Reports of Retrospective Studies


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Summary: Case records of 200 horses treated with metronidazole were reviewed. Horses were treated for respiratory tract infections (90 cases), peritonitis or abdominal abscess (39 cases), celiotomy (49 cases), orthopedic infections (6 cases), and miscellaneous soft tissue infections (16 cases). Bacteria of the genus Bacteroides were most prevalent (55 of 167 anaerobic isolates). Metronidazole was always used in combination with other antimicrobial drugs.

Only 4 of the 200 horses had signs of adverse effects associated with metronidazole treatment. Those 4 horses had poor appetite that resolved when metronidazole treatment was discontinued.

Metronidazole (1-2-hydroxyethyl-2-methyl-5-nitroimidazole) is an antibacterial agent used for the treatment of infections caused by anaerobic protozoa and bacteria. The importance of anaerobic bacterial infections in horses has been described,1-3 and the resistance of anaerobic bacterial pathogens (isolated from human patients) to commonly used antimicrobial agents has been recognized.4-6 Metronidazole has a broad spectrum of antibacterial activity against anaerobes in vitro,5-7 and the successful use of metronidazole for the treatment and prevention of anaerobic infections in human patients has been described.7-10 The pharmacokinetics of metronidazole in the horse have been described,11,12 but reports of the clinical use of metronidazole are scarce.13,14 The purpose of the study reported here was to review the clinical use of metronidazole in horses in an attempt to describe the response to treatment and the rate of complications associated with metronidazole usage.

Criteria for Selection of Cases

Records of horses admitted to the George D. Widener Hospital for Large Animals, New Bolton Center, University of Pennsylvania School of Veterinary Medicine between July 31, 1984 and June 1, 1989 were reviewed. Case records of horses treated with metronidazole were evaluated. The diagnosis, duration of treatment, bacteriologic culture results, concurrent antimicrobial treatment, clinical outcome, and complications were reviewed.

Results

There were 21,058 horses admitted to the hospital during the period studied. Records from 200 horses treated with metronidazole were retrieved. An additional 19 horses were treated with metronidazole during this period but were not included in the study because of incomplete or unavailable case records. There were 103 males and 97 females. The mean age was 5.2 years (sd = 4.9 years), with a range of 2 weeks to 30 years, and 15 horses were < 6 months old. The breed distribution was as follows: 105 Thoroughbred, 60 Standardbred, 11 Quarter Horse, 8 Arabian, 6 Warmblood, 2 Morgan, 2 Appaloosa, 2 Paint Horse, and 4 ponies. There were 2 cases in the second half of 1984, 23 in 1985, 48 in 1986, 50 in 1987, 51 in 1988, and 26 in the first 5 months of 1989.

The most common dosage of metronidazole used was 15 mg/kg of body weight given q 6 h in 162 cases and q 8 h in 4 cases. A dosage of 20 to 25 mg/kg was used q 6 h in 21 horses and q 12 h in one horse. A dosage of 7.5 mg/kg q 6 h (the dosage in people) was used in 12 cases. The drug was administered orally to 196 of the 200 horses. Of those 196 horses, 9 with a gastrointestinal problem were given the drug IV and 13 were given the drug (crushed tablets suspended in water) per rectum because of ileus or intestinal obstruction. Four horses were given metronidazole only per rectum.

Infections involving the respiratory or gastrointestinal systems (where anaerobic bacteria are known to reside and anaerobic infections can frequently develop) were most commonly treated with metronidazole (Table 1). The 6 miscellaneous diagnoses not specified included protozoal myelitis, fever of unknown origin, hepatitis, perforated esophagus, salmonellosis, and open diagnosis. Metronidazole was used prophylactically in 49 celiot-
into the peritoneal cavity was possible. The most common; 51 of the 54 horses with peritonitis, the difference in the survival rates for horses with negative culture results (9/15) was not significant. From many specimens, more than one anaerobe was cultured; 167 organisms were isolated in some horses, and the diarrhea resolved while the horse was still being medicated with metronidazole.

Metronidazole was always used in combination with other antimicrobial drugs, including aqueous penicillin and gentamicin (159 of 200 horses), penicillin and amikacin (21 horses), trimethoprim-sulfa (15 horses, various sulfas, depending on product used). Of the 180 horses initially treated with metronidazole, penicillin, and an aminoglycoside (amikacin or gentamicin), 48 were switched to treatment with metronidazole and trimethoprim-sulfa for continued oral treatment after parenteral antimicrobial treatment was discontinued. Deleterious drug interactions were not observed in these horses. Other antimicrobials used with metronidazole, in lesser frequency, included ampicillin, erythromycin, neomycin, and rifampin.

Complications attributed to metronidazole were rare. Of the 200 horses treated with metronidazole, only 4 had complications attributed to metronidazole. These four horses had reduced appetite that improved or resolved within 24 hours after administration of the drug was discontinued. One additional horse developed mild, self-limiting diarrhea, but this horse was concurrently treated with a liquid diet that is known to cause diarrhea in some horses, and the diarrhea resolved while the horse was still being medicated with metronidazole.

**Discussion**

Metronidazole was used most commonly to treat horses with infections of the respiratory tract.
and abdominal cavity, or in cases in which contami-
nation of the abdomen with intestinal contents was considered possible. Metronidazole was fre-
cquently used in cases of pleuropneumonia, because of the known prevalence of anaerobic infections at these sites,\(^1,3\) and also because of the known resi-
dent anaerobic bacterial flora in the upper respira-
atory tract than can result in contamination or in-
fection with anaerobes. Similarly, metronidazole was frequently used to treat horses with peritonitis (or prevent peritonitis), because leakage of anaer-
oblic bacteria from the gastrointestinal tract can re-
result in anaerobic infection of the abdominal cavity. Additional evidence of anaerobic infection, such as foul breath odor and ultrasonographic findings, give even stronger indication for metronidazole treat-
ment in cases of pleuropneumonia.\(^1,3\)

Metronidazole was always used in combina-
tion with antimicrobials with antibacterial activity against aerobic bacteria. Of the 54 horses with positive anaerobic culture results, 94.4% also had aerobic bacteria isolated from the same specimen. Although metronidazole has bactericidal activity against some facultative anaerobic bacteria (when tested under anaerobic conditions), the activity is not uniform, and additional antimicrobials should be used.\(^7\) Bacteria of the genus *Bacteroides* were most prevalent in this study, and these (not just *B fragilis*) commonly are resistant to penicillin because of \(\beta\)-lactamase production.\(^5,6\) Although sim-
ilar data are not available for *Bacteroides* isolates of equine origin, and antimicrobial susceptibility testing was not performed on anaerobic bacteria iso-
lated in this report, possible resistance might be expected and metronidazole could be used if anaerobic infection is considered a possibility. Be-
cause anaerobic bacterial culture results are usually not available for several days after specimen sub-
mission, we recommend empiric treatment with metronidazole at the onset of treatment in severe cases of pleuropneumonia, because of the known prevalence of anaerobic infections (especially *Bac-
teroides* sp) in those horses.

The dosage of metronidazole used most fre-
cquently in the horses of this report was 15 mg/kg, po, q 6 h. This dosage was recommended in one report,\(^1,4\) although in another study,\(^1,2\) a dosage of 25 mg/kg q 12 h was suggested to be adequate.\(^1,2\) Only one horse in our study was medicated with 25 mg/kg q 12 h, so response to treatment of the 2 dosages cannot be compared. Therapeutic concentra-
tions of metronidazole in serum and peritoneal fluid are rapidly achieved with oral administration, and IV administration is necessary only if oral treatment is prevented by ileus.\(^1,11,12\) Metronidazole was used IV in some horses in this study, when the need for antianaerobic bacterial treatment was determined during surgery (eg, enterotomy), or when postoperative ileus prevented its use by the oral route. Although metronidazole is well ab-
sorbed when administered per rectum to human

\(^9\) the bioavailability of this drug when ad-
ministered per rectum to the horse is not known. Posttreatment serum concentration of metronida-

zole was not obtained in the horses in this study. Adverse effects following administration per rec-
tum were not observed.

In a review of pleuropneumonia,\(^1\) anaerobic bacterial infections were confirmed in 21 of 46 horses (45.7%) from which specimens were sub-
mitted for anaerobic bacteriologic culture, similar to the prevalence in the cases reported here (47.3%). A group of horses not treated with metroni-
dazole was not available for comparison of clinical outcome in this report. However, in the review\(^1\) of horses with pleuropneumonia (not treated with metronidazole), 7 of 21 horses (33.3%) with positive anaerobic bacterial culture results survived, compared with 18 of 36 (50%) in our study. Although improved survival may be in part attributable to improved antianaerobic bacterial treatment with metronidazole, other improvements in patient care might have affected survival rates. Even with metronidazole, the survival rate for horses with a positive anaerobic bacterial culture result (50%) was less than that for horses with a negative result (90%).

Complications or adverse effects attributable to metronidazole treatment in horses are appar-
ently rare. Gastrointestinal side effects, in particular nausea and vomiting, develop in 5 to 10% of human patients treated with metronidazole.\(^7\) Appetite suppression was apparent in 4 of the 200 horses (2%) in this report. Other complications re-
ported in people include dark urine, rash, and with prolonged or high-dose treatment, convulsions and peripheral neuropathy.\(^7\) Acute CNS dysfunction has been reported in dogs treated with metronidazole.\(^1,7\) Comparable adverse effects were not ob-
erved in these horses. Postanesthetic hindlimb paralysis in 2 horses treated with approximately 3 mg of metronidazole/kg by intraperitoneal injec-
tion at the time of celiotomy\(^14\) may have been asso-
ciated with anesthesia and recumbency. Several horses in this study were medicated with higher doses while under anesthesia, with no adverse ef-

Metronidazole has been used with few adverse effects in 200 horses with various conditions. Pro-
longed duration of treatment (up to 217 days) and treatment with metronidazole in combination with other antimicrobials (especially penicillin, genta-
micin, and trimethoprim-sulfamethoxazole) caused no apparent adverse effects. We believe that the survival rate for horses with anaerobic infections, particularly anaerobic pleuropneumonia, has improved since the usage of metronidazole was instituted in our hospital.

References


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**New Veterinary Biological Products**

<table>
<thead>
<tr>
<th>Product name</th>
<th>Species and indications for use</th>
<th>Route of administration</th>
<th>Remarks</th>
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<tbody>
<tr>
<td><em>Haemophilus somnus</em> ‒ <em>Pasteurella haemolytica</em>-multocida- <em>Salmonella typhimurium</em> bacterin (Texas Vet Lab, Inc, San Angelo, TX 76903)</td>
<td>For use in stocker and feeder calves as an aid in the prevention of respiratory disease associated with <em>Haemophilus somnus</em>, <em>Pasteurella haemolytica</em>, and <em>P. multocida</em> and salmonellosis caused by <em>Salmonella typhimurium</em></td>
<td>Subcutaneous</td>
<td>For veterinary use only</td>
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