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There is no evidence that the addition of antimicrobials reduce the risk of sepsis after intra-articular corticosteroids in horses with arthritis

A Knowledge Summary by

Elena Gogua DVM [1*]

[1] Moscow State Academy of Veterinary Medicine and Biotechnology named K.I. Skryabin, Moscow, Russia

[*] Corresponding Author (goguaveter@gmail.com)

ISSN: **2396-9776**
Published: **14 Jan 2020**
in: **Vol 5, Issue 1**
DOI: 10.18849/VE.V5I1.220
Reviewed by: **Nick Parkinson (MA, MS, VetMB, CertEM(Int.Med.), DACVIM, MRCVS)and Matthieu Cousty (DVM, ECVS)**
Next Review Date: **May 4th 2021**

KNOWLEDGE SUMMARY

PICO question

In horses with arthritis, does the treatment with intra-articular antimicrobials concurrently with intra-articular corticosteroids reduce the risk of sepsis compared to intra-articular corticosteroids alone?

Clinical bottom line

The three studies identified did not demonstrate a reduction of risk when antimicrobials were used. However, the strength of evidence provided by the studies was weak. The power of the studies to detect an effect of antimicrobials was low due to the small number of sepsis cases recorded. Further studies are therefore required to draw conclusions.

The evidence

Despite appearing to be common practice, there is no convincing evidence that the use of intra-articular antimicrobials concurrently with intra-articular corticosteroids reduces the risk of sepsis. Literature searches uncovered three papers that partially addressed the PICO question. In these papers the authors among other things considered the result of the addition of antimicrobials to corticosteroids for intra-articular injection, therefore it were included in the evidence. One of these works is a cross-sectional study (Gillespie et al., 2016), two other works (Smith et al., 2018 and Steel et al., 2013) are retrospective cohort studies, one of which (Steel et al., 2013) includes a case-control design. The authors of all three publications detected no effect of the addition of antimicrobials on the risk of sepsis after intra-articular corticosteroids. However, due to low numbers of adverse outcomes and consequent low power, conclusions should be interpreted with caution.

Summary of the evidence

Smith et al. (2018)	
Population:	Data from clinical records of all horses undergoing intrasynovial medication by 10 ambulatory clinicians in the UK 2006–2011
Sample size:	9456 intrasynovial injections in 4331 sessions in 1732 horses
Intervention details:	A similar protocol of aseptic technique was used for each joint injection. The concurrent use of medications was dependent on clinician preference. Corticosteroids were used in 3869 of 4331 (89.3%) sessions, including triamcinolone acetonide in 3592 of 4331 sessions (82.9%). Amikacin sulphate was used in 4044 of 4331 (93.4%) sessions Information on dosages is not reported.
Study design:	Retrospective cohort study

Outcome studied:	Objective assessment. Frequency of sepsis after joint injection. The intrasynovial medications studied: • Triamcinolone acetonide • Dexamethasone phosphate • Methylprednisolone acetate • Autologous conditioned serum • Stanazolol • Platelet Rich Plasma • Polysulphated glucosaminoglycans (PSGAG) • Hyaluronate • Amikacin sulphate
Main findings: (relevant to PICO question):	4/9456 horses developed post medication synovial sepsis (0.04%) of all medications. In one of the sepsis cases there was a combination of triamcinolone acetonide with amikacin, one sepsis case was triamcinolone without amikacin, and two sepsis cases was polysulphated glycosaminoglycan. Hyaluronate was used in all four of the sepsis cases.
Limitations:	Due to the low incidence of cases statistical analysis was not performed. Non-random treatment allocation.

Gillespie et al. (2016)	
Population:	Equine veterinarians
Sample size:	241 surveys
Intervention details:	Online cross-sectional survey of veterinarians – members of the American Association of Equine Practitioners (AAEP)
Study design:	Cross-sectional survey
Outcome studied:	Objective assessment. Data from medical records for a period of up to 10 years prior to the survey for the number of intra-articular injections performed and the number of joints that developed septic arthritis. Variables studied: • number of years in practice • duration of skin preparation at injection site (and details) • use of sterile gloves (and details) • use of individual medication vials • one-time use of each needle • antibiotic added to other medication
Main findings: (relevant to PICO question):	The number of septic joints following intra-articular injection was 67 joints out of 319,760 intra-articular injections, giving an incidence of 2.1 septic joints per 10,000 intra-articular injections. Intra-articular antimicrobial usage as an adjunct for all intra-articular injections was used by 46.5% of veterinarians (112/241) and

	additional 39.4% of veterinarians (95/241) used antimicrobials some of the time. The data from the 64 veterinarians providing data from medical records did not show a reduction in joint sepsis associated with the use of antimicrobial administration.
Limitations:	There is no way of determining validity. Data obtained from surveys may be inexact.

Steel et al. (2013)	
Population:	Horses having intra-articular medication at the Singapore Turf Club 2002–2005 Excluded: injection of local anaesthesia alone
Sample size:	16,624 joints injected in 1103 horses Study population included septic arthritis in 13 joints from 13 horses
Intervention details:	15,934 intra-articular injection of corticosteroid. 824 intra-articular injections of amikacin sulphate. The combination of drugs, doses, frequency determined by the clinical situation. Any information on dosages is not reported. Joints were prepared using a standardised procedure. Control group – 224 horses
Study design:	Retrospective and prospective descriptive cohort study, and case-control study
Outcome studied:	Objective assessment. Septic arthritis was diagnosed if bacterial culture of synovial fluid was positive or if synovial fluid analysis was consistent with sepsis. Assessment potential risk factors septic arthritis following intra-articular medication: • using corticosteroids • repeated joint injections • using amikacin sulphate with the intra-articular medication
Main findings: (relevant to PICO question):	Septic arthritis was diagnosed following intra-articular medication in 13 joints from 13 horses of the 16,624 injections – a risk of 7.8 per 10,000 joints injected. Statistically significant risk factors: • veterinarian • type of corticosteroid Septic arthritis was diagnosed in 12 of the 15,934 joints injected with a corticosteroid (risk of 7.5 per 10,000 injections, 95% CI 3.9–13.1). Betamethasone injection had a lower risk of septic arthritis than dexamethasone (P=0.024). None of the 824 joints in which amikacin sulphate was injected developed septic arthritis (risk of 0.0 per 10,000 injections, 95% CI 0.0–44.7), but 13 of the 15,800 joints injected without amikacin sulphate or any antimicrobial did develop sepsis (risk of 8.2 per 10,000 injections, 95% CI 4.4–14.1). However, this was not statistically significant.
Limitations:	13 cases is a small number and statistical analysis of risk factors is

	difficult. Non-random treatment allocation.

Appraisal, application and reflection

Intra-articular injections of corticosteroids are employed in horse practice for the treatment of non-inflammatory synovitis and osteoarthritis. The risk of developing iatrogenic septic arthritis after intra-articular injections is well known. The aim of this knowledge summary was to critically appraise published evidence where the addition of intra-articular antimicrobials is to reduce the risk of sepsis.

The search strategy did not include the terms corticosteroid, antibiotic, and their derivatives, since specific drug names may have been used in publications. The search gave a lot of results, as it was not very specific, but it makes sure that relevant publications were not missed. However, only two publications related to the PICO question were found and one publication (Smith et al. 2018) was mentioned by a reviewer but was not picked up in the searches due to search query restrictions. One paper was a cross-sectional study and the other two were retrospective cohort studies, one of which includes a case-control design. None of these publications respond directly to the PICO question, but the authors looked at the result of using antimicrobials in addition to intra-articular injections of corticosteroids. In general, the risk of sepsis after intra-articular injections is very low – 7.8 cases per 10,000 injections (Steel et al. 2013) or 2.1 cases per 10,000 injections (Gillespie et al. 2016) or 4.2 cases per 10,000 injections (Smith et al. 2018). The veterinarian and type of corticosteroid were identified as risk factors (Steel et al. 2013). While the use of intra-articular amikacin sulphate or gentamicin was not a statistically significant factor (Gillespie et al. 2016 and Steel et al. 2013) or did not prevent the development of synovial sepsis (Smith et al. 2018). These observations should be interpreted with caution – due to the low incidence of sepsis after intra-articular injections, the statistical power of the studies may not be sufficient to reflect true results.

Thus, the use of antimicrobials is a very common practice – 46% (Gillespie et al. 2016) to 93% (Smith et al. 2018) of veterinarians combine intra-articular corticosteroids with intra-articular antimicrobials to reduce the risk of septic inflammation of the joint, but there is no evidence of efficiency of this approach and this treatment is pure empirical. Prospective randomised controlled trials using standardised treatment protocols could answer this clinical question. Smith at al. (2018) estimated that approximately 12,500 medication sessions would be needed to provide a power of 80% for relative risk estimation. But such clinical trials are unlikely to be of practical value given the low incidence of sepsis.

Methodology Section

Search	
Databases searched and dates covered:	CAB Abstracts on OVID Platform; 1973 to Week 13 2019 PubMed via the NCBI website; 1910 to Week 13 2019
Search strategy:	CAB Abstracts: 1. (equine* or horse* or mare* or equus or equid*).mp. or exp equidae/ or exp equus/ or exp horses/ or exp mares/ 2. (arthrit* or osteoarthrit* or arthros* or osteoathros* or 'joint disease*' or DJD or OA).mp. or exp osteoarthritis/ or exp arthritis/ or exp joint diseases/ 3. ('joint injection*' or 'synovial injection*' or intraarticular or intrasynovial) 4. ('synovial sepsis' or 'joint sepsis' or 'septic arthritis' or sepsis or 'septic infection').mp. or exp sepsis/ 5. 1 and 2 and (3 or 4)

	PubMed: 1. equine OR horse OR mare OR equus OR equid 2. arthritis OR osteoarthritis OR DJD OR OA OR degenerative joint disease 3. joint injection OR synovial injection OR intra-articular OR intraarticular OR intrasynovial 4. synovial sepsis OR joint sepsis OR septic arthritis OR sepsis OR septic infection 5. 1 and 2 and (3 or 4)
Dates searches performed:	CAB abstracts: 25/4/18 PubMed: 4/5/18

Exclusion / Inclusion Criteria	
Exclusion:	Non-English language publications Conference paper or thesis Articles not relevant to the PICO Book chapters
Inclusion:	Articles available in English which were relevant to the PICO

Search Outcome

Database	Number of results	Excluded – non-English Language	Excluded – Conference paper or thesis	Excluded – Not relevant to PICO	Excluded – Book chapters	Total relevant papers
CAB abstracts	458	81	50	316	9	2
PubMed	466	10	0	454	0	2
Hand Search						1
Total relevant papers when duplicates removed						**3**

CONFLICT OF INTEREST

The author declares no conflicts of interest.

I would like to acknowledge Clare Boulton for her help with the search strategy and finding full-text papers, Bridget Sheppard for her support throughout the process, the reviewers for their helpful and detailed comments, and Jennifer Morris for her thorough copyediting.

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