Incidence of bacteremia following upper gastrointestinal endoscopy and biopsy in healthy dogs before, during, and after treatment with omeprazole

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Objective—To determine the incidence of bacteremia, as detected by routine methods for bacterial culture of blood samples, following routine endoscopic biopsy of the stomach and duodenum in healthy research dogs and to determine whether treatment with omeprazole administration affected the incidence of bacteremia.

Animals—8 healthy purpose-bred research dogs.

Procedures—All dogs underwent gastroduodenoscopy with biopsy at 4 points: twice prior to treatment with omeprazole, once following 15 days of omeprazole treatment (20 mg, PO, q 12 h), and once 14 days after treatment ceased. Dogs had a mean ± SD body weight of 18.6 ± 2.0 kg. Blood samples were aseptically obtained at 3 points during each procedure (before, immediately following, and 24 hours after endoscopy), and routine aerobic and anaerobic bacterial culture of blood was performed.

Results—96 cultures were attempted for each culture method, yielding positive results of aerobic culture for 2 dogs at separate time points and no positive results of anaerobic culture.

Conclusions and Clinical Relevance—Routine gastrointestinal endoscopy with biopsy in healthy dogs did not result in a detectable bacteremia in most dogs. Treatment with the gastric acid–suppressing medication omeprazole did not affect the incidence of bacteremia as detected via standard techniques. (*Am J Vet Res* 2013;74:239–242)

The overall safety of endoscopic procedures has been evaluated for colonoscopy, esophageal and gastric foreign body removal, and esophageal stricture dilation in dogs[1–3]; however, little information is available concerning the incidence and clinical importance of transient bacteremia in animals following minimally invasive procedures such as gastrointestinal endoscopy and biopsy. No evidence exists to suggest that clinically relevant bacteremia is associated with gastrointestinal biopsy specimen collection, and there are no reports of bacteremia as a complication of this routine procedure. Dating back to the early 1970s, the human literature contains reports[4–6] of studies involving patients that underwent endoscopic procedures, including gastroduodenoscopy, esophageal dilation, and colonoscopy. Bacteremia resulting from routine gastroduodenoscopy appears to be uncommon, with the incidence of bacteremia ranging from 0% to 12% of procedures performed.[7] Biopsy specimen collection does not appear to increase the risk of bacteremia.[7]

People at greatest risk for clinically relevant complications secondary to transient bacteremia include those with considerable heart disease (eg, prosthetic valves, cyanotic congenital heart disease, or valvular dysfunction), those with other prosthetic implants, and those who are immunosuppressed.[8] Through evaluation of the results of studies involving humans undergoing elective endoscopic procedures, the American Society for Gastrointestinal Endoscopy determined that the risk for clinically relevant bacteremia is low and therefore the relative risk for endocarditis following endoscopic procedures is also low, with the highest risk found in people undergoing esophageal dilation.[9]

Prophylactic antimicrobial administration is recommended only for high-risk cardiac patients (eg, those with a cardiac prosthetic valve, previous history of endocarditis, or surgically corrected congenital cardiac anomaly) undergoing the highest risk medical procedures, such as esophageal dilation or endoscopic retrograde cholangiopancreatography.[9] Prophylactic

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antimicrobial administration is not currently recommended for patients undergoing routine gastroduodenoscopy with moderate heart disease (ie, mitral valve prolapse with regurgitation).

Omeprazole is a proton pump inhibitor, the administration of which results in potent gastric acid suppression, yielding much greater suppression of gastric acid secretion in dogs than treatment with H2-receptor blockers.[10,11] In recent years, gastric acid suppressors, particularly proton-pump inhibitors, have gained attention for their potential to predispose humans to adverse effects, including upper gastrointestinal bacterial overgrowth and possibly pneumonia or community-acquired infections with organisms such as *Clostridium difficile*.[12–15] Although the reported findings are variable, the evidence is growing to support that use of potent gastric acid–suppressing medications can result in changes to the composition of gastrointestinal flora and to host defenses. Indeed, several studies[16–18] have demonstrated gastric and duodenal bacterial overgrowth in humans receiving gastric acid–suppressing medications.

Various molecular methods have revealed changes to the microfloral population in healthy research dogs treated with omeprazole, including increases in the amount of bacteria attached to the gastric and duodenal mucosa and in the proportion of bacteria of the phyla Firmicutes or Proteobacteria.[19] Bacteria belonging to these phyla, particularly *Staphylococcus* spp and *Streptococcus* (Firmicutes) spp or *Escherichia coli* (Proteobacteria), are among those most commonly associated with clinical bacteremia[20] or endocarditis[21] in dogs. The changes induced by omeprazole to the balance of microbial flora may also increase the risk of bacterial translocation following routine gastroduodenoscopy with biopsy in dogs treated with proton-pump inhibitors.

To the authors' knowledge, no studies have been conducted to evaluate the incidence of bacteremia following routine gastroduodenoscopy and biopsy in dogs. The objective of the study reported here was to prospectively obtain and evaluate data on the incidence of detectable bacteremia (through bacterial culture of blood) following these procedures in healthy research dogs before, during, and after treatment with omeprazole.

Materials and Methods

Dogs—Eight purpose-bred hound-mix research dogs (4 sexually intact males and 4 sexually intact females) were used in this study. At the time of enrollment, the dogs were 10 months of age, with a mean ± SD body weight of 18.6 ± 2.0 kg. All dogs were determined to be healthy by performance of a CBC, serum biochemical analysis, fecal analysis, and physical examination. All dogs were prophylactically treated with fenbendazole[a] (50 mg/kg, PO, for 5 days) twice prior to initiation of the study. They were fed a dry kibble diet,[b] with the amount selected on the basis of calculated energy requirement. The research protocol was approved by the University of Illinois Animal Care and Use Committee.

Endoscopy—Gastroduodenoscopy with biopsy was performed in each dog at 4 points: 30 days (phase 1) and 15 days (phase 2) prior to omeprazole treatment, 15 days after treatment began (phase 3), and 2 weeks after treatment ceased (phase 4). Treatment consisted of 20 mg of omeprazole,[c] PO, twice daily for 15 days (mean dosage, 1.1 ± 0.1 mg/kg, q 12 h).

Food was withheld from all dogs for 12 hours prior to each endoscopic procedure. In preparation, each dog received butorphanol[d] (0.2 mg/kg, IM) and an IV catheter was placed in a cephalic vein. Anesthesia was induced with thiopental[e] (15 mg/kg, IV) to effect, and dogs were endotracheally intubated. Anesthesia was then maintained with sevoflurane[f] delivered in 100% oxygen. Endoscopy was performed with a veterinary endoscope[g] (working length, 1,400 mm; diameter, 8.6 mm; accessory channel diameter, 2.8 mm). A minimum of 16 duodenal and 16 gastric biopsy specimens was collected from each dog with single-use flexible endoscopy biopsy forceps.[h] Dogs were monitored closely for 24 hours after each procedure for any signs of discomfort or illness. They were allowed free access to water after recovery from anesthesia; however, no food was offered until 24 hours after endoscopy concluded.

Bacterial culture of blood—Blood samples for bacterial culture were obtained from each dog at each of the following points: immediately prior to endoscopy (following anesthetic induction), immediately following endoscopy with gastric and duodenal biopsy (during anesthetic recovery), and 24 hours after endoscopy concluded (before food was offered). For sample collection, the hair on the area over the right jugular vein was clipped 48 hours prior to the planned collection date. Immediately prior to blood sample collection, the area was aseptically prepared with 0.75% povidone iodine solution and sterile saline (0.9% NaCl) solution. A minimum of 7 mL of blood was aseptically collected from the right jugular vein with a 21-gauge needle attached to a 12-mL syringe. The needle was exchanged for a new sterile needle, through which 3 mL of whole blood was injected into each of two 20-mL sterile trypticase soy broth bottles.[i] The bottle intended to be used for aerobic culture was immediately vented with a sterile filter needle, and all bottles were incubated at 37°C.

Aerobic culture bottles were incubated for 24 hours, after which a sterile swab was used for inoculation of the contents onto culture plates containing Columbia blood agar, Columbia blood agar with colistin and naladixic acid, MacConkey agar, and chocolate agar.[j] These plates were routinely streaked for isolation, then incubated at 37°C with 5% CO_2. After 48 hours of incubation, the contents of bottles intended for anaerobic culture were used to inoculate plates containing *Brucella* blood agar and the plates were incubated in a mixed gas anaerobic environment chamber. All culture plates were monitored daily for evidence of growth and all bottle contents were plated as described after 5 days of incubation, with these plates observed for 2 days before a given sample was recorded as having negative culture results.

Statistical analysis—For the purpose of statistical comparisons, results of aerobic and anaerobic bacterial cultures of blood were considered as negative (no growth) or positive (growth). With the aid of statistical software,[k] the Cochran Q test was used to evalu-

ate the effect of endoscopy or biopsy on the results of bacterial culture. For each phase of the study, culture results were compared immediately prior to endoscopy (following anesthetic induction), immediately after endoscopy with gastric and duodenal biopsy (during anesthetic recovery), and 24 hours after endoscopy concluded. The Cochran Q test was also used to assess the effect of omeprazole treatment by comparing the overall culture results at phases 1, 2, 3, and 4. Values of $P \leq 0.05$ were considered significant.

Results

All 8 dogs underwent anesthesia and gastroduodenoscopy on 4 occasions, resulting in 96 blood samples for aerobic bacterial culture and 96 samples for anaerobic culture. No dogs had any clinical indication of illness or pain following the procedure. Results of all anaerobic culture attempts were negative. On the other hand, bacteria were cultured from the blood samples of 2 dogs at different time points. A *Lactobacillus* sp was recovered from a blood sample collected prior to endoscopy during phase 3 (immediately after 15 days of omeprazole treatment), and *Staphylococcus pseudointermedius* was isolated from the 24-hour postendoscopy sample during phase 4 of the experiment. Neither of the dogs from which these samples were obtained developed any indication of clinical illness.

The incidence of bacteremia detection after routine endoscopy and biopsy was approximately 3% (1 positive sample/32 endoscopic procedures). Endoscopy or biopsy ($P = 0.368$) or omeprazole treatment ($P = 0.572$) had no significant effect on culture results.

Discussion

The purpose of the present study was to estimate the overall incidence of bacteremia following gastroduodenoscopy with multiple pinch biopsies in a controlled sample of research dogs. In addition, we sought to determine whether the incidence of detectable bacteremia would be influenced by treatment with a potent gastric acid–suppressing medication (omeprazole). An overall low incidence of bacteremia (as determined by standard technique) was found. Following 15 days of omeprazole administration, *Lactobacillus* sp was isolated from the blood sample collected from 1 dog prior to endoscopy. Subsequent blood samples obtained immediately following endoscopy and 24 hours after endoscopy yielded no growth. This dog was noted at the time of endoscopy to have fecal material within its stomach. Therefore, the importance of this positive culture result remains unknown. The finding may have been attributable to coprophagia, inadvertent contamination, or a true bacteremic event. The dog was not clinically ill or identified as febrile at any point.

Staphylococcus pseudointermedius was isolated from a blood sample obtained from another dog 24 hours after the endoscopy and biopsy session that was performed 2 weeks after treatment with omeprazole had stopped (phase 4). Unlike blood samples collected immediately prior to and after endoscopy, this sample was obtained from a nonsedated dog and may have become contaminated.

Routine bacterial culture of blood remains the gold standard diagnostic test for bacteremia in human and veterinary patients. Between 1 and 3 attempts at bacterial culture of blood are considered necessary to detect clinically relevant bacteremia.[22,23] In the present study, aerobic and anaerobic cultures were attempted at 3 points for each endoscopic event. Cultures were obtained prior to endoscopy to establish that the dogs were nonbacteremic prior to the procedure. The time point for collection of the second sample (immediately after endoscopy) was selected on the basis of the sporadic and short-lived nature of bacteremic events following endoscopy in humans. Previous studies[5,7] in humans have demonstrated that culture-positive blood samples were most likely to be obtained between 5 and 30 minutes after endoscopy. The final sample in our study was obtained 24 hours after the procedure to allow documentation of the duration of bacteremic events and to test our hypothesis that any induced bacteremia would be short-lived.

Medications that reduce gastric acidity are commonly prescribed in veterinary medicine, but little is known about the effect of altered gastric pH on bacterial flora and the possibility of altering the gastrointestinal microbiome. Our findings suggested there was no increased risk for bacteremia following 15 days of omeprazole treatment (mean dosage, 1.1 mg/kg, PO, q 12 h) in healthy research dogs. However, although unlikely, it cannot be excluded that omeprazole treatment was a predisposing factor for transient bacteremia in the coprophagic dog.

The study had several limitations. First, blood samples were obtained at only 3 points, and therefore, transient bacteremia may have occurred and remained undetected. Additionally, because of the frequency of blood collection and the concern of inducing anemia in the dogs, a small-volume system was used, in accordance with the system manufacturer's instructions for blood volume-to-broth ratio. These small volumes of blood may have resulted in a decrease in culture yield.[22,24] Only routine bacterial culture of blood was used to detect bacteremia, and more sensitive molecular techniques, such as PCR assay of the 16 S ribosomal gene, were not performed. In a study[21] of dogs with endocarditis, although a PCR assay did not have a better sensitivity than bacterial culture of blood, a combination of bacterial culture and PCR assay increased the likelihood of identifying bacteria in the blood. However, PCR assay also increases the risk of false-positive results due to contaminants and of detecting dead bacteria that might be of little importance. Our study included only a small sample of healthy purpose-bred dogs. Dogs with clinical disease would likely have a much different microfloral balance, and the changes induced by proton pump inhibitors and any risk of bacteremia may be different. Therefore, additional evaluations in clinically ill dogs are warranted to supplement our preliminary findings.

a. Panacur, Intervet, Summit, NJ.
b. Teklad 8755, Harlan, Indianapolis, Ind.
c. Zegerid (omeprazole/sodium bicarbonate capsules), Santarus Inc, San Diego, Calif.
d. Torbugesic, Fort Dodge Animal Health, Fort Dodge, Iowa.

e. Pentothal, Hospira Inc, Lake Forest, Ill.
f. SevoFlow, Abbott Animal Health, Abbott Park, Ill.
g. Veterinary Videoscope, model VQ-8143A, Olympus, Center Valley, Pa.
h. Endojaw FB 220U-A biopsy forceps, Olympus, Center Valley, Pa.
i. BBL Septi-Check TSB, Becton Dickinson Microbiology Systems, Sparks, Md.
j. Remel Inc, Lenexa, Kan.
k. SPSS, version 17.0, SPSS Inc, Chicago, Ill.

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