Article

Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital

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Abstract — Perioperative antimicrobial administration practices were evaluated retrospectively in 97 horses undergoing elective arthroscopy, and antimicrobial use was compared with standard recommendations for perioperative prophylaxis. Parenteral antimicrobials were administered perioperatively to 95/97 (98%) horses, 88 of which received intravenous sodium penicillin. Time from 1st dose until 1st incision ranged from 30 to 390 min [142 ± 55.6 min, mean ± standard deviation (*s*), median 135 min], and the first incision was performed greater than 2 half-lives after administration of sodium penicillin in 86/95 (91%) cases. Overall duration of therapy was 30.8 ± 24.2 h (mean ± *s*). Six (6.3%) horses received only a single preoperative dose, while 63 (66%) horses were treated for 24 h or less. While objective data regarding optimal perioperative antimicrobial prophylaxis are limited, the antimicrobial use practices observed here commonly deviated from standard recommendations for perioperative prophylaxis.

Résumé — Étude rétrospective des pratiques d'utilisation périopératoire des antimicrobiens chez les chevaux subissant une chirurgie arthroscopique non urgente dans un hôpital d'enseignement vétérinaire. Les pratiques d'administration périopératoire des antimicrobiens ont été évaluées rétrospectivement chez 97 chevaux subissant une arthroscopie non urgente et l'utilisation des antimicrobiens a été comparée aux recommandations standard pour la prophylaxie périopératoire. L'administration périopératoire d'antimicrobiens parentéraux a été effectuée pour 95/97 (98 %) chevaux, dont 88 ont reçu de la pénicilline sodique intraveineuse. Le délai écoulé entre la première dose et la première incision variait de 30 à 390 minutes (142 ± 55,6 minutes, moyenne + SD, médiane de 135 minutes) et la première incision a été réalisée à plus de deux demi-vies après l'administration dans 86/95 (91 %) des cas. La durée totale de la thérapie était de 30,8 ± 24,2 heures (moyenne ± SD). Six (6,2 %) chevaux ont reçu une seule dose préopératoire tandis que 63 (66 %) chevaux ont été traités pendant 24 heures ou moins. Bien que des données objectives concernant la prophylaxie périopératoire optimale soient limitées, les pratiques d'utilisation d'antimicrobiens observées ici ont couramment dévié des recommandations standard pour la prophylaxie périopératoire.

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Introduction

The discovery and subsequent availability of antimicrobials was a landmark event in medicine and resulted in significant beneficial effects on morbidity and mortality of humans and animals. When properly applied, perioperative antimicrobial therapy can significantly reduce postoperative morbidity and mortality (1). However, perioperative antimicrobial prophylaxis has come under scrutiny in human medicine because it is often poorly applied and accounts for a large percentage of overall antimicrobial use. In general human hospitals, surgical prophylaxis often accounts for 30% of antimicrobial prescriptions, while this can reach 95% in surgical centers (2).

The objectives of surgical prophylaxis are to reduce postoperative infection at the surgical site, thereby reducing morbidity, mortality, and treatment costs, while producing no (or minimal) adverse consequences for the patient or his/her environment (1). Pharmacologically, the goal is to have adequate serum and tissue antimicrobial levels at the time of surgery in situations where bacterial contamination of the surgical site is a reasonable possibility. Standard perioperative guidelines developed in human medicine are presented in Table 1.

Little attention has been paid to perioperative antimicrobial use in equine medicine, despite increasing concerns about veterinary antimicrobial use. Excessive or inappropriate antimicrobial administration could result in suboptimal clinical effect and selection for antimicrobial resistance while exposing the patient to a risk of development of antimicrobial-associated complications such as colitis. Specific concerns regarding antimicrobial

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Table 1. Standard guidelines for perioperative antimicrobial prophylaxis in human medicine (adapted from references 1 and 7)

Antimicrobials are only indicated in clean-contaminated, contaminated, or dirty procedures, not clean procedures (except with implant placement).
Antimicrobials should be administered pre-operatively, ideally within 1 h of the 1st incision.
Prophylactic antimicrobials should be administered intravenously.
The antimicrobial spectrum should encompass the likely bacterial contaminants. Broad-spectrum therapy is usually required.
The use of newer broad-spectrum antimicrobials should be avoided to decrease emergence of resistant bacterial strains.
Therapy should be restricted to a single dose, or less than 24 h of therapy, except in certain situations such as gross contamination of the surgical site or pre-existing infection.
Dosing should be repeated intra-operatively if the procedure is still ongoing 2 half-lives after the 1st dose.
Antimicrobials should not be used to compensate for deficiencies in surgical technique or infection control practices.

use practices include administration of antimicrobials when not indicated, administration of ineffective antimicrobials, improper timing of administration, and unnecessarily prolonged therapy. The objective of this study was to describe perioperative antimicrobial administration in horses undergoing elective arthroscopy at a veterinary teaching hospital and compare this administration with standard perioperative antimicrobial use recommendations.

Materials and methods

A search of the Ontario Veterinary College Veterinary Teaching Hospital electronic medical records was used to identify all horses on which arthroscopy had been performed between August 23, 2001 and May 1, 2005. Records were reviewed and horses having undergone elective arthroscopic surgery were eligible for inclusion. Horses with an infectious orthopedic disease or with a co-morbidity that may have had an effect on the choice of antimicrobial therapy were excluded. Additionally, cases in which a surgical procedure in addition to arthroscopic surgery was performed were excluded. Perioperative antimicrobial use information was obtained from the medical records. Specifically, dosing regimen (drug, dose), time from administration to the 1st surgical incision, duration of antimicrobial therapy, length of surgical procedure, surgeon, and the presence of clinical signs consistent with postoperative surgical site infection were evaluated. Any complications that developed during or after surgery were also recorded.

Descriptive statistics were used for most categories. Surgeons who carried out fewer than 5 surgeries were grouped together for analysis. Fisher's exact test was used to evaluate the association between antimicrobial use and diarrhea. Normality of continuous data was assessed using the Shapiro-Wilk test. A Kruskal-Wallis test was used for comparisons between groups. A P value of < 0.05 was considered significant for all comparisons. A statistical software package was used for data analysis (JMP 5.1, SAS Institute, Cary, North Carolina, USA).

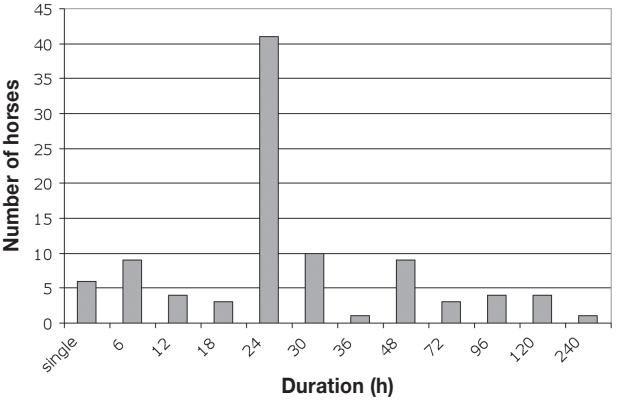

Figure 1. Duration of perioperative antimicrobial therapy in horses undergoing elective arthroscopy ($n = 95$).

Results

Ninety-seven horses ranging from 6 mo to 11 y of age [3.0 ± 2.2 y, mean ± standard deviation (s)] satisfied the inclusion criteria. Standardbred horses were most common (n = 35), followed by Thoroughbred (n = 27), and Hanoverian (n = 12). A variety of breeds accounted for the remaining horses. Surgical sites included bilateral hock (n = 27), single hock (n = 25), single carpus (n = 12), single stifle (n = 12), single fetlock (n = 11), bilateral fetlock (n = 3), bilateral stifle (n = 3), bilateral shoulder (n = 2), single shoulder (n = 1), and bilateral carpus (n = 1). Twelve primary surgeons were involved; however, 2 accounted for 53 (55%) cases.

Parenteral antimicrobials were administered perioperatively to 95/97 (98%) horses. Intravenous penicillin was administered preoperatively to 88/95 (93%) horses that received antimicrobials, while a combination of intravenous penicillin and gentamicin was administered to the remaining 7 (7.4%). In 7 cases (7.4%), oral trimethoprim/sulfa replaced penicillin 6 to 72 h after the preoperative dose. Time from 1st dose until 1st incision was reported in 89/95 (94%) cases, and ranged from 30 to 390 min (142 ± 55.6 min, mean ± s, median 135 min). Six of 95 (6.3%) horses received antimicrobials within 60 min of the 1st incision. Using a $t_{1/2}$ for sodium penicillin of 39 min (3), the 1st incision was performed more than 2 half-lives after administration in 86/95 (91%) cases and surgery was still ongoing in all cases after 2 half-lives had passed since the preoperative penicillin dose. Because the half-life for gentamicin is much longer (3 h) (4), intraoperative gentamicin dosing was not indicated in any of the 7 horses that received sodium penicillin and gentamicin perioperatively.

One of the horses that had not been treated with parenteral antimicrobials was treated with intraarticular amikacin postoperatively. The other horse received no antimicrobials whatsoever. Five horses that were treated preoperatively also received intraarticular amikacin postoperatively

Overall duration of therapy was 30.8 ± 24.2 h (mean ± s). Six (6.3%) horses received only a single pre-operative dose while a total of 63 (66%) horses were treated for 24 h or less (Figure 1). There was no apparent reason for prolonged

antimicrobial treatment for any case based on scrutiny of the medical record.

All procedures were classified as noncomplicated. Infectious complications at the surgery site were not identified in any case. In 1 horse, oozing of serous fluid from the surgical site was identified postoperatively, but no signs of septic arthritis or incision infection were reported and antimicrobial therapy was only administered for 24 h. A limb laceration occurred in 1 horse during recovery; however, antimicrobials were only administered for 6 h and no further problems developed.

Six (6.3%) horses developed diarrhea within 7 d of surgery. All had received antimicrobials. There was no significant association between antimicrobial use and diarrhea ($P = 1.00$), but statistical power was extremely limited because of the high prevalence of antimicrobial use. In all but 1 case, diarrhea was mild; however, 1 horse died after developing diarrhea following discharge from the hospital.

Surgical time ranged from 30 to 240 min (mean 85 $\pm$ 36 min). There was no association between surgeon and use of antimicrobials, drug choice, time from administration to incision, duration of therapy, or surgical time (all $P > 0.15$).

Discussion

This is the first study that provides detailed information on antimicrobial use practices in equine arthroscopy. While evidence-based guidelines have not been developed for horses, and care must be taken when extrapolating between species, there were differences between antimicrobial practices in this case series compared with standard recommendations for human beings. Some of these may reflect a lack of adequate information regarding the need for antimicrobial therapy in equine arthroscopy and lack of evaluation of different antimicrobial regimens. Some differences, such as the timing of administration with respect to onset of surgery, however, represent a deviation from standard antimicrobial practice recommendations. This has also been reported in elective surgery for cranial cruciate ligament rupture in dogs (5).

One area of discrepancy from guidelines for human beings was the timing from 1st dose to incision. The standard guideline that antimicrobials should be administered within 1 h of incision was only followed in 6.3% of cases, with the mean interval being $>$ 2 h. It is unlikely that this reflects a lack of understanding of principles of therapy. Rather, it is more likely based on logistical reasons related to standard daily practices. Perioperative antimicrobials are often administered based on an anticipation of the time of surgery, which is often delayed because of case management, emergencies, or other factors that are common in a busy hospital with a heavy emergency caseload. Administration of antimicrobials shortly before, or at the time of, induction of anesthesia would be preferable, but antimicrobials have not traditionally been administered to horses at this time because of concerns about transient hypotension associated with administration of penicillin (6). Administration of antimicrobials at the time of induction of anesthesia is considered safe in human beings (7) and the clinical significance of this concern in horses is unclear. While concerns about anesthesia should not be dismissed, antimicrobial administration at the time of induction of anesthesia, or shortly thereafter, would be preferable to the current practice of administration based on an estimate of when surgery will be performed.

Another area of discrepancy is the dosing regimen following the preoperative dose. It has been recommended that the antimicrobial should be readministered if surgery on human beings is ongoing after 2 half lives of the drug have passed, to ensure that adequate levels are present at the time of closure (7). While this has not been objectively evaluated in other species, it is a reasonable general recommendation, particularly for time-dependent drugs such as beta-lactam antimicrobials that do not have a significant postantibiotic effect. Intraoperative dosing did not occur in any horse, despite the fact that, in all cases, surgery was ongoing after 2 half-lives of sodium penicillin had passed. Thus, sub-therapeutic levels may have been present at the time of surgery, when peak antimicrobial levels are required. In many cases, based on the delay from 1st dose to the start of surgery and the duration of the procedures, a single pre-operative antimicrobial dose might reach such low levels by the time of the procedure that it could be similar to using no antimicrobials (in terms of prevention of infection, not development of resistance). Further, if antimicrobial therapy was continued after surgery it would be akin to starting antimicrobial therapy after surgery, something that has been shown in human beings to be no more effective than no administration of antimicrobials (8).

The duration of therapy was another area that could be of concern, with 34% of horses being treated beyond 24 h. In human beings, no benefit of extended ($>$ 24 h) therapy has been identified in orthopedic surgery (9). Additionally, multiple doses rarely confer any benefit over single dose therapy in general surgery (7) and prolonged prophylactic administration may be associated with emergence of resistant bacteria (10,11). There was no apparent reason for prolonged therapy of horses treated for $>$ 24 h, although it is possible that there were reasons for prolonged therapy in some or all cases that were not documented in the medical record or discharge orders.

Penicillin was the most commonly used antimicrobial, similar to what has been reported elsewhere (12). Optimal drugs for perioperative prophylaxis in horses have not been evaluated. While widely used, there could be concerns regarding penicillin use because of the relatively high prevalence of resistance among the more common bacteria that cause septic arthritis (12). Comparative study of different antimicrobial regimens would be useful; however, a very large sample size would be required because of the low incidence of infection.

One aspect that is difficult to assess is the need for perioperative antimicrobial therapy in procedures such as elective arthroscopic surgery. Arthroscopy is classified as a 'clean' procedure and perioperative antimicrobial therapy is not usually recommended in human medicine in the absence of co-morbidity or implant placement (1,7), although conflicting opinions do exist (13). The high prevalence of antimicrobial use in this study is in contrast to the 39% rate reported in a previous study of elective arthroscopies (12). Considering both studies evaluated elective arthroscopic cases, it is interesting that there was such a difference in overall antimicrobial use. There is no reason to suspect that the risk of infection was higher in our study

population versus that of the other study population. Typical rates of postoperative infectious complications in human beings range from 0.01 to 0.48%, with 1.3% being reported in 1 study (14–17). The incidence of infections in this study (0%) is therefore consistent with studies on human beings and other studies of surgical site infections in carpal arthroscopy in horses (0.5 to 0.9%) (12,18). A randomized, placebo-controlled blinded clinical trial in humans did not identify a difference in the incidence of postarthroscopy infections with or without perioperative antimicrobial prophylaxis; it was concluded that antimicrobials were not warranted because of the very low incidence of infection (19). However, perioperative prophylaxis may be justifiable in situations where postoperative infection is rare but associated with catastrophic effects. It could be argued that this is the case in horses because postoperative septic arthritis in horses can be a performance- or life-threatening complication. The influence of antimicrobial administration on the incidence of postoperative septic arthritis following elective arthroscopy in horses has not been clearly evaluated. One study reported no association between antimicrobial use and infection (12); however, the low incidence of infection may have compromised the ability of that study to detect the presence of a significant difference. A randomized, blinded, placebo-controlled trial evaluating the need for antimicrobial prophylaxis and evaluating different protocols would be desirable, but may be difficult based on the large sample size required to study such a low-incidence disease.

It is unreasonable to suspect that all surgeons (and owners) will be comfortable, at this point and without objective evidence, stopping the use of perioperative antimicrobials in elective arthroscopic surgery. The emphasis should be on prudent antimicrobial use while objective evidence is being gathered. While evidence-based guidelines are not available at this point, interim guidelines can be designed based on an understanding of equine orthopedic surgery, prudent use guidelines in development for veterinary medicine and established guidelines for human medicine. Regular review of antimicrobial use practices, infection rates, and passive surveillance of pathogens involved in postoperative infections can be used to monitor response to perioperative antimicrobial use guidelines and to determine if future changes are required.

An inherent problem with a study such as this is reliance on the medical record to capture retrospective data. Incompleteness and inaccuracy of the medical records can affect the results. Some cases that would have met the inclusion criteria were possibly not identified because of deficiencies in the computerized medical record. The small number of horses that were not treated with antimicrobials also prevents us from making any conclusions regarding the efficacy of antimicrobial therapy. This study, however, provides important information about antimicrobial use patterns, suggests areas that should be evaluated to facilitate prudent use, and highlights the need for prospective studies on the necessity of antimicrobials in surgical procedures. The data herein indicate that surgical and infection control personnel should scrutinize antimicrobial practices at their facilities to determine whether or not logical practices are being used and if other measures are needed to improve perioperative antimicrobial use practices.

Authors' contributions

Dr. Weese initiated the study and performed the initial data collection. Dr. Cruz performed a secondary review of cases to clarify certain items and provide a second level of review. The article was written by Dr. Weese with the participation of Dr. Cruz. CVJ

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