exceed 6 Way™** with excellent palatability, high owner satisfaction and measurable reduction in the degree of lameness in performance horses with pre-existing osteoarthritis.