Retrospective Study

Journal of Veterinary Emergency and Critical Care 19(5) 2009, pp 489–495
doi: 10.1111/j.1476-4431.2009.00463.x

Antimicrobial therapy and aerobic bacteriologic culture patterns in canine intensive care unit patients: 74 dogs (January–June 2006)

Dorothy M. Black, DVM, MPVM; Shelley C. Rankin, BSc, PhD and
Lesley G. King, MVB, DACVECC, DACVIM

Abstract

Objective – Describe antimicrobial therapy and aerobic bacteriologic culture patterns in canine intensive care unit (ICU) patients in a university hospital.
Design – Retrospective descriptive.
Setting – A tertiary university referral hospital.
Animals – Seventy-four canine ICU patients.
Interventions – From January to June 2006 patient antimicrobial use, minimum inhibitory concentration (MIC) results, and clinical data were recorded. Appropriate antimicrobial use was analyzed relative to the time of culture submission and MIC results.
Measurements and Main Results – Mean ± SD age was 7.2 ± 4.2 years. Median (range) length of ICU and hospital stays were 3 days (1–25 d) and 4 days (1–27 d), respectively. A total of 106 cultures were submitted; 47 of 106 (44%) cultures were positive for 70 isolates, including *Escherichia coli* (16/70 [23%]), *Staphylococcus intermedius* (7/70 [10%]), and *Acinetobacter baumannii* (5/70 [7%]). A multidrug resistant pattern occurred in 19 of 70 (27%) isolates, and was significantly more likely after 48 hours of hospitalization ($P < 0.001$). Antimicrobials were administered before culture submission in 42 of 74 dogs (57%) and included enrofloxacin (23/42 [55%]), ampicillin (20/42 [48%]), and amoxicillin/clavulanic acid (8/42 [19%]). Antimicrobial choices were appropriate 19% of the time. While pending culture results, antimicrobials were administered to 67 of 72 (94%) dogs remaining alive, and were appropriate 75% of the time. The most common antimicrobials administered while awaiting culture results were ampicillin (52/67 [78%]), enrofloxacin (49/67 [73%]), and amikacin (9/67 [13%]). Post-MIC antimicrobials were appropriate 89% of the time. Of 45 dogs remaining alive, 17 (37%) continued to receive antimicrobials despite negative cultures.
Conclusions – Antimicrobial use was extensive in this patient population, but when available, MIC results were used to guide antimicrobial therapy. Many patients with negative cultures continued to receive antimicrobial therapy. Multidrug resistant bacteria were more likely in cultures taken after 48 hours of hospitalization.

(J Vet Emerg Crit Care 2009; 19(5): 489–495) doi: 10.1111/j.1476-4431.2009.00463.x

Keywords: antimicrobial surveillance, infectious disease, multidrug resistance

Introduction

Bacterial resistance to antimicrobial drugs is a pressing multifactorial problem in veterinary and human medicine. Inappropriate use of antimicrobials is implicated as 1 factor contributing to the development of bacterial resistance.[1–3] Studies evaluating antimicrobial use in human intensive care units (ICUs) have demonstrated increases in antimicrobial resistance correlating with increased antimicrobial use.[4] Other studies have shown that septic hospitalized human patients who initially receive incorrect empirical antimicrobial therapy have increased morbidity and mortality.[5–8]

In humans, antimicrobial surveillance programs and antimicrobial-use studies have highlighted areas of concern and have helped improve appropriate antimicrobial use.[9–11] The Intensive Care Antimicrobial Resistance Epidemiology project, for example, is 1 study that has showed increased antimicrobial use and increased anti-

From the Departments of Clinical Studies (Black, King) and Pathobiology (Rankin), School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104.

This study was presented as a poster at the 12th International Veterinary Emergency and Critical Care Symposium, New Orleans, LA.
The authors have declared no conflicts of interest.

Address correspondence and reprint requests to:
Dr. Dorothy M. Black, Department of Veterinary Medicine Small Animal Clinical Sciences, College of Veterinary Medicine, Texas A&M University, 4474-TAMU, College Station, TX 77843, USA.
Email: doeblack@gmail.com

microbial resistance within the human ICU setting.[9] This study has also documented a relationship between antimicrobial use within hospitals and patterns of multidrug resistance (MDR). Antimicrobial education, stewardship, and antimicrobial rotation programs have shown promising results, including decreased resistance patterns, decreased antimicrobial use, decreased morbidity and mortality, and decreased patient cost.[12–17]

In veterinary medicine few studies have focused on antimicrobial surveillance and control programs. A study of antimicrobial prescriptions in dogs and cats in Finland demonstrated that β-lactams were the most frequent antimicrobials prescribed, and that less than half of the prescriptions listed a clinical indication.[18] A 15-year review of records at Ontario Veterinary Teaching Hospital showed a complex correlation between antimicrobial use and resistance patterns in *Staphylococcus* spp.[19] Following implementation of antimicrobial use guidelines in that hospital, overall antimicrobial prescriptions (in particular the use of broad-spectrum drugs) decreased significantly.[20] All of these studies evaluated a broad population of small animal patients and did not focus on high-risk hospital populations. Human ICU patients often receive aggressive antimicrobial therapy and may be at increased risk of infections with MDR bacteria.[9] It is commonly believed that a similar situation occurs in the veterinary ICU, but no data currently exists about this population. The paucity of studies and the lack of information about antimicrobial use in veterinary intensive care settings highlight the need for further information within this subset of the hospital population.

The objective of this study was to describe antimicrobial use in a small animal ICU. Specifically this study describes antimicrobial use and its relationship to aerobic bacteriologic culture results in canine ICU patients with varying conditions at a tertiary referral veterinary teaching hospital.

Materials and Method

The medical records of all canine patients admitted to the ICU of a tertiary referral veterinary teaching hospital from January 1 through June 30, 2006, were retrospectively analyzed. Dogs were excluded from the study if they were admitted to the ICU for <24 hours, had no bacteriologic culture submitted before or during the ICU hospitalization period, or if the medical record was unavailable.

Samples were routinely submitted for bacteriologic culture and susceptibility testing at the discretion of the clinician attending the case with input from board-certified critical care specialists. All samples were submitted to the in-house microbiology laboratory for analysis that included aerobic bacteriologic culture and susceptibility testing. The samples were cultured using standard laboratory procedure, and subcultures of all individual bacterial isolates were made. Individual bacterial colonies were identified and minimum inhibitory concentration (MIC) susceptibility testing was performed by an automated analyzer.[a]

The medical records were reviewed and for all subjects the following data were recorded: age, sex, breed, body weight, diagnosis, surgeries, use of indwelling urinary catheters, use of mechanical ventilation, date of bacteriologic culture(s), bacteriologic culture source, bacteria isolated, the presence of MDR, MIC susceptibility results, antimicrobial administration, length of ICU stay, total duration of hospital stay, and survival to discharge.

For the purpose of data analysis, antimicrobial use was broken down into 3 reference periods for each animal. Preculture antimicrobials were defined as all antimicrobials received by the animal within the month before submission of the bacteriologic culture sample. Postculture/pre-MIC antimicrobials were defined as antimicrobials received by the patient following submission of the bacteriologic culture sample but before receiving the final bacteriologic culture and MIC results. The final reference period included antimicrobials administered after receipt of the final bacteriologic culture results and MIC. Patients that died and those that were euthanized were grouped together. Deceased animals were excluded from further analysis in later time periods. Individual antimicrobials and combinations of antimicrobials were prescribed according to each clinician's preference.

The MIC susceptibility results were reviewed to identify the single antimicrobial or the antimicrobial combination that would have provided the most complete coverage to treat all bacterial isolates grown. We also evaluated routine combination therapy protocols to determine the efficacy of their coverage of the isolates grown.

For each animal and each time period, antimicrobial use was assessed and placed into one of the following categories:

Appropriate antimicrobial use

- if the organism isolated was susceptible,
- if antimicrobial use was clinically supported by other testing, such as clinical suspicion or positive testing for leptospirosis, tick-borne disease, or *Campylobacter* spp. infection,
- if the patient did not receive antimicrobials and had a negative bacteriologic culture.

Inappropriate antimicrobial use

- if the organism(s) isolated was (were) resistant to the antimicrobial chosen,
- if the patient did not receive antimicrobials and had a positive bacteriologic culture.

Possible appropriate or inappropriate antimicrobial use

- if patients received antimicrobials but had a negative bacteriologic culture.

For animals with multiple bacteriologic cultures, antimicrobial use was assessed based on the bacteriologic culture sample most relevant to their underlying disease process. Bacteria identified as contaminants were not evaluated for appropriate antimicrobial use.

All data were recorded in a computer spreadsheet[b] and analyzed using commercially available computer software.[c] Data were expressed as percent, mean (SD) or median (range). Data that were normally distributed are presented as mean ($\pm$ SD), and data that were not normally distributed are presented as median (range). χ^2 analysis was used to compare groups, where appropriate. A $P < 0.05$ was considered significant.

Results

Patient population

A total of 455 dogs were admitted to the ICU during the study period from January 1 to June 30, 2006. Of those, 83 canine patients met all of the inclusion criteria. Nine of these animals could not be included because their medical records were unavailable or incomplete, leaving a study population of 74 dogs.

This was the first visit to MJR VHUP for 50 of 74 (68%) patients. Twenty-seven were female and 47 were male dogs. The mean age was 7.2 years ($\pm$ 4.2 y). The median body weight was 21.3 kg (1.2–69.9 kg). Patients spent a median of 4 days (1–27 d) in the hospital and a median of 3 days (1–25 d) in the ICU.

There were 39 primary diagnoses for this patient population. Thirty-nine of 74 (53%) patients had multiple diagnoses. Based on the final diagnoses coded in the medical record, 45 of 74 (60.8%) of the patients had a confirmed or suspected diagnosis with an underlying bacterial cause. The most frequent diagnosis was pneumonia (29/74 [39%]). Thirty-seven of the 74 (50%) patients had some form of respiratory embarrassment, including pneumonia, lung parenchymal disease, pulmonary thromboemboli, brachycephalic syndrome, and noncardiogenic pulmonary edema. Septic peritonitis and renal disease were each diagnosed in 7 patients (9%).

Anesthesia requiring endotracheal intubation (including anesthesia for endotracheal washes and other short procedures) occurred at least once in 50 of 74 (68%) dogs; a urinary catheter was utilized in 21 of 74 (28%) dogs; at least 1 dose of corticosteroids was administered to 18 of 74 (24%) dogs; surgery occurred in 17 of 74 (23%) dogs; total parenteral nutrition was used in 14 of 74 (19%); positive pressure ventilation was performed in 8 of 74 (11%); at least 1 vasopressor was utilized in 8 of 74 (11%), and a feeding tube was placed in 3 of 74 (4%) dogs. Individual patients received a mean of 3 ($\pm$ 1.4) different antimicrobials during their hospital stay. Forty patients (54%) survived to discharge. Of the deceased patients, 32 of 34 (94%) were euthanized and 2 of 34 (6%) died.

Bacterial isolates

A total of 106 bacteriologic culture samples were submitted from the 74 patients. Seventeen different sources were sampled, with the most frequent being endotracheal washes (40/106 [38%]), urine (29/106 [27%]), and peritoneal fluid (8/106 [8%]). More than 1 bacteriologic culture sample was submitted in 23 dogs. The majority of the samples were taken within the first 24 hours of hospitalization (80/106 [75%]). Thirty-seven patients (50%) were positive for growth on their first bacteriologic culture.

Cytologic evaluation was performed on 63 of 106 culture samples. Bacteria were seen cytologically on 25 of 63 (40%) samples. Of these, 18 had positive bacteriologic cultures and 7 produced no growth. For the remaining 38 cytologic samples in which no bacteria were seen, 18 (47%) were positive for growth on bacteriologic culture.

Forty-seven of the 106 (44%) samples were positive for aerobic bacteriologic growth, and 18 of 47 (32%) bacteriologic cultures grew >1 organism. There were 70 distinct bacterial isolates: 39 of 70 (56%) were gram-negative bacteria, 26 of 70 (37%) were gram-positive bacteria, and 5 of 70 (7%) had variable Gram staining determination. Thirty-four of 70 (49%) were bacilli, 26 of 70 (37%) were cocci, and 10 of 70 (14%) were coccobacilli. Twenty-five different bacteria were represented: *Escherichia coli* was the most frequent organism isolated (16/70 [23%]), followed by *Staphylococcus intermedius* (7/70 [10%]), and *Acinetobacter baumanii* (5/70 [7%]). *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa* were equally represented (4/70 [6%]).

Of these isolates, 19 of 70 (27%) were considered to be MDR as described previously.[21] *A. baumanii* represented 4 of the 19 MDR isolates (21%). *E. coli* (3/19 [15%]) and *Enterobacter* spp. (2/19 [11%]) were the next most frequent MDR isolates, respectively. There was a significant increase in the frequency of MDR bacteria when cultures taken in the first 48 hours were compared with those taken after 48 hours of hospitalization ($P < 0.001$). Of 17 isolates from cultures taken after 48 hours of hospitalization, 10 (59%) were MDR.

There was no association between positive bacteriologic cultures and patient outcome with regard to survival to discharge ($P > 0.1$).

MIC findings

According to the MIC results, no single antimicrobial or any combination of antimicrobials would have been

effective for all of the organisms isolated during this period. Regardless of whether the isolate was gram-negative, gram-positive, cocci, bacilli, or coccobacilli, the MIC results demonstrated susceptibility as follows: imipenem 55 of 70 (79%), gentamicin 52 of 70 (74%), trimethoprim sulfamethoxazole (TMS) 48 of 70 (69%), enrofloxacin 42 of 70 (60%), cefotaxime 34 of 70 (49%), ampicillin 27 of 70 (39%), and ampicillin/sulbactam 20/of 70 (29%). In combination, imipenem with either ampicillin or gentamicin would have been effective for 62 of 70 (89%) of the isolated organisms. Amikacin plus clindamycin would have been effective for 59 of 70 (84%) of the isolates. TMS plus ampicillin would have been effective for 54 of 70 (77%) of the isolates. The combinations of enrofloxacin plus ampicillin, or cefotaxime plus clindamycin, would each have been effective for 50 of 70 (71%) of the isolates.

Antimicrobial use

Antimicrobial use in this patient population is summarized in Tables 1 and 2. Before bacteriologic culture submission, 57% of the dogs had received antimicrobials prescribed by referring veterinarians and by in-hospital clinicians. Antimicrobials had been administered to the patient before submission of 66 of 106 (62%) culture samples; of these, 29 of 66 (44%) were positive for bacterial growth. There was no association between the receipt of antimicrobials preculture and the percent of culture samples that were positive for growth ($P > 0.9$).

After submission of the bacteriologic culture sample, 72 patients remained in the study population. Of these, 28 of 72 (39%) had not previously been on antimicrobials, which were then started; 19 of 72 (26%) had a complete change in antimicrobial drugs; 12 of 72 (17%) had no change in antimicrobial drugs; 8 of 72 (11%) had an antimicrobial drug added to their previous regimen; 1 of 72 (1%) had an antimicrobial drug discontinued; and 4 of 72 (6%) were still not on any antimicrobial drug.

Following receipt of the MIC results 45 patients remained in the study population. Of these, 14 of 45 (31%) dogs had 1 or more antimicrobial drugs removed from their treatment regimen; 13 of 45 (29%) had no change in antimicrobial coverage; 10 of 45 (22%) had an antimicrobial drug added; 5 of 45 (11%) were changed to an appropriate antimicrobial combination; 2 of 45 (4%) had antimicrobial drugs discontinued, and anti-

Table 1: Antimicrobial therapy in relation to bacteriologic culture results in 74 canine patients admitted to a small animal intensive care unit

Time period		Before bacteriologic culture submission	After bacteriologic culture submission but before MIC result was available	After bacteriologic culture and MIC results were available
Total # of dogs that received antimicrobials		42/74 (57%)	67/72 (93%)*	38/45 (84%)†
Total # of bacteriologic cultures that were positive for growth		37/74 (50%)	36/72 (50%)	19/45 (42%)
Positive bacteriologic culture and received antimicrobials	Appropriate antimicrobials for bacteria identified (isolates were susceptible)	20/37 (54%) 6/20 (30%)	36/36 (100%) 27/36 (75%)	18/19 (95%) 17/18 (94%)
	Appropriate antimicrobials for 1 isolate but not all	5/20 (25%)	1/36 (3%)	1/18 (6%)
	Inappropriate antimicrobials for bacteria identified (isolates were resistant)	9/20 (45%)	8/36 (22%)	0/18 (0%)
Positive bacteriologic culture and not treated with antimicrobials		17/37 (46%)	0/36 (0%)	1/19 (5%)
Appropriate antimicrobials for suspected or confirmed leptospirosis, tick borne disease, *Campylobacter* spp., etc., and negative culture		4/37 (11%)	2/36 (5%)	3/26 (12%)
Negative bacteriologic culture and received antimicrobials		18/37 (49%)	29/36 (81%)	17/26 (65%)
Negative bacteriologic culture and not treated with antimicrobials		15/37 (40%)	5/36 (14%)	6/26 (23%)

*Two patients were euthanized immediately after bacteriologic culture submission, reducing the study population to 72 dogs.

†A further 27 patients died, were euthanized or were transferred before receipt of the bacteriologic culture and MIC results, leaving a population of 45 hospitalized patients.

MIC, minimum inhibitory concentration.

Table 2: Antimicrobial therapy in relation to subsequent minimum inhibitory concentration (MIC) results in 74 dogs admitted to a small animal intensive care unit

Antimicrobial administered	Before bacteriologic culture submission	After bacteriologic culture submission but before MIC result was available	After bacteriologic culture and MIC results were available
Enrofloxacin	23/42 (55%)	49/67 (73%)	21/38 (55%)
Appropriate, bacteria sensitive	3/23 (13%)	19/49 (39%)	6/21 (29%)
Bacteria identified resistant	7/23 (30%)	11/49 (22%)	1/21 (5%)
One or more bacteria identified were resistant	1/23 (4%)	1/49 (2%)	
Negative bacteriologic cultures	12/23 (52%)	18/49 (37%)	14/21 (67%)
Ampicillin	20/42 (48%)	52/67 (78%)	13/38 (34%)
Appropriate, bacteria sensitive	2/20 (10%)	18/52 (35%)	3/13 (23%)
Bacteria identified were resistant	5/20 (25%)	14/52 (27%)	1/13 (8%)
One or more bacteria identified were resistant	1/20 (5%)		
Negative bacteriologic cultures	12/20 (60%)	20/52 (38%)	9/13 (69%)
Amoxicillin/clavulanate	8/42 (19%)		12/38 (32%)
Appropriate, bacteria sensitive	2/8 (25%)		3/12 (25%)
Bacteria identified were resistant	1/8 (13%)		1/12 (8%)
Negative bacteriologic cultures	5/8 (62%)		8/12 (67%)
Amikacin		9/67 (13%)	1/38 (3%)
Appropriate, bacteria sensitive		5/9 (56%)	1/1 (100%)
Bacteria identified were resistant or drug used inappropriately		2/9 (22%)	
Negative bacteriologic cultures		2/9 (22%)	
Cefotaxime		7/67 (10%)	3/38 (8%)
Appropriate, bacteria sensitive		2/7 (29%)	2/3 (67%)
Bacteria identified were resistant		3/7 (42%)	
Negative bacteriologic cultures		2/7 (29%)	1/3 (33%)

microbials selected in 1 dog were inappropriate because resistant bacteria had been identified.

Overall post MIC antimicrobial therapy was appropriate or possibly appropriate in 43/45 cases (96%). Specifically, patients with positive cultures received appropriate therapy in 17/19 cases (89.5%). Two patients continued to receive inappropriate therapy. One patient had been sent home for euthanasia at the local veterinarian and the owners declined continuation of any medication. The second patient was discharged before completion of the MIC result and the antimicrobial therapy was not changed. Three isolates grew on culture and antimicrobial therapy was appropriate for 2 of the 3 isolates. This patient's pneumonia resolved despite treatment with inappropriate antimicrobials.

There was no association between appropriate or inappropriate initial antimicrobial coverage and patient outcome, with regard to antimicrobials administered before culture submission ($P = 0.37$) and before receiving culture/MIC results ($P > 0.70$).

Discussion

This is the first study that retrospectively documents the use of antimicrobial drugs over a 6-month period in a canine intensive care population for which bacteriologic culture results were available. Antimicrobial use was extensive in this patient population with an average of 3 antimicrobials per patient throughout hospitalization. Ampicillin and enrofloxacin were used most frequently at all time periods, especially pending results of specimens submitted for bacteriologic culture. Over half of the patients (57%) received antimicrobials before any bacteriologic culture submission. When antimicrobials were administered before collection of a culture, the selected antimicrobials were appropriate only 30% of the time.

Once a bacteriologic culture had been submitted, almost all of the dogs received antimicrobials, presumably because there was a high index of suspicion that bacterial infection was contributing to the disease process. Because there is a delay until final results are available, clinicians are initially required to make empiric antimicrobial choices. While waiting for the MIC results, clinicians selected appropriate antimicrobial drugs 75% of the time. This increased use of an appropriate antimicrobial may reflect greater expertise of clinicians who chose to submit a sample for bacteriologic culture and thoughtfully selected antimicrobials that were more likely to be effective for that site and the

particular organisms predicted. Once MIC results were available, the rate of use of appropriate antimicrobials increased to 89.5%. Thus, clinicians were attentive to positive bacteriologic culture results and adjusted therapy accordingly when MICs were available for guidance.

Many patients received antimicrobials but their bacteriologic cultures were subsequently negative for growth. Of the animals that had no bacteriologic growth on their cultures, 49% (22/37) had received antimicrobials before collection of the culture sample. We found no statistically significant difference in the rate of positive cultures when patients who had received antimicrobials before obtaining the sample were compared with those that had not received antimicrobials. While waiting for the MIC results after bacteriologic culture submission, 80.5% of this population was treated with antimicrobials, presumably because they were clinically deemed to be at risk of having bacterial infection.

Once results showing no growth on bacteriologic cultures were received, antimicrobial use decreased to 65%. Thus, only 35% of the dogs with negative cultures were managed without antimicrobials. We can only speculate about the continued administration of antimicrobials to the remaining dogs, despite negative culture results. Other supportive evidence of infection may have been present, such as a known source, leukocytosis or leukopenia with toxic changes in white blood cells, fever, cytologic confirmation of bacteria, or an apparent response to antimicrobial therapy. The majority ($>60\%$) of patients in this population had a primary diagnosis of a confirmed or suspected bacterial infection. In review of these cases, clinicians appear to have weighed many of the above questions before continuing antimicrobials.

However, the continued use of ampicillin, enrofloxacin, and other antimicrobials in this ICU despite negative bacteriologic cultures warrants further investigation, as this has the potential to promote antimicrobial abuse and expose other ICU patients to even greater risk of infection. Appropriate antimicrobial use might be improved by adopting clear guidelines for specific disease processes (ie, pneumonia, cellulitis, and abdominal disease), by which antimicrobials should be discontinued or continued in patients with negative bacteriologic culture results.

A similar study performed on human patients in a large European teaching hospital found that antimicrobial therapy was inappropriate in 37.4% (351/938) of the patients.[10] They used similar definitions of appropriate and inappropriate antimicrobial use. The decision for antimicrobial appropriateness, however, was not based solely on MIC results but also included the hospital antimicrobial prescription guidelines. In that study, an incorrect choice of antimicrobial drugs was made in 140 patients (14.9%), antimicrobials were unjustified in 123 patients (13%), and in 88 patients (9.4%) the correct antimicrobial was prescribed, but it was used incorrectly.[10]

This patient population included critically ill, dyspneic, and septic dogs with significant exposure to immunosuppressive drugs, total parenteral nutrition, and frequent use of multiple antimicrobials before a bacteriologic culture was obtained. Additional stressors included anesthesia, surgery, and mechanical ventilation. Central IV and urinary catheters were used extensively. All of these factors have been demonstrated to contribute to the risk of nosocomial infections and the creation of MDR bacteria.[22–24]

Research has shown that the use of antimicrobials, in particular ampicillin and fluoroquinolones, contributes to the creation of MDR.[25–28] In this type of high-risk patient, antimicrobials kill susceptible organisms, but can select for growth of resistant subpopulations of bacteria. Invasive procedures allow these resistant pathogens to penetrate and proliferate in tissues, causing nosocomial (hospital-acquired) infections. The presence of an MDR infection in 1 ICU patient may increase the risk for MDR infection in other ICU patients because of transmission by caregivers and fomites.[29–31]

In this study, we demonstrated that there was a significantly greater likelihood of MDR in samples submitted after 48 hours of hospitalization. In fact, more than half of the bacteriologic cultures submitted after this time period were MDR. Thus, it appears that patients who develop new infections after >2 days of hospitalization are likely to require very aggressive antimicrobial therapy. In our dogs, the combinations of either ampicillin and enrofloxacin or cefotaxime and clindamycin only treated approximately 70% of the isolates. Ideally, pending the results of the submitted bacteriologic cultures, these patients would receive antimicrobial therapy that approaches 100% coverage for all possible isolates. For our study population, this did not exist. Using the findings of this study, if gram-negative sepsis is highly suspected in a critically ill animal that has been hospitalized for >48 hours, gentamicin, amikacin, and potentially even imipenem could be recommended as empiric therapy. If methicillin-resistant *Staphylococcus* spp. are suspected, however, imipenem should be avoided, as the 4 isolates resistant to imipenem in this population were all *Staphylococcus* spp. Antimicrobials that maintained efficacy against methicillin-resistant staphylococci in this study, such as TMS or doxycycline, should be considered instead.

In conclusion, this description and review of antimicrobial use in a small animal ICU highlighted antimicrobial usage patterns and exposed factors contributing to antimicrobial resistance. This study was limited by

its design as a retrospective analysis. Most importantly, there was a selection bias because we excluded dogs from the study if no bacteriologic culture was submitted or if they were hospitalized in the ICU for <24 hours. In fact, this excluded $>80\%$ of the ICU population during this time period. However, our clinical practice promotes vigilance for infections and early submission of bacteriologic cultures in patients deemed at risk. Therefore, despite the selection bias, we believe that the results of this study provide useful information about antimicrobial use in critically ill dogs. Review of MIC results and empiric antimicrobial prescriptions in this ICU population identified areas of antimicrobial use that need further study and improvement. This analysis could be expanded to all patients within the ICU or hospital, and could be performed on a regular basis. The results of such antimicrobial surveillance would help to create antimicrobial guidelines and improve empiric therapy choices.

Footnotes

[a] Microscan WalkAway SI 40, Siemens Healthcare Diagnostics Inc, Sacramento, CA.
[b] Microsoft Excel, Microsoft Corp, Seattle, WA.
[c] SPSS Statistics, SPSS Inc, Chicago, IL.

References

1. Neu HC. The crisis in antibiotic resistance. Science 1992; 257(5073): 1064–1073.
2. Appelbaum PC. MRSA – the tip of the iceberg. Clin Micro Infect 2006; 12(s2):3–10.
3. Hooper D. Emerging mechanisms of fluoroquinolone resistance. Emerg Infect Dis 2001; 7(2):337–341.
4. Kollef MH. Antibiotic resistance in the intensive care unit. Ann Intern Med 2001; 134:298–314.
5. Degoricija VSM, Legac A, Gradiser M, et al. Survival analysis of 314 episodes of sepsis in medical intensive care unit in university hospital: impact of intensive care unit performance and antimicrobial therapy. Croat Med J 2006; 47:385–397.
6. Kollef MH, Sherman G, Ward S, et al. Inadequate antimicrobial areatment of anfections: a risk factor for hospital mortality among critically ill patients. Chest 1999; 115(2):462–474.
7. Hyle EP, Lipworth AD, Zaoutis TE, et al. Impact of inadequate initial antimicrobial therapy on mortality in infections due to extended-spectrum {beta}-lactamase-producing Enterobacteriaceae: variability by site of infection. Arch Intern Med 2005; 165(12):1375–1380.
8. Lautenbach E, Metlay JP, Bilker WB, et al. Association between fluoroquinolone resistance and mortality in *Escherichia coli* and *Klebsiella pneumoniae* infections: the role of inadequate empirical antimicrobial therapy. Clin Infect Dis 2005; 41(7):923–929.
9. Fridkin SK SC, Edwards JR, Pryor ER, et al. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. Clin Infect Dis 1999; 29:245–252.
10. Willemsen I, Groenhuijzen A, Bogaers D, et al. Appropriateness of antimicrobial therapy measured by repeated prevalence surveys. Antimicrob Agents Chemother 2007; 51(3):864–867.
11. Lautenbach E, Larosa LA, Kasbekar N, et al. Fluoroquinolone utilization in the emergency departments of academic medical centers: prevalence of, and risk factors for, inappropriate use. Arch Intern Med 2003; 163(5):601–605.
12. Kollef MH, Vlasnik JON, Sharpless L, et al. Scheduled change of antibiotic classes. a strategy to decrease the incidence of ventilator-associated pneumonia. Am J Respir Crit Care Med 1997; 156(4): 1040–1048.
13. Allegranzi B, Luzzati R, Luzzani A, et al. Impact of antibiotic changes in empirical therapy on antimicrobial resistance in intensive care unit-acquired infections. J Hosp Infect 2002; 52(2):136–140.
14. Apisarnthanarak A, Danchaivijitr S, Khawcharoenporn T, et al. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. Clin Infect Dis 2006; 42(6): 768–775.
15. Gruson D, Hilbert G, Vargas F, et al. Rotation and restricted use of antibiotics in a medical intensive care unit. impact on the incidence of ventilator-associated pneumonia caused by antibiotic-resistant gram-negative bacteria. Am J Respir Crit Care Med 2000; 162(3):837–843.
16. Zahar JR, Rioux C, Girou E, et al. Inappropriate prescribing of aminoglycosides: risk factors and impact of an antibiotic control team. J Antimicrob Chemother 2006; 58(3):651–656.
17. Martinez JA, Nicolas JM, Marco F, et al. Comparison of antimicrobial cycling and mixing strategies in two medical intensive care units. Crit Care Med 2006; 34:329–336.
18. Holso K, Rantala M, Lillas A, et al. Prescribing antimicrobial agents for dogs and cats via university pharmacies in Finland – patterns and quality of information. Acta Vet Scand 2005; 46 (1–2):87–93.
19. Prescott J, Hanna W, Reid-Smith R, et al. Antimicrobial drug use and resistance in dogs. Can Vet J 2002; 43:107–116.
20. Weese JS. Investigation of antimicrobial use and the impact of antimicrobial use guidelines in a small animal veterinary teaching hospital. J Am Vet Med Assoc 2006; 228(4):553–558.
21. Kluytmans-VandenBergh J, Klytmans J, Voss A. Dutch guideline for preventing nosocomial transmission of highly resistant microorganisms (HRMO). Infection 2005; 33:309–313.
22. Ogeer-Gyles JSMK, Boerlin P. Nosocomial infections and antimicrobial resistance in critical care medicine. J Vet Emerg Crit Care 2005; 16(1):1–18.
23. Weber D, Raasch R, Rutala W. Nosocomial infections in the ICU. The growing importance of antibiotic-resistant pathogens. Chest 1999; 115:42S–41S.
24. Emori T, Gaynes R. An overview of nosocomial infections, including the role of the microbiology laboratory. Clin Microbiol Rev 1993; 6(4):428–442.
25. Kollef M, Fraser V. Antibiotic resistance in the intensive care unit. Ann Intern Med 2001; 134:298–314.
26. Hirsh D, Jang S. Antimicrobial susceptibility of selected infectious bacterial agents obtained from dogs. J Am Anim Hosp Assoc 1994; 30:487–494.
27. Cooke C, Singer R, Jang S. Enrofloxacin resistance in *Escherichia coli* isolated from dogs with urinary tract infections. J Am Vet Med Assoc 2002; 220(2):190–192.
28. Cohn L, Gary A, Fales W, et al. Trends in fluoroquinolone resistance of bacteria isolated from canine urinary tracts. J Vet Diagn Invest 2003; 15(4):338–343.
29. Richards M, Edwards J, Culver D, et al. Nosocomial infections in medical intensive care units in the United States. Crit Care Med 1999; 27(5):887–892.
30. Lipsitch M, Samore M. Antimicrobial use and antimicrobial resistance: a population perspective. Emerg Infect Dis 2002; 8(4):347–354.
31. Trott D, Filippich L, Bensink J, et al. Canine model for investigating the impact of oral enrofloxacin on commensal coliforms and colonization with multidrug-resistant *Escherichia coli*. J Med Microbiol 2004; 53:439–443.

