



Positive impact of an emergency department protocol on time to antimicrobial administration in dogs with septic peritonitis

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Abstract

Objective – To determine whether the development of a specific antimicrobial protocol for the treatment of canine intra-abdominal sepsis would improve time to appropriate antimicrobial administration following diagnosis of bacterial peritonitis.

Design – Case controlled observational study.

Setting – A tertiary referral small animal teaching hospital.

Animals – Twenty dogs undergoing surgery for septic peritonitis prior to the deployment of the abdominal sepsis protocol served as a case control population and 40 dogs identified as having septic peritonitis after deployment of the protocol served as the study population.

Interventions – None.

Measurements and Main Results – Median time from diagnosis of septic peritonitis to antimicrobial administration was 6 hours (range 1–10 h) in the preprotocol group (PRE), and 1 hour (range 1–2 h) in the postprotocol group (POST) ($P = 0.001$). Five of 20 (25%) culture and sensitivity results yielded negative cultures in the PRE versus 6 of 34 (17.6%) in the POST. Inappropriate empirical antimicrobials were selected 3 of 20 times (15%) in the PRE and 3 of 34 times (8.8%) in the POST. The overall survival to discharge was 60% in the PRE and 70% in the POST ($P = 0.425$).

Conclusions – The development of an emergency department antimicrobial protocol significantly decreased time to antimicrobial administration following identification of septic peritonitis in dogs.

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Introduction

Canine septic peritonitis is a challenging disease process to treat, with survival rates reported between 54% and 79%.^{1–8} Despite advances in surgical technique, anesthetic monitoring, and postoperative veterinary care, a recent veterinary study suggested that little to no improvement in survival has occurred over the last two and a half decades.¹ Studies in people suggest that early

Abbreviations

ED	emergency department
PRE	preprotocol group
POST	postprotocol group
MDR	multidrug resistant
SSCG	Surviving Sepsis Campaign Guidelines

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and aggressive treatment of sepsis in the emergency department (ED) may improve survival, and that early intervention with appropriate empirical antimicrobials decreases morbidity and mortality.^{9–11} Based on these studies, the Surviving Sepsis Campaign of 2008 (SSCG) made several recommended guidelines for early interventional therapy including antimicrobial administration within 1 hour of diagnosis of severe sepsis or septic shock, and source control within 6 hours of recognition.¹²

Despite these recommendations, it can be challenging in a busy ED to meet the time frame outlined by these guidelines. In an attempt to improve the management of abdominal sepsis in the ED and adhere to the SSCG, a canine abdominal sepsis protocol was created for the ED at our institution. The aims of this protocol were to assist clinicians in earlier identification of dogs with septic peritonitis, aid in early medical intervention, and to reduce the time to antimicrobial administration.

The purpose of this observational study was to determine whether the creation and implementation of the canine abdominal sepsis protocol decreased time to antimicrobial administration in dogs identified with septic peritonitis. A further aim was to determine whether there was an overall improvement in empirical antimicrobial selection, and in survival in dogs with septic peritonitis following protocol deployment.

Materials and Methods

Protocol development and antimicrobial selection

The sepsis protocol was a paper-based protocol developed by 4 clinicians from the Emergency and Critical Care department at the Foster Hospital for Animals at the Cummings School of Veterinary Medicine, Tufts University. The aim of the protocol was to assist ED clinicians in identifying dogs with abdominal sepsis more rapidly and initiating therapy in a timely fashion. The protocol consisted of several components including a screening tool to help identify patients with septic peritonitis, a checklist of suggested diagnostics, guidelines for appropriate antimicrobial therapy, resuscitation endpoints, and interventions that could be undertaken to improve transfer into the operating room from the ED. (Appendix 1).

In order to determine where significant delays occurred that prevented timely antimicrobial administration, a review of 20 medical records of dogs presented to the ED with intra-abdominal sepsis was performed, and a timeline of each case was reconstructed. Additionally, ED clinicians were questioned as to what would help them improve their identification of abdominal sepsis and to administer antimicrobials to their patients in a more timely fashion. The most common time delays identified included waiting for abdominal radiographs to be performed, waiting for abdominal cultures to be acquired, obtaining antimicrobials from the pharmacy, and transfer to the operating room.

Empiric antimicrobial selections were determined by performing a computer database search for all positive canine abdominal bacterial cultures and sensitivities submitted at our institution between January 1, 2001 and December 1, 2006. The bacterial culture results were analyzed using commercial software^a to identify

Table 1: Empiric antimicrobial guidelines used for treatment of dogs with septic peritonitis as described in a devised emergency department septic abdomen protocol

Initial empiric antimicrobial guidelines for canine abdominal sepsis in the ED

Option 1: Community acquired infection No evidence of renal insufficiency*	Amikacin 15 mg/kg IV now and then once daily, and clindamycin 12 mg/kg IV now and in 12 hours.
Option 2: Community acquired infection and evidence of renal insufficiency*	Cefotaxime 22 mg/kg IV now and then every 8 hours, and clindamycin 12 mg/kg IV now and then every 12 hours.
Option 3: Hospital acquired infections where <i>Enterococcus</i> is a concern	Select either of the above protocols and add ampicillin 22 mg/kg IV now and then every 8 hours.

*Renal insufficiency was defined as by presence of creatinine >221 $\mu\text{mol/L}$ [>2.5 mg/dL], or presence of findings such as obstructive uropathy.

the most common bacterial isolates, as well as community and hospital acquired bacterial resistance patterns. A hospital-acquired infection was defined as an isolate displaying a multidrug resistance (MDR) pattern cultured from a dog admitted to a veterinary hospital during the previous 2 months prior to presentation. This information was taken to a larger committee of clinicians from a variety of specialties and 3 antimicrobial protocols were created for use in dogs identified as having septic peritonitis with the intent of decreasing inappropriate initial antimicrobial selection. (Table 1) To decrease delays in diagnosis and antimicrobial administration, clinicians were instructed to perform a cursory abdominal sonogram to evaluate for the presence of free abdominal fluid in any patient suspected of having abdominal sepsis prior to obtaining abdominal radiographs, to administer antimicrobials before obtaining cultures in surgery, and select antimicrobial agents were moved from the pharmacy to the ED. Finally, a checklist was made to assist in facilitation of the transfer of patients from the ED to the surgery service (Appendix 1).

Animal selection

Preprotocol animals

The preprotocol group (PRE) included all dogs undergoing surgery for septic peritonitis at our institution between January 1, 2008 and December 1, 2008, where abdominal sepsis was confirmed at the time of surgery. Dogs were identified retrospectively by searching a hospital computer database for keywords including "peritonitis," "abdominal sepsis," and "exploratory

laparotomy." Dogs were included in the study group if they had septic peritonitis diagnosed by identification of intracellular bacteria on abdominal cytological examination performed by the ED clinician, or during abdominal surgery, and the time of diagnosis as well as time of antimicrobial administration could be determined from the record. Dogs were excluded if they had received antimicrobials from a primary care veterinarian prior to referral to our institution.

Postprotocol animals

Dogs in the postprotocol group (POST) were presented to the ED between January 2009 and January 2011. Cases were identified retrospectively by using the same database search used to identify the PRE, as well as from a log of all patients receiving antimicrobials from the ED septic protocol kit. Unlike in the PRE group, dogs euthanized prior to abdominal surgery were included in the study as they were easily identified due to the ED log sheet, the remaining inclusion and exclusion criteria were the same as for the PRE group.

Data retrieval

The medical records from both the PRE and POST were searched and data were incorporated into an electronic spreadsheet.^a Variables collected included time of arrival to the ED, time of identification of septic peritonitis either via identification of intracellular bacteria on abdominal fluid cytology or strong suspicion based on abdominal ultrasound, time of antimicrobial administration, antimicrobials administered, whether abdominal bacterial cultures were positive or negative, bacteria cultured, whether the antimicrobials administered were appropriate for the bacteria cultured based on minimum inhibitory concentration results, whether there was suspicion of a hospital acquired infection, and patient survival status (defined as survival to discharge). Due to the difficulty in determining exact times from the medical record, all times recorded were rounded to the nearest hour. Additional data collected on the POST dogs included whether dogs were euthanized prior to the initial surgery.

Protocol deployment

The protocol was deployed in January 2009. As part of the protocol implementation, an informational meeting was open to all staff members and flyers were placed around the hospital describing the protocol, with contact names for additional information and support. Additionally, an informational email was sent to all members of the ED describing the protocol. Finally, for all new

clinicians that joined the staff at the ED, a mandatory informational session was held as part of their orientation.

Statistical Methods

Descriptive statistics including mean, median, and SD were calculated for all parameters. Distribution of data was examined for normality using the Shapiro–Wilk test. Data were analyzed using Fisher exact probability test for categorical variables and a Mann–Whitney U test for continuous variables. A *P*-value < 0.05 was considered statistically significant. All data analyses were performed using commercial statistical software.^b

Results

Case identification

For the PRE group, 23 dogs were identified from the hospital database as having undergone surgery for septic peritonitis. Of these, 3 were excluded due to inability to determine time of antimicrobial administration, yielding a total of 20 dogs in the PRE group. For the POST group, 35 dogs were identified via a search of the hospital's database and 52 dogs were identified using the ED patient registry log. All dogs identified via the computerized search had also been identified on the ED patient registry log. Of the 52 dogs identified using the ED patient registry log, 10 received antimicrobials from the septic protocol kit for causes other than intra-abdominal sepsis and 2 were excluded due to inability to determine time of antimicrobial administration for a total of 40 dogs in the POST group. Of the 10 dogs receiving the septic protocol kit that did not have intra-abdominal sepsis, 6 had sepsis of another source, and 4 did not have any identifiable source of infection and received antimicrobials inappropriately. No dogs in either group were excluded due to antimicrobial administration immediately prior to presentation.

Time to antimicrobial administration and survival

Median time from diagnosis to antimicrobial administration was 6 hours (range 1–10 h) in the PRE, and 1 hour (range 1–2 h) in the POST which was significantly different (*P* = 0.001; Table 2). In the PRE, 5 of 20 dogs (25%) received antimicrobials within 2 hours of diagnosis of septic peritonitis versus 40 of 40 dogs (100%) in the POST, (*P* = 0.0001). The number of dogs meeting the SSCG of receiving antimicrobials within 1 hour of diagnosis was 2 of 20 dogs (10%) in the PRE, versus 35 of 40 dogs (87.5%) in the POST, (*P* = 0.0001). Twenty of 20 dogs underwent exploratory laparotomy in the PRE versus 34 of 40 dogs in the POST groups, and the remaining 6 dogs were euthanized in the ED. A statistical difference

Table 2: Time from diagnosis of septic peritonitis time of antimicrobial administration in dogs

Time from diagnosis to antimicrobial administration	PRE n = 20	POST n = 40
< 1 h	1	35
1–2 h	4	5
3–6 h	6	0
7–10 h	4	0
> 10 h	4	0
No antimicrobial administered	1	0

in overall survival rates between dogs in the PRE group (survival rate 12 of 20 [60%]) versus dogs in the POST group (survival rate 24 of 34 [70%]) was not detected ($P = 0.425$).

Antimicrobials administered and bacterial culture and sensitivity results

Dogs in the PRE group received a variety of antimicrobial combinations based on the preference of the clinician. All dogs in the POST group received antimicrobials from 1 of the 3 outlined protocols. Table 3 shows the specific antimicrobial regimens administered in the PRE and POST groups. All dogs undergoing surgery from both groups had bacterial culture and sensitivity results available. There were 5 of 20 (25%) negative culture results in the PRE versus 6 of 34 (17.6%) negative culture results in the POST. Based on available culture results, inappropriate antimicrobials were selected in 3 of 20 dogs (15%) in the PRE and 3 of 34 dogs (8.8%) in the POST ($P = 0.485$). All instances of inappropriate antimicrobial selection in the POST group involved MDR *enterococcus* species, whereas in the PRE, 2 bacteria cultured were MDR *Escherichia coli* and 1 was an MDR *Enterococcus* species. All cases of MDR *Enterococcus* were suspected to result from hospital acquired intra-abdominal sepsis where patients developed peritonitis after recent abdominal surgery.

Discussion

This study supports the beneficial effect of a protocol and readily available antimicrobials on shortening time to antimicrobial administration in dogs with septic peritonitis. Evidence in people supports that the interventions made during the early hours of severe sepsis and septic shock are vital to patient outcome.^{10,13,14} The SSCG was created with the intent of decreasing morbidity and mortality resulting from sepsis in people. To this end, the campaign published a variety of recommendations on therapeutic interventions that are believed to improve survival in patients with sepsis. One of the central themes of management of this group of patients is early and ap-

Table 3: Antimicrobial regimens administered to dogs with septic peritonitis

Antimicrobials administered	PRE	POST
Amikacin, clindamycin	0	30
Cefotaxime, clindamycin	0	9
Cefotaxime, clindamycin, ampicillin	0	1
Enrofloxacin, ampicillin, metronidazole	3	0
Amikacin, ampicillin	3	0
Ampicillin, enrofloxacin	3	0
Cefazolin, enrofloxacin, metronidazole	3	0
Cefazolin, ampicillin, enrofloxacin, metronidazole	2	0
Amikacin, ampicillin, metronidazole	1	0
Amikacin, cefazolin	1	0
Cefazolin, metronidazole	1	0
Cefazolin, ceftiofur	1	0
Enrofloxacin	1	0
None	1	0

propriate administration of empirical antimicrobials. In 2006, Kumar *et al*¹⁰ published a landmark study that demonstrated that in patients with hypotensive shock secondary to bacterial infection, for each hour of delay of appropriate antimicrobial administration, mortality rate increased by 7.6%.¹⁰ Overall survival if antimicrobials were delayed by just 6 hours, was 42% compared to 79.9% if antimicrobials were given within the first hour. Since the publication of that study, several additional studies have confirmed the survival benefit of early and appropriate antimicrobial administration.^{13,14} Our primary goal in creating this protocol was to improve time to antimicrobial administration. Although we were unable to demonstrate a statistically significant improvement in survival between the 2 groups, the protocol did achieve our goal of improving time to antibiotic administration, with 100% of dogs receiving antimicrobials within 2 hours of diagnosis of bacterial peritonitis, versus the PRE where 25% of dogs received antimicrobials during the same time period.

A second aim of the septic abdomen protocol was to assist ED clinicians in selecting appropriate empirical antimicrobials. Numerous studies have documented that inappropriate empirical antimicrobial selection is associated with a prolonged hospital stay and worse prognosis in patients with sepsis.^{13–15} Our study failed to show a significant difference in empirical antimicrobial selection, although inappropriate antimicrobials were selected 15% of the time in the PRE versus 8.8% of the time in the POST group. It is not surprising that all inappropriate antimicrobial selections in the POST involved MDR *Enterococcus* species. This is because the sepsis committee purposely elected not to treat *Enterococcal* abdominal contaminations in straightforward cases of abdominal sepsis. This controversial decision was based on the fact that in people, *Enterococcus* is considered a questionable

pathogen in cases of intra-abdominal sepsis, and many treatment guidelines call for anti-*Enterococcal* therapy to be initiated only in hospital-acquired cases of intra-abdominal sepsis, or with patients that have other confounding factors and morbidities.^{16,17} We attempted to follow these guidelines by creating an option in the protocol for the treatment of hospital acquired abdominal sepsis, where ampicillin was combined with amikacin or cefotaxime in the treatment regimen to provide a synergistic effect (Table 1). It would appear, however, that this protocol is inadequate to cover for the current nosocomial MDR *Enterococcus* infection of our geographic region and highlights the importance of monitoring changing bacterial resistance patterns closely.

The SSCG states that whenever possible, samples should be collected for bacterial culture prior to antimicrobial administration. It further states, however, that antimicrobials should not be delayed in order to obtain cultures.¹² One concern of many clinicians is that the administration of antimicrobials prior to obtaining adequate bacterial cultures may affect culture and sensitivity results, making it difficult to tailor specific antimicrobial therapy to individual patients. Based on this study, the administration of antimicrobials prior to collection of abdominal fluid samples did not increase the number of negative bacterial culture results. In fact, we found a greater percentage of negative bacterial results in the PRE than the POST group. This is unlikely related to the timing of the antimicrobial administration and more likely the result of diverse culture strategies employed by various clinicians, as well as the different amounts of bacterial contamination among patients. If obtaining abdominal samples for bacterial culture prior to antimicrobial administration remains a top priority, samples should be obtained in the ED via abdominocentesis and antimicrobials do not need to be delayed until the time of surgery.

This study also identified obstacles for timely provision of care that can be overcome with appropriate planning. In our hospital, significant delays were noted while waiting for abdominal radiographs to be obtained, withholding antimicrobial administration until abdominal samples for bacterial culture were obtained at the time of surgery, waiting for antimicrobials to arrive from pharmacy, and waiting for the surgery and anesthesia services to transfer the patient to the operating room. Delays of this nature are likely to be hospital-specific, and each hospital should perform an internal review to discover where delays might be occurring, and to create a plan to expedite timely treatment. In order to determine whether our checklist resulted in an improvement of the time to transfer to the surgery service and was effective, we should have compared the time from diagnosis to time to surgery; however, these data were not collected.

One problem associated with the initiation of the protocol was the inappropriate application of the protocol in 4 dogs that did not have an identifiable source of infection. In all 4 dogs, adherence to the protocol was not maintained as intracellular bacteria were not identified on examination of abdominocentesis sample, nor was there a very strong suspicion of intra-abdominal sepsis found on ultrasonographic examination prior to antimicrobial administration. It is likely that the strong emphasis placed on early antimicrobial administration played a role in the clinical decisions to administer antimicrobials prematurely. However, due to the retrospective nature of the study we are unable to determine how many dogs received inappropriate antimicrobials before initiation of the protocol. In addition, 6 dogs received antimicrobials according to the protocol for infections from areas other than intra-abdominal sources. While antimicrobials selected were likely appropriate choices, there is a possibility that other antimicrobials may have been a better selection depending on the source of infection and the convenience of the protocol skewed the clinicians' decisions.

One limitation of this study is its retrospective nature, which relied heavily on accurate documentation in the medical records. This can be a particular source of error when determining exact times of interventions. In an attempt to make any time bias equal between groups, all times were rounded to the nearest hour. This limitation could have been alleviated with a prospective study design. Additionally, it is possible that as a result of the protocol, staff were more diligent about recording the time of antimicrobial administration in the medical record, creating a false improvement in time.

In conclusion, our study demonstrates that the creation of a specific antimicrobial protocol for the treatment of canine abdominal sepsis significantly improves time to antimicrobial administration. It would seem that additional protocols could be developed for a variety of causes of canine sepsis to improve time to antimicrobial administration in other septic models. Future prospective studies are needed to elucidate whether there is a survival benefit from early antimicrobial administration in this group of dogs.

Footnotes

^a Microsoft Excel, Microsoft Corporation, Redmond, WA.

^b Systat 11.0, SPSS, Chicago, IL.

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Appendix I. Protocol for the treatment of canine intra-abdominal sepsis used.

Patient NAME/Number _____

CANINE – Acute Abdomen/ Abdominal Sepsis Bundle

Circle the following identified:

- Abdominal Pain
- Hypoglycemia
- Febrile
- Vomiting
- Abdominal Effusion

If 2 or more are circled ensure the following are completed:

1. IVC, electrolyte panel, TPR, BP, PCV/TS, Blood smear
2. Cursory AUS +/- abdominocentesis, glucose/lactate Blood-Fluid differential

- (a) if #2 is non-diagnostic or inflammatory but not clearly septic effusion then order a complete AUS

If septic abdomen confirmed

- O Notify Senior House Officer/Faculty

Initiate Fluid Therapy with the following goals:

- Systolic BP > 90 mmHg
- Lactate < 2.5
- HR < 150 bpm if possible
- Good pulse quality, CRT – 1–2 seconds

Diagnostic tests to submit:

Check all that apply:

- Abdominal fluid C&S
- CBC, platelet, Chem
- UA
- ER PT/PTT or TEG
- Blood type
- Recheck electrolytes, PCV/TS

Preparing for surgery:

- Call Surgery/Anesthesia Team
- Place second IVC
- Shave Abdomen
- Externally Warm (if hypothermic)

Transfusion Therapy:

- If PCV <30 at recheck then consider 10 mL/kg pRBC
- If PTT >1.5× prolonged start thawing 10–20 mL/kg FFP

Immediately Postoperatively:

- Analgesia
- Fluid therapy with goals as before
- Recheck PT/PTT/TEG if coagulopathic pre-op, or excessive bleeding
- Re-check electrolytes/PCV/TS
- Standard monitoring: BP, ECG, Urine output if U-cath, RR/effort
- Check to ensure antibiotics were administered and continue previous antibiotic protocol as selected in the ED on appropriate time schedule:

Cultures:

- Source and time taken: _____
- Postoperatively: check cultures submitted
- Day 1 postoperatively: check cultures accessioned
- Daily postoperatively: check cultures until finalized:

Abbreviations: IVC = IV catheter; AUS = abdominal ultrasound; TEG = thromboelastogram; RR = respiratory rate; BP = blood pressure; TPR = temperature, pulse rate, respiratory rate; ; TS = total solids; u-cath = urinary catheter; ED = emergency department; PT = prothrombin time; APTT = activated partial thromboplastin time; FFP = fresh frozen plasma; pRBC = packed RBC; UA = urinalysis; Chem = biochemistry profile.