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Antimicrobial Use in Horses Undergoing Colic Surgery

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Background: Recommendations for antimicrobial prophylaxis for surgery are well-described in human medicine, but information is limited for veterinary practice.

Objective: To characterize antimicrobial use in horses undergoing emergency colic surgery.

Animals: A total of 761 horses undergoing emergency colic surgery (2001–2007).

Methods: Retrospective case review. Antimicrobial dose and timing, surgical description, and duration of treatment were collected from medical records. Associations between antimicrobial use and the occurrence of fever, incisional inflammation or infection, catheter-associated complications, or *Salmonella* shedding during hospitalization were analyzed using rank-sum methods and logistic regression.

Results: A total of 511 (67.2%) horses received an inappropriate amount of drug preoperatively. Median time from preoperative dose to incision was 70 (IQR 55–90) minutes; median total surgery time was 110 (IQR 80–160) minutes. Seventy-three horses were euthanized under anesthesia because of poor prognosis. Of 688 horses, 438 should have been redosed intraoperatively based on the duration of surgery. Only 8 (1.8%) horses were redosed correctly. Horses remained on perioperative antimicrobials a median of 3 (IQR 2–4.5) days. Antimicrobial therapy was reinstituted in 193 (28.9%) horses, and median days of total treatment were 3.8 (IQR 2–6). Signs that led to reinstituting therapy were fever (OR 3.13, $P = .001$) and incisional inflammation/infection (OR 2.95, $P = .001$). Horses in which treatment was reinstituted had 2.3 greater odds of shedding *Salmonella* ($P = .003$). Increased surgical time was associated with longer duration of antimicrobial therapy (OR 1.02, $P = .001$).

Conclusions and Clinical Relevance: Despite published recommendations regarding antimicrobial prophylaxis, compliance is poor; improvement might reduce postoperative complications.

Key words: Antibiotic choices; Clinical trials; Equine species; Evidence-based medicine; Perioperative management; Pharmacology.

In both human and veterinary medicine, antimicrobial administration for prevention and treatment of disease has led to important improvements in patient outcome. Antimicrobial administration is not without risk and indiscriminant antimicrobial use has been implicated in the emergence of drug resistant organisms commonly responsible for nosocomial infections and burgeoning human health care costs. In recent years, increased focus has been placed on the appropriate use of antimicrobials and adherence to recommended guidelines, including efforts in veterinary medicine.[1] Guidelines for appropriate antimicrobial use are targeted at maximizing therapeutic benefit, while minimizing the risks of patient complications and any negative impact on public health.

Perioperative prophylaxis is one of the most common reasons for antimicrobial administration, and might account for up to 95% of overall use in human surgical facilities. The goal of perioperative prophylaxis[1–3] is to decrease the likelihood of infection after exposure to bacteria during the surgical period (induction, surgery, recovery). In human patients, appropriate perioperative prophylaxis has been shown to decrease the incidence of surgical site infection (SSI) by almost 80% in clean-contaminated and contaminated surgeries when used in conjunction using aseptic technique.[4,5] Decreased SSIs correlate with shorter hospitalization, reduced risk of postoperative complications, and lower treatment costs.[4,6,7] Antimicrobial prophylaxis is recommended for surgeries with an increased risk of infection, procedures in which complications associated with infection can be life threatening, or those that involve implanted prosthetic material.[8] To maximize efficacy of prophylaxis, antimicrobials should be selected based on the sensitivity of likely bacterial contaminants, administered intravenously in time to allow appropriate concentrations to accumulate in serum and tissues before incision, and be maintained at a therapeutic concentration throughout the surgery.[9,10]

Abbreviations:

IQR	interquartile range (25 and 75%)
SSI	surgical site infection

Reported compliance with prophylaxis guidelines in human medicine is variable.[11] The percentage of human patients receiving preoperative doses within 60 minutes of the start of surgery range from 56 to 98%.[11–13] Published guidelines regarding prophylactic antimicrobial use in veterinary patients are few,[1,14–18] and in many cases, recommendations are extrapolated from human literature.[19,20] In studies reporting on prophylactic antimicrobial use in veterinary medicine, compliance with guidelines varied with the species evaluated. Only 6.3%

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of horses undergoing elective arthroscopy received preoperative antibiotics within 60 minutes of the 1st incision, while 78% of dogs received their preoperative dose within the appropriate time frame.[17,18]

Colic surgery in the horse is typically an emergency procedure, classified in the best circumstances as a clean-contaminated surgical procedure. Suggested guidelines for perioperative antimicrobial prophylaxis in clean-contaminated procedures such as colic surgery are presented in Table 1. Complications after colic surgery that might be reduced by increasing the efficacy of antimicrobial prophylaxis include SSI, peritonitis, thrombophlebitis, and pneumonia. Antimicrobial therapy has been identified as a risk factor for the development of colitis[21] and salmonellosis[22,23] in the horse. In addition, horses undergoing colic surgery are at increased risk for shedding *Salmonella*.[24] Evaluation of antimicrobial use in horses undergoing colic surgery and degree of adherence to accepted guidelines is warranted in this population of animals. The purpose of this retrospective study was to describe antimicrobial use in horses undergoing colic surgery and evaluate factors that influenced prescribing behavior. Our hypothesis was that antimicrobial use and compliance would reflect published guidelines for prophylaxis, but that clinical factors would influence prescribing behavior.

Materials and Methods

A retrospective study was conducted at the George D. Widener Hospital of the University of Pennsylvania School of Veterinary Medicine to evaluate antimicrobial use practices in horses undergoing colic surgery. Medical records of horses having had colic surgery between January 2001 and December 2007 were reviewed. Horses administered antimicrobials before colic surgery for preexisting conditions (including other surgical procedures), or horses with a comorbidity not associated with colic surgery that could have impacted prescribing behavior were excluded.

Information obtained from the medical record included signalment, preoperative drug/dose information, number of antimicrobial classes administered, time from antimicrobial administration to 1st surgical incision, and duration of surgical procedure. Based on the horse's weight recorded in the medical record and both expert opinion and published doses for commonly used antimicrobials (Table 2), it was determined if the horse received an appropriate preoperative dose.

Surgical diagnosis was collected and categorized as follows: (1) simple obstruction, (2) nonstrangulating small or large intestine displacement, (3) small or large intestine inflammatory disease, or (4) strangulating/vascular compromise of the small or large intestine. Antimicrobial administration during surgery, such as intravenous redosing, intra-abdominal antimicrobial lavage, or peri-incisional antimicrobial infusion, was also recorded. To determine if antimicrobials should have been redosed during surgery, the time of preoperative administration was compared with the total duration of surgery. Horses that were still in surgery more than $2 \times t^{1/2}$ for time-dependent antimicrobials (Table 2) were identified as needing to be redosed intraoperatively.[25–30] With the exception of ceftiofur, all half-lives given in Table 2 are based on IV administration. Because of presence of active metabolites, consensus data on the half-life of ceftiofur in adult horses after IV administration are lacking. We therefore used the most detailed information available after IM dosing to derive the half-life for ceftiofur.[30] Horses euthanized on the table were excluded from this part of the analysis.

Surgical outcome was recorded as either recovering from anesthesia, or euthanasia during surgery; overall outcome was recorded as discharged from the hospital, or euthanized postoperatively during hospitalization. Perioperative antimicrobial therapy was defined as the number of days of continuous antimicrobial administration starting with the preoperative dose until treatment was discontinued. Changes in drug administered, drug class, or dose were recorded. Reinstituting antimicrobial therapy was defined as discontinuation of treatment for $\geq$ 24 hours, before reinitiating antimicrobial therapy in the postoperative period. Total days of antimicrobial therapy during hospitalization was also collected.

Information regarding the occurrence of fever, incisional complications, thrombophlebitis or catheter-associated complications, and *Salmonella* shedding were collected. Fever was defined as rectal temperature > 101.5°F at any point in the postoperative

Table 1. Suggested guidelines for antimicrobial prophylaxis in patients undergoing clean-contaminated surgical procedures.

Antimicrobials are indicated for all clean-contaminated surgical procedures
Antimicrobial selection should be based on efficacy against common bacterial contaminants for the type of procedure performed
Broad-spectrum antimicrobials are recommended, but prophylactic therapy should consist of lower generation drugs, in an effort to minimize emergence of resistant bacterial strains
Antimicrobials should be administered intravenously, ideally within 30–60 minutes before the 1st surgical incision
Patients should be redosed intraoperatively if surgery is still ongoing 2 half-lives after the preoperative dose
Standard aseptic technique and infection control measures should be rigorously followed during clean-contaminated procedures; antimicrobial therapy should not be expected to compensate for poor technique

Adapted from references 1, 15, 26, and 27.

Table 2. Dose range and half-lives (time-dependent drugs only) of antimicrobials used for surgical prophylaxis and postoperative treatment in horses undergoing colic surgery.

Antimicrobial Drug	Dose Range	Half-Life (t½)
Potassium Penicillin G	22,000–44,000 IU/kg	40 minutes[34]
Gentamicin	6.6–8.8 mg/kg	—
Ceftiofur[a]	2.2–5.0 mg/kg	189 minutes[30]
Procaine Penicillin G	25,000 IU/kg	19.7 hours[35]
Cefazolin	11.0–22.0 mg/kg	46 minutes[40]
Ampicillin	15.0–20.0 mg/kg	120 minutes[41]
Enrofloxacin	5.0–10.0 mg/kg	—
Metronidazole	15.0–25.0 mg/kg	—
Ticarcillin-clavulanate[b]	50.0 mg/kg	60 minutes[42]
Amikacin	15.0–25.0 mg/kg	—
Oxytetracycline[c]	6.6 mg/kg	12.95 hours[43]

[a]The half-life given is for ceftiofur and metabolites after IM administration, t½ of ceftiofur per se is 16 minutes.

[b]The half-life given is for ticarcillin, t½ for clavulanic acid after IV administration is 24 minutes.

[c]Tetracyclines have both time- and concentration-dependent features.

period. Incisional complications were characterized by any of the following: drainage from incision, observation of clinical signs that led the clinician to culture the incision (regardless of microbiological findings), continuation of antimicrobial therapy targeting incisional infection described in the medical record, or evidence that the horse was discharged while being treated with antimicrobials caused by a suspected incisional infection. For this study, a catheter-associated complication was defined as inflammation at the catheter site or along the jugular vein that required treatment, or confirmed diagnosis of jugular vein thrombosis or thrombophlebitis sonographically. From August 2004 to December 2007, infection control protocols required fecal sampling for *Salmonella* from all horses admitted for colic both on admission and twice weekly during hospitalization; additional samples were collected based on the development of clinical signs of fever > 102.5°F, leukopenia, or diarrhea. A single positive culture result identified the animal as shedding *Salmonella*.

Statistical Analysis

A statistical software program was used to perform all statistical analyses.[a] Descriptive statistics were determined for all variables. For categorical variables, 95% confidence intervals were calculated using the Agresti–Coull method. Descriptive statistics were used to assess both preoperative dose, and timing relative to 1st surgical incision. Similarly, intraoperative antimicrobial use, such as redosing during surgery, and administration of intra-abdominal or peri-incisional drug, were reported descriptively. As clinical efficacy of an antimicrobial drug relates to dose and timing of administration, 2 new categorical variables were created that were defined as the horse receiving both the correct dose, and within either 30 or 60 minutes of the 1st incision. Wilcoxon rank-sum methods were used to determine preliminary associations between preoperative antimicrobial administration and complications. Logistic regression was used to quantify associations where applicable. The association between reinstituting antimicrobial therapy or changing antimicrobial class in the postoperative period, and development of clinical findings such as fever, evidence of incisional complication, catheter-associated complication or *Salmonella* shedding were similarly examined.

To evaluate the relationships of surgical diagnosis and duration to prescribing pattern, antimicrobial use was classified as: 0 = perioperative antimicrobials $\leq$ 24 hours, 1 = 24–72 hours perioperative antimicrobials, and 2 = >72 hours antimicrobial administration. A proportional odds model (ordered logistic regression) was used to determine the association between surgical duration and prescribing pattern. Spearman's correlation and Kendall's tau were used to determine whether surgical diagnosis (disease category) was correlated with antimicrobial prescribing pattern.

The relationship between reinstituting antimicrobial therapy or changing antimicrobial class during hospitalization, and presence or absence of postoperative complication, was analyzed using Wilcoxon rank-sum methods to determine preliminary associations, and quantified using logistic regression where applicable. A P value of $< .05$ was considered significant for all comparisons.

Results

A total of 761 horses with a median age of 8 years (IQR: 3–13 years, range 0.5–32 years) met the inclusion criteria. A total of 348 females (45.7%), 111 males (14.6%), and 302 geldings (39.7%) comprised the study population. Thoroughbreds were the most common breed (n = 351, 46.1%), followed by Standardbred (n = 88, 11.6%), Quarter Horse/Quarter Horse cross (n = 82, 10.8%), Warmblood (n = 73, 9.6%), pony or miniature horse (n = 48, 6.3%), and Arabian breeds (n = 43, 5.7%). Draft or draft crosses (n = 17, 2.2%) and a variety of other breeds (n = 59, 7.8%) made up the remainder of the study population.

A total of 599 horses received potassium penicillin G (IV) and gentamicin (IV) preoperatively, 81 received a combination of procaine penicillin G and gentamicin, 16 were given ceftiofur and gentamicin, and 21 received cefazolin and gentamicin. Other less commonly used preoperative antimicrobials were amikacin, enrofloxacin, oxytetracycline, and ticarcillin-clavulanate (Table 3). Average doses for the most commonly used antimicrobials used were as follows: potassium penicillin G 24,800 iu/kg; gentamicin 7.3 mg/kg; ceftiofur 3.1 mg/kg, and cefazolin 21.6 mg/kg.

Based on the dose ranges shown in Table 2, only 250/761 horses (32.9%) received the appropriate dose for antimicrobials administered. For the most common antimicrobial combination (potassium penicillin G and gentamicin administered intravenously), 207/599 (34.6%) horses were given the appropriate dose of both drugs. Two hundred and fifty (41.7%) horses were dosed inappropriately for 1 drug. In 182 horses in which the penicillin dose was correct, 122 horses were underdosed with gentamicin, and 62 were overdosed. When the dose of gentamicin was appropriate, 64 horses received too low a dose of penicillin, and 2 were given a dose higher than the reference range. The dose of both drugs was inappropriate in 142 (23.7%) horses; in 123, both antimicrobials were too low, 8 both were too high, 10 penicillin was low and gentamicin was high, and 1 penicillin was high and gentamicin low. For all horses given the potassium penicillin G, gentamicin drug combination, underdosing was the most common error (320/406 errors, 78.8%). Gentamicin was underdosed 41.1% of the time (246/599 horses) and penicillin 32.9% of the time (197/599 horses).

In horses underdosed with penicillin or gentamicin, the mean difference between the amount of drug given and the lowest acceptable dose (Table 2) was 2.3 IU

Table 3. Preoperative combinations of antimicrobials used for surgical prophylaxis in horses undergoing colic surgery (N = 761).

Preoperative Antimicrobial Combination	Surgical Colics Treated N (%)
Potassium Penicillin and Gentamicin	599 (78.7)
Potassium Penicillin and Ceftiofur	1 (0.1)
Potassium Penicillin and Enrofloxacin	6 (0.8)
Potassium Penicillin and Amikacin	5 (0.7)
Potassium Penicillin alone	7 (0.9)
Cefazolin and Gentamicin	21 (2.8)
Ceftiofur and Gentamicin	16 (2.1)
Ceftiofur alone	9 (1.2)
Ampicillin and Gentamicin	1 (0.1)
Procaine Penicillin G and Gentamicin	81 (10.6)
Procaine Penicillin G alone	8 (1.1)
Ticarcillin and Clavulanic Acid	1 (0.1)
Gentamicin alone	6 (0.8)

(95% CI 2.1–2.6, range 0.1–12, average 10.7% lower than the bottom of the dose range) for penicillin and 1.1 mg/kg (95% CI 0.9–1.2, range 0.1–5.9, average 16.1% lower than the bottom of the dose range) for gentamicin. In horses that received doses above the reference range, the difference for penicillin was 10.7 IU (95% CI 1.5–19.9, range 1–44, average 24.3% higher than the top of the dose range) and for gentamicin was 3.3.mg/kg (95% CI 0.9–5.7, range 0.1–54.4, average 37.4% higher than the top of the dose range).

Of the 162 horses that received a less common antimicrobial combination (Table 3), 30 received a single preoperative medication, which was appropriately dosed on 12 (40%) occasions and inappropriately dosed on 18 (60%). One hundred and thirty-two were given a combination of antimicrobials, doses of which were appropriate in 31 (23.5%) cases, 1 antimicrobial was inappropriately dosed in 53 (40.2%) cases and both were inappropriate in 48 (36.4%) cases. The most common error observed in horses receiving perioperative antimicrobials other than the potassium penicillin G/gentamicin combination was again underdosing (134/167 errors, 80.2%). For all preoperative antimicrobials given, 79.2% of the errors were those of underdosing.

Horses were administered the preoperative dose a median of 70.0 minutes (IQR 55–80 minutes, range 0–455 minutes, mean 77.8 ± 1.5 minutes, sd 42.1 minutes) before the start of the surgical incision. The largest proportion of horses undergoing emergency colic surgery had a strangulating or vascularly compromising lesion (n = 317, 41.7%), followed by simple displacement or malposition of either the large or small bowel (n = 249, 32.6%). One hundred and fifty-two (20%) horses taken to surgery had a simple intraluminal obstruction, whereas far fewer were explored for what was ultimately identified as a primary inflammatory lesion (n = 43, 5.7%). Total surgery time was a median of 110 minutes (IQR 80–160, range 35–400 minutes, mean 125.7 ± 2.4 minutes, sd 62.7 minutes). Based on surgical findings and associated prognosis, 73 horses were euthanized under anesthesia. Of the 688 remaining horses in which surgical treatment was pursued, 438 (63.7% ± 1.8, 95% CI 60.0–67.2) should have been redosed with a time-dependent antimicrobial based on surgical duration and drug half-life (because of the long half-life, horses receiving procaine penicillin G were classified as not requiring redosing). Twelve horses were redosed intraoperatively (1.7% ± 0.5, 95% CI 1.0–3.1); interestingly, 4 of these horses did not need to be redosed, indicating that only 8 horses were redosed correctly. Ninety-nine (14.4% ± 1.3, 95% CI 12.0–17.2) horses received additional intra-abdominal antimicrobials in the form of lavage. Combination of potassium penicillin G (5–20 IU) and gentamicin (0.5–2 g) was the most common intra-abdominal treatment (70/99 horses, 70.7%). Other agents used intra-abdominally included combinations of cefazolin and gentamicin (n = 6), ceftiofur and gentamicin (n = 1), as well as potassium penicillin G (n = 4), gentamicin (n = 4), cefazolin (n = 7), ceftiofur (n = 1) and triple antibiotic (n = 1) given alone. On 5 occasions, the anesthesia record indicated that intra-abdominal lavage of antimicrobials had taken place, but the agents used were not recorded. Although doses of antimicrobial administered intra-abdominally are given here, they were only recorded 47.4% of the time; hence, the accuracy of the dose information remains uncertain. There were also 13 horses (1.9% ± 0.5, 95% CI 1.1–3.2) that had an antimicrobial drug placed peri-incisionally; only amikacin (500–750 mg) was used for this purpose.

Horses remained on perioperative antimicrobials a median of 3.0 continuous days (IQR 2.0–4.5 days, range 0–32 days, mean 3.8 days ± 0.1, 95% CI 3.6–4.0, sd 2.9 days). Four hundred and fifteen (60.3% ± 1.9, 95% CI 56.6–63.9) horses developed fever (T > 101.5°F) during the postoperative period. Of 688 horses recovered from surgery, 107 (15.5% ± 1.4, 95% CI 13.0–18.4) developed clinical signs consistent with incisional infection during hospitalization, and 77/688 (11.2% ± 1.2, 95% CI 9.0–13.8) horses either required treatment for a catheter-associated complication or had a confirmed diagnosis of thrombophlebitis sonographically. Horses were hospitalized for a median of 7.0 days (IQR 5–10 days, range 0–71, mean 8.9 days ± 0.3, 95% CI 8.1–9.1, sd 7.0 days). Of the 761 horses undergoing colic surgery from 2001 to 2007, 82.1% (n = 625) were discharged. Seventy-three horses were euthanized under general anesthesia at the recommendation of the surgeon. In the 688 horses in which surgical treatment was pursued, 42 horses (6.7%) required repeat celiotomy at least once (excluded from further analysis), and 63 were euthanized in hospital during the recovery period. The survival rate of horses treated surgically was 90.8%, with 9.2% euthanized postoperatively.

Preoperative timing was investigated in 2 ways: as the horse receiving the preoperative drug 30 minutes before 1st surgical incision, and the horse receiving the preoperative drug 60 minutes before 1st surgical incision. With the more rigid criterion of 30 minutes before the start of surgery, only 23 horses received antimicrobials at the correct dose and correct time (3.0%), with 738 horses (97.0%, 95% CI 95.8–98.2%) receiving either the incorrect dose or the drug more than 30 minutes before the 1st surgical incision. Using the timing criterion of 60 minutes before incision, 88 horses were medicated correctly (11.6%), with 673 (88.4%, CI 86.2–90.7%) medicated incorrectly. There were no statistically significant associations between preoperative antimicrobial use pattern and postoperative complications, regardless of the timing criterion used.

Prescribing pattern (0–2) during hospitalization was not correlated with surgical diagnosis identified intraoperatively (Spearman's $P = .120$, Kendall's tau $P = .220$). Prescribing pattern was associated with duration of the surgery; for every additional minute of surgical time, the horse had a 2% increase in the log odds of staying on antimicrobials for a longer period of time (OR = 1.02, 95% CI 1.01–1.02, $P < .001$).

In the postoperative period, antimicrobial therapy was reinstituted in 193 horses (28.9 ± 1.8, 95% CI 25.4 –32.3). Febrile (>101.5°F) horses had 3 times greater odds of having antimicrobial therapy reinitiated (OR = 3.13, 95% CI 2.13–4.60, $P < .001$) compared with those that remained afebrile in the postoperative period. Similarly, horses with clinical signs consistent with incisional infection were also at increased odds for having antimicrobial treatment reinstituted, OR = 3.30, 95% CI 2.15–5.07, $P < .001$. There was no association between signs of catheter-associated complication and reinstitution of antimicrobial therapy ($P = .440$). One hundred and sixty-nine horses (24.6% ± 1.6, 95% CI 21.5–27.9) underwent a change in antimicrobial class in the postoperative period. Change in class was similarly associated with fever or signs of incisional infection (OR = 2.98, 95% CI 1.99–4.45, $P < .001$ and OR = 2.95, 95% CI 1.91–4.53, $P < .001$, respectively), but was not significantly associated with signs of catheter-associated complication. There were no apparent associations ($P > .05$) between change in antimicrobial dose (N = 53, 7.0% ± 0.9, 95% CI 5.4–9.0) and any postoperative complication. *Salmonella* status was only evaluated after implementation of active surveillance in August 2004 (n = 365 horses). Seventy-four horses were confirmed as positive on fecal culture (20.3% ± 2.1, 95% CI 16.1–24.4). Horses reinstituted on antimicrobials were at increased odds for shedding *Salmonella,* OR = 2.3, 95% CI 1.3–4.0, $P = .003$. There were no associations between change in antimicrobial class ($P = .362$) or change in dose ($P = .690$), and *Salmonella* status.

Discussion

This study revealed the majority of horses treated for surgical colic in our hospital received inaccurate antimicrobial prophylaxis, both in terms of dose received and when the drug was given. As clinical trials evaluating antimicrobial use in veterinary patients are limited,[15–18,31] many institutions base antimicrobial use on consensus statements,[1] recommendations for human patients,[19,20,28,29] or common practice. The need for surgical prophylaxis has been demonstrated in veterinary surgery.[18] Moreover, the efficacy of timing and duration of antimicrobial prophylaxis has been reported; a single, preoperative dose of antibiotic proved as effective as a longer course of treatment in reducing complications after rumentomy in cattle.[17] Based on a recent meta-analysis in human patients, which concluded that the efficacy of antimicrobial prophylaxis was independent of surgery type,[32] it seems justified to apply general published recommendations to colic surgery in the horse (Table 1). Following discussions on antimicrobial prophylaxis in formal rounds settings and section meetings, the general consensus in our hospital was that a horse undergoing colic surgery was appropriately dosed within 60 minutes of the start of surgery. The clinical impression of surgeons and criticalists during these discussions was that the guidelines for antimicrobial prophylaxis were being observed. Until this study, no formal evaluation of how well in-hospital prescribing practices adhere to published guidelines had been performed at our institution. Information reported here describes deviation from both the in-hospital perception of antimicrobial administration, and published recommendations for prophylaxis.

The majority of horses in this study received an inaccurate antimicrobial dose preoperatively. Underdosing was the most common dosing mistake made for all combinations of antimicrobial prophylaxis. Given that this was a retrospective study, it was impossible to know for certain the precise cause of the error in all cases, but failure to weigh the horse before surgery and failure to calculate the dose correctly (versus what appeared to be an estimate) were both observed in the medical record. Granted, in some violent colic patients, obtaining a weight might be impossible, but certainly in some cases it was overlooked or deemed inconvenient. Weighing a horse (and recording the weight in the record) can be made part of the standard admission, thus increasing the ease and accuracy of drug calculation.

In addition to horses receiving the incorrect dose of antimicrobials preoperatively, often the timing of administration was inadequate. Horses frequently received the preoperative dose more than an hour before the start of surgery (mean interval, 77.8 minutes) even though these patients were being taken to surgery on an emergency basis. Only 88 (11.6%) horses in the study received the appropriate preoperative dose within 60 minutes of the start of surgery. The association between administering penicillin under general anesthesia and the development of hypotension often results in preoperative antimicrobials being given before induction. In the original study[33] evaluating the physiologic effects of sodium penicillin administered under general anesthesia in 5 horses, mean arterial pressure did undergo a statistically significant decrease (8–15 mmHg, depending on the horse), but the clinical importance of this might be animal-dependent. The authors' recommendations[33] were to monitor blood pressure if penicillin is to be administered under anesthesia. Interestingly, the degree to which mean arterial pressure decreased with the administration of sodium cefazolin was similar, but did not reach statistical significance.

As a result of the findings reported here, a formal protocol for prophylactic antimicrobial therapy was developed in our hospital. The protocol was reviewed by the relevant sections (Anesthesia, Emergency/Critical Care, Surgery) and those involved in performing colic surgery. In horses undergoing emergency colic surgery, the preoperative dose is now administered following induction and instrumentation with cardiovascular monitoring equipment. Once appropriate mean arterial pressures are confirmed, the preoperative medications are slowly given while the patient is closely monitored and prepared aseptically for surgery. If the anesthesiologist has concerns regarding the cardiovascular stability of the patient, an alternative

antimicrobial can be administered. To date, this approach has not been associated with observed hemodynamic complications, but is in the process of prospective evaluation. Similar recommendations for antimicrobial prophylaxis given on or shortly after induction seem to be safe in human patients.[28]

Given the pharmacokinetic data[25,30,34–36] available for the most commonly used prophylactic antimicrobials (potassium penicillin G, gentamicin); we also chose to evaluate how many horses received the appropriate dose of antimicrobials within 30 minutes of the start of surgery. Very few horses fell into this category, with only 23 (3.0%) meeting this criterion. Therapeutic drug concentrations for penicillin[34] and gentamicin[36] reach peak levels at the surgical site from 15 to 30 minutes after administration, and decline rapidly. Our recently implemented protocol targets a 30-minute interval from administration to 1st surgical incision in an attempt to maximize antimicrobial efficacy. Although no association was identified between preoperative dose and timing and the occurrence of postoperative complications, the number of horses correctly dosed at either 30 or 60 minutes before the 1st incision was very small (3.0 and 11.6%, respectively). We might therefore have failed to detect any positive effect of appropriate administration on decreasing the complication rate.

In some horses, additional antimicrobial therapy was used during surgery, either in the form of intraoperative abdominal lavage, or placed along the incision during closure. Unfortunately, because of the retrospective nature of this study and our suspicion that this information was not reliably entered in the record, we were unable to determine the actual frequency with which these treatments were administered, or draw any conclusions regarding efficacy.

Similar to a previously reported study,[15] compliance was poor with respect to published recommendations on redosing of antimicrobials during surgery. Animals should be redosed with time-dependent antimicrobials intraoperatively if surgical duration exceeds 2 half-lives of the drug.[28] Redosing only occurred in 12 (1.7%) horses, 4 of which were not required to be redosed at that time. It is impossible to determine in a retrospective study the exact cause of poor compliance. Surgeons might not be aware that the half-life of penicillin, the time-dependent antimicrobial most commonly used in surgical prophylaxis, is reported to be 30–40 minutes in horses.[25,34,35] The findings of this study suggest that antimicrobial concentrations could have been subtherapeutic during portions of the procedure considered at high risk for causing infection, such as complicated resection and anastomosis, or recovery from anesthesia.

In the majority of cases, antimicrobial therapy was continued for > 24 hours after surgery (mean 3.8 days). The benefit of prolonged antimicrobial therapy in the postoperative period has not been supported in the literature,[3,4,7,10] even in clean-contaminated surgeries.[37] Given concerns over the emergence of multidrug resistant bacteria in veterinary medicine,[1,14] antimicrobial administration should be evidence-based and risk-adverse, particularly, in a patient population that might be more susceptible to shedding *Salmonella*.[24]

Postoperative complications associated with clinicians choosing to prolong or reinstitute therapy were fever and signs of incisional inflammation/infection. While these are logical drivers of prescribing pattern, documentation of the incorrect dose, inappropriate timing preoperatively, lack of intraoperative redosing, and continuation of antimicrobials well into the postoperative provides strong evidence of misguided antimicrobial prophylaxis. This study revealed a relatively high incisional complication rate (15.6%), which might be underestimated because it is a large retrospective focused on data collected during hospitalization. As a result, incisional complications that developed after the horse was discharged would not have been included. The incisional complication rate, possibly indicative of ineffective antimicrobial prophylaxis, and increased risk of shedding *Salmonella* in patients reinstituted on antimicrobials, a further complication of antimicrobial use, suggest that closer scrutiny of antimicrobial use in the large animal veterinary setting is warranted. Additional studies are needed to confirm suggested guidelines are effective in large animal surgical patients. More importantly, antimicrobial use policies should be evaluated with the assurance of appropriate compliance. This study demonstrates there is often discrepancy between perceived adherence (ie, clinical impression) to commonly published recommendations and actuality (ie, evidence-based medicine).

It is possible that the level of critical illness in horses undergoing colic surgery could play a role in antimicrobial efficacy. In human patients, degree of critical illness,[38] volume of intravenous fluid resuscitation[39] and general anesthesia[39] have been identified as altering pharmacokinetics of commonly used antimicrobials. All these factors could play a role in the efficacy of antimicrobial prophylaxis in the horse undergoing colic surgery. Additional studies are needed to evaluate pharmacokinetics of commonly used antimicrobials in this patient population, and the possible influence of resuscitation and critical illness on efficacy of prophylaxis. While the cardiovascular effects of penicillin have been studied in horses under general anesthesia,[33] the influence of critical illness or volume of fluid resuscitation on penicillin pharmacokinetics has not been evaluated. In addition, periodic review of antimicrobial susceptibility patterns from bacteria recovered from surgical site infections could help inform prophylactic antimicrobial choices for colic surgery. Findings reported here also emphasize the importance of compliance monitoring with respect to antimicrobial guidelines for surgical prophylaxis; ample room for improvement exists.

Footnote

[a] STATA IC, version 11.2, College Station, TX

Acknowledgment

Conflict of Interest: Authors disclose no conflict of interest.

References

1. Morley PS, Apley MD, Besser TE, et al. Antimicrobial drug use in veterinary medicine. J Vet Intern Med 2005;19:617–29.

2. Bergquist EJ, Murphey SA. Prophylactic antibiotics for surgery. Med Clin North Am 1987;71:357–68.

3. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20(4):250–78.

4. Stone HH, Hooper CA, Kold LD. Antibiotic prophylaxis in gastric, biliary, and colonic surgery. Annal Surg. 1976;184:443–52.

5. Nichols RL. Preventing surgical site infections: A surgeon's perspective. Emerg Infect Dis 2001;7(2):220–4.

6. Southwood LL. Principles of antimicrobial therapy: What should we be using? Vet Clin Equine 2006;22:279–96.

7. Stratchounski LS, Taylor EW, Dellinger EP, Pechere JC. Antibiotic policies in surgery: A consensus paper. Int J Antimicrob Agent 2005;26:312–322.

8. Sanderson PJ. Antimicrobial prophylaxis in surgery: Microbiological factors. J Antimicrob Chemother 1993;31(Suppl B): 1–9.

9. Vasseur PB, Paul HA, Enos LR, Hirsh DC. Infection rates in clean surgical procedures: A comparison of ampicillin prophylaxis vs. a placebo. J Am Vet Med Assoc 1985;187(8):825–7.

10. Classen DC, Evans RS, Pestotnik SL, et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 1992;326(5):281–6.

11. Vaisbrud V, Raveh D, Schlesinger AM. Surveillance of antimicrobial prophylaxis for surgical procedures. Infect Control Hosp Epidemiol 1999;20(9):610–3.

12. Weed HG. Antimicrobial prophylaxis in the surgical patient. Med Clin North Am 2003;87(1):59–75.

13. Kao LS, Lew DF, Doyle PD, et al. A tale of 2 hospitals: A staggered cohort study of targeted intervention to improve compliances with antibiotic prophylaxis guidelines. Surgery 2010;148(2):255–62.

14. Traub-Dargatz JL, Dargatz DA, Morley PS. Antimicrobial resistance: What's the big deal? Importance of antimicrobial resistance to the equine practitioner. AAEP Proceedings 2002;48:138–44.

15. Weese SJ, Cruz A. Retrospective study of perioperative antimicrobial use practices in horses undergoing elective arthroscopic surgery at a veterinary teaching hospital. Can Vet J 2009;50:185–8.

16. Weese JS, Halling KB. Perioperative administration of antimicrobials associated with elective surgery for cranial cruciate ligament rupture in dogs: 83 cases (2003–2005). J Am Vet Med Assoc 2006;229(1):92–5.

17. Haven ML, Wichtel JJ, Bristol DG, et al. Effects of antibiotic prophylaxis on post-operative complications after rumenotomy in cattle. J Am Vet Med Assoc 1992;200:1332–5.

18. Whittem TL, Johnson AL, Smith CW, et al. Effect of perioperative prophylactic antimicrobial treatment in dogs undergoing elective orthopedic surgery. J Am Vet Med Assoc 1999;215:212–216.

19. Page CP, Bohnen JM, Fletcher JR, et al. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. Arch Surg 1993;128(1):79–88.

20. Steinberg JP, Braun BI, Hellinger WC, et al. Timing of antimicrobial prophylaxis and the risk of surgical site infections: Results from the trial to reduce antimicrobial prophylaxis errors. Annal Surg 2009;250(1):10–6.

21. Baverud V, Gustafsson A, Franklin A, et al. *Clostridium difficile* associated with acute colitis in mature horses treated with antibiotics. Equine Vet J 1997;29(4):279–84.

22. Hird DW, Casebolt DB, Carter JD, et al. Risk factors for salmonellosis in horses. J Am Vet Med Assoc 1986;188(2): 173–7.

23. House JK, Mainar-Jaime RC, Smith BP. Risk factors for nosocomial *Salmonella* infections among hospitalized horses. J Am Vet Med Assoc 1999;214(10):1511–6.

24. Ekiri AB, Mackay RJ, Gaskin JM, et al. Epidemiologic analysis of nosocomial *Salmonella* infections in hospitalized horses. J Am Vet Med Assoc 2009;234:108–19.

25. Dowling PM, Davis JL. Antimicrobial therapy. In: Reed SM, Bayly WM, Sellon DC, eds. Equine Internal Medicine, 3rd ed. St. Louis, MO: Saunders Elsevier; 2010:169–89.

26. Prescott JF. Beta-lactam antibiotics: Penam penicillins. In: Prescott JF, Baggot JD, Walker RD, eds. Antimicrobial Therapy in Veterinary Medicine, 3rd ed. Ames, IA: Iowa State Press University; 2000:120.

27. Sullivan-Hackett E, Orsini JA, Divers TJ. Equine emergency drugs: Approximate doses and adverse drug reactions. In: Orsini JA, Divers TJ, eds. Equine Emergencies: Treatment and Procedures, 3rd ed. St. Louis, MO: Saunders Elsevier; 2008:739–52.

28. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project. Am J Surg 2005;189:395–404.

29. Howe LM, Booth HW Jr. Antimicrobial use in the surgical patient. Vet Clin Small Anim 2006;36:1049–60.

30. Jaglan PS, Roof RD, Yein FS, et al. Concentration of ceftiofur metabolites in the plasma and lungs of horses following intramuscular treatment. J Vet Pharmacol Therap 1994;17:24–30.

31. Freeman KD, Southwood LL, Lane J, et al. Postoperative infection, pyrexia, and perioperative antimicrobial drug use in surgical colic patients. Equine Vet J 2012;44:476–81.

32. Bowater RJ, Stirling SA, Lilford RJ. Is antibiotic prophylaxis in surgery a generally effective intervention? Testing a generic hypothesis over a set of meta-analyses. Annal Surg 2009;249 (4):551–6.

33. Hubbell JA, Muir WW, Robertson JT, Sams RA. Cardiovascular effects of intravenous sodium penicillin, sodium cefazolin, and sodium citrate in awake and anesthetized horses. Vet Surg 1987;16(3):245–50.

34. Horspool LJI, McKellar QA. Disposition of penicillin G sodium following intravenous and oral administration to equidae. Br Vet J 1995;151:401–12.

35. Love DN, Rose RJ, Martin CA, Bailey M. Serum concentrations of penicillin in the horse after administration of a variety of penicillin preparations. Equine Vet J 1983;15(1):43–8.

36. Magdesian KG, Hogan P, Cohen ND, et al. Pharmacokinetics of a high dose of gentamicin administered intravenously or intramuscularly to horses. J Am Vet Med Assoc 1998;213:1007–11.

37. De Chiara S, Chiumello D, Nicolini R, et al. Prolongation of antibiotic prophylaxis after a clean and clean-contaminated surgery and surgical site infection. Minerva Anestesiol 2010;76 (6):413–9.

38. Goncalves-Pereira J, Povoa P. Antibiotics in the critically ill patient: A systematic review of the pharmacokinetics of β-lactams. Crit Care 2011;15:R206.

39. Pea F, Viale P, Furlanut M. Antimicrobial therapy in critically ill patients: A review of pathophysiological conditions responsible for altering disposition and pharmacokinetic variability. Clin Pharmacokinet 2005;44(10):1009–34.

40. Sams RA, Ruoff WW Jr. Pharmacokinetics and bioavailability of cefazolin in horses. Am J Vet Res 1985;46:348–52.

41. Sarasola P, McKellar QA. Pharmacokinetics and applications of ampicillin sodium as an intravenous infusion in the horse. J Vet Pharmacol Therap 1993;16:63–9.

42. Sweeney RW, Beech J, Simmons RD, Soma LR. Pharmacokinetics of ticarcillin and clavulanic acid given in combination to adult horses by intravenous and intramuscular routes. J Vet Pharmacol Therap 1988;11:103–8.

43. Horspool LJI, McKellar QA. Disposition of oxytetracycline in horses, ponies and donkeys after intravenous administration. Equine Vet J 1990;22:284–5.