Continuous infusion of gentamicin into the tarsocrural joint of horses

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Objective—To develop a method for continuous infusion of gentamicin into the tarsocrural joint of horses, to determine pharmacokinetics of gentamicin in synovial fluid of the tarsocrural joint during continuous infusion, and to evaluate effects of continuous infusion of gentamicin on characteristics of the synovial fluid.

Animals—12 healthy adult horses.

Procedure—An infusion catheter consisting of flow control tubing connected to a balloon infuser was used. Gentamicin solution (100 mg/ml) was infused in the right tarsocrural joint and balanced electrolyte solution was infused in the left tarsocrural joint for 5 days. Synovial fluid and serum gentamicin concentrations were measured by use of a fluorescence polarization immunoassay.

Results—17 of the 24 (71%) infusion catheters initially placed functioned without complications for the entire 5-day infusion period. Median gentamicin concentration in synovial fluid from treated joints during the 5-day infusion period ranged from 287.5 to 982 µg/ml. Median serum gentamicin concentration during this period ranged from 2.31 to 2.59 µg/ml. Mean (± SD) elimination half-life and total clearance of gentamicin from the synovial fluid were 6.25 ± 1.01 hours and 1.52 ± 0.96 ml/min, respectively.

Conclusions and Clinical Relevance—An infusion catheter can be used for continuous infusion of gentamicin into the tarsocrural joints of horses for up to 5 days. At a gentamicin dosage of 0.17 ± 0.02 mg/kg/h, continuous intra-articular infusion results in synovial fluid gentamicin concentrations greater than 100 times the minimal inhibitory concentration reported for common equine pathogens. (*Am J Vet Res* 2000;61:407–412)

Septic arthritis is a serious, potentially life-threatening condition in horses.[1-4] Infectious organisms gain entry into the synovial cavity hematogenously or via direct penetration, invoking an acute inflammatory response within the joint. The complex structure of the synovial membrane with its villous projections may allow bacteria to evade host defense mechanisms.[2] Additionally, severe inflammation results in impaired microcirculation, thrombosis, and necrosis of the synovial membrane.[2,3] Successful treatment of septic arthritis requires rapid elimination of the infection before permanent lameness develops secondary to irreversible cartilage damage, fibrosis, and osteoarthritis.[1-4]

Treatment of septic arthritis should always include administration of antibiotics.[1-5] Adjunct treatments used in horses with septic arthritis include systemic administration of anti-inflammatory medications, joint lavage, arthroscopic debridement, and open joint drainage with sterile bandaging.[4] Open joint drainage has been recommended for horses with persistent or severe septic arthritis.[1]

Aminoglycosides such as gentamicin are often used for treatment of horses with septic arthritis.[1,2,4,6,7] These antimicrobials have a concentration-dependent bactericidal action,[8,9] and clinical response to treatment correlates with the ratio of mean peak aminoglycoside concentration to minimal concentration of the aminoglycoside that will inhibit growth of the bacterial pathogen.[10] The **minimal inhibitory concentration (MIC)** of gentamicin for various common equine pathogens reportedly ranges from 2 to 4 µg/ml.[11,12] *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* are commonly isolated from horses with septic arthritis,[7] and MIC of gentamicin for these organisms are 0.8, 6.3, and 8.0 µg/ml, respectively.[13]

Recent investigations into treatment of horses with septic arthritis have focused on improving delivery of antimicrobials to the site of infection.[14,15] Peak mean concentrations of gentamicin in synovial fluid of the antebrachiocarpal joint following direct injection[11] (1,828 µg/ml) or regional limb perfusion[15,16] (589 µg/ml) were significantly higher than concentration obtained following systemic administration (2.5 µg/ml).[11] Administration of gentamicin into a joint to maintain synovial fluid drug concentrations well above the MIC would likely improve penetration of gentamicin into areas of the synovial membrane where bacterial colonization and impaired microcirculation limit effectiveness of systemic antibiotic treatment and would likely be advantageous in the treatment of horses with septic arthritis.[14,16] The purposes of the study reported here were to develop a method for continuous infusion of gentamicin into the tarsocrural joint of horses, to determine concentration and pharmacokinetics of gentamicin in synovial fluid of the tarsocrural joint during continuous infusion, and to evaluate the effects of continuous infusion of gentamicin on characteristics of the synovial fluid.

Materials and Methods

Horses—Twelve healthy adult horses of either sex and various breeds were used in the study. Prior to the study, horses did not have any signs of lameness associated with the tarsocrural joints, and results of CBC were normal. Horses

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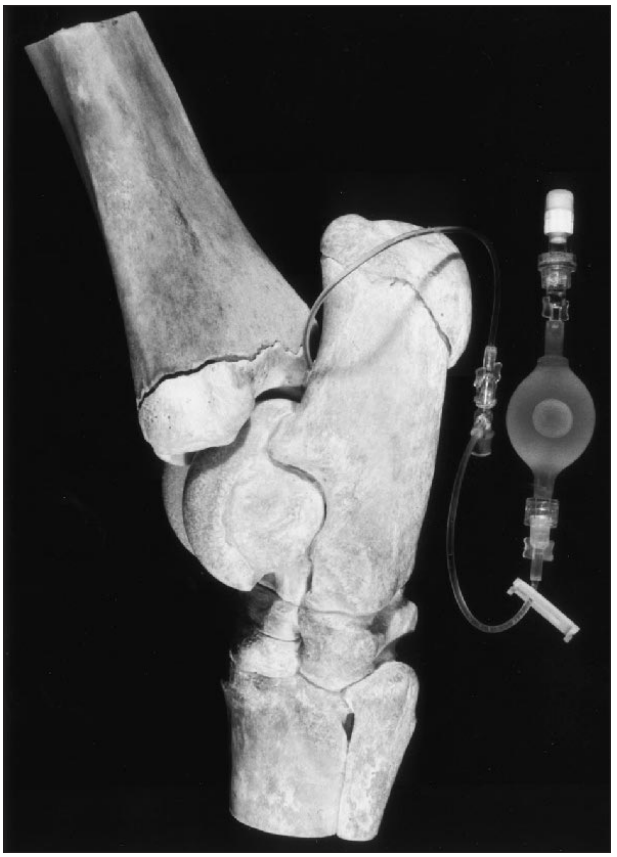

Figure 1—Photograph of an infusion catheter for continuous administration of gentamicin in the plantarolateral pouch of the tarsocrural joint in horses. The infusion catheter consisted of flow control tubing connected to a balloon infuser by use of an extension set with a T-connector.

were confined to box stalls throughout the study. The Purdue University Animal Care and Use Committee approved the study protocol.

Catheter and infusion system—Catheters used in the study were created by modifying commercially available flow control tubing.[a] Rate of flow of a **balanced electrolyte solution (BES)** through the tubing had previously been determined to be 10 ml every 8 hours. To create the catheters used in the study, the male adapter end was cut off the flow control tubing, and an extension set with a T-connector[b] was used to connect the tubing to a 36-ml latex balloon infuser[c] **(Fig 1)**.

Because the effect that viscosity of the gentamicin solution to be used in the study would have on flow rate through the infusion catheter was not known, in vitro rates of flow of the gentamicin sulfate solution (100 mg/ml) and of BES through the infusion catheter were determined. Infusion balloons for 12 infusion catheters were filled with 20 ml of gentamicin solution (n = 6) or BES (n = 6), and fluid passing through each catheter was collected. Balloons were assessed after 12 hours and refilled to a volume of 20 ml if required. Total volume of fluid collected over a 24-hour period was measured, and mean and SD were calculated. Room temperature remained constant at 22.5 C throughout the measurement period.

Experimental protocol—Horses were restrained in stocks and sedated with detomidine hydrochloride (0.01 mg/kg of body weight). Skin overlying the plantarolateral pouch of the tarsocrural joints was prepared for aseptic catheterization, and 2 ml of 2% mepivacaine hydrochloride was used to desensitize the skin. Using aseptic technique, infusion catheters were assembled, and infuser balloons were filled with 20 ml of gentamicin solution or BES. The extension set and flow control tubing were also filled with gentamicin solution or BES prior to insertion of the catheter.

Arthrocentesis of the dorsomedial pouch of the tarsocrural joint was performed, and a synovial fluid sample was collected. Forty to sixty milliliters of BES was then injected into the joint, and a sterile 12-gauge stainless-steel needle was inserted into the plantarolateral joint pouch. The infusion catheter was introduced into the joint through the needle to a depth of approximately 5 cm. The needle was withdrawn from the joint and taped over the tubing, and the tubing was sutured in position with 2-0 polypropylene suture material and affixed with cyanoacrylate. A bandage was then applied to hold the balloon infuser in place over the distolateral aspect of the crus. In the final horse enrolled in the study, a peel-away introducer[d] was used, instead of a 12-gauge needle, for placement of the tubing, so that the needle did not have to remain in place.

In all horses, an infusion catheter containing gentamicin solution (100 mg/ml) was inserted in the right tarsocrural joint, and an infusion catheter containing BES was inserted in the left tarsocrural joint. After catheters were inserted, horses were returned to their stalls. Infuser balloons were examined every 12 hours for signs of leakage, rupture, and failure to empty. If needed, balloons were refilled at these times to a volume of approximately 20 ml. Volume of fluid added to each balloon was recorded, and total volume of gentamicin solution administered was calculated. If a balloon ruptured, it was replaced, and the new balloon was initially filled to a volume of 20 ml. Any infusion catheter that stopped flowing was replaced.

Catheter sites were assessed daily for evidence of discharge from the catheter site, swelling, signs of pain during palpation, and change in position of the catheter. Horses were examined daily for signs of lameness. No analgesic or anti-inflammatory medications were administered to the horses during the study.

Catheters were removed 5 days after insertion. Three horses were euthanatized immediately after catheter removal in conjunction with a separate study. The remaining 9 horses were evaluated daily for another 9 days (ie, day 14 of the study).

Sample collection—Synovial fluid samples were collected from the right and left tarsocrural joints before (time 0) and 6, 24, 48, 72, 96, 120, 132, and 144 hours and 14 days after catheter placement. Samples were collected aseptically by means of arthrocentesis of the dorsomedial pouch of the tarsocrural joint and immediately placed in evacuated tubes containing EDTA. Samples used for determination of gentamicin concentrations were immediately transferred to plastic collection tubes and frozen at –20 C until analyzed.

Blood samples were collected from all horses 24, 48, 96, 120, and 144 hours after catheter placement. Serum was harvested and stored at –20 C until used for determination of gentamicin concentrations.

Measurement of synovial fluid and serum gentamicin concentrations—Concentration of gentamicin in synovial fluid from treated joints was determined 6, 24, 48, 72, 96, 120, 132, and 144 hours and 14 days after catheter placement. Concentration of gentamicin in synovial fluid from control joints was determined 6, 72, and 120 hours after catheter placement. Serum gentamicin concentrations were determined 24, 48, 96, 120, and 144 hours after catheter placement.

Gentamicin concentrations were determined by use of a fluorescence polarization immunoassay.[e] Calibration curves were established with 6 human serum standards, as described.[15,16] Samples of normal equine synovial fluid spiked with gentamicin at concentrations of 2,000, 500, 200, 50, 20,

and 5 µg/ml were analyzed to verify validity of the assay for equine synovial fluid. Six samples at each concentration were analyzed; coefficients of variation for these samples were 8.7, 5.4, 7.7, 5.2, 5.5, and 2.5%, respectively. Test synovial fluid samples were diluted 10-fold with buffer solution as necessary until measured concentration was < 10 µg/ml. The lower limit of detection of the assay was 0.01 µg/ml.

Synovial fluid analysis—Synovial fluid samples collected before and 24, 96, and 144 hours and 14 days after catheter placement were tested for WBC count, RBC count, total protein concentration, and pH. Samples that were clotted because of collection difficulties were excluded from analysis because of inability to determine objective data. However, only 3 samples were excluded for this reason. An automated cytometer was used to measure WBC and RBC counts. Total protein concentration was measured with a refractometer. The pH of the samples was determined with a pH meter.

Pharmacokinetic analyses—A synovial fluid gentamicin concentration versus time curve was constructed for each treated joint. The **elimination constant** (k_e) was calculated as the slope of the portion of the natural logarithm of the gentamicin concentration versus time curve after catheter removal. Synovial fluid gentamicin concentrations 120, 132, and 144 hours after catheter placement were analyzed by use of linear regression; synovial fluid gentamicin concentrations 14 days after catheter placement were less than the lower limit of detection of the assay. The **apparent half-life** ($T_{½}$) of gentamicin in synovial fluid was calculated from the following equation:

$$T_{½} = 0.693/k_e$$

Clearance of gentamicin from synovial fluid (Cl_{sf}) was calculated by use of 2 methods.[11,14,17] With the first method, Cl_{sf} was calculated by dividing total dose of gentamicin by the **area under the concentration versus time curve** (AUC); AUC was calculated by use of the trapezoidal method.[18] With the second method, Cl_{sf} was calculated by dividing infusion rate by the estimated steady-state synovial fluid gentamicin concentration. Mean synovial fluid gentamicin concentration during the infusion period was used as an estimate of steady state concentration for each joint. Infusion rate was calculated from volume of gentamicin solution infused into each joint during the infusion period.

Statistical analyses—Analysis of variance was used to compare synovial fluid characteristics between joints (treated vs control) at each time interval and, for joints grouped as treated or control, among collection days. Results were expressed as mean ± SD. Values of $P < 0.05$ were considered significant. Synovial fluid gentamicin concentrations are presented as median values and range. Values of Cl_{sf} obtained with the 2 methods were compared by calculating the linear correlation coefficient. Correlations between synovial fluid gentamicin concentration and WBC count and TP concentration were also evaluated.

Results

In vitro and in vivo flow rates—In vitro rates of flow of the gentamicin solution and the BES were 15.2 ± 0.8 and 26.8 ± 1.0 ml/d, respectively. In vivo rates of flow of the gentamicin solution and the BES were 16.4 ± 2.5 and 24.4 ± 7.7 ml/d, respectively.

Clinical observations—Horses tolerated the procedure well and did not show any signs of discomfort while the catheters were in place. None of the horses became lame during the study. Seventeen of the 24 (71%) infusion catheters initially placed functioned without complication for the entire 5-day infusion period.

Complications encountered during the study were primarily associated with failure of the infuser balloons and blockage of the catheters. One catheter (treated joint) was dislodged from the joint but not from the leg during the course of the study, resulting in low synovial fluid gentamicin concentrations in this joint. One horse dislodged the leg bandages repeatedly, causing the infusion catheters to be disrupted. Fluid flow was stopped during the infusion period in 2 treatment joints and 2 control joints and could not be re-established without replacing the entire infusion catheter. In all cases, an air lock was identified as the cause of the obstruction to fluid flow. Four balloon infusers ruptured during the course of the study, resulting in an air lock in the flow control tubing in all cases. Two balloon infusers leaked fluid during the infusion; however, flow was re-established in these cases by replacing the balloon.

Throughout the study, catheter sites were free from discharge, heat, and swelling; signs of pain were not evident during palpation of the sites. At the time of catheter removal on day 5, 11 of 24 catheter sites (46%) leaked a small volume of synovial fluid. Sterile bandages were applied, and these sites sealed within 24 hours.

Synovial fluid gentamicin concentrations and pharmacokinetic analyses—Median (range) gentamicin concentrations in synovial fluid from treated joints on days 0 through 5 of the study were 982 (101 to 2,230), 578.5 (57.8 to 3,510), 536.5 (25.6 to 2,360), 432 (17.3 to 1,730), 369.5 (13.9 to 2,390), and 287.5 (11.9 to 2,910) µg/ml, respectively. Median (range) gentamicin concentrations in synovial fluid from control joints 6, 72, and 120 hours after the beginning of the infusion were 1.27 (0.71 to 2.6), 2.62 (0.15 to 3.38), and 2.01 (0.01 to 3.89) µg/ml, respectively.

Data from the 3 horses euthanized immediately after catheter removal were not included in pharmacokinetic analyses. In addition, data from 2 other horses were excluded from pharmacokinetic analyses because problems with the infusion catheters resulted in synovial fluid gentamicin concentrations < 15 µg/ml at the time of catheter removal that did not decrease during the following 24-hour period.

For the remaining 7 horses, mean dosage of gentamicin was 0.17 ± 0.02 mg/kg/h (**Table 1**). The correlation between values of Cl_{sf} obtained with the 2 calculation methods was 0.98.

Synovial fluid analysis—White blood cell and RBC counts for synovial fluid from treated and control joints were not significantly different at any time during the study (**Table 2**). Total protein concentration in synovial fluid from treated joints was significantly higher than concentration in synovial fluid from control joints on day 14, and pH of synovial fluid from treated joints was significantly lower than pH of synovial fluid from control joints on days 1 and 4. For treated and control joints, WBC count and total protein concentration on day 1 was significantly higher than values obtained on day 0. For treated joints, correlation coefficient for WBC count versus synovial

Table 1—Pharmacokinetics of gentamicin in synovial fluid following continuous infusion in the tarsocrural joints of horses

Variable	Horse No. 1	2	3	4	5	6	7	Mean ± SD
K_e (h^{-1})	0.13	0.12	0.12	0.09	0.13	0.12	0.09	0.11 ± 0.02
$T_{½}$ (h)	5.33	5.78	6.02	7.7	5.46	5.78	7.7	6.25 ± 1.01
Total dose (g)	9.8	8.8	8.6	7.4	9.2	6.0	9.2	8.4 ± 1.3
Dose rate (mg/kg/h)	0.17	0.18	0.16	0.15	0.22	0.15	0.17	0.17 ± 0.02
IR (mg/min)	1.36	1.22	1.19	1.03	1.28	0.83	1.28	1.17 ± 0.18
C_{ss} (mg/ml)	697.3	454.7	1,245.2	2,027.2	1,877.8	650.0	535.3	1,069.6 ± 655.7
AUC (mg • h/ml)	83.62	46.35	158.46	254.0	226.34	79.29	69.98	131.15 ± 82.44
Cl_{sf}[a] (ml/min)	1.95	3.16	0.90	0.49	0.68	1.26	2.19	1.52 ± 0.96
Cl_{sf}[b] (ml/min)	1.95	2.68	0.96	0.51	0.68	1.28	2.39	1.49 ± 0.85

K_e = Elimination constant for gentamicin from synovial fluid. $T_{½}$ = Apparent half-life of gentamicin in synovial fluid. IR = Infusion rate. C_{ss} = Steady-state synovial fluid gentamicin concentration. AUC = Area under the concentration-versus-time curve. Cl_{sf} = Clearance of gentamicin from synovial fluid.
[a]Clearance calculated from total dose of gentamicin and AUC. [b]Clearance calculated from infusion rate and steady-state synovial fluid gentamicin concentration.

Table 2—Results of analyses of synovial fluid from the tarsocrural joints of horses in which gentamicin was infused continuously for 5 days (treated) and in the contralateral control joints

Variable	Time (d) 0 (n = 12)	1 (n = 11)	4 (n = 12)	6 (n = 9)	14 (n = 8)
WBC count (cells/ml)					
Treated	193 ± 124	10,547 ± 5,954†	4,063 ± 2,643†	2,948 ± 2,728	1,020 ± 757
Control	145 ± 75	8,411 ± 7,416†	11,081 ± 2,341	4,262 ± 2,673	463 ± 400†
RBC count (cells X 10^3/ml)					
Treated	53 ± 103	98 ± 167	291 ± 373	312 ± 652	45 ± 58
Control	55 ± 59	433 ± 972	398 ± 608	452 ± 400	205 ± 456
Total protein (g/dl)					
Treated	2 ± 0	2.8 ± 0.8†	2.7 ± 0.7	3.2 ± 0.8	2.6 ± 0.6*
Control	2 ± 0	3.0 ± 0.8†	2.7 ± 1.0	2.8 ± 0.7	2.2 ± 0.2†
pH					
Treated	7.43 ± 0.12	7.13 ± 0.23* †	7.15 ± 0.18 *	7.24 ± 0.11	ND
Control	7.44 ± 0.10	7.33 ± 0.17	7.33 ± 0.12	7.34 ± 0.14	ND

Values are given as mean ± SD.
*Significantly ($P < 0.05$) different from value for control group at the same time. †Significantly ($P < 0.05$) different from value obtained at the previous measurement time for the same group.
ND = Not determined.

fluid gentamicin concentration was 0.81, and correlation coefficient for TP concentration versus synovial fluid gentamicin concentration was 0.72.

Serum gentamicin concentrations—Median (range) serum gentamicin concentrations 24, 48, 96, 120, and 144 hours after the gentamicin infusion was started were 2.31 (0.27 to 3.66), 2.47 (0.01 to 3.98), 2.59 (0.6 to 3.99), 1.85 (0.27 to 2.78), and 0.24 (0.01 to 0.79) µg/ml, respectively. For all horses, serum gentamicin concentration was < 0.8 µg/ml within 24 hours after the infusion was discontinued.

Discussion

Results of this study suggest that this infusion catheter can be used for continuous infusion of gentamicin into the tarsocrural joints of horses for up to 5 days. However, 7 of the 24 (29%) catheters initially placed in horses in this study developed complications necessitating replacement of the catheter or balloon.

During the infusion period, gentamicin concentration in synovial fluid from treated joints of horses in this study ranged from 11.9 to 3,510 µg/ml. Horses with low concentrations had technical problems with the catheter system, contributing to the large range of values obtained. Surveys of antimicrobial susceptibility of bacterial isolates from horses have shown a trend toward greater resistance to the more commonly used antibiotics, including aminoglycosides.[6,19] A survey of 233 isolates from equine musculoskeletal infections showed gentamicin effectiveness ranged from 70 to 84.5% for most groups of pathogen tested.[6] Similarly, unpublished data from the animal disease diagnostic laboratory microbiology service at Purdue University indicated that 34.5% of all bacterial pathogens obtained during 1997 were resistant in vitro to gentamicin at a concentration of 4 µg/ml. All of these bacterial pathogens were susceptible to gentamicin at a concentration of 500 µg/ml. However, the MIC of gentamicin for some bacterial isolates in other animal species is greater than 2,000 µg/ml, with 15% of isolates having an MIC greater than 250 µg/ml in 1 study on enterococci.[20] These findings support the use of gentamicin concentrations within the synovial fluid well above the MIC to improve the spectrum and bactericidal activity of the drug. Further, strong correlation between high serum peak concentration of amino-

glycoside relative to the MIC of an infecting organism and the clinical response to treatment has been established.[10] Maintenance of high peak aminoglycoside concentration during the time required for development of adaptive resistance has also been recommended.[21] These findings give support to the concept of attaining high concentrations of gentamicin within the synovial fluid during treatment of septic arthritis, providing local and systemic toxicoses can be avoided.

It is not known what concentration of gentamicin is required in the synovial fluid to achieve synovial membrane concentrations sufficient to kill colonizing bacteria and bring about resolution of septic arthritis. Septic arthritis causes severe inflammation, thrombosis of the synovial vascular bed, and necrosis of the synovial membrane,[2,16] restricting penetration of drug to this area following systemic administration. Entrapment of bacteria within fibrin and necrotic synovial crypts further retards the ability of systemically administered antibiotics to be effective.[2] The high synovial fluid concentrations obtained with intra-articular infusion may improve penetration of gentamicin into these ischemic areas of infected synovial membrane, resulting in a higher likelihood of cure.

Mean (± SD) $T_{½}$ of gentamicin in the synovial fluid of the tarsocrural joints in this study was 6.25 ± 1.01 hours. This was similar to the value reported following intra-articular administration of gentamicin to clinically normal (4.32 ± 2.05 hours)[11] and experimentally infected (5.18 ± 1.58 hours)[14] antebrachiocarpal joints in horses. Pharmacokinetics of gentamicin following intra-articular administration to the tarsocrural joints of horses are not available for comparison to our study.

Two methods were used to measure Cl_{sf} in this study, and values obtained with these 2 methods were similar. Individual steady state concentrations of gentamicin could not be estimated from the concentration-vs-time graphs because of variability in synovial fluid gentamicin concentrations. Possible reasons for this may have included variation in the infusion catheters (the manufacturer reports a possible 20% variation among balloon infusers),[f] individual animal variation (including technical problems with catheters), relatively large sampling volume relative to total synovial fluid volume, and variation in the gentamicin concentration assay.

The flow control tubing used in this study was resistant to external occlusion, providing a relatively constant flow of gentamicin into the joint. Catheter occlusion and the inability to regularly monitor drug delivery have hindered previous efforts at continuous intra-articular infusion.[g] The flow control tubing has a thick wall and small inner lumen, and when catheters were folded on themselves during in vitro testing, the flow rate was unchanged. In 1 horse, the tubing was compressed and flattened inside the joint during the study; however, fluid continued to flow through the catheter, although at a slower rate than expected from day 2 to day 5.

The length and internal diameter of the flow control tubing and the viscosity of the infusion fluid determine the flow rate through the tubing. An increase in temperature results in a decrease in fluid viscosity and an increase in flow rate. Temperatures of the balloon infuser and the infusion solutions were not measured in this study; however, room temperature during the in vitro and in vivo portions of the study were kept constant at 22.5 C. The close correlation between the in vivo and in vitro fluid flow rates suggest that any increase in temperature of the infusion fluid and balloon infuser associated with bandaging had little effect on flow rate.

An air lock in the flow control tubing was identified as the cause of blockage for infusion catheters that became blocked. Modifications in the infusion catheters to make balloon infusers more resistant to rupture and to prevent entry of air in the case of balloon rupture, leakage, or disconnection should help prevent this complication and make the catheter more reliable.

The pharmacokinetics of gentamicin following systemic administration to healthy horses and horses with sepsis have been reported,[8,12] and extrapolation of data from human studies suggested that trough serum gentamicin concentrations < 2 µg/ml were associated with a lower prevalence of toxicoses.[12] In the present study, serum gentamicin concentrations ranged from 0.01 to 3.99 µg/ml. This variability in serum gentamicin concentration is consistent with previous studies in the horse.[11,12] Further investigation, therefore, is required to determine dosing regimens that will result in effective synovial fluid gentamicin concentrations in conjunction with serum gentamicin concentrations that will be unlikely to result in nephrotoxicosis. In the present study, mean dosage of gentamicin was 0.17 mg/kg/h. This dosage could be adjusted by using solutions containing a lower concentration of gentamicin or by diluting the gentamicin solution in the balloon infuser. Alternatively, continuous infusion followed by periods without infusion, combined with therapeutic drug monitoring could be used to avoid toxicoses.

Gentamicin was detected in synovial fluid from control joints of horses in this study; however, the concentrations of gentamicin in the synovial fluid from these joints were lower than the serum gentamicin concentrations and less than the concentrations expected following systemic administration of gentamicin.[11]

We did not detect significant differences in WBC and RBC counts between treated and control joints in this study. On day 14, total protein concentration in synovial fluid from treated joints was significantly higher than concentration in synovial fluid from control joints. In a previous study, administration of a single dose of gentamicin (150 mg) into clinically normal antebrachiocarpal joints of horses resulted in an increase in the synovial fluid total protein concentration for 9 days and a mild inflammatory response within the joint that resolved over 7 days.[22] Similarly, pH of the synovial fluid from treated joints was significantly lower than pH of synovial fluid from the control joints. The pH of the gentamicin solution (3.2) may account for this difference.[22] Inflammation has also been shown to result in a decrease in synovial fluid pH[14]; however, there was no apparent difference in inflammatory response between treated and control joints in the present study.

Arthrocentesis,[22-24] intra-articular injection of BES,[11,23,24] joint lavage with BES,[25] and multiple joint injections[26] all produce significant increases in synovial

fluid WBC count and total protein concentration. In the present study, synovial fluid WBC counts and total protein concentrations for the treated and control joints were increased on day 1, compared with day 0 values. However, values were similar to those reported for control groups in previous studies.[22-26] It was not possible in this study to distinguish among the contributions of daily arthrocentesis, joint catheterization, and gentamicin or BES infusion to synovial inflammation; however, the overall response was mild.

[a]Flow control tubing, Mila International Inc, Erlanger, Ky.
[b]Minivolume extension set, Baxter Healthcare Corp, Deerfield, Ill.
[c]Latex balloon infusor, catheter No. VB101, Mila International Inc, Erlanger, Ky.
[d]Peel away introducer set, Vascor Medical Corp, Tarpon Springs, Fla.
[e]TDx Analyzer, Abbott Diagnostics Inc, Abbott Park, Ill.
[f]Flowline fluid delivery systems informational brochure, Pacific Medical Supplies Pty Ltd, Richmond, Victoria, Australia.
[g]Lescun TB, Adams SB, Bill RP. Constant gentamicin administration into the antebrachiocarpal joint of the horse using a subcutaneously implanted osmotic pump (abstr), in *Proceedings*. Vet Orthop Soc 1998;49.

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