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Current joint therapy usage in equine practice: Changes in the last 10 years

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Abstract

Background: Osteoarthritis is a common clinical condition in the performance horse. In the last 10 years, there has been substantial growth in understanding of the disease and in the development of novel therapies.

Objectives: To document changes in clinical use of joint therapies over the past 10 years. We also aimed to understand how newly developed therapies have been added to routine clinical practice.

Study design: Survey of veterinary professionals.

Methods: We administered an electronic survey to members of the American Association of the Equine Practitioners. Questions from a similar survey in 2009 were repeated and new questions were added. The responses were tabulated, analysed and compared to those of the previous survey.

Results: A total of 407 completed surveys were returned. There were no significant differences between the current and previous surveys with respect to demographic parameters. Triamcinolone acetonide (TA) remained the most common corticosteroid used to treat high-motion joints. Methylprednisolone acetate (MPA) remained the most common corticosteroid to treat low-motion joints. The use of MPA for high-motion joints was significantly more common in 2009 than in 2019 (odds ratio [OR]: 2.38, 95% confidence interval [CI]: 1.66-3.42, $P = .001$). Biological therapies became more popular, and the likelihood of respondents reporting having used autologous conditioned serum was substantially higher in 2019 than in 2009 (OR: 4.24, 95% CI: 3.16-5.68, $P < .001$). Concomitant use of antibiotics with intra-articular medications became more common as well.

Main limitations: This is a report of survey data and not directly measured treatments.

Conclusions: There is a decrease in the use of MPA to treat high-motion joints. The use of biological therapies in joints has become more prevalent. There are clear differences in the use of joint therapies over time. While some differences agree with the scientific evidence, others are not fully concordant or are in direct conflict with the scientific literature.

KEYWORDS

articular treatment, biological therapies, corticosteroid, horse, osteoarthritis

The abstract is available in French in the Supporting Information section of the online version of this article

1 | INTRODUCTION

Osteoarthritis is a common clinical problem in performance horses that can result in disability and economic losses.[1,2] Equine osteoarthritis is characterised by progressive deterioration of the articular cartilage associated with changes in the subchondral bone and associated soft tissues.[3] Commercially available systemic and intra-articular therapies focus on providing symptom modification and/or disease-modifying effects.[4,5]

In 2009, a survey was administered to members of the American Association of Equine Practitioners (AAEP) designed to provide understanding of the clinical usage of various medications used for joint therapy in horses.[6] Of note, regarding corticosteroid use, triamcinolone acetonide (TA) was the most commonly used to treat high-motion joint, while methylprednisolone acetate (MPA) was the most commonly used to treat for low-motion joint. The most commonly disease-modifying products were polysulphated glycosaminoglycan (Adequan) and hyaluronate sodium (Legend). The majority of the respondents reported always or occasionally including amikacin when injecting a joint. Also, 54% of the respondents reported using IRAP products.[6] Since then, new scientific literature has been published regarding these therapies, and new therapeutics such as biological therapies have become widely available and might have changed how some therapies are used currently. For these reasons, the goal of the present study was to compare current uses of joint therapies in horses with those from 10 years ago and to determine how new therapies are being used clinically.

2 | MATERIALS AND METHODS

A cross-sectional survey of members of the AAEP was performed using a web-based survey (Surveymonkey.com) (Survey S1). Responses were collected over 45 days, from April to May 2020. The present survey included questions from the 2009 survey, with minimal adaptation if needed, as well as other questions to reflect currently available joint therapies (platelet-rich plasma, autologous protein solution, stem cells and bone marrow aspirate concentrate). Respondents were assigned unique identifiers to eliminate duplicates; however, they were not directly linked to the individual responses to ensure that all survey answers were confidential. Low-motion joints were defined as distal intertarsal and tarsometatarsal joints and high-motion joints included the coffin joint, carpus, fetlock and stifle.

2.1 | Data analysis

Summaries and percentages were calculated by the survey programme (Surveymonkey.com). The data were all categorical variables. All other statistical analyses were performed using SAS v9.4 (SAS Institute Inc). The chi-square test was used to compare frequencies of the responses in the current survey with those from the 2009 survey.[6] When any of the response counts in any category were less than 5, Fisher's exact test was performed instead. Percentages were calculated to describe data in each of the categories. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated to evaluate the likelihood of the outcome, wherever applicable. A P value of .05 was designated as the limit of statistical significance.

3 | RESULTS

3.1 | Demographic responses and clinician perceptions

A total of 407 individuals completed the survey and all were included in the study: 199/407 (48.9%) of the respondents in this survey reported practicing veterinary medicine for over 20 years; 96/407 (23.6%) reported practicing for 10-20 years; 54/407 (13.3%) reported practicing for 5-10 years; and 58/407 (14.3%) reported practicing for less than 5 years. The majority of the respondents (90.9%) indicated that they spend most of their time (>75%) dedicated to equine practice; and most (70%) reported performing joint injections in fewer than 20 horses per month. These findings were not statistically significant different from those of the 2009 survey.

Respondents responded that the most common performance classes they worked with were racehorses (Thoroughbred/Quarter-Horse) (52.4% [55/105]) and hunters/jumpers (50.6% [136/269]). Overall, the four largest groups of performance horses represented in this survey were as follows: hunters/jumpers (269/407), dressage (237/407), recreational riding horses (213/407) and eventers/fox hunters (146/407). Thoroughbreds, Quarter-Horses, Warmbloods, and Sport-Horse crosses were reported to be the most commonly served breeds. There were statistically significant differences between 2009 and 2019 only with respect to Thoroughbreds (P = .03) and Warmbloods (P = .003): thoroughbreds as the main breed treated decreased from 31.8% (188/591) in 2009 to 22.2% (76/342) to 2019, while Warmbloods as the main breed treated increased from 36.3% (186/512) in 2009 to 49.7% (155/312) in 2019.

The majority of the clinicians (66.4% [269/405]) reported seeing frequent joint treatments as a problem in the equine industry. Furthermore, 75.8% (273/360) reported believing that joints are harmed by overly frequent treatments. Regarding frequency of repeated intra-articular corticosteroid therapy, most of the clinicians (50.4% [203/403]) considered 6 months as the shortest interval between injections that they felt comfortable with, while 3 months was selected by 29.8% (120/405). Only one respondent (0.3% [1/403) reported believing that corticosteroids caused no harm, regardless of interval. The majority of respondents (79.8% [324/406]) reported not considering the use of a compounded replacement for an intra-articular injection if their preferred medication were unavailable.

3.2 | Intra-articular corticosteroids

3.2.1 | Use of corticosteroid

TA was the most commonly reported corticosteroid for high-motion joints, either alone or in combination with other corticosteroids (80.3%), while MPA was the most commonly reported corticosteroid for low-motion joints, either alone or in combination with other corticosteroids (69.9%). The likelihood of MPA use for high- versus low-motion joints was higher in 2009 than in 2019 (OR: 2.38, 95% CI: 1.66-3.42, $P < .001$). Betamethasone esters (Betavet®, BM, American Regent Animal Healthy) for high-motion joints was selected by 33.4% of the respondents, while 17.3% of the respondents reported using it on low-motion joints. The likelihood of a respondent reporting use of BM in high- and low-motion joints were higher in 2019 than in 2009 (OR: 2.29, 95% CI: 1.75-3.00, $P < .001$; low-motion joint OR: 2.13, 95% CI: 1.45-3.12, $P < .001$). Isoflurane acetate (Predef® 2x, IPA, Zoetis) was reported used in high-motion joints by 9.8% and in low-motion joints by 9.6%; this proportion was not significantly different from that of 2009. Dexamethasone SP (DEX) was reported used in high-motion joints by 5.4% of respondents and in low-motion joint by 5.1% of respondents (Table 1).

3.2.2 | Association of corticosteroids and laminitis

TA was considered somewhat likely or very likely to contribute to laminitis when used in an intra-articular application by 72.2% (289/400) of the respondents. BM, IPA and MPA were more often considered unlikely to contribute to laminitis when used intra-articularly (58.8% [217/369], 61.1% [206/337] and 59% [229/388], respectively).

3.2.3 | Dose of corticosteroids

The most commonly reported dose range of TA for a single joint was 5-10 mg, followed by 3-5, >10 and <3 mg. The most commonly reported dose range of MPA in a single joint was 20-40 mg, followed by 40-80, <20 and >80 mg. There was a statistically significant difference in MPA dose selections between 2009 and 2019 surveys, with the respondents in 2009 being more likely to use doses >40 mg compared to 2019 respondents (OR: 2.97, 95% CI: 2.28-3.85, $P < .001$). For BM, the most commonly reported dosage for a single joint was 4-6 mg, followed by 6-12, <4 and >12 mg. For those respondents reporting use of IPA or DEX, the most common dose ranges for a single joint were 5-10 and 4-10 mg, respectively (Table 2).

For 51.1% (208/407) of the respondents, the maximal total body dosage in a single treatment for TA was less than 18 mg, while 38.3% (156/407) responded that the maximal total body dosage was between 18 and 40 mg, with the remaining 6.6% (27/407) of the respondents considering the maximal total body dosage to be >40 mg (6.14% responded 40-80 mg and 0.49% responded >80 mg). Respondents in 2009 were more likely than 2019 respondents to

TABLE 1 Preferred corticosteroid for treatment of high- and low-motion joints reported by AAEP members in surveys conducted in 2009 and 2019

	Triamcinolone acetonide		Methylpredinisolone acetate		Betamethasone esters		Isuflupredone acetate		Dexamethasone Sp	
Year	High-motion joint	Low-motion joint	High-motion joint	Low-motion joint	High-motion joint	Low-motion joint	High-motion joint	Low-motion joint	High-motion joint	Low-motion joint
2009	621	276	206	584	149	58	69	56		
2019	326	119	42	284	136	60	40	39	22	21
Chi-square	2.13		22.48		0.21		0.24		N/A	
P value	.1		**<.001**		.6		.6		N/A	

Bold values emphasis the comparasions with statistical significance.

TABLE 2 Doses most commonly used for intra-articular corticosteroid injections reported by AAEP members in surveys conducted in 2009 and 2019

		Triamcinolone acetonide					
		<3 mg	3-5 mg	5-10 mg	>10 mg	Do not commonly use	Total
2009	n	49	275	335	51	44	754
	%	6.5	36.47	44.43	6.76	5.84	
2019	n	14	138	183	19	18	372
	%	3.76	37.1	49.19	5.11	4.84	
		Methylprednisolone acetate					
		<20 mg	20-40 mg	40-80 mg	>80 mg	Do not commonly use	Total
2009	n	19	221	399	74	45	758
	%	2.51	29.16	52.64	9.76	5.94	
2019	n	36	172	120	18	26	372
	%	9.68	46.24	32.26	4.84	6.99	
		Betamethasone esters					
		<4 mg	4-6 mg	6-12 mg	>12 mg	Do not commonly use	Total
2009	n	9	112	109	5	477	712
	%	1.26	15.73	15.31	0.7	66.00	
2019	n	21	111	96	9	122	359
	%	5.85	30.92	26.74	2.51	33.98	
		Isuflupredone acetate					
		<5 mg	5-10 mg	10-15 mg	>15 mg	Do not commonly use	Total
2009	n	31	91	42	13	524	701
	%	4.42	12.98	5.99	1.85	74.75	
2019	n	26	71	22	11	192	322
	%	8.07	22.05	6.83	3.42	59.63	
		Dexamethasone SP					
		<4 mg	4-10 mg	10-20 mg		Do not commonly use	Total
2009							
2019	n	10	20	6		120	156
	%	8.07	22.05	6.83		76.92	

answer that the total body dosage was over 18 mg (OR: 1.72, 95% CI: 1.35-2.20, $P < .001$).

3.2.4 | Specific indications

The three main joints that typically respond best to IA corticosteroid therapy according to the respondents' perspective were as follows: lower hock joints (58.2% [237/407]), coffin joints (33.9% [138/407]) and fetlock joints (20.4% [83/407]). The majority of the respondents (57% [232/407]) reported not injecting the same joint more than four times per year. Long-term negative effects of chronic intra-articular corticosteroid use (>4 injections into the same joint annually for more than 4 years) were reported as occurring occasionally by 62.8% (110/175) and as occurring routinely by 10.3% (18/175), while 26.8% (47/175) reported never having observed long-term negative effects from chronic intra-articular corticosteroid use. When administering an intra-articular therapy, respondents usually or always included corticosteroid in 79% (320/405) of chronic joint inflammation cases and in 69.6% (282/405) in joints with chronic radiographic changes. Only 3.7% (15/407) of the clinicians reported rarely or never including corticosteroid in intra-articular medications.

3.2.5 | Joint flare or sepsis associated with intra-articular corticosteroid

The incidence of joint flare following intra-articular corticosteroid injection was considered fewer than 1:1000 by 33.9% (138/407), fewer than 1:10 000 by 29.5% (120/407), and fewer than 1:500 by

23.3% (95/407) of the clinicians. Furthermore, 13.3% (54/407) of the respondents reported not having experienced joint flares after intra-articular corticosteroid injections. The estimated prevalence of joint sepsis after intra-articular corticosteroid injection was considered fewer than 1:10 000 by 37.1% (151/407), fewer than 1:1000 by 21.1% (86/407) and fewer than 1:500 by 8.8% (36/407) of the respondents. A total of 134/407 (32.9%) indicated they had never experienced post-injection (sepsis) complications following intra-articular corticosteroid injection. Many clinicians (55.6% [225/405]) said they always included an antibiotic such as amikacin when injecting medication into a joint, while 28.6% (116/405) reported rarely or occasionally doing so. Only 15.8% (64/405) of the respondents said they never used antibiotics when injecting medications into a joint. Compared to the 2009 survey, there was a statistically significant difference ($P < .001$) with respect to the percentage of clinicians who reported never using antibiotic when injecting medications into a joint, decreasing from 32.4% to 15.8%. In other words, the reported likelihood of a clinician not using an antibiotic when injecting medications into a joint was lower in 2019 than in 2009 (OR: 0.39, 95% CI: 0.28-0.53, $P < .001$; Table 3). The main three reported reasons for clinicians using antibiotics in joint injections were as follows: in the context of poor environmental conditions (38.1% [150/394], at any time corticosteroids are injected (37.6% [148/394]), and with all injections except biological therapies (37.1% [146/394]).

3.2.6 | Combination with other medications

Respondents selected amikacin (60.3% [270/407]) and Hylartin-V (Boehringer Ingelheim Vetmedica Inc, St Joseph, Missouri, USA)/Hyvisc (Luitpold Pharmaceuticals Inc, Shirley, New York, USA) (65.8% [268/407] as the two most commonly drugs mixed in the same syringe when injecting a joint with corticosteroid. This was similar to the responses in the 2009 survey.

3.2.7 | Factors affecting choice of corticosteroid

Scientific data and published articles on the efficacy and chondroprotective qualities of individual products were selected as the factors that most commonly affected the choice of corticosteroid used by 34.9% (142/407) of the respondents. The joint being treated was selected as the most common factor affecting the choice of corticosteroid by 29.7% (121/407), and personal experience with the product was selected as the most important factor affecting the choice of corticosteroid by 9.8% (40/407) of the respondents. The top three factors that most commonly influenced the choice of corticosteroid were as follows: what joint was being treated (269/407), scientific data and published articles on the efficacy and chondroprotective qualities of the individual products (232/407), and the severity and chronicity of the condition to be treated (168/407). No statistically significant differences were observed between 2019 and 2009 responses with respect to these responses.

TABLE 3 Frequency of use of amikacin when injecting a joint reported by AAEP members in surveys conducted in 2009 and 2019

Year		Always	Never	Rarely/occasionally	Total
2009	n	341	239	158	738
	%	46.21	32.38	21.41	
2019	n	225	64	116	405
	%	55.56	15.8	28.64	

3.3 | Biological therapy

3.3.1 | Therapy selection

For 45.7% (186/407) of the respondents, the primary reason for choosing a biological therapy over corticosteroid for intra-articular use was long-term efficacy. Safety was selected by 19.4% (79/407), client request was selected by 10.8% (44/407), and short-term efficacy was selected by 5.6% (23/407) of the respondents. A total of 75/407 (18.4%) reported not using many biologicals. The majority of the respondents (87% [354/407]) reported that they had patients who benefited from intra-articular biological therapy. The benefit of intra-articular biological therapy was rated an average of 4 on 1-5 scale (1 = *minimal benefit*, 5 = *maximal benefit* or as positive of an outcome that could have been hoped for).

The majority of the respondents (83.3%) answered they had used autologous conditioned serum (IRAP), followed by platelet-rich plasma (72.5%), autologous protein solution (53.8%) and stem cells (53.7%). A minority of the respondents (22.4%) reported having used bone marrow aspirate concentrate. Compared to the 2009 survey, there was a statistically significant increase in the proportion of respondents reporting having used autologous conditioned serum, from 54.1% in 2009 to 83.3% in 2019. This indicates that the likelihood of use of autologous conditioned serum was significantly higher in 2019 than in 2009 (OR: 4.38, 95% CI: 3.28-5.84, $P < .001$). The three main reported factors most commonly influencing the choice of biological therapy were as follows: scientific data and published articles on the efficacy and chondro-protective qualities of individual products, cost, and the severity or chronicity of the condition to be treated (weighted averages = 1.7, 1.9 and 2.0, respectively). Biological therapies were reported most commonly used in cases of joint soreness when biological therapy was available, in cases that are not responsive to corticosteroid treatment, and when treating diseased soft-tissue within a joint such as a meniscus or a ligament. From the respondent's perspective, the three main joints that typically responded best to biological therapy were fetlock, stifle and coffin joint. Stifle was considered the joint that responded best to biological therapy (33.2% [135/407]), while fetlock

was considered the second best (23.6% [96/407]), and the coffin joint was considered the third best joint (22.6% [92/407]).

3.3.2 | HA products

Choice of hyaluronic acid (HA) product (Hyvisc [Boehringer Ingelheim Vetmedica In.], Adequan [Luitpold Pharmaceuticals Inc] and Legend [Merial Inc]) were the most often selected HA produces frequently used by the respondents. Intra-muscular Adequan (Luitpold Pharmaceuticals Inc) was the most commonly reported product used for preventive/prophylactic measures in a high-performance horse (86% [350/407]), for chronic cases involving 'maintenance' or routine injections, for chronic cases with radiographic evidence of osteoarthritis, for acute disease in low-motion joints, and for ligament and tendon lesions. Legend (Merial Inc) was reported most commonly used for acute disease in high-motion joints and tendon sheath applications. The most important factor that influenced the choice of non-corticosteroid intra-articular medication was reported to be the scientific data and published articles on the efficacy and chondroprotective qualities of individual products (35.6% [145/407]), followed by which joint was being treated (22.8% [93/407]), and personal experience with efficacy/response to therapy (18.4% [75/407]).

4 | DISCUSSION

This study contributes to understanding how joint therapies are being used clinically. Compared with survey data gathered in 2009, we were able to observe some differences in the use of intra-articular therapy.[6] Of particular importance, in the intervening 10 years, there were differences in terms of the use of intra-articular corticosteroid, increased popularity of biological therapy, and increased frequency of use of intra-articular antibiotics. Some of these differences accord with recent evidence from the scientific literature, while others are not fully supported from the scientific perspective and appear to be related to anecdotal observation.

TA remained the most common corticoid used in high-motion joints. Even though the most common dose of TA used to treat a single joint did not change between surveys, there was a significant decrease in the reported maximum total body dose, with clinicians now reporting being less likely to provide more than 18 mg in a single treatment. This is likely due to the association of triamcinolone and laminitis. However, triamcinolone does not appear to increase the risk of laminitis in healthy horses,[7,8,9] and a safe total body dose has not yet been established. MPA remained the most commonly reported corticoid used in low-motion joints. By contrast, the use of MPA in high-motion joint decreased over the last decade, probably associated with evidence of harmful effects on cartilage metabolism.[10,11] Furthermore, the most commonly reported dose range of MPA in a single-joint application decreased from 40-80 to 20-40 mg, with doses over 40 mg being almost three times less likely to be used than reported in our previous survey.[6] An increase in the use of betamethasone esters (Betavet®) was noted. BM was 2.2 and 2.4 times more likely to be used for the treatment of high- and low-motion joints, respectively, in 2019 than it was in 2009. This increase in the use of BM may be explained by the fact that it is now easily available on the market.

Another interesting finding of this study was the increased use of biological therapies. Autologous conditioned serum (IRAP/IRAPII) was the most popular therapy that was reported by more than 80% of the clinicians in this study. The likelihood of a clinician reporting having used autologous conditioned serum was now substantially higher in 2019 than in 2009. Also, the majority of the clinicians responded that they had used platelet-rich plasma, autologous protein solution or stem cells routinely; however, comparisons with the previous survey were not possible because these products were not included in the 2009 survey. The least popular reported therapy for the treatment of joint disease was bone marrow aspirate and concentrate with 77.6% of the clinicians reporting they had not used this therapy. Similar to intra-articular corticosteroid therapy, among the main reasons that most commonly influenced the choice of biological therapy were scientific data and published articles on the efficacy and chondro-protective qualities of individual products, as well as the severity or chronicity of the condition to be treated. Unlike the case for corticosteroids, respondents selected the cost of the product as an important factor. Furthermore, the main reported reason for using biological therapy was for case of joint soreness when biological therapy was available. These findings highlight the importance of a cost-effectiveness analysis among biological therapies and other commonly used therapies such as triamcinolone and HA for long-term management of joint disease in performance horses.

The increase used of antibiotics in the joint was an alarming finding. The literature suggests that septic arthritis is uncommon following intra-articular therapies.[12,13] Furthermore, there is evidence of chondrotoxic effects of amikacin[14] as well as increased concern regarding antibiotic resistance.[15] The reasons mentioned by clinicians for using antibiotics in the joint were poor environmental conditions and coincident corticosteroid injections. However, intra-articular corticosteroid does not appear to be associated with increased risk of joint infection.[12,16] This highlights the importance of disseminating scientific knowledge to clinicians and the introduction of more evidence-based approaches in the decision-making processes surrounding use of antibiotics in joints.

Overall, the current study represents an actual picture of the clinical use of joint therapies. Small demographic differences were observed when the present study was compared to a survey published 10 years prior. However, these differences were minor and are unlikely to significantly impact the present findings. The study was conducted on an anonymized, individual basis; the responses might be influenced by practices' protocols or product availability. Nevertheless, these should have minimal influences on our results based on the large number of responses retrieved and the fact that the previous study was conducted in a similar way. In conclusion, we identified similarities and differences in the use of joint therapies over the last 10 years. Although new scientific evidence could partially explain some of the differences observed, few points still not fully concordant or are in direct conflict

with the scientific literature. New data regarding current therapies that were unavailable years ago were collected and presented here.

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CONFLICT OF INTERESTS

No competing interests have been declared.

AUTHOR CONTRIBUTIONS

G. Zanotto contributed to data acquisition and interpretation, manuscript preparation and has approved the final version. D. Frisbie was responsible for the study concept and design, contributed to data acquisition and interpretation, revised and approved the manuscript final version.

ETHICAL ANIMAL RESEARCH

Research ethics committee oversight not currently required by this journal: survey of veterinary professionals.

INFORMED CONSENT

Completion of the questionnaire was taken as participant consent.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/evj.13489.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Texas Data Repository at https://doi.org/10.18738/T8/DQSNVI, reference number MD5: 8fc566e205e2b4d8a13b39b3b47da23d.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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