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# Are bisphosphonates a more effective treatment than intra-articular steroids in horses with distal hock osteoarthritis?

A Knowledge Summary by

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## KNOWLEDGE SUMMARY

### Question

In horses that are lame due to osteoarthritis of the distal tarsal joints (bone spavin), is intra-articular medication with corticosteroids compared to systemic bisphosphonate treatment more effective in long-term lameness reduction?

### Clinical bottom line

**Category of research question**

Treatment

**The number and type of study designs reviewed**

Three papers were critically reviewed. Two were randomised controlled trials, and one was a retrospective study.

**Strength of evidence**

Weak

**Outcomes reported**

There is insufficient evidence to support the use of systemic bisphosphonates over intra-articular corticosteroids to treat distal hock osteoarthritis in horses.

**Conclusion**

Horses with distal hock osteoarthritis should not be treated with systemic bisphosphonates until further blinded randomised controlled trials are completed. Additionally, supportive evidence for the use of intra-articular corticosteroids as a treatment for degenerative hock osteoarthritis is limited to a retrospective study where modest, short-term improvements are reported: 58% of horses improved after an average of 56 days (Labens et al., 2007). Evidence does not support significant improvement in long-term outcomes: 50% of horses improved after 4 months (Watts et al., 2016) and only 38% of horses improved after a mean follow-up period of 787 days (Labens et al., 2007).

### How to apply this evidence in practice

The application of evidence into practice should take into account multiple factors, not limited to: individual clinical expertise, patient's circumstances and owners' values, country, location or clinic where you work, the individual case in front of you, the availability of therapies and resources.

Knowledge Summaries are a resource to help reinforce or inform decision making. They do not override the responsibility or judgement of the practitioner to do what is best for the animal in their care.

## The evidence

Labens et al. (2007) is a retrospective study that followed the outcomes of 51 horses treated with intra-articular (IA) corticosteroids for distal hock osteoarthritis (OA). The authors used lameness scores, radiographs and scintigraphy to assess the outcomes of treatment with IA corticosteroids in either the tarsometatarsal (TMT) or distal intertarsal (DIT) joints. The authors concluded that after a single treatment with an IA corticosteroid, lameness improved in 34/59 (58%) of treated limbs at a median of 56 days post-treatment. At telephone follow-up a mean of 787 days after treatment, 38% of horses had a positive outcome: they were used as intended, had no detectable lameness according to the owner and were not receiving nonsteroidal anti-inflammatory drugs (NSAIDs). This study provides the strongest experimental design in absence of a randomised controlled trial among studies that examine IA corticosteroids as the sole treatment in chronic, degenerative OA. While the treatments were not uniform between cases, they do reflect the day-to-day clinical treatment of distal hock OA.
This study reports a positive correlation between treatment with IA corticosteroids for distal hock OA and a modest, improved outcome.

Gough et al. (2010) is a randomised controlled trial that compared two treatment groups of horses with distal hock OA. The first group was treated with a 1 mg/kg tiludronate IV infusion and the second group was given an IV placebo infusion. The study used lameness scores, level of exercise and radiographs to assess outcomes at day 60. The authors concluded that the lameness scores for the tiludronate group were significantly lower than the placebo group at day 60 (P=0.0318). Furthermore, they concluded that 60% of horses in the tiludronate group improved by 2 or more lameness scores at day 60. Despite the type of experimental design (randomised controlled trial), there were significant limitations to the quality of the evidence such that a wholescale change to clinical practice is not recommended based on this trial alone. These limitations are further addressed in the appraisal section below.

Watts et al. (2016) is a randomised controlled trial of resveratrol supplementation and IA triamcinolone to treat distal hock OA. Resveratrol is a compound with anti-inflammatory properties that is naturally found in grape skins. In this study the placebo group was treated with IA triamcinolone and a placebo powder (fermentation solubles*, S. cerevisiae* 1026, diatomaceous earth) 2 scoops fed every 12 hours. Additionally both groups were treated with 2 g phenylbutazone IV immediately after IA injection and 2 g phenylbutazone PO every 24 hours for the next 3-7 days. There was no control group (i.e. IA saline) to assess the efficacy of triamcinolone as a sole intervention, as the authors did not wish to withhold standard IA triamcinolone treatment from lame horses. To eliminate the majority of effects from IA triamcinolone, the authors chose to assess outcomes at 2 and 4 months post-treatment. At 2 months post-treatment, lameness was expected to recur in 90% of horses (Labens et al., 2007) and at 3 months post-treatment 50% of horses were expected to be lame (de Grauw et al., 2016). In effect, the authors assumed that treatment with IA triamcinolone alone will fail by either 2 or 4 months post-treatment and the outcome of resveratrol supplementation can be interpreted without IA triamcinolone treatment effects. The authors conclude that horses injected with IA triamcinolone and supplemented with resveratrol had better performance than horses injected with triamcinolone alone at 2 and 4 months post-treatment. While the efficacy of the resveratrol intervention is not the subject of this PICO question, Watts et al. (2016) found that 4 months after IA corticosteroid (triamcinolone) injection, only 35% of horses had returned to full work, confirming that long-term outcome of IA triamcinolone treatment is not favourable for distal tarsal OA. Further study limitations are outlined in the appraisal section below.

## Summary of the evidence

| Labens et al. (2007) | |
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| **Population:** | Horses treated at the University of Glasgow Veterinary School for OA of the TMT and/or DIT joint between 1998 and 2005<br>• Sex: 35 geldings, 15 mares, one stallion<br>• Age: Median = 9 years (range 4–18 years)<br>• Breed: 28 Thoroughbreds (TB), Warmbloods (WB) or TB x WB crosses; 23 undisclosed breeds<br>• Use: 29 general purpose, 10 showjumping, four dressage, two eventing, two hunting, four unknown use |
| **Sample size:** | n=51 |
| **Intervention details:** | *Case Selection*<br>Horses were identified by a database search of horses treated at Weipers Centre Equine Hospital, University of Glasgow Veterinary School. The study included horses treated for distal tarsal joint OA between 1998 and 2005. Horses accepted into the study met each of the following conditions:<br>• analgesia of the TMT and/or DIT joint reduced lameness by 50% or more based on the AAEP 5 point lameness score<br>• There was radiographic evidence of TMT and/or DIT joint OA<br>• The horses received an IA injection of methylprednisolone acetate (MPA) or triamcinolone acetonide (triamcinolone) with or without hyaluronic acid (HA) into the TMT and/or DIT joint<br>Horses with bilateral hindlimb lameness (25/51 at first examination) were also included in the study if they met the following criteria:<br>• IA analgesia reduced lameness by 50% or more in one hindlimb<br>• There was increased uptake of a radiopharmaceutical by the DIT and/or TMT joint in the other hindlimb on scintigraphic examination<br>Horses were split into two groups:<br>• Group 1 = moderate or severe radiographic evidence of OA of DIT and TMT joints<br>• Group 2 = mild or no radiographic evidence of OA of DIT and TMT joints<br><br>*Intervention*<br>Dose:<br>• MPA median = 55 mg (range 20-120 mg)<br>• Triamcinolone median = 9.8 mg (range 5–20 mg)<br>First Treatment:<br>• 49/51 horses (59 hindlimbs) were treated once with an IA corticosteroid<br>• Specific joint treated not identified |

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| | • Choice of IA corticosteroid was determined by the attending clinician's preference:<br>  ○ Triamcinolone only in four hindlimbs<br>  ○ Triamcinolone with HA in 17 hindlimbs<br>  ○ MPA only in 38 hindlimbs<br>• Median interval between first treatment and second exam = 56 days (range 18-1436 days)<br>• Median interval between the first and second treatment = 69 days<br>Second Treatment:<br>• 14/51 horses were treated two or more times with an IA corticosteroid<br>• 12 of these horses (13 hindlimbs) were treated twice and re-examined by the same clinician<br>  ○ MPA only in 12/13 hindlimbs<br>  ○ Triamcinolone with HA in 1/13 hindlimbs<br>• Joints treated:<br>  ○ DIT and TMT 5/13 hindlimbs<br>  ○ TMT only in 8/13 hindlimbs<br>• Median interval between second treatment and re-examination = 50 days (range 25-194 days) |
| **Study design:** | Retrospective study |
| **Outcome studied:** | *Subjective Assessment: Lameness Scores*<br>1) Difference between lameness scores at initial and follow-up examinations was calculated if the clinician was the same for both exams<br>2) The horse was classified as 'lame' or 'sound' if two different clinicians performed initial and follow up examinations<br>• Positive outcome = horse fulfilled intended use without the owner detecting lameness and without receiving oral NSAIDs<br>• Negative outcome (excluded from analysis) = horse developed unrelated problems that prevented its return to exercise and/or horse received surgical treatment<br>• Follow up information was obtained for 42/51 horses at a mean of 787 days after the last appointment (range 114–1942 days)<br>Lameness variables assessed at initial and follow-up exam<br>• Based on AAEP lameness score (0 = not lame, 5 = not weight bearing; including half-point scores)<br>• During initial exams lameness was assessed in the following conditions:<br>  ○ Walk and trot, straight line, hard surface<br>  ○ Walk and trot, right and left circles on the lunge, hard and soft surfaces<br>• During follow-up exams lameness was assessed only in the condition which exacerbated the lameness in the initial exam. |

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| | *Objective Assessment: Radiographic Examination*<br>• Radiographs were available at time of inclusion and were not repeated after treatment<br>• Standing dorsoplantar, dorsolateral-plantaromedial oblique, dorsomedial-plantarolateral oblique and lateromedial radiographs of all affected tarsi<br>• Blinded assessment of radiographic signs of OA by first author<br>  ○ Signs included: irregular subchondral bone, subchondral bone sclerosis, narrowed joint, osteophytes, bony bridge formation, subchondral bone lysis and ankylosis<br>  ○ Each sign was graded as absent, mild, moderate or severe<br><br>*Objective Assessment: Scintigraphy*<br>• 12/51 horses underwent scintigraphy (lateral and plantar views)<br>  ○ Only included horses with bilateral lameness<br>• Six veterinary surgeons experienced in scintigraphic interpretation conducted a blind assessment of the images |
| **Main findings: (relevant to PICO question):** | After a single treatment with MPA or triamcinolone (+/-HA) lameness improved in 34/59 (58%) of treated limbs.<br>  ○ The median improvement was 0.75 grades (range 1.5–3 grades) on the 0–5 lameness scale (P<0.001)<br>  ○ 15/59 (25.4%) of limbs were sound at the first re-examination<br>  ○ 46/51 (90.2%) of horses remained lame at the second examination<br>• Horses treated twice showed no improvement when assessed at a median of 50 days after the second treatment (P=0.141)<br>• None of the horses that improved by two or more grades of lameness had radiographic evidence of OA in the proximal intertarsal (PIT) joint<br>• No significant differences observed between horses with varying degrees of radiographic severity<br>• No significant differences observed between effects of MPA and triamcinolone (p-value or raw numbers not provided)<br>• No significant differences observed between horses in which only the TMT joint or both the DIT and TMT joint were treated<br>• At telephone follow-up (on average 787 days after the last exam):<br>  ○ 38.2% of horses had a positive outcome (used as intended with no NSAIDs)<br>  ○ The horses with a positive outcome tended to have moderate to severe OA more frequently than horses with a negative outcome |

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| | • 12/12 horses showed significant radiopharmaceutical uptake in the distal tarsal joints<br>  ○ Scintigraphy was available at time of inclusion and not repeated after treatment<br>  ○ The horses with diffuse uptake showed significant improvement in their lameness score after one treatment (P=0.032).<br>  ○ The horses with focal uptake did not show significant improvement<br>  ○ There was no significant association between the type of uptake (i.e. focal or diffuse) and the outcome of treatment at telephone follow-up |
| **Limitations:** | • As a retrospective study, this study lacks a control group and cannot prove causation; i.e., differences between treatments cannot be causally linked to treatment alone, as disease status may have influenced treatment allocation to MPA or triamcinolone. Further limitations include:<br>• Lameness grading was subjective and not blinded<br>• The horses were from a wide age range (4–18 years) and effect between age and outcome was not calculated<br>• The intervention (MPA or triamcinolone +/-HA, and dose) was not uniform between groups<br>• No information on ancillary treatment/chondroprotective supplements etc.<br>• Follow-up exams and treatments did not occur within a uniform date range and were not performed by the same observer<br>• The inclusion criteria for distal hock OA (positive response to IA analgesia) did not rule out other conditions such as PSD and intertarsal ligament enthesopathy. These other differentials respond differently to treatment and scintigraphic examination<br>• Insufficient power for radiographic and scintigraphic evidence. Imaging was not conducted following treatment |

| **Gough et al. (2010)** | |
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| **Population:** | Horses in the UK and Ireland with a clinical diagnosis of distal hock OA<br>• Sex: 35 non-pregnant mares, 73 geldings (108 initially included)<br>• Age: mean 11 years (range 5–20 years)<br>• Use: pleasure horses, event horses, showjumpers or other |
| **Sample size:** | n=108 initially included; only 87 met the final inclusion criteria |
| **Intervention details:** | *Case Selection*<br>Horses with a clinical diagnosis of distal hock OA that met each of the following conditions:<br>• Clinical signs of spontaneous lameness from 6 weeks–1 year in duration |

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| | • Decreased level of performance according to owner<br>• A lameness score 3/10 or greater on the lamest limb after IA analgesia of TMT and/or DIT joint of the least lame limb<br>• A 50% or greater improvement in lameness score after IA analgesia of TMT and/or DIT joint of the lamest limb<br>• Radiographic assessment that included signs of OA on one of four standard views of the lamest limb. Horses were excluded from the study for any of the following reasons:<br>  ○ Less than 3 years of age<br>  ○ Pregnancy<br>  ○ Lameness less than 6 weeks duration or more than 1 year duration<br>  ○ Feed additives with chondroprotective substances given within 4 weeks of the study<br>  ○ Treated with NSAIDs or chondroprotective drugs (i.e. HA, chondroitin, glucosamine, polysulfated glycosaminoglycan) within 14 days prior to the study<br>  ○ Treated with corticosteroids within 60 days prior to the study<br>  ○ Treated with IA medications within 60 days prior to the study<br>  ○ A history of two or more hock joint injections in the past year<br>  ○ A change in pattern of shoeing within 4 weeks prior to the study<br>  ○ Underwent nuclear scintigraphy within 60 days prior to the study<br>  ○ A lameness score of 2/10 or less after IA analgesia was administered to the least lame limb<br>  ○ Level of exercise was not significantly reduced (8/10 or greater)<br>  ○ A less than 50% improvement in lameness score following IA analgesia of TMT and/or DIT joint of the lamest limb<br>  ○ No radiographic evidence of distal hock OA<br>  ○ A possible diagnosis of PSD confirmed by a high metatarsal 4 point block, local infusion or tibial block with ultrasonographic evaluation<br>Initially included horses were excluded for any of the following reasons (n=108 at initial inclusion, 21 horses excluded, n=87 at final inclusion):<br>• When concomitant disease interfered with the assessment of the efficacy of treatment<br>• Any event occurred with potential influence on clinical outcome<br>• Prescription of forbidden treatments |

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| | • Horses were diagnosed with another orthopedic problem on day 60 that was not apparent on day 0<br>Horses were split into two groups (n=87):<br>• Group 1 = Tiludronate group, 42 horses<br>• Group 2 = Placebo group, 45 horses<br>• Imbalanced groups not addressed<br>• 40 horses needed in each group for 80% power to evidence an average of one lameness grade difference<br><br>*Intervention*<br>Dose:<br>• Group 1 = 1 mg/kg tiludronate diluted with normal saline to 1 litre by IV infusion over 30 minutes<br>• Group 2 =1 mg/kg placebo powder diluted with normal saline to 1 litre by IV infusion over 30 minutes<br>First Treatment, Day 0:<br>• Treatments were determined by a biometrician-generated randomisation list<br>• Horses were divided into blocks with four horses in each block. ("In each list, treatments were randomly allocated by blocks of four horses (two tiludronate treated and two placebo horses per block)." Whether or not there was a group of three is unspecified.)<br>• Double blinded: Neither the owner nor the veterinarian knew if the infusion was the treatment or the placebo at day 0<br>• All horses were given IV sedation before infusion (20 mcg/kg bwt detomidine hydrochloride or 40 mcg/kg bwt romifidine)<br>Second Treatment, Day 60:<br>• Horses with an inadequate response at day 60 were given 1 mg/kg bwt tiludronate diluted with normal saline by IV infusion over 30 minutes<br>• Day 60 treatments were not blinded so there was no placebo administered<br>During the trial horses could receive the following treatments:<br>• Hoof trimming or reshoeing. The type of shoe could not be altered<br>• NSAIDs. Horses with lameness were treated with NSAIDs if deemed necessary (e.g. Phenylbutazone or flunixin). Horses with a concomitant disease such as colic or trauma were also treated with NSAIDs (e.g. phenylbutazone, flunixin meglumine), butylscopolamine or metamizole but not anti-microbials In each case there had to be 15 days between treatment and the next control visit<br>• Feed additives. Horses who had been receiving chondroprotective feed additives in the four weeks prior to the study continued to receive these additives at the same |

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| | dose throughout the studyNo other treatments were allowed |
| **Study design:** | Randomised controlled trial |
| **Outcome studied:** | *Subjective Assessment: Lameness Scores*<br>• Lameness was assessed on a 10 point scale based on clinician observation. Not specified if same or different clinician<br>• Lameness was assessed on a straight line on hard ground<br>• Lameness was monitored at days 0, 60 and 120<br>  ○ On days 60 and 120 critical lameness scores were obtained: lameness was assessed on the most lame limb after the least lame hock was given IA analgesia<br><br>*Subjective Assessment: Level of Exercise*<br>• Exercise was graded on a 10 point scale<br>• Exercise grading scores were specific to the horse's discipline (e.g. racing, trotters, showjumpers and eventers, dressage, pleasure and endurance)<br><br>*Objective Assessment: Radiographs*<br>• Radiographic findings were compared between the treatment and control group.<br>• Radiographic findings were not graded by severity of disease Findings noted included: thickening of subchondral bone, subchondral bone lysis, subchondral bone sclerosis, narrowing or loss of joint space, periarticular osteophytes, periosteal new bone |
| **Main findings: (relevant to PICO question):** | • The lameness scores for the tiludronate group were significantly lower than the placebo group at day 60 (P=0.0318)<br>  ○ Tiludronate group lameness score group mean 2.6/10 (s.d. 1.7)<br>  ○ Placebo group lameness score group mean 3.3/10 (s.d. 2.0)<br>• Approximately 60% of horses in the tiludronate group improved by 2 or more lameness scores at day 60 (distribution not provided)<br>• The number of horses in the placebo group that improved by 2 or more lameness scores is not provided<br>• Lameness grading varied significantly between investigators (covariate investigator effect P=0.0395)<br>• Horses with a higher lameness score at day 0 had a higher lameness score at day 60 (covariate baseline effect P=0.0007)<br>• In horses with periarticular osteophytes there was a significant improvement in lameness scores in the |

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| | tiludronate group as compared to the placebo group (P=0.006). Number of horses with periarticular osteophytes or subchondral bone thickening not given |
| **Limitations:** | • The 60 day outcome of the placebo group is not provided<br>• From day 60, the study was no longer blinded<br>• The study was funded by the makers of Tildren® (CEVA) as part of the regulatory licensing trial. Two authors work for CEVA and the third author was paid by CEVA for his clinical expertise. Because the study was not double blinded past day 60, this could introduce bias<br>• The study relies on the investigator's clinical experience to eliminate horses with PSD. It was also assumed that the majority of horses with PSD would not have a greater than 50% positive response to TMT IA analgesia within 10 minutes (Dyson and Romero, 1993 and Dyson, 1994)<br>• Outcomes were assessed with subjective lameness grading that varied significantly between investigators<br>• There was a significant interaction between investigator (P=0.0083) and treatment (P=0.0223) in the exercise results. The authors suggest this was due to differences in at home exercise protocols between investigators, but other biases could be responsible. As a result, improvement in exercise scores could not be associated with treatment<br>• The statistical results on lameness did not include a p-value for a possible interaction between treatment and investigator. Including this p-value would provide more evidence that the treatment effect on lameness was not due to differences in investigator<br>• There was a significant difference in bodyweight between the two groups. The placebo group had a mean weight of 568 kg, while the tiludronate group had a mean weight of 521 kg (P=0.01). Differences in bodyweight are difficult to interpret without breed information and likely clinically irrelevant<br>• Results were only presented in percentages, means, standard deviations and p-values. Frequencies (e.g. 5/9 horses) were not supplied<br>• The radiographic evidence exclusion criteria was based on investigator's clinical experience alone and did not include a standardised, objective grading scale of radiographic lesions<br>• The paper does not address potential side effects of tiludronate. The authors do not specify that adverse events were monitored or reported |

| Watts et al. (2016) | |
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| **Population:** | Horses in the Southern US with hindlimb lameness or poor performance<br>• Sex: 12 non-pregnant mares, 28 geldings, one stallion<br>• Breed: 10 warmbloods, 21 Quarter Horses or Paints, nine Thoroughbreds, one Arabian<br>• Mean Age: 12.4 (+/- 6.5) in treatment group; 10.7 +/- 6.0 in placebo group<br>• Use: dressage (8), eventing (7), jumping (5), western performance (11), pleasure or trail riding (3) and western show (7). Use not-specified for four horses lost to follow up. |
| **Sample size:** | n=45 |
| **Intervention details:** | *Case Selection*<br>Horses with a hindlimb lameness or poor performance that met each of the following conditions:<br>• ≥ 3 years old<br>• Primary hindlimb lameness localised to distal tarsal joints with diagnostic anesthesia<br>Horses were excluded for any of the following reasons:<br>• Treated with IA medication in any tarsal joint in the previous 6 months<br>• Treated with NSAIDs in the previous 7 days<br>• Pregnant<br>• Lameness > 4/5<br>• Required additional lameness treatments (e.g. shoeing changes, other IA injections)<br>Horses were split into two groups (n=45):<br>• 20 horses needed in each group to detect an improvement from 50% (placebo group) to 90% (resveratrol group) with 80% power and $\alpha$=0.05<br>• 5% predicted loss<br>• 45 horses enrolled<br>• Group 1 = Resveratrol group, 23 horses<br>• Group 2 = Placebo group, 22 horses<br><br>*Intervention*<br>• Group 1 = 1,000 mg microencapsulated resveratrol in powder (70% resveratrol, 30% microencapsulant, fermentation solubles, *Saccharomyces cerevisiae* 1026, diatomaceous earth) two scoops fed every 12 hours<br>• Group 2 = placebo powder (fermentation solubles, *S. cerevisiae* 1026, diatomaceous earth) 2 scoops fed every 12 hours<br>• All enrolled horses received 4.5 mg of triamcinolone acetonide in each of the centrodistal and TMT joint of both hindlimbs |

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| | • Four horses also received 62.5 mg of amikacin in each joint (this was a single clinician's preference, it was not specified in which group these horses were enrolled)<br>• IA injection confirmed by either 1) joint fluid in needle hub or 2) radiography or fluoroscopy to confirm needle placement<br>• All horses were treated with 2 g phenylbutazone IV after IA injections<br>• Owners instructed to give 2 g phenylbutazone PO q 24 h for 3–7 days and return to full work in 3–7 days depending on clinician instructions. Diet, turnout and exercise programs maintained as before study enrollment<br>• Owners recorded medications or supplements added or stopped during treatment period |
| **Study design:** | Randomised controlled trial |
| **Outcome studied:** | *Subjective Assessment: Lameness Scores*<br>• Lameness was assessed on a 5 point scale based on clinician observation. Lameness was also noted to be unilateral or bilateral<br>• Lameness was assessed on a 40 m straight line and in a 20 m half circle on hard ground in both directions<br>• Lameness was monitored at enrollment and 4 months post-enrollment<br>• Diagnostic anesthesia was only performed at enrollment<br><br>*Subjective Assessment: Level of Exercise*<br>• Owner questionnaire at 2 and 4 months<br>• Clinician asked owner or rider about horse's perceived performance<br><br>*Objective Assessment: Inertial Sensor System*<br>• Parameters measured were pelvic asymmetry (MAXDIFF and MINDIFF) and vertical pelvic movement vs. expected pelvic movement (A1:A2 ratio) |
| **Main findings: (relevant to PICO question):** | • Two horses in each group (four total) lost to follow-up at 2 months; 41 horses analysed<br>• 2 months after enrollment, the percentage of horses whose performance was better, compared with worse or the same, was significantly (P=0.04) higher for the resveratrol group (20/21 [95%]) than for the placebo group (14/20 [70%])<br>• 4 months after enrollment, the percentage of horses whose performance was better, compared with worse or the same, was still significantly (P=0.02) higher for the resveratrol group (18/21 [86%]) than for the placebo group (10/20 |

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| | [50%]). 2 months after enrollment 70% (14/20) of riders reported that the horse's performance was better in the IA triamcinolone only group compared to baseline<br>• 4 months after enrollment 50% (10/20) of horses improved in the IA triamcinolone only group compared to baseline<br>• 4 months after treatment, 35% of horses had returned to full work in placebo group 2 (vs 38% of horses in treatment group 1; not significant) |
| **Limitations:** | • Many key performance indicators in the rider questionnaire were not significantly different between groups. These included: whether the horse had returned to full work (yes vs no), whether signs of lameness were present (yes vs no), performance compared with expectations (at/above vs below) and whether the owner/rider was satisfied with how the horse was doing (yes vs no)<br>• There was no difference in pelvic asymmetry from inertia sensor between the two groups<br>• Confidence intervals were not provided to substantiate changes in A1:A2 ratio (only scatterplots and p-values given)<br>• Other differentials for distal tarsal lameness (e.g. proximal suspensory desmopathy) were not excluded<br>• Radiographic evidence was not considered |

## Appraisal, application and reflection

Labens et al. (2007) provides the strongest experimental design in support of IA corticosteroids as the sole treatment in chronic, degenerative OA. There is no randomised controlled trial to support the use of IA corticosteroids as a treatment for degenerative hock OA. This study reports a positive correlation between treatment with IA corticosteroids for distal hock OA and a modest, improved outcome.

The limitations of the study include non-uniform treatments (doses, site of injection and choice of corticosteroid varied), non-uniform time to follow-up, and non-uniform time between subsequent exams and treatments. Another weakness was that the cases studied did not conclusively rule out other disease processes that would not respond to IA corticosteroid treatment (e.g. proximal suspensory desmitis and intertarsal ligament enthesopathy). One strength of this study is that it uses a moderately large sample size (n=51). More importantly, it provides the strongest experimental design in absence of a randomised controlled trial among studies that examine IA corticosteroids as the sole treatment in chronic, degenerative OA. While the treatments were not uniform between cases, they do reflect the day-to-day clinical treatment of distal hock OA. The modest therapeutic success in this study indicates that clinicians can expect about half of horses to have a positive outcome 2 months after treatment, but only 34/59 (58%) of horses to have a long-term positive outcome. These outcomes are restricted to IA corticosteroid treatment as a sole intervention and do not consider other treatments for distal hock OA.

Gough et al. (2010) is a randomised controlled trial that evaluated efficacy of tiludronate as a treatment for distal hock OA. The authors concluded that the lameness scores for the tiludronate group were significantly lower than the placebo group at day 60 (P=0.0318). Furthermore, they concluded that 60% of horses in the tiludronate group improved by 2 or more lameness scores at day 60. Finally, the authors report that for the subset of horses with periarticular osteophytes in both groups, lameness scores were lower in the tiludronate group as compared to the placebo group (P=0.006).

There are a number of limitations associated with this study, the main ones are highlighted here. First, the distribution of lameness scores for both the placebo group and the treatment group was not reported. Second, the study became unblinded at/after day 60. The study was also funded by the makers of Tildren® (tiludronate disodium). While this funding source was clearly disclosed, it may have introduced bias. Third, lameness grading varied significantly between investigators (covariate investigator effect P=0.0395), which may have impacted outcome assessment. There was also a significant effect of investigator (P=0.0083) and an interaction between investigator and treatment (P=0.0223) in the exercise results. This suggests that differences in at home exercise protocols were significant between investigators and centres. As a result, improvement in exercise scores could not be utilised as a treatment outcome as this was more likely to be associated with investigator rather than treatment. A final limitation is that this study does not address potential side effects of tiludronate. Despite the type of experimental design (randomised controlled trial), there were significant limitations to the quality of the evidence such that a wholescale change to clinical practice is not recommended based on this trial alone.

Watts et al. (2016) is a randomised controlled trial of resveratrol supplementation and IA triamcinolone to treat distal hock OA. The authors conclude that horses injected with IA triamcinolone and supplemented with resveratrol had better performance than horses injected with triamcinolone alone at 2 and 4 months post-treatment. Better performance was indicated subjectively by owner reported performance improvement and objectively by vertical pelvic movement measured by inertial sensor system (The A1:A2 ratio is calculated for each hindlimb and compares the horse's actual vertical pelvic movement with an expected vertical pelvic movement). Yet certain key performance indicators did not vary between the treatment and placebo groups: subjective lameness scores by a clinician, pelvic asymmetry from inertial sensor, and the owner/rider's perception that the horse had returned to full work. While the efficacy of the resveratrol intervention is not the subject of this PICO question, Watts et al. (2016) found that 4 months after IA corticosteroid (triamcinolone) injection, only 35% of horses had returned to full work, confirming that long-term outcome of IA triamcinolone treatment is not favourable for distal tarsal OA.

Evaluating the comparative efficacy of treatments for distal hock OA comes with many challenges. One challenge is that to date, there is no published randomised controlled trial to directly compare the efficacy of IA corticosteroids with systemic bisphosphonates. The strongest evidence for either treatment comes from randomised controlled trials where each intervention is examined separately. Watts et al. (2016) is a randomised controlled trial of resveratrol supplementation and IA triamcinolone to treat distal hock OA. While the efficacy of the resveratrol intervention is not the subject of this PICO question, Watts et al. (2016) does provide evidence that long-term outcome of IA triamcinolone treatment for distal tarsal OA is suboptimal: at 2 months post IA triamcinolone treatment, 70% (14/20) horses' performance improved while at 4 months post IA triamcinolone treatment, only 50% (10/20) of horses' performance improved.

De Grauw et al. (2016) conducted another randomised controlled trial that compared efficacy of IA triamcinolone with IA triamcinolone + hyaluronate acid (HA). It was excluded from this knowledge summary because OA was not confirmed radiographically and no tarsal joints were included in the study; therefore, conclusions about the intervention relative to tarsal OA cannot be drawn. But this study does shed light on IA triamcinolone efficacy at various intervals post-treatment. At 3 weeks post-treatment, 88% of patients treated with IA triamcinolone had improved by 2 lameness grades. At 3 months post-treatment, owners reported only 50% of horses were back in full work, which is very similar to the proportion found by Watts et al. (2016). Again, there was no placebo control group due to ethical implications of withholding treatments from lame horses. De Grauw et al. (2016) also note that the 3 week improvement in lameness may in part have been due to the resting protocol they implemented.

Another prospective case series, although investigating the outcomes of a different treatment (IA ethanol injection) in cases of distal tarsal joint OA (Lamas et al., 2012), is also relevant to the PICO question at hand, given the study's population and inclusion criteria: of the 24 horses included, all horses had lameness recur

within 4 months of receiving IA corticosteroids (triamcinolone or MPA) in the TMT joint (Lamas et al., 2012). This suggests that failure of IA corticosteroids for long-term management of distal tarsal OA is certainly not uncommon.

While IA corticosteroids are commonly used in everyday practice, prospective, randomised controlled trials with adequate power are necessary to assess their efficacy in treating distal hock OA. While it may not be ethically feasible to include a control group treated with IA saline in these studies, a non-treated group with controlled exercise should be included at a minimum. Additionally, placement of IA treatments should be confirmed radiographically as injection into distal tarsal joints — especially the DIT joint — is not always accurate (Seabaugh et al., 2017 and Hoaglund et al., 2019). Additional blinded randomised controlled trials are needed to assess efficacy of bisphosphonate treatment for distal hock OA, as various shortcomings for Gough et al. (2010) were noted above. Regardless of the intervention studied, a combination of subjective and objective outcomes should be assessed. These may include (blinded) lameness scores, rider reported performance improvement, and ideally some form of quantitative motion analysis (e.g. vertical pelvic movement from inertial motion unit sensor systems).

## Methodology Section

| **Search Strategy** | |
|---|---|
| Databases searched and dates covered: | CAB Abstracts on the OVID Platform 1973 to 2018 Week 19<br>PubMed accessed via the NCBI website 1910 to May 2018 |
| Search terms: | **CAB Abstracts**<br>(equine* or horse* or equus or equid* or mare or mares or broodmare* or 'brood mare*' or pony or ponies or filly or fillies or colt or colts or yearling* or stallion* or thoroughbred* or standardbred* or racehorse* or 'race horse*').mp. or (exp horses/ or exp equus/ or exp equidae/ or exp mares/ or exp colts/ or exp foals/ or exp stallions/ or exp thoroughbred/ or exp racehorses/)<br>AND<br>(arthropat* or arthrit* or osteoarthrit* or osteo-arthrit* or synovitis or tenosynovitis or 'joint disease*' or OA or DJD or osteoarthrosis or lame or lameness or spavin or gait).mp. or (exp osteoarthritis/ or exp arthritis/ or exp joint diseases/)<br>AND<br>(tarsal* or tarsus* or carpus* or carpal*).mp. or exp tarsus/ or exp carpus/<br>AND<br>((corticosteroid* or glucocorticoid* or corticoid* or dexamethason* or methylprednisolon* or triamcinolon* or TMC or betamethason* or prednisolon* or prednison* or prednicare* or steroid*).mp. or (exp prednisolone/ or exp prednisone/ or exp glucocorticoids/ or exp steroids/)<br>OR<br>(bisphosphonat* or biphosphonat* or bisphosponat* or biphosponat* or disphosponat* or diphosphonat* or diphosponat* or disphosphonat* or tiludron* or clodron*))<br><br>**PubMed**<br>(horse OR equine OR equus OR equidae OR equid OR mare OR broodmare OR “brood mare” OR pony OR filly OR colt OR yearling |

| | |
|---|---|
| | OR stallion OR thoroughbred OR standardbred OR racehorse OR "race horse")<br>AND<br>(arthropathy OR arthritis OR osteoarthritis OR osteo-arthritis OR synovitis OR tenosynovitis OR "joint disease" OR OA OR DJD OR osteoarthrosis OR lame OR lameness OR spavin OR gait)<br>AND<br>(tarsal OR tarsus OR carpal OR carpus)<br>AND<br>((corticosteroid OR glucocorticoid OR corticoid OR dexamethasone OR methylprednisolone OR triamcinolone OR TMC OR betamethasone OR prednisolone OR prednisone OR prednicare OR steroid)<br>OR<br>(bisphosphonate OR biphosphonate OR bisphosphonate OR biphosponate OR disphosponate OR diphosphonate OR diphosponate OR disphosphonate OR tiludronate OR tiludronic OR clodronate OR clodronic)) |
| Dates searches performed: | 21 May 2018 |

| **Exclusion / Inclusion Criteria** | |
|---|---|
| Exclusion: | Papers that did not answer the PICO question were excluded for the following reasons:<br>1. the therapeutic intervention was not a corticosteroid or a bisphosphonate (e.g. gold, resveratrol, NSAIDs, surgery, ethanol, polysulfated glycosaminoglycans, hyaluronic acid, dimethyl sulphoxide), or<br>2. the therapeutic interventions were not administered according to the PICO requirements (i.e. corticosteroids were not given intra-articularly or bisphosphonates were not given systemically), or<br>3. the study was based on a non-osteoarthritic disease (e.g. osteochondrosis, infection, hemoarthrosis, tarsal sheath effusion, stringhalt), or<br>4. a non-equine model was used. Also excluded were non-English language, non-systematic review articles, case reports, conference proceedings or duplicates |
| Inclusion: | Either IA corticosteroids or systemic bisphosphonates were studied in horses with distal tarsal joint lameness due to OA |

| Search Outcome | | | | |
|---|---|---|---|---|
| **Database** | **Number of results** | **Excluded – did not answer PICO question** | **Excluded – conference proceedings, case report or non-systematic review articles** | **Total relevant papers** |
| CAB Abstracts | 81 | 55 | 23 | 3 |
| PubMed | 36 | 32 | 1 | 3 |
| Total relevant papers when duplicates removed | | | | **3** |

## CONFLICT OF INTEREST

The author declares no conflicts of interest.

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