Effects of an Oral Nutraceutical on Clinical Aspects of Joint Disease in a Blinded, Controlled Clinical Trial: 39 Horses

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Myristol is a nutraceutical, containing cetyl myristoleate, glucosamine hydrochloride, methylsulfonylmethane, and hydrolyzed collagen, available to veterinarians for use in osteoarthritis (OA) in horses. This study investigated the efficacy of Myristol to alleviate clinical signs of OA in horses. Thirty-nine horses with OA were used in a randomized, double-blinded, placebo-controlled clinical trial. Each horse was scored using American Association of Equine Practitioners (AAEP) guidelines for lameness severity and 0-10 cm visual analog scales (VAS) for lameness at walk (LAW), lameness at trot (LAT), response to joint flexion (RJF), lameness after flexion (LAF), and quality of life (QOL). Horses were assessed on day O and 14, 28, and 42 days after treatment. A responder was defined as improving 1 grade on the AAEP lameness scale or 2 cm on the VAS. Parameter differences between treatment groups were evaluated by repeated-measures analysis of variance. Cross-tabulations of the number of responders versus nonresponders were evaluated by Fischer's exact test. Level of significance was set at $p = 0.05$. The Myristol group improved significantly more than the placebo group in AAEP lameness score ($p=0.03$), LAW ($p=0.02$), RJF ($p=0.04$), LAF ($p=0.05$) and QOL ($p=0.05$). The Myristol group had significantly more responders than the placebo group in one measured parameter (RJF). Oral administration of Myristol had beneficial clinical effects on horses with naturally occuring OA. Authors' addresses: C163A Clydesdale Hall, 379 East Campus Drive, Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, Columbia, MO 65211 (Keegan); Peterson & Smith Equine Hospital, 4747 SW 60th Avenue, Ocala FL 34474 (Hughes); 17200 SE 58th Avenue, Summerfield, FL 34491 (Lane); and Serengeti Consulting, 6880 NW 21st Street, St. Louis, MO 63005 (Buonomo, Downer); e-mail: fcbuonomo@att.net.

1. Introduction

Joint disease and osteoarthritis (OA) are common causes of impaired performance and economic wastage in the equine industry. Traditional therapy often targets symptom modification through the use of either locally or systemically administered agents that control symptoms of pain and impaired function (corticosteroids and non-steroidal anti-inflammatory drugs [NSAIDS]).[1] Interest has also developed in preventive approaches to joint disease. Some injectable agents, such as hyaluronan products and polysulfated glycosaminoglycan, are frequently used with these goals in mind. Oral nutraceuticals, like glucosamine and chondroitin

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sulfate, are also used for their supposed symptom-modifying effects.[2–7] In humans, there is some evidence to suggest that nutraceuticals may be effective for the treatment of OA;[5–6] however, there are few controlled and blinded prospective studies evaluating the efficacy of nutraceuticals in the horse.

Myristol[a] is a nutraceutical that has recently become available to veterinarians for use in horses for the treatment of OA. Myristol contains cetyl myristoleate (CM), glucosamine hydrochloride (GLN), methylsulfonylmethane (MSM), and hydrolyzed collagen (HC). Each individual ingredient has shown some positive effect in either human clinical trials (CM, GLN, and MSM)[8–14] or in vitro in horses (GLN and HC).[2,4,15] The purpose of this study was to investigate the efficacy of Myristol to alleviate clinical signs associated with OA in horses. Our hypothesis was that oral supplementation of Myristol would not improve clinical signs of OA in horses compared with placebo in a blinded, controlled trial.

2. Materials and Methods

Selection of Horses

A total of 39 adult horses were selected in Missouri (n = 27) and Florida (n = 12) for enrollment in the study after a complete physical and lameness evaluation by an American College of Veterinary Surgeons (ACVS) board-certified equine surgeon (KGK or FEH) for the diagnosis of naturally occurring OA. Horses were client owned and originated from four sources: a broodmare farm, a local Thoroughbred retirement center, and two local college/university equestrian programs. To be selected into the program, each horse had to have a diagnosis of naturally occurring OA and an American Association of Equine Practitioner (AAEP) lameness score between 2 and 4. Diagnosis was made on the basis of clinical examination; if the joint affected with OA was not noticeable by clinical examination alone, radiographs were used. If bilateral lameness was evident, the more severely affected limb was selected for study. Suitable horses were excluded if they had had surgery in the last 120 days, intra-articular injections within the last 90 days, systemic polysulfated glycosaminoglycans within the last 30 days, systemic steroids or NSAIDS within the last 7 days, or any other dietary supplements with potential beneficial effect on joint health initiated within the last 60 days.

Study Design

Two treatment groups were used in the study: a negative control using a pelleted vehicle and an oral-supplementation group using pelleted Myristol. Each 2.67 oz or 2 scoops of Myristol contains cetyl myristoleate fatty-acid complex (5000 mg), glucosamine HCl (4500 mg), methylsulfonylmethane (4500 mg), hydrolyzed collagen (3000 mg), DL methionine (1534 mg), ascorbic acid (1000 mg), manganese (250 mg), zinc (250 mg), and copper (50 mg). Horses were fed Myristol or negative-control pellets as a top dressing over normal concentrate feed at 3 scoops (4 oz) one time a day for 14 days. Then, 2 scoops (2.67 oz) were fed one time a day for 28 days; there was a total of 42 days of supplementation. Horses were blocked for forelimb or hindlimb OA and randomly assigned to one of the two treatment groups. Lameness evaluations were performed on day 0 and on days 14, 28, and 42 after the start of treatment. Treatment was administered by the caretaker in charge of the particular horse at the normal place of boarding. Veterinarians performing the lameness evaluations and caretakers administering treatment to the horses were blinded to the treatment group. An individual from a consulting firm contracted to run the study performed the randomization and treatment group designation.

Lameness Evaluations

All lameness evaluations on a selected horse were performed by the same veterinarian. Lameness data were recorded on a form provided by the consulting company in the order listed below. The affected and contralateral limbs were scored separately for AAEP lameness grade. Only affected limb(s) were scored for all other parameters. Both limbs were scored for all parameters if the horse showed bilateral lameness at any evaluation day. Parameters were quantified with a visual analog scale (VAS) by marking on a horizontal line from 0 to 10 with 0 being no response or no lameness and 10 being extreme response or maximum possible lameness (non-weight bearing). In addition to AAEP lameness score, the following parameters were measured: lameness at a walk (LAW), lameness at a trot (LAT), pain to manual joint flexion (RJF), and lameness after a 1-min flexion test using the VAS (LAF). Passive joint flexion was performed by manually manipulating the involved joint into a position of maximum passive flexion and then trying to force the joint to flex a little more. Lameness after flexion was evaluated immediately after assessment of pain to manual joint flexion.

Quality of Life Evaluations

Quality of life (QOL) was subjectively assessed using all of the above parameters as well as the horse's demeanor at the time of examination on a 10-cm VAS; 0 was excellent QOL (i.e., no obvious discomfort associated with the existing OA), and 10 was poor QOL.

Data Analysis

Horses were classified as responders or non-responders for each measured parameter. For AAEP lameness score, a responder horse was defined as a horse having decreased by one lameness grade by day 43 after initiation of treatment. For all other parameters, a responder horse was defined as a horse having increased (improved) in VAS measure-

Table 1. Estimate Marginal Means of Lameness and Quality of Life Parameters for Myristol and Placebo-Treated Groups at Days 0, 14, 28, and 42

	Treatment Group								
	Placebo				Myristol				
Overall Mean of Measured Parameter	Day 0	Day 14	Day 28	Day 42	Day 0	Day 14	Day 28	Day 42	p Value
AAEP Score	2.6	2.4	2.4	2.5	2.7	1.9	1.8	2.0	0.034
Lameness at walk (VAS)	0.8	1.1	1.4	0.8	2.5	1.7	1.7	1.3	0.021
Lameness at trot (VAS)	4.7	3.4	3.4	4.3	4.7	3.1	2.9	4.1	0.428
Pain to flexion (VAS)	3.4	3.6	4.4	4.1	4.3	3.3	3.2	3.0	0.038
Lameness after flexion (VAS)	7.4	6.6	6.5	7.0	6.9	5.0	5.0	5.2	0.054
Quality of life (VAS)	2.0	1.7	1.9	1.2	2.6	1.9	1.5	1.2	0.054

Values decreasing indicate improvement in lameness.

ment by ≥2 cm along the 10-cm scale by day 42 after initiation of treatment. After day 42, the treatment-group code was revealed. The differences between baseline and each study day for each horse were calculated and arranged by treatment group and study day.

Differences in measured parameters between day 0 and subsequent treatment days for treatment and control groups were evaluated by general linear models and repeated measures analysis of variance. Cross-tabulations of responders versus non-responders for each measured parameter were evaluated for difference between treatment and control groups by Fischer's exact test. Cross-tabulations of numbers of responders and non-responders to 4, 3, 2, and 0 measured parameters were also evaluated. Level of significance was set at 0.05.

3. Results

Four horses did not complete the entire study (Table 1). One horse was given away to a new home and did not complete the day 42 evaluation. Two horses were injected with corticosteroids into the affected limbs: one the day before the day 28 evaluation and one the day before the day 42 evaluation. No data was collected from these two horses after the interventions. One other horse could not be evaluated on day 28. All data from horses that did not complete the entire study were retained and used in cross-tabulation analysis but not in the repeated measures analysis of variance. All treatment administrations were completed on time, and all horses consumed treatment and control preparations without hesitation.

Horses in the Myristol group improved significantly more than horses in the placebo group in AAEP lameness score ($p = 0.03$), LAW ($p = 0.02$), RJF ($p = 0.04$), LAF ($p = 0.05$), and QOL ($p = 0.05$). Horses in both the Myristol and placebo groups improved significantly in QOL over baseline ($p < 0.01$). For both the Myristol and placebo groups, time had a significant impact ($p = 0.02$) on test results; both groups improved at days 14 and 28 but then regressed toward baseline in LAT on day 42.

One measured parameter, RJF, had significantly more responders in the Myristol group (7 responders and 12 non-responders) compared with the placebo group (1 responder and 19 non-responders).

4. Discussion

This study was performed on a heterogenous population of horses with a wide variety of naturally occurring OA. Horses from two states (Missouri and Florida) were evaluated by different practitioners in variable weather and surface-hardness conditions. Lack of control of potential compounding variables increased variance and may have made it difficult to find differences in some parameters between Myristol and placebo treatment. The substantial group variance resulting from the natural but highly variable evaluation conditions may explain why cross-tabulation analysis (difference in number of responders) did not show a significant difference in many measured parameters, but analysis of variance (difference in group means) was significantly different between treatments in many parameters. Also, our selections of cutoffs for definition of responder and non-responder were arbitrary (no previous definitions for these parameters exist). It is somewhat confusing that we saw a difference between Myristol and placebo for AAEP subjective lameness score, but we did not see a difference for VAS score of LAT. The VAS should be more sensitive than the more limited AAEP lameness score. Varying interpretations of the VAS for LAT by the different evaluators may have contributed to this result. Prior standardized training in VAS measurement may help to reduce this potential problem in the future. Nevertheless, despite high group variation, we detected significant differences ($p \leq 0.05$) in five of the six variables measured. Therefore, we conclude that oral administration of Myristol had beneficial clinical effects on horses with naturally occurring OA. First, there were significantly more responders in the Myristol group compared with the placebo group in the RJF category. Second, both variables relating to joint flexion were significantly different between the Myristol

and placebo groups. Third, the trends of the marginal means between Myristol and placebo for the RJF parameter were most obviously contrasting. Therefore, we suggest that the most apparent beneficial effects were in parameters related to joint flexion. Reducing pain to passive flexion and lameness after flexion are positive clinical effects for horses with OA.

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References and Footnote

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[a]Myristol, Tryan Enterprises, Dennis, TX 76439.