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Original Research

Use of a 2.5% Cross-Linked Polyacrylamide Hydrogel in the Management of Joint Lameness in a Population of Flat Racing Thoroughbreds: A Pilot Study

Leigh T. de Clifford [a,*], Jason N. Lowe [b], Campbell D. McKellar [c], Charlotte Bolwell [d], Florent David [e]

[a] Matamata Veterinary Services Limited, Matamata, New Zealand
[b] Innovative Medical Solutions Limited, New Zealand
[c] AK & K Equine Services, Victoria, Australia
[d] Massey University, Massey Equine, Palmerston North, New Zealand
[e] Equine Veterinary Medical Center - Al Shaqab, A member of Qatar Foundation, Al Rayyan, Doha, Qatar

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ABSTRACT

Osteoarthritis is one of the most common disease processes effecting equine athletes, causing up to 60% of all lameness. This prospective longitudinal study reports on the effect of treatment of carpal and metacarpophalangeal joint lameness with 2.5% cross-linked polyacrylamide hydrogel (PAAG). A total of 49 flat-racing Thoroughbreds at a single training facility were included in the study. The results show a significant improvement in lameness grades at weeks 1 ($P < .01$), 4 ($P < .001$), 12 ($P < .001$), and 24 ($P < .001$) when compared to baseline lameness at week 0. This pilot study suggests that 2.5% cross-linked PAAG is a safe and effective joint treatment for managing joint lameness in Thoroughbred racehorses and warrants further blinded and controlled studies to fully evaluate the efficacy of the 2.5% cross-linked PAAG and its mode of action.

1. Introduction

Osteoarthritis (OA) is cited as the most important musculoskeletal disorder in both humans and horses [1]. Several medications have been evaluated in the treatment of horses with OA, including nonsteroidal anti-inflammatory drugs (NSAIDs), polysulfated glycosaminoglycans (PSGAGs), corticosteroids, glucosamine, hyaluronic acid, and a combination of the above, along with biological substances such as gene therapy, recombinant or autologous growth factors (platelet-rich plasma and autologous conditioned serum), and stem cells (allogenic and autologous) [2]. The 2.5% cross-linked polyacrylamide hydrogel (PAAG) (Arthramid Vet; Mepivacaine Injection, Ceva Animal Health Pty Ltd, Glenorie, NSW, Australia), is a synthetic, nondegradable hydrogel, which is biocompatible, nontoxic, and has water-exchanging capabilities [3,4]. The hydrogel has been used in the augmentation of soft tissues, and studies from mice, rats, rabbits, pigs, and humans have shown it exerts its effect by being integrated within the tissue through a combination of vessel in-growth and molecular water exchange [5]. Vessel in-growth begins immediately after gel injection with host macrophages entering the gel, which are unable to engulf the polymer, and it is incorporated into the synovium over a period of approximately 14 days [4]. By day 30 in horse joints, the gel had formed a subsynovial layer, which was traversed by thin strands of connective tissue with vessels and covered by a synovial lining facing

Animal welfare/ethical statement: The study was conducted in accordance with EU Directive 2010/63/EU and approved by the Animal Research Authority and AEC from NSW, case number 14/1284.

Conflict of interest statement: Dr Leigh de Clifford consultants to Innovative Medical Solutions Limited that hold rights to Arthramid Vet in Australasia, with contribution being in conception and design of the study, interpretation of the data, and drafting the article. Dr Jason Lowe contributed to conception and design of the study and interpretation of the data. Dr C.D. McKellar was the examining and treating veterinarian. Dr C. Bolwell performed the statistical analysis and also assisted with interpretation of the data. Dr F. David assisted in drafting the article and interpretation of the data.

* Corresponding author at: de Clifford, L.T., Matamata Veterinary Services Limited, 26 Tainui Street, Matamata 3400, New Zealand.
E-mail address: leigh@matavet.co.nz (L.T. de Clifford).

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Table 1
Lameness scoring.

Score	Definition
0	Lameness not perceptible under any circumstances.
1	Lameness is difficult to observe and is not consistently apparent, regardless of circumstances.
2	Lameness is difficult to observe at a walk or when trotting in a straight line on a grassed surface, but consistently apparent after a flexion test or when examined on bitumen.
3	Lameness is consistently observable at a trot under all circumstances, on the grassed surface and bitumen.
4	Lameness is obvious at a walk.
5	Lameness produces minimal weight bearing in motion and/or at rest or a complete inability to move.

the joint cavity [4], with the histological appearance persisting up to 2 years postinjection in horse joints.

Recent clinical trials have investigated the effect of 2.5% cross-linked PAAG on improving clinical signs of equine OA unresponsive to previous treatments, with promising results [6–8]. Another long-term field study evaluated the efficacy of 2.5% cross-linked PAAG in 43 mostly sport horses with OA, with 82.5% of horses being lame-free at 24 months [9]. A standardized experimental study to explore the efficacy of 2.5% cross-linked PAAG in the treatment of induced OA in a goat model also gave encouraging results, with 3 of 4 being clinically lame-free at 4 months postinjection [10]. Recently an observational pilot study of 118 humans with femoro-tibial joint OA treated with 2.5% cross-linked PAAG showed significant improvement ($P < .0001$) of OA symptoms, up to 1 year [11].

It has been demonstrated [10] that the joint capsule elasticity and synovial membrane of OA affected goat joints improved following 2.5% cross-linked PAAG intra-articular treatment. A hypothesis as to a mechanism of action of 2.5% cross-linked PAAG is that it may have a stabilizing effect on the joint capsule and synovium, increasing elasticity and tensile strength and a subsequent reduction in mechanoreceptor activation [12]. This could in turn reduce synovitis and subsequent deleterious effects as a result.

The purpose of this study was to report on the effect and persistence of 2.5% cross-linked PAAG (Arthramid Vet; Mepivacaine Injection, Ceva Animal Health Pty Ltd, Glenorie, NSW, Australia) on clinical signs of joint lameness in the metacarpophalangeal (MCP) and carpal (antebrachiocarpal and middle carpal) joints of flat-racing Thoroughbreds, to determine if further, more rigorous studies, are warranted. Our hypothesis was that lameness scores would improve after treatment with 2.5% cross-linked PAAG compared to baseline lameness.

2. Materials and Methods

The study was conducted between June 1, 2015 and May 31, 2016 at a single Thoroughbred training facility. Horses were selected from those presenting for routine veterinary clinical examination for lameness, using a modified AAEP lameness scale formatted for the study (Table 1). Horses were included in the study based on a confirmed diagnosis of joint lameness in one or more joints associated with clinical signs of joint inflammation (effusion, heat, swelling, pain) and when a positive response to intra-articular analgesia (100 mg mepivacaine, Mepivacaine Injection, Ceva Animal Health Pty Ltd, Glenorie, NSW, Australia; hydrochloride per joint, horses re-examined after 10 minutes) was obtained. Horses with lameness from multiple joints had intra-articular analgesia performed in a different sequence at least 4 hours after initial assessment. This allowed sufficient time for the analgesia to subside, to accurately determine the grade of lameness in all affected joints. Radiographs were acquired and assessed using the indexed radiological grading scale detailed in (Table 2) by a clinician experienced in equine radiology, and all structures assessed to ensure no confounding factors. Radiographic projections of carpal and metacarpophalangeal joints were dorso-palmar, dorsolateral-palmaromedial oblique, dorsomedial-palmarolateral oblique, flexed lateromedial, dorso30°proximo-dorsodistal oblique, dorso65°-proximo-dorsodistal oblique and dorso-45°-palmar, dorso30°-lateral-palmaromedial oblique, dorso30°medial-palmarolateral oblique, flexed lateromedial, and flexed dorso-palmar views, respectively.

Exclusion Criteria

(1) Horses with osteochondral fragmentation or articular fracture were excluded from the study.
(2) Joint lameness secondary to joint infection.
(3) Horses with lameness grades of 4 and 5 were excluded from the study, as they were more likely to be severe or chronic in nature and were unable to be continued in training.
(4) Horses having undergone surgery of the joint within 3 months preceding the study.
(5) Any antiarthritic treatment administered to the affected joint within 2 months preceding the study.

Owners/agents then gave written informed consent for the horses to be included in the study. Postinclusion exclusion criteria were any additional intra-articular antiarthritic treatment administered, or surgery performed during the study period, involving the joint(s) under investigation. Systemic anti-inflammatories were permitted to be used throughout the study, for routine use, but were not permissible within 14 days of examination. The use of systemic nutraceuticals throughout the study was not permitted.

To increase homogeneity between study individuals, only horses that were at the stage of galloping were included into the study and were racing over distances of 1,200–2,000 meters.

On day zero, horses were injected with 2 mL of 2.5% cross-linked PAAG (Arthramid Vet; Contura International A/S, Soborg, Denmark) and 100 mg Gentamicin (Gentamax 100, CEVA Animal Health, NSW, Australia) in the affected joint(s) under aseptic conditions. The horses were followed up at 1 week, 4 weeks, 12 weeks, and 24 weeks postinjection. All horses were rested for 48 hours after treatment, before re-entering an unaltered training regime. Horses were evaluated in-hand, on a grassed surface, and bitumen, in straight lines.

Variables at each examination point were recorded by a veterinarian independent to data analysis and included: limb and joint involved, lameness scoring (0–5 scale) (Table 1), radiological scoring (0–3 scale) (Table 2), joint effusion scoring (0–3; 0 = no

Table 2
Radiological grading scale compiled to assess common radiographic findings associated with OA. Whichever was the highest was the overall grading of the horse.

Overall score	Subchondral Bone Sclerosis	Subchondral Bone Lysis	Extra-Articular Enthesiophytes	Periarticular Remodeling/Osteophytes
0	Absent	Absent	Mild	Absent
1	Mild	Mild	Moderate	Mild
2	Moderate	Moderate	Severe	Moderate
3	Severe	Severe		Severe

effusion, 1 = mild effusion, 2 = moderate effusion, 3 = severe effusion), and response to flexion test (0–3; 0 = no reaction, 1 = mild reaction, 2 = moderate reaction, 3 = severe reaction). Follow-up included re-evaluation of lameness, joint effusion and response to flexion test of the horse, and personal interview with the trainer. Postinjection complications were recorded throughout the entire study period.

2.1. Statistical Analysis

Multilevel mixed-effects ordered logistic regression was used to investigate the effect of time, joint affected, joint effusion scores, reaction to flexion tests, previous treatments, and radiographic score on the outcome lameness score. Because of low numbers, reaction to flexion tests was regrouped into a binary variable coding 0 for reaction score 0 and 1 for reaction scores 1, 2, and 3. Univariable ordered logistic regression was used to identify variables associated with lameness score (0, 1, 2, 3) at $P < .20$. A backward stepwise regression process was used to identify variables significantly associated with lameness score in the multivariable model at $P < .05$. This method of analysis provided a proportional odds ratio for each variable in the model across each level of the outcome variable "lameness score". This enabled a comparison of horses with a high lameness score to baseline lameness (Day 0), that is, the probability of having a high lameness score compared to the probability of having a low lameness score. The model also generates a Wald test *P*-value for each variable. A random effect for horse was used to adjust for potential clustering at the horse level due to the inclusion of multiple joints per horse [13].

3. Results

Forty-nine horses with a total of 89 affected joints satisfied the inclusion and postinclusion exclusion criteria, with Table 3 summarizing the data of the study population. The age of the horses treated was between 3 and 7 years (mean 5 years), and all horses were actively involved in flat-racing. At day zero, 54% (48/89) of the included joints had a radiological grading of zero. Synovitis, early OA without radiographic signs, subchondral bone injury, capsulitis, or intra/periarticular soft tissue injury formed the differential diagnosis list on these cases. At day zero, 46% (41/89) had mild, moderate, or severe radiological grades of OA (Table 3). Lameness was localized predominately to the middle carpal joint, representing 87.6% (78/89) of the included joints, the antebrachiocarpal joint only 1% (1/89), and the MCP joint represented 11.2% (10/89) (Table 3). Before treatment the percentage of horses with a lameness score of 1 was 6% (3/49), of 2 was 45% (22/49), and of 3 was 49% (24/49). Of the total number of horses, 20% (10/49) had been nonresponsive to other joint treatments previously attempted. The type or dose of medication as well as the exact duration of lameness was not recorded on these cases.

The percentage of lame-free horses at each evaluation was 0% at 1 week, 43% (21/49) at 4 weeks, and 67.3% (33/49) at 12 weeks (Fig. 1). One horse regressed after that time so at 24 weeks 65.3% (32/49) of the horses were lame-free, and a further 14.3% (7/49) had improved to some degree and enough to remain in race training. The distribution of the change in lameness grades for individual joints over the observed time periods is shown in Fig. 2. The largest reduction in lameness scores occurred at 4 weeks, with some taking up to 12 weeks after treatment to respond, and no further improvement in lameness between 12 and 24 weeks was observed. No side effects or adverse reactions were observed in any of the treated joints.

Whether a previous treatment was administered in the included joints, the type of joint affected, the effusion score, and the radiological score were not significantly associated with the lameness scores at the univariable level. Results of the final statistical model are shown in (Table 4) and showed a statistically significant improvement in lameness grades at weeks 1 ($P < .01$), 4 ($P < .001$), 12 ($P < .001$), and 24 ($P < .001$) when compared to week 0. A positive response to flexion tests was associated with higher lameness grade ($P < .01$) in the final model. The random effect for horse was significant in the final regression model.

Table 3
Summary data of study population.

Variable	Number (%)
Thoroughbred racehorses included	49
Total number of joints injected	89
Age range (y)	3–7
Mean age (y)	5
SD (y)	1.68
Joint involved	
Metacarpophalangeal	10 (11%)
Intercarpal	78 (88%)
Radiocarpal	1 (1%)
Lameness scoring at baseline	
0	0 (0%)
1	3 (6%)
2	22 (45%)
3	24 (49%)
4	0 (0%)
5	0 (0%)
Radiological score at baseline	
0 (none)	48 (54%)
1 (mild)	32 (36%)
2 (moderate)	4 (4%)
3 (severe)	5 (6%)
Reaction to flexion test score at baseline	
0 (none)	66/89 (74%)
1 (mild)	20/89 (23%)
2 (moderate)	3/89 (3%)
3 (severe)	0 (0%)
Reaction to flexion test score at 24 wk	
0 (none)	76/89 (85%)
1 (mild)	13/89 (15%)
2 (moderate)	0 (0%)
3 (severe)	0 (0%)
Horses free of lameness (grade 0)	
0 wk	0 (0%)
1 wk	0 (0%)
4 wk	21 (42.9%)
12 wk	33 (67.3%)
24 wk	32 (65.3%)

4. Discussion

This study demonstrates that intra-articular use of 2.5% cross-linked PAAG in the management of carpal and metacarpophalangeal joint lameness in a flat-racing Thoroughbred group was well tolerated, with no side effects such as joint inflammation or infection, and resulted in 65.3% of horses (32/49) being lame-free at 24 weeks postinjection. In addition to this, there were no subsequent injuries to any treated joint or surrounding soft tissue structures, such as subchondral bone disease, fracture, suspensory ligament desmitis, etc.

There were some obvious limitations to the study including the lack of randomization, the lack of blinding, and the lack of controls. The lack of control/placebo group represents the main weakness of the study. Therefore, it does not allow us to draw any conclusion on the direct effect of 2.5% cross-linked PAAG on the study results. However, the authors' clinical experience seems to indicate that the single intra-articular injection of 2.5% cross-linked PAAG appears superior to and longer-lasting than other treatments used in the past in a similar population, which could have positive benefits on

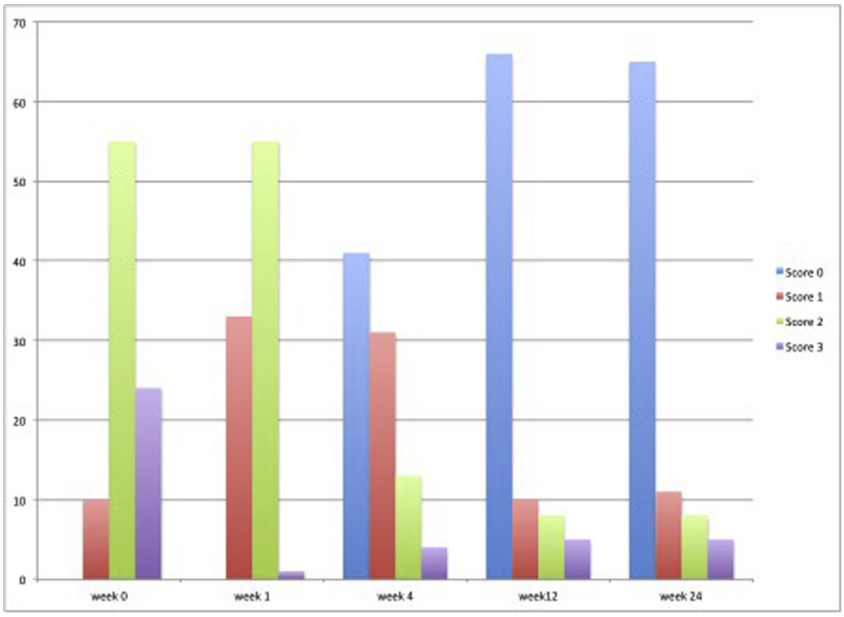

Fig. 1. Distribution of lameness scores (0, 1, 2, and 3 out of 5) at baseline (Day 0) and at 1, 4, 12, and 24 wk following treatment with 2.5% cross-linked PAAG.

animal welfare for those individuals participating in racing disciplines. The lack of change in lameness grade between 12 and 24 weeks and that owner satisfaction remaining high would also tend to support this interpretation. Further studies should however be conducted to investigate this clinical impression.

Animal ethics concerns and owner/trainer compliance remain a challenge in clinical trials. Randomization could be introduced but in a clinical trial setting, it is difficult to manage owner expectations around what treatment their horse receives or what the control product is. The use of a positive control may be a practicable solution to achieve this desired outcome, such as triamcinolone acetonide and/or sodium hyaluronate, which are typically used as a first line of joint pain treatment in this situation. Some subjects (20%) had already failed to respond to other joint treatments in this study, so they may have acted as their own positive controls as suggested in previous studies [8] but no statistical analysis was done on this due to the small numbers and lack of detailed information available.

It is important to note that no adverse reactions were observed in any of the treated joints. Adverse reactions in humans are rarely reported where quality hydrogel products have been used under tight control and according to intended use [14]. Arthramid Vet (Arthramid Vet, Contura International A/S, Soborg, Denmark) is a ready-to-use preparation delivered in a sterile single use syringe of 1 mL. Early reports indicated the use of 1–2 mL per equine joint [6]. A volume of 2 mL of 2.5% cross-linked PAAG was selected for this study, but this volume selection remains empirical as dose/volume-response curves have yet to be established for each equine joint.

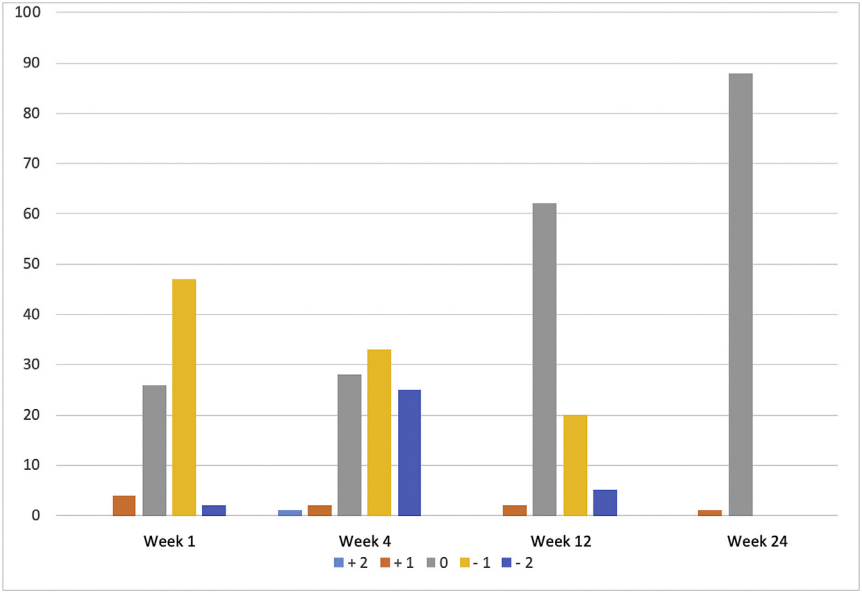

Fig. 2. Distribution of change in lameness grades of individual joints over consecutive time points.

Table 4
Results of ordered logistic regression for the variables week and reaction to flexion tests on lameness score.

Variable	Odds Ratio	95% Confidence Interval	*P* Value
Time			
Week 1 versus Week 0	0.033	0.014–0.084	<.01
Week 4 versus Week 0	0.002	0.0006–0.006	<.001
Week 16 versus Week 0	0.0005	0.0001–0.002	<.001
Week 24 versus Week 0	0.0006	0.0002–0.002	<.001
Positive response to a passive flexion associated with presence/persistence of lameness	3.16	1.32–7.53	<.01

Odds ratios and 95% confidence intervals are reported.

Our findings (Figs. 1 and 2) indicate that horses took between 1 to 12 weeks to respond to treatment, with the greatest response occurring by 4 weeks postinjection. Also, 7/49 horses had partially responded to the treatment by this time. These findings indicate that re-examination at 4–6 weeks would be an important time point to evaluate the response to this treatment, but this is yet to be investigated. In our studied population, a positive response to flexion tests showed increased odds for the horse to still being lame. Whether this indicates an absence or an insufficient/partial response to the treatment is difficult to say. The random effect for horse was also significant in the final regression model, indicating that some of the variance in the lameness score were explained by individual variations in pain expression/tolerance. However, in the proposed mechanism of action that 2.5% cross-linked PAAG improves joint capsule elasticity, it is possible that the dosage used was insufficient to restore a pain-free joint motion. Repeating the 2.5% cross-linked PAAG treatment in these partial responders could make sense but this was not tested in our study. Interestingly, the majority (32/33) of horses that were lame-free at 12 weeks remained so until the 24-week examination period, indicating that the treatment has a prolonged effect, as shown previously [9], and despite continuous racing/training activity.

This study took place in a single clinical setting with a single observing clinician. This could be seen as a weakness of the study but it is the authors' opinion that this removes the potential for inconsistencies in the application of lameness grading's among clinicians and within clinicians at different examinations. Videographic recording of each assessment could have been performed for a blinded observer to assess retrospectively to improve the overall power of the study; however, the aim of the study was to act as a pilot for future investigation. Other factors that were consistent between study patients include management and training regimens, nutrition, shoeing effects, track effects, weather, and animal handling during the examinations. Trot ups were consistently performed on the same surfaces and in the same examination area. The clinician grading lameness in this study had up to 30 horses from both within and outside the study group being presented at any one session. Although not completely blinded to the treatment, the clinician was unaware of the horse's name or previous treatments, if any, before examining and recording their lameness scores. This may add to the validity of the results, although it does not fully address the issues of blinding and having separate treating and examining veterinarians, reducing the bias to its minimum.

Response to intra-articular analgesia, especially of the metacarpophalangeal and carpal joints, is highly repeatable by an experienced clinician and is used to clinically diagnose conditions affecting those joints including OA, capsulitis, desmitis, and subchondral bone injury [15]. However, understanding the complexity of disease processes associated with joint pain remains a constant dilemma in clinical practice and as with any disease process, an accurate diagnosis is essential. The horses in this study were subjected to only single intra-articular analgesia and radiographs to provide a diagnosis of each affected joint, which corresponds to a practical racetrack approach. As shown in MRI studies [16], carpal or fetlock pain without radiographic changes is associated with a myriad of diagnoses. It is therefore possible that several horses of the 54% that showed no radiographic changes normally associated with osteoarthritis at T0 were affected by conditions other than early OA. This may also explain why some individuals were nonresponsive to treatment. Forty-six percentage of the horses did have radiological changes consistent with osteoarthritis, and the severity of those radiographic changes overall was unrelated to treatment outcome, meaning even those with marked radiographic signs of OA responded well to the 2.5% cross-linked PAAG.

The low dose of mepivacaine and short time frame from administration to reassessment was the method adopted for this particular study as it was the examining veterinarians preferred protocol, which had been developed over 45 years of clinical practice.

Previous studies have demonstrated a significant reduction in joint effusion scores over time and suggest a possible disease-modifying effect as a result [9]. In the present study, no significant decrease was seen, and only 37/89 (38%) of joints had any effusion at presentation. Synovitis (and capsulitis) is important to the horse because it produces pain, increased synovial effusion/thickening, elimination of the normal small negative pressure within the joint, leading to microinstability, and it produces deleterious products that affect joint health as a whole and articular cartilage in particular [17]. The lack of clinically relevant effusion noted in the carpal joints in this study was possibly due to what the examining veterinarian considered within normal limits in young racing Thoroughbreds. There is no gold-standard evaluation to objectively measure synovial effusion, making this parameter subject to error.

Earlier studies have focused on using 2.5% cross-linked PAAG as an end-stage treatment [6–8]. Only 20% (10/49) of the horses had been nonresponsive to previous treatments in the present study, indicating a switch to 2.5% cross-linked PAAG as a first line of treatment. Treatment of joint disease is intended to reduce pain and minimize the progression of joint degeneration [18,19]. Welfare of the equine athlete warrants careful consideration when treating joint lameness and although the mechanism of action still remains unclear for 2.5% cross-linked PAAG, this and other studies indicate it is effective at alleviating clinical signs of joint lameness and has a long-lasting effect that may support an earlier use in the therapeutic approach to degenerative joint disease.

5. Conclusion

This study shows 2.5% cross-linked PAAG is a safe and practical first line treatment option for joint lameness isolated to the metacarpophalangeal and carpal joints of TB racehorses. The percentage of horses that were lame-free at 4 weeks and 24 weeks postinjection was 43% and 62%, respectively, following a single intra-articular injection of 2 mL of a 2.5% cross-linked PAAG. This encouraging clinical impression warrants further investigation, in the format of a double-blind randomized clinical trial to ascertain the beneficial and long-term effect of 2.5% cross-linked PAAG as an early intra-articular treatment of degenerative joint disease in racehorses.

References

[1] van Weeren P, de Grauw J. Pain in osteoarthritis. Vet Clin Equine 2010;26:619–42.

[2] Sandoval J, Lopez C, Carmona J. Therapies intended for joint regenerations in the horse. Arch Med Vet 2013;45:229–36.
[3] Zarini E, Supino R, Pratesi G, Laccubue D, Totoreto M, Ghisleni G, et al. Biocompatibility and tissue interactions of a new filler material for medical use. Plast Reconstr Surg 2003;114:934–42.
[4] Christensen L, Camitz L, Illegen K, Hansen M, Sarvaa R, Conaghan P. Synovial incorporation of polyacrylamide hydrogel after injection into normal and osteoarthritic animal joints. Osteoarthritis Cartilage 2016;24:1999–2002.
[5] Christensen L, Nielson J, Mouritsen L, Sorensen M, Lose G. Tissue integration of polyacrylamide hydrogel: an experimental study of periurethral, perivascular, and mammary gland tissue in the pig. Dermatol Surg 2008;34:S68–77.
[6] Janssen I, Koene M, Lischer C. Intra-articular use of Polyacrylamide hydrogel as a treatment for osteoarthritis in the distal interphalangeal joint: a case series of 12 horses. Pferdeheilkunde 2012;6:650–6.
[7] Tnibar A, Schougaard H, Koene M, Christensen L, Marussen B. A controlled clinical trial on the efficacy of an intra-articular polyacrylamide hydrogel in horses with osetoarthritis. In: Proceedings of the European College of Veterinary Surgeons Annual Scientific Meeting. Denmark: Copenhagen; 2014. p. 71.
[8] Bathe A, Read R and Briggs C. Intra-articular polyacrylamide hydrogel for the treatment of 20 horses with non-responsive osteoarthritis of the interphalangeal joints; a prospective study. Conference Abstracts of the Veterinary Orthopaedic Society 43rd Annual Conference 2016 Feb 27-March 5, Big Sky, Montana, USA. p 4-5.
[9] Tnibar A, Schougaard H, Camitz L, Rasmussen J, Koene M, Jahn W. An international multi-centre prospective study on the efficacy of an intraarticular polyacrylamide hydrogel in horses with osteoarthritis: a 24 month follow up. Acta Vet Scand 2015;57:8.
[10] Tnibar A, Perrson A, Nielsen H, Svalastoga E, Westrup U, McEvoy F, et al. Evaluation of a polyacrylamide hydrogel in the treatment of induced osteoarthritis in a goat model: a pilot randomized controlled study. Osteoarthritis Cartilage 2014;22:s477.
[11] Henrikson M, Overgaard A, Bliddal H. Initial estimates of efficiency of intra-articular 2.5% polyacrylamide hydrogel for the treatment of knee osteoarthritis: an observational proof-of-concept study (abstract). Arthritis Rheumatol 2017;69(Suppl 10). http://acrabstracts.org/abstract/initial-estimates-of-ecacy-of-intra-articular-2-5-polyacrylamide-hydrogel-for-the-treatment-of-knee-osteoarthritis-an-observational-proof-of-concept-study/. [Accessed 21 February 2018].
[12] Tnibar A, Persson A, Jensen H. Mechanism of action of an intraarticular 2.5% polyacrylamide hydrogel (Arthramid Vet) in a goat model of osteoarthritis: preliminary observations. SM J Biomed Eng 2017;3:1022.
[13] Dohoo I, Martin W, Stryhn H. Veterinary epidemiologic Research. 2nd ed. Charlottetown: VER Inc; 2010.
[14] Narrins R, Schmidt R. Polyacrylamide hydrogel differences: getting rid of the confusion. J Drugs Dermatol 2011;10:1370–5.
[15] Caron J. Osteoarthritis. In: Ross M, Dyson S, editors. Diagnosis and management of lameness in the horse. 2nd ed. Missouri: Saunders; 2011. p. 655–68.
[16] Kawcak C, Barrett M. Carpus. In: McIlwraith C, Frisbie D, Kawcak C, van Weeren P, editors. Joint disease in the horse. 2nd ed. St Louis: Elsevier; 2016. p. 318–32.
[17] McIlWraith C. Traumatic arthritis and posttraumatic arthritis in the horse. In: McIlwraith C, Frisbie D, Kawcak C, van Weeren P, editors. Joint disease in the horse. 2nd ed. St Louis: Elsevier; 2016. p. 33–48.
[18] Caron J. Intra-articular injections for joint diseases in horses. Vet Clin North Am Equine Pract 2005;21:559–73.
[19] McIlwraith C. Principles and practices of joint disease treatment. In: Ross M, Dyson S, editors. Diagnosis and management of lameness in the horse. 2nd ed. Missouri: Saunders; 2011. p. 840–52.