The combination of unsaponifiable oil extracted from avocado and soybeans has been investigated over the last decade with promising results in experimental animal models and human patients but blinded controlled studies in a target species such as the horse are lacking. The purpose of this study was to evaluate ASU compared to placebo treatment in an equine model of OA.
Methods: This study was a blinded experimentally controlled randomized block design that utilized 16 horses in an established model of osteoarthritis. On day 0 of the study, arthroscopic surgery was performed, and OA was induced unilaterally in the mid-carpal joint of all horses. Also on day 0, horses were divided into two treatment groups: placebo control and ASU treated. The placebo control horses (n = 8) received molasses orally once daily, while the ASU treated horses (n = 8) received 6g of ASU plus a similar volume of molasses orally, both treatments were continued throughout the study period.
On day 14 horses began and continued treadmill exercise for the remaining 8 weeks of the study. Synovial fluid and serum were assessed every other week for total protein concentration, white blood cell count (WBC) and levels of the inflammatory marker, prostaglandin E2 (PGE2). Horses were assessed for lameness using the AAEP grading scale every two weeks. At the termination of the study, operated joints were evaluated grossly, and tissues were harvested for biochemical and routine histologic examinations.
Results: All horses completed the study and no adverse events were recorded. At the termination of the study horses treated with ASU were observed to have significantly improved total gross examination score (articular cartilage erosion + synovial membrane hemorrhage score) in their OA joint when compared to placebo treated horses. The degree of lameness and other outcome parameters were not significantly different when ASU and Placebo treatments were compared although numerically they appeared improved.
Conclusions: While the significant improvements were modest, it is more than has been seen with some other parenteral (Polysulfated glycosaminoglycan and intravenous hyaluronan) and oral (hyaluronan) products tested using the same model of equine OA. These data suggest further research both using in vitro and clinical trials should be undertaken to evaluate ASU.

519 EVALUATION OF BONE MARROW DERIVED STEM CELLS AND ADIPOSE DERIVED STROMAL VASCULAR FRACTION FOR TREATMENT OF OSTEOARTHRITIS USING AN EQUINE EXPERIMENTAL MODEL

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Purpose: Joint disease and specifically osteoarthritis (OA) is one of the most prevalent and debilitating diseases affecting both humans and horses. While claims that adipose derived stem cells improve horses with clinical OA, no controlled clinical studies have been published in horses or humans to date. Furthermore no controlled studies have been published on bone marrow derived stem cells for the treatment of OA in either humans or horse OA. Bone marrow derived stem cells expanded in culture have been used to regenerate and/or repair a variety of tissues but to date only one study has been published evaluating the in vivo effects of intraarticular stem cell injection on decreasing the progression of experimental OA in a goat model of OA This study used a medial meniscectomy and cranial cruciate transection model to induce OA. The decrease in OA seen in the study was thought to be secondary to the regeneration of the medial meniscal tissues, which was dramatic in 7 of 9 cases. The design of the study did not lend itself to determining if the stem cells had a direct effect on the articular cartilage. Based on unpublished data there is some evidence that stem cells have a tropism for fibrillated articular cartilage. This coupled with the overwhelming capacity of stem cells for regeneration of many tissue types, the current study was undertaken. Unlike the study by Murphy et al., the model used in the current study does not rely on joint instability (medial meniscal model) to create secondary OA but rather an osteochondral fragment in concert with articular cartilage and bone debris created at the time of fragmentation. It is believed that the progression of OA in this model is largely enzymatically and particle mediated.
Methods: This study was a blinded experimentally controlled randomized block design that utilized 24 horses in an established model of osteoarthritis. On day 0 of the study, bilateral mid-carpal arthroscopic surgery was performed, and OA was induced unilaterally in one mid-carpal joint of all horses. On day 14 horses received either Placebo, bone derived culture expanded stem cells (BDMSC) or adipose derived stromal-vascular fraction (ADSVF). Also on day 14 the horses began a strenuous exercise regime 5 days per week for the remaining 8 weeks of the study. Pivotal parameters assessed included clinical pain, radiographic and gross examinations as well as articular cartilage and synovial membrane morphology and synovial fluid prostaglandin E2 (PGE2).
Statistical analysis utilized both a Mixed model analysis of variance and a Least Square mean when individual comparisons were made, and p-values <0.05 were considered significant.
Results: All horses completed the study and no adverse events were recorded. Horses receiving Placebo treatment in the OA joint had a significant increase in all of the pivotal parameters. Neither horses receiving BDMSC or ADSVF in their OA joints showed any significant improvement in any of the same pivotal parameters except PGE2 which was significantly decreased in BDMSC treated horses.
Conclusions: The results of the current study and Murphy et al. combined suggest that the regeneration of the medial meniscus in Murphy et al.'s study may have in fact been the reason for less OA progression. Furthermore, the current study also suggests that MSC's by themselves do little to counteract the progression of OA mediated by enzymatic degradation and joint debris except for decreasing PGE2. It would appear modification of the MSC's is needed if they are to be clinically useful in treating the OA represented in the current model.

520 EVALUATION OF AUTOLOGOUS CONDITIONED SERUM USING AN EXPERIMENTAL MODEL OF EQUINE OSTEOARTHRITIS

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Purpose: Interleukin-1 (Il-1) is thought to be the major mediator of joint disease. Studies in both humans and horses have evaluated the use of a natural antagonist (interleukin-1 receptor antagonist, Il-1Ra) to block Il-1 activity and decrease the progression of joint disease.
A novel product to the United States has been introduced for the treatment of equine OA, autologous conditioned serum (ACS). This product has been shown to stimulate the production of Il-1Ra from cultured peripheral blood of human patients by 140 fold. The purpose of this study was to evaluate ACS compared to placebo treatment using a horse model of OA.
Methods: This study was a randomized blinded controlled study that utilized 16 horses in an established model of osteoarthritis. On day 0 of the study, arthroscopic surgery was performed, and OA was induced unilaterally in the mid-carpal joint of all horses. On day 14, horses were divided into two treatment groups: placebo control and ACS treated. The placebo control horses had 6 ml of saline injected into the OA joint on days 14, 21, 28 & 35 while the ACS treated joints (OA joints) received 6 ml of serum prepared as directed by the manufacturer at similar time periods. On day 14 the horses began a strenuous exercise regime 5 days per week for the remaining 8 weeks of the study. Synovial fluid and serum were assessed every other week for total protein concentration, white blood cell count (WBC) and levels of the inflammatory marker, prostaglandin E2 (PGE2). Horses were assessed for pain using a standardized scale every two weeks. At the termination of the study, operated joints were evaluated grossly, and tissues were harvested for biochemical and routine histologic examinations.
Statistical analysis utilized an analysis of variance and a Least Square mean for individual comparisons, p-values <0.05 were considered significant.
Results: All horses completed the study and no adverse events. ACS processed serum had a significant increase in Il-1Ra concentrations when compared to control serum (234±27 versus 45±29 pg/mL, respectively). Horses treated with ACS were observed to have significantly improved lameness in OA joints, even five weeks after the last treatment when compared to placebo treated horses (1.3±0.2 versus 2.1±0.2, respectively). A significant reduction in synovial membrane hyperplasia was also seen in the treated compared to placebo OA joints at day 70 (0.4±0.3 versus 1.3±0.3, respectively). The levels of IL1-Ra were also significantly elevated in the joints of ACS treated horses after day 35 and were estimated to be 71±13 versus 44±13 pg/mL on day 70 when treated versus placebo synovial fluid was compared respectively.
Conclusions: The ACS system used here stimulates peripheral white blood cells to produce an "anti-inflammatory soup". An import finding of this study was no negative side effects associated with the intraarticular administration of ACS. Significant clinical improvement was seen following treatment of induced OA at the last point measured during the study. Significant improvement was also noted in synovial membrane parameters, as well as trends for gross improvement, further supporting a therapeutic