PRACTICE MANAGEMENT GUIDELINES FOR PROPHYLACTIC ANTIBIOTIC USE IN PENETRATING ABDOMINAL TRAUMA

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I. Statement of the Problem

Fullen et al. first described the role for antibiotics in patients sustaining penetrating abdominal injuries.[1] They retrospectively reviewed 295 patients who underwent celiotomy after sustaining penetrating abdominal wounds and categorized patients according to the timing of their first antibiotic dose: preoperative (n=16); intraoperative (n=98); and postoperative (n=81). The reported rate of trauma-related infections (incisional and intra-abdominal abscess) were 7%, 33%, and 30%, respectively. Individuals with colon injuries had postoperative infection rates of 11%, 57%, and 70% for each group, respectively. These rates remained constant even when the data were analyzed for additional risk factors, including the number of associated intra-abdominal organs injured, frequency of shock, and need for transfusion of blood products. The average time from hospital admission to laparotomy was the same for all three groups. Regardless of whether the observed difference was due to the intraoperative or postoperative groups having a longer interval between injury and antibiotic administration or that the preoperative group had antibiotics circulating at the time of incision, this was the first study to suggest that the timing of antibiotic administration can impact the development of injury related infections in patients with penetrating abdominal injuries.

The importance of broad-spectrum antibiotic coverage for these patients was demonstrated by Thadepalli et al. in 1973.[2] This study was a prospective, randomized comparison of kanamycin and cephalothin to kanamycin and clindamycin. Both antibiotic combinations were administered preoperatively. The clindamycin group had a significantly lower rate of infection in the postoperative period compared to the cephalothin group (10% versus 27%). They further demonstrated that the difference was due to significantly more anaerobic infections in the cephalothin group (21%) compared with the clindamycin group (2%).

These two studies demonstrated a significantly lower rate of infection when antibiotics providing aerobic and anaerobic coverage are administered prior to operative treatment. Prophylactic antibiotics for patients sustaining penetrating abdominal injuries with intestinal contamination have a role for reducing the rate of incisional wound infection subjected to gastrointestinal soiling. A single dose providing sufficient concentration within the wound during the vulnerable period is optimal. The other aspect of prophylactic antibiotic administration in trauma is the potential therapeutic role. The problem is to define the time period when contamination of the abdominal cavity becomes an established infection. At celiotomy, the intestinal wound is closed, eliminating further contamination and soiling of the peritoneal cavity. Thus, no further antibiotic should be necessary.

Surgeons have concluded that Aprophylactic antibiotics@ in penetrating abdominal trauma can reduce the incidence of postoperative infectious complications. Since the mid 1970s, no study has included a placebo control group because of the high incidence of infectious complications after intestinal injury. However, many studies in the past two

decades have compared various antibiotic regimens to evaluate single agents versus combination regimens, duration of administration, and, more recently, the pharmacokinetics and cost implications of single versus combination therapy.

II. Process

A. Identification of references

The recommended guidelines for prophylactic antibiotic use for trauma patients sustaining penetrating abdominal wounds are evidence-based. A MEDLINE search from 1976 to 1997 was performed using the following subject words: antibiotic prophylaxis; penetrating abdominal injuries; abdominal injuries-complications; peritonitis; wound infection-prevention and control; pharmacokinetics; trauma; and cost analysis. This search identified 55 English language references. The bibliography of each article was reviewed for additional references which were not identified in the original MEDLINE query. Letters to the editor, case reports, and review articles were deleted from further evaluation. Thirty-nine articles were identified for this evidentiary review. Thirty-two pertained to comparisons of various antibiotic regimens and comprise the first table subtitled AOutcome@. The remaining seven articles include six clinical studies and one meta-analysis. These articles addressed pharmacokinetics and cost and are listed in the table subtitled APharmacokinetics and Cost@. The articles were reviewed by five general surgeons and two pharmaceutical outcome researchers with interest in pharmacokinetics and health care economics. These individuals then collaborated to produce the guidelines.

B. Quality of the references

The references were classified using methodology established by the Agency for Health Care Policy and Research (AHCPR) of the U.S. Department of Health and Human Services. Additional criteria and specifications were used for Class I articles from a tool described by Oxman et al.[3]

Thus, the classifications were:

Class I: Prospective, Randomized, Double-Blinded Study.
Class II: Prospective, Randomized, Non-Blinded Trial.
Class III: Retrospective Series of Patients or Meta-Analysis.

In the evidentiary section are three tables. The first table includes 32 studies comparing various antibiotic regimens for infectious outcome. The second table is a summary of the seven articles pertaining to pharmacokinetics and cost, and the third table lists data from Class I studies regarding combination versus single agent antibiotics.

III. Recommendations

A. Level I

There is sufficient Class I and II data to recommend a single preoperative dose of prophylactic antibiotics with broad-spectrum aerobic and anaerobic coverage as a standard of care for trauma patients sustaining penetrating abdominal wounds. Absence of a hollow viscus injury requires no further administration.

B. Level II

There is sufficient Class I and Class II data to recommend continuation of prophylactic antibiotics for only 24 hours in the presence of injury to any hollow viscus.

C. Level III

There is insufficient clinical data to provide meaningful guidelines for reducing infectious risks in trauma patients with hemorrhagic shock. Vasoconstriction alters the normal distribution of antibiotics, resulting in reduced tissue penetration. To circumvent this problem, the administered dose may be increased two- or threefold and repeated after every 10^{th} unit of blood product transfusion until there is no further blood loss (see Pharmacokinetics Table). Once hemodynamic stability has been achieved, antibiotics with excellent activity against obligate and facultative anaerobic bacteria should be continued for periods that depend on the degree of wound contamination. Aminoglycosides have been demonstrated to exhibit sub-optimal activity in patients with serious injury, probably due to altered pharmacokinetics of drug distribution.

IV. Scientific Foundation

A. Historical background

The reports by Fullen et al.[1] and Thadepalli et al.[2] set the standard for use of antibiotic prophylaxis in patients with penetrating abdominal injuries. Multiple studies in the 1980s compared the efficacy of various antibiotic regimens. These articles have been summarized by Dellinger,[4] who discusses specific issues regarding choice of agent, duration of therapy, and optimum dose for the various antimicrobial agents. Several studies since that review have compared third generation cephalosporins and ß-lactam penicillin derivatives with combination therapy (see Evidentiary Tables). There have been several studies evaluating the duration of therapy. Dellinger concluded in 1989 that the studies reported up to that time did not permit a definitive statement regarding the preferred antimicrobial

agent for patients sustaining penetrating abdominal injuries, and we would agree with this statement. The additional studies identified in this review address some of the concerns raised by Dellinger and will be the focus of this evidentiary review.

Many difficulties exist with interpreting the literature to date regarding prophylactic antibiotics for penetrating abdominal wounds. Specifically, there continues to be a lack of standardization in study design and reporting of data and results. There is also the lack of definition according to the risk factors identified by Nichols et al.[5] and Dellinger et al.[6] Most studies did not mention the importance of transfusion requirements, length of operation, age, and penetrating abdominal trauma index as significant risk factors for development of any postoperative infection. With the trend towards primary repair of all colon injuries, the surgical management of the colon is rarely mentioned nor standardized in the study design. The frequency of colostomy versus primary repair, particularly regarding left colon injury in high risk patients, is not standardized in the design or discussed in the results. Thus, the goal of this evidentiary review is to evaluate the literature regarding mechanism of injury, choice of agent, duration of therapy, the unique pharmacokinetics of the trauma patient and its effect on dosing considerations, and cost analysis.

B. Risk factors for trauma-related infections (wound infection, intra-abdominal abscess, bacteremia, drain tract infection, and urinary tract infection).

1. Mechanism of injury.

The majority of studies have included patients sustaining stab wounds and gunshot wounds.[5-23] Four reports enrolled patients by controlling for types of penetrating forces. Moore et al. compared three antibiotic regimens in only firearm wounds.[24] Of the 86 patients studied, less than half had colon injuries (n=39). The infection rate ranged from 13 to 23% with no significant difference between the three groups. Three studies evaluated patients primarily injured by knives.[19,25,26] Heseltine et al. only enrolled stab wounds to compare gentamicin and clindamycin against cefoxitin.[25] Both drugs were administered for 72 hours. The infection rates were 7% and 9%, respectively. Of the 75 patients studied, less than one-third had colon injuries (n=21). Demetriades et al. studied 123 patients (76% stab wounds) receiving 48 hours of ceftriaxone or cefoxitin and observed a 7 to 8% rate of infection.[19] Van Rensburg et al. observed a 1.4 % infection rate in 290 patients (89% stab wounds) receiving ceftriaxone and metronidazole for 24 hours.[26] However, only 16% had colonic injuries. None of these studies reported the management of colonic injury. These three studies suggest that prophylactic antibiotics in abdominal stabbing injuries can be stopped after 24 hours.

In several studies, the mechanism of injury was not reported,[10,11,14,22,27] while others also included non-penetrating injuries. Ericsson et al. compared the duration and dose of amikacin and clindamycin in 150 randomized patients.[28] Bowel injuries occurred from gunshot wounds (n=76), blunt trauma (n=40), or knives (n=24). Hofstetter et al. also included blunt bowel wounds (20%) and observed no difference in infection rates for patients treated with cefoxitin or triple antibiotics for 24 hours (14% versus 18%, respectively).[29]

2. Choice of antimicrobial agents

The 33 articles included in the evidentiary outcome table compared various antibiotics for differences in infectious complications. Twelve of these studies were Class I data (prospective, randomized, double-blinded). Three series that controlled for mechanism of injury at the time of enrollment were discussed in section 1.[24,25,27] Another study evaluated duration of therapy.[9] Other articles included mixed populations of patients (blunt, gunshot, stab) comparing various single agents against combination therapy.[5,14,20,22,23,27,30-33] Fabian et al. compared various classes of cephalosporins and limited the duration of use to 24 hours.[30] The number of colon injuries in each of the three groups was less than 20% of the patients enrolled in each. The trauma-related infections were not significantly different (range 9 to 17%). Nichols et al. compared cefoxitin to clindamycin and gentamicin.[5] Both groups had an infection rate of 24% despite 5 days of therapy. Jones et al. compared tobramycin plus clindamycin to cefamandole and cefoxitin in 257 patients.[31] Ninety-six patients (37%) had colon injuries and were equally distributed between the three treatment groups. They concluded that cefoxitin and tobramycin plus clindamycin were superior to cefamandole in reducing infections (18%, 29% versus 36%, respectively) with only 48 hours of therapy. In a comparison of moxalactam to a combination of tobramycin plus clindamycin, Nelson et al. observed no difference in postoperative infections (19% versus 23%).[14] Cefoxitin and cefotetan were compared to each other using two different treatment durations (1 day versus 5 days).[27] There was no difference in trauma-related infection rates between agents or between the duration of use. Aztreonam was compared to gentamicin when both agents were used in combination with clindamycin.[22] The authors concluded aztreonam was superior to gentamicin (3% versus 13%) because of the under-dosing of the gentamicin and subsequent subtherapeutic levels compared to the more stable pharmacokinetics of aztreonam. Unfortunately, of the 63 patients enrolled in this trial, only 17 (27%) had colon injuries.[22] The role of *enterococci* in abdominal infectious complications was evaluated by Sims et al.[23] Using cefoperazone, which has no enterococcal coverage, or combination therapy with enterococcal

coverage, both regimens were administered for at least five days. Trauma-related infections ranged from 2 to 8%. They concluded that coverage for *enterococcus* is not necessary in penetrating abdominal wounds. In contrast, Weigelt et al.[34] in a prospective, randomized open labeled study (Class II data) concluded ampicillin / sulbactam therapy resulted in a significantly lower wound infection rate in patients with colonic injuries compared to cefoxitin (9% versus 17%, respectively). This difference between the two groups was due to an increased incidence of enterococcal infections in the cefoxitin-treated patients. However, there were some methodologic problems with the study, ie, almost twice as many patients (N=21) receiving ampicillin / sulbactam had surgical wounds left open compared to the cefoxitin group (N=11), making interpretation of the data difficult.

In these six Class I studies, the trauma-related infectious complication rate ranged from 3%[22] to 36%.[31] The only study with a significant reduction in infections was based on a small study population (n=63) with only 17 colonic wounds.[22] It does not justify any definitive statement. No other study showed superiority of any agent compared to an aminoglycoside in combination with clindamycin or metronidazole (Class I data table). Finally, one Class I study evaluated duration of therapy using penicillin G plus doxycycline administered for either 12 hours or 5 days.[9] There was no difference in the trauma-related infections between the two groups. These Class I data indicate that single and combination therapy are equally effective in minimizing trauma-related infections following penetrating abdominal wounds. The antibiotics need not be continued for more than 24 hours following injury.

One meta-analysis included 17 studies assessing the effectiveness of single agent versus combination therapy containing aminoglycosides for penetrating wounds. This report concluded that single ß-lactam agents were as effective as combination therapy.[35]

3. Duration of therapy

There is a small amount of Class I data regarding duration of therapy. Griswold et al. stated that injury severity, as measured by the abdominal trauma index (ATI), should dictate the duration of therapy.[20] While there were no significant differences in abdominal abscess rates for the antibiotic groups (cefoxitin, ceftriaxone, and mezlocillin), there were differences in abscess rates for those with a lower ATI. The authors concluded that antibiotics should be given longer than 12 hours for high-risk patients. Fabian et al. analyzed 515 patients who were randomized to receive either cefoxitin or cefotetan for either 1 or 5 days.[27] There were no differences in abdominal infection rates for the different antibiotics or for the duration of

therapy. When the duration of therapy was compared in the high-risk population (colon wounds or ATI > 25), there was also no statistical difference in infection rates. In fact, infections tended to be more frequent in the 5-day group. These authors concluded that 24 hours of therapy was an adequate duration of therapy for all penetrating abdominal wounds.

The Class II data (prospective, randomized, non-blinded) included several trials evaluating various lengths of therapy.[11,16,19,21,36,37] Rowlands and Ericsson incorporated two independent studies in their review comparing various antibiotics for 3 or 5 day courses.[11] Unfortunately, they did not identify colon or other hollow viscus injuries in any treatment. Although infection rates were lowest with the 5-day therapy, the lack of knowledge about organ injuries does not allow any convincing conclusion. Dellinger et al. evaluated 116 patients with penetrating wounds of the colon and/or small bowel randomized to receive 12 hours or 5 days of antibiotics.[37] There was no statistical difference in the rate of trauma-related infections. In contrast, a second study by Rowlands et al. used intraoperative findings to define patients as high or low risk for infection.[16] The high-risk group included one or more of the following injuries: penetration of the GI tract; major liver or pancreatic injury; close range shotgun wounds; patients in whom complete hemostasis was not obtained; and patients in whom nonviable tissue was present at the time of wound closure and following major splenic repair. Patients without any of these injuries were considered low-risk and received antibiotics for less than 24 hours, whereas prophylaxis for the high-risk patients was for 72 hours. Each group had a second stratification for one of two antibiotic combinations. Despite this randomization by operative findings, their data reported one colon and one small bowel injury in the low-risk group receiving less than 24 hours of antibiotics with a 6% rate of infection. The high-risk group included 53 colon injuries in 103 patients. The infection rates for the two antibiotic regimens were 16% and 25%.[16] Lou et al. compared mezlocillin to gentamicin plus clindamycin.[18] Both therapies were continued for 5 to 10 days if there was a colon injury. The trauma-related infection rate was similar between the two groups (9% versus 10%). Moore et al. compared the same two antibiotic regimens as Lou et al.[18] but limited therapy to a 5-day course for patients sustaining a colon injury.[38] They reported a 13 to 15% incidence of infections. Even when antibiotic therapy was continued for up to 15 days, the trauma-related infection rate remained 7 to 8% as reported by Sims et al.[21] These Class II data further support limiting prophylaxis to 24 hours or less since there was no documented benefit with a longer course.

4. Pharmacokinetics (Optimal Dosage)

Most current studies evaluating the efficacy of various antibiotic regimens have used standard drug doses recommended for healthy patients undergoing elective procedures. This is of particular concern in patients sustaining penetrating wounds in whom abnormal perfusion and shock is common. It is this group of patients that presents with shock and receives inappropriate doses of antibiotics when standard dosing is followed and not adjusted for the reduced circulating volume. The ideal dose of antibiotics has not been established for these patients. Ericsson et al.[28] first questioned adequate dosing because of large fluid shifts and the hyperdynamic physiologic response seen in trauma patients. They compared clindamycin 600 mg every 6 hours against a 1200 mg dose every 12 hours over a 72-hour course. There was no difference in infection rates. However, early in the study they measured the serum concentration of a second agent, amikacin, and found the average peak level was subtherapeutic. They subsequently increased the dose of amikacin to 11 mg/kg and saw an inverse correlation between increasing dose of amikacin and the rate of infection. Similarly, Townsend et al. reported that the volume of distribution for aminoglycosides in trauma patients was greater than predicted and serum levels were subtherapeutic (not in table).[39] In order to maintain adequate levels of aminoglycosides in the serum, wound fluid, or target tissue, they recommended an initial loading dose of 3 mg/kg.

The relationship of volume of distribution being altered in trauma patients by massive fluid resuscitation was further elucidated by Reed et al.[40] They compared standard amikacin dosing to dosing based on pharmacokinetic analysis of serum levels. Both groups had a significant expansion of the volume of distribution (71%) during the first 24 hours post-injury. For study days 2 and 3, the volume expansion was only 43% over the expected values, whereas the elimination rates remained elevated. Because of the expanded volume of distribution during resuscitation, they concluded that empiric prophylactic antibiotic dosing should be high, rather than low. They also recommended frequent dosing during the fluid resuscitation phase. Once bacterial contamination of tissues has ceased, the antibiotic should be stopped. Because of the relatively narrow therapeutic index associated with aminoglycosides and the highly variable volumes of distribution in trauma patients, they concluded that standard dosing of these agents would result in subtherapeutic serum and tissue levels and thus inadequate prophylaxis. Rosemurgy et al. evaluated the effects of volume of distribution on serum concentrations of ceftizoxime and subsequent infection rates.[41] They demonstrated that early peak serum concentrations were significantly lower in patients who experienced infections because of the increased volume of distribution of the drug compared to patients who did not develop infection.

These four studies, although with small numbers of patients, raise serious questions about the adequacy of antibiotic dosing of aminoglycosides in previous trials that included patients in shock. Pharmacokinetic studies of aminoglycosides suggest that standard dosing is subtherapeutic for patients in hemorrhagic shock (see Pharmacokinetics Table). Some of the high infection rates reported in earlier studies could be explained by inadequate dosing.

5. Cost analysis

In the past 10 years, there have been four studies evaluating the cost of antibiotic therapy in trauma patients with penetrating abdominal wounds. Crots et al. compared moxalactam to gentamicin plus clindamycin in 50 patients.[42] The strength of this study is the well-performed cost analysis which included hospital costs for drugs, laboratory tests, personnel time, and supplies. They observed no symptomatic, trauma-related infections in either treatment group. There were also no direct toxic effects from either agent. The mean drug cost for each regimen did not differ. However, when laboratory tests, personnel time, and supply cost were added to the drug cost, the mean cost of therapy per patient was 38% greater with gentamicin plus clindamycin compared to moxalactam. This study demonstrated the importance of considering all treatment costs when performing cost-effectiveness analysis of combination therapy. In a similar study design, Bivins et al. compared cefotaxime, cefoxitin, and gentamicin plus clindamycin.[43] Twenty-five patients were entered into each treatment arm, and the septic complications were 8%, 4%, and 8%, respectively. The cost analysis included the same four categories (drug cost, laboratory tests, personnel time, and supply cost). The mean cost of therapy per patient was significantly less with the cefotaxime. Unfortunately, the authors did not specify the number of patients who had high-risk factors for the development of infection. In a subsequent report using the same study design, Bivins et al. used the same three antibiotic regimens for a 3- to 5-day course of prophylaxis in 129 patients.[44] Only 17 patients had colon injuries. The infection rate for cefotaxime was 6.9%, cefoxitin was 2.3%, and gentamicin plus clindamycin was 6.9%. There was no statistical difference between groups. As in their previous study, the mean cost of therapy per patient was significantly lower for the cefotaxime group. Fabian et al.[45] compared aztreonam plus clindamycin with gentamicin plus clindamycin in 85 trauma victims with suspected penetrating intra-abdominal injury. There were 34 colon injuries. They further analyzed the hospital cost by stratifying patients as infected versus non-infected. They concluded that, despite a lower infection rate in the aztreonam group, neither hospital nor pharmacy costs were significantly different compared with those in the gentamicin plus clindamycin group. These cost analysis

studies of antibiotic therapy would suggest that consideration of single agent therapy using a drug with aerobic and anaerobic coverage may be a cost-effective choice compared to the more traditional combination antibiotic regimen (gentamicin plus clindamycin).

C. Evidentiary Table

There are three evidentiary tables in this review. The first table includes outcome studies and contains 33 articles arranged chronologically by class. The conclusion section lists the antibiotic, number of patients, days of therapy, organs injured (when identified), and percent of trauma-related infections. These infections included wound infection, intra-abdominal abscess, drain tract wound infection, urinary tract infection, or bacteremia. The rate of infection was determined by reviewing each result section for the specific infections and dividing this by the number of patients. The table includes 11 Class I articles (prospective, randomized, double-blinded) and 19 Class II (prospective, randomized, non-blinded). The second table delineates studies on pharmacokinetics and cost analysis. It includes 7 articles listed by chronologically by class (one Class I, 5 Class II, and one Class III). Three articles address the cost of antimicrobial therapy, three evaluate pharmacokinetics, and the last article is a meta-analysis of safety of ß-lactam penicillin derivatives compared with aminoglycoside combinations. The use of quinolones has not been tested for prophylaxis in penetrating abdominal wounds with GI contamination. The third table contains data from Class I studies addressing single versus combination antimicrobial agents.

V. Summary

The proven role of prophylactic antibiotics in penetrating abdominal trauma is to reduce the incidence of wound infections. However, numerous studies from the past two decades have compared one therapeutic agent against another without an appropriate placebo control. The reduced incidence of remote infections (urinary tract infection, thrombophlebitis, and pneumonia) found by these investigators without appropriate controls is of questionable benefit. The altered pharmacokinetics of drugs in patients undergoing resuscitation with crystalloid and/or blood products needs further investigation. Most authors agree that the increased volume of drug distribution with appropriate resuscitation suggests that standard dosing regimens are subtherapeutic. Prophylactic antibiotics are optimally administered prior to incision, the duration should be brief (✍ 24 hours) with no additional benefit associated with prolonged therapy. An adjusted dose for the hemodynamically unstable patients, may be of benefit.

VI. Future Studies

Future studies need to be double-blinded in their design and clearly define the criteria for trauma-related infections. Other risk factors such as time to administration, shock, short

versus long half-life antibiotics, duration, and organ injuries should be evaluated. More studies need to be conducted evaluating the interaction of hemodynamic status with volume of distribution. The specific organisms responsible for trauma-related infections need further study.

VII. References

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PROPHYLACTIC ANTIBIOTICS IN PENETRATING ABDOMINAL TRAUMA: EVIDENTIARY TABLE - OUTCOME

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Fabian TC	1982	Use of antibiotic prophylaxis in penetrating abdominal trauma. *Clin Ther 5:38-47*	I	Cefotaxime Cefotaxime Cefazolin	117 127 116	< 1 1 1	colon 19/hv 45 colon 19/hv 41 colon 16/hv 32	17 10 9
Oreskovich MR	1982	Duration of preventive antibiotic administration for penetrating abdominal trauma. *Arch Surg 117:200-5*	I	Penicillin G + Doxycycline	42 39	12 hrs 5	colon 9/hv 17 colon 9/hv 12	26 15
Moore FA	1983	Preoperative antibiotics for abdominal gunshot wounds. A prospective, randomized study. *Am J Surg 146:762-5*	I	Ampicillin + Clindamycin + Amikacin Penicillin + Doxycycline Carbenicillin	30 26 30	5 for colon 2 hv 1 no injury	colon 15/hv 24 colon 12/hv 20 colon 12/hv 23	20 23 13
Nichols RL	1984	Risk of infection after penetrating abdominal trauma. *N Engl J Med 311:1065-70*	I	Cefoxitin + placebo Clindamycin + Gentamycin	70 75	5 5	colon 40/sb 30 colon 35/sb 40	24 24
Jones RC	1985	Evaluation of antibiotic therapy following penetrating abdominal trauma. *Ann Surg 201:576-85*	I	Tobramycin + Clindamycin Cefamandole Cefoxitin	85 78 94	2 2 2	colon 39/hv 61 colon 26/hv 55 colon 31/hv 64	29 36 18
Heseltine PN	1986	The efficacy of cefoxitin vs. clindamycin/ gentamicin in surgically treated stab wounds of the bowel. *J Trauma 26:241-5*	I	Gentamicin + Clindamycin Cefoxitin	41 34	? 3	colon 14/hv 27 colon 7/hv 27	7 3
Nelson RM	1986	Single-antibiotic use for penetrating abdominal trauma. *Arch Surg 121:153-6*	I	Tobramycin + Clindamycin Moxalactam	85 78	5 5	colon 26/hv 54 colon 30/hv 50	11 16
Fabian TC	1992	Duration of antibiotic therapy for penetrating abdominal trauma: A prospective trial. *Surgery 112:788-95*	I	Cefoxitin Cefotetan Cefoxitin Cefotetan	135 130 117 133	1 1 5 5	colon 28 colon 28 colon 26 colon 29	11 6 7 13

* hv = hollow viscus injuries
sb = small bowel injuries

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Griswold JA	1993	Injury severity dictates individualized antibiotic therapy in penetrating abdominal trauma. *Am Surg 59:34-9*	I	Cefoxitin Ceftizoxime Mezlocillin Cefoxitin Ceftizoxime Mezlocillin	25 23 20 6 13 15	6 or 12 hrs Primary repair, no shock,? 3 organs 6 or 12 hrs Colostomy, shock, ? 3 organs	colon 5 colon 3 colon 3 colon 5 colon 3 colon 5	12 8.7 10 50 15 53
Fabian TC	1994	Superiority of aztreonam/clindamycin compared with gentamicin/clindamycin in patients with penetrating abdominal trauma. *Am J Surg 167:291-6*	I	Gentamicin + Clindamycin Aztreonam + Clindamycin	36 37	4/1 4/1	colon 9/hv 27 colon 8/hv 29	13 3
Sims EH	1997	How many antibiotics are necessary to treat abdominal trauma victims? *Am Surg 63:525-35*	I	Cefoperazone Ceftriaxone+Metronidazole Ampicillin+Gentamicin+ Metronidazole	101 95 95	 All ? 5	colon 29/hv 53 colon 25/hv 53 colon 37/hv 69	8 2 5
O=Donnell V	1978	Evaluation of carbenicillin and a comparison of clindamycin and gentamicin combined therapy in penetrating abdominal trauma. *Surg Gynecol Obstet 147:525-8*	II	Clindamycin + Gentamicin Carbenicillin	66 60	no injury ? 4 any injury ? 6	colon 15 colon 15	16 21
Crenshaw C	1983	A prospective random study of a single agent versus combination antibiotics as therapy in penetrating injuries of the abdomen. *Surg Gynecol Obstet 156:289-94*	II	Cefamandole Tobramycin + Cephalothin	49 45	 ? 3	colon 16 colon 16	6 11
Gentry LO	1984	Perioperative antibiotic therapy for penetrating injuries of the abdomen. *Ann Surg 200:561-6*	II	Cefamandole Cefoxitin Ticarcillin + Tobramycin	51 50 51	2 2 2	colon 22/sb 37 colon 21/sb 40 colon 26/sb 37	18 6 10

* hv = hollow viscus injuries
sb = small bowel injuries

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Hofstetter SR	1984	A prospective comparison of two regimens of prophylactic antibiotics in abdominal trauma: Cefoxitin versus triple drug. J Trauma 24:307-10	II	Cefoxitin Ampicillin +Clindamycin + Aminoglycoside	69 50	1 1	hv 31 hv 25	14 18
Rowlands BJ	1984	Comparative studies of antibiotic therapy after penetrating abdominal trauma. Am J Surg 148:791-5	II	Cefamandole Cefoxitin Clindamycin + Tobramycin Moxalactam Clindamycin + Tobramycin	51 54 46 47 45	3 3 3 5 5	 N/A N/A	20 20 11 2 9
Fabian TC	1985	Antibiotics in penetrating abdominal trauma. Comparison of ticarcillin plus clavulanic acid with gentamicin plus clindamycin. Am J Med 79:157-60	II	Gentamicin + Clindamycin Ticarcillin / Clavulanate	32 53	1 1	all all	13 2
Lou MA	1985	Comparison of cefamandole and carbenicillin in preventing sepsis following penetrating abdominal trauma. Am Surg 51:580-6	II	Cefamandole Carbenicillin	47 58	3 or 5	colon 13/hv 33 colon 15/hv 36	6.4 19
Dellinger EP	1986	Efficacy of short-course antibiotic prophylaxis after penetrating intestinal injury. A prospective randomized trial. Arch Surg 121:23-30	II	Doxycycline + Penicillin G Cefoxitin Doxycycline + Penicillin G Cefoxitin	31 30 25 28	12 hrs 12 hrs 5 5	colon 18/sb 13 colon 15/sb 15 colon 14/sb 11 colon 14/sb 14	16 17 24 11
Feliciano DV	1986	Single agent cephalosporin prophylaxis for penetrating abdominal trauma. Results and comment on the emergence of the enterococcus. Am J Surg 152:674-81	II	Cefotaxime Cefoxitin Moxalactam	124 149 153	2 2 2	colon 52/hv 101 colon 65/hv 117 colon 66/hv 111	2 13 7
Kreis DJ Jr	1986	A prospective randomized study of moxalactam versus gentamicin and clindamycin in penetrating abdominal trauma. Surg Gynecol Obstet 163:1-4	II	Gentamycin +Clindamycin Moxalactam	22 20	> 3	colon 2/hv 4 colon 2/hv 7	23 0

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sb = small bowel injuries

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Posner MC	1987	Presumptive antibiotics for penetrating abdominal wounds. Surg Gynecol Obstet 165:29-32	II	Mezlocillin Clindamycin + Gentamycin	61 69	colon 5 hv 2	colon 14 colon 19	15 13
Rowlands BJ	1987	Penetrating abdominal trauma: The use of operative findings to determine length of antibiotic therapy. J Trauma 27:250-5	II	Tobramycin + Metronidazole Tobramycin + Clindamycin Tobramycin + Metronidazole Tobramycin + Clindamycin	49 53 31 27	3 3 < 1 < 1	colon 21/sb 19 colon 32/sb 14 colon 1/sb 1 colon 0/sb 0	16 25 6 0
Fifer T	1988	A prospective randomized comparison of a single antibiotic (moxalactam) versus combination therapy (gentamicin and clindamycin) in penetrating abdominal trauma. Henry Ford Hosp Med J 36:52-55	II	Gentamicin + Clindamycin Moxalactam	25 25	? 3 ? 3	colon 4/hv 12 colon 2/hv 11	0 0
Lou MA	1988	Safety and efficacy of mezlocillin: A single-drug therapy for penetrating abdominal trauma. J Trauma 28:1541-7	II	Mezlocillin Clindamycin + Gentamicin	74 73	colon 5-10 hv 2-10 no injury 1	colon 20/hv 49 colon 24/hv 48	9 10
Ericsson CD	1989	Prophylactic antibiotics in trauma: The hazards of underdosing. J Trauma 29:1356-61	II	Amikacin + Clindamycin 1200 Amikacin + Clindamycin 1200 Amikacin + Clindamycin 600	47 52 51	1 3 3	colon 13 colon 14 colon 18	19 21 12
Moore FA	1989	Presumptive antibiotics for penetrating abdominal wounds. Surg Gynecol Obstet 169:99-103	II	Mezlocillin Gentamycin +Clindamycin	136 142	colon 5 hv 2	colon 31 colon 35	15 13
Demetriades D	1991	Short-course antibiotic prophylaxis in penetrating abdominal injuries: Ceftriaxone versus cefoxitin. Injury 22:20-24	II	Ceftriaxone Cefoxitin	60 63	colon 2 hv 1	colon 12/hv 38 colon 13/hv 45	7 8

* hv = hollow viscus injuries
sb = small bowel injuries

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Van Rensburg LC	1991	Ceftriaxone (Rocephin) in abdominal trauma. *J Trauma 31:1490-4*	II	Ceftriaxone + Metronidazole	290 (89% stabs)	1	colon 47/ hv 129	1.4 (all infections), 0 deep
Sims EH	1993	Piperacillin monotherapy compared with metronidazole and gentamicin combination in penetrating abdominal trauma. *J Trauma 34:205-10*	II	Gentamicin + Metronidazole Piperacillin	89 33 94 30	5-15 2 5-15 2	colon 20 hv 40 colon 26 hv 49	8 0 7 0
Weigelt JA	1993	Abdominal surgical wound infection is lowered with improved perioperative enterococcus and bacteroides therapy. *J Trauma 1993;34:579-84*	II	Cefoxitin Ampicillin / Sulbactam	309 283	1 1	colon 54 colon 57	17 9
O=Donnell VA	1978	Role of antibiotics in penetrating abdominal trauma. *Am Surg 44:574-7*	III	Cephalosporin / Penicillin / Chloramphenicol, Gentamicin Kanamycin, Clindamycin, Gentamicin + Clindamycin	107	variable ? 7	N/A N/A	15.8 7.4
Dellinger EP	1984	Risk of infection following laparotomy for penetrating abdominal injury. *Arch Surg 119:20-7*	III	Penicillin + Tetracycline or Doxycycline	330	N/A	colon 78 hv 118	13

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sb = small bowel injuries

PROPHYLACTIC ANTIBIOTICS IN PENETRATING ABDOMINAL TRAUMA: EVIDENTIARY TABLE PHARMACOKINETICS AND COST

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Lab Test	Cost Analysis
Fabian TC	1996	Pharmacoeconomics of aztreonam-clindamycin versus gentamicin-clindamycin in the treatment of penetrating abdominal injury. *Pharmacotherapy 16:951-7*	I	Gentamicin + Clindamycin Aztreonam + Clindamycin	41 44	4 (colon) or 1 4 (colon) or 1	$66,336 Mean hosp. cost: $ 8,014	14.6 2.3
Crots LD	1985	Twice-daily moxalactam versus gentamicin and clindamycin in patients with penetrating abdominal trauma. *Clin Pharmacokinet 4:316-20*	II	Clindamycin + gentamicin Moxalactam	25 25	5.4 6.0	165 173	$ 475.11 $ 331.88
Bivins BA	1988	Preventive antibiotics for penetrating abdominal trauma --single agent or combination therapy? *Drugs 35:100-105*	II	Cefotaxime Cefoxitin Clindamycin + gentamycin	25 25 25	3 - 98 3 - 98 3 - 98	170 185 158	$ 471.90 $ 530.24 $ 528.54
Bivins BA	1989	Antibiotics for penetrating abdominal trauma: A prospective comparative trial of single agent cephalosporin therapy versus combination therapy. *Diagn Microbiol Infect Dis 12:113-8*	II	Cefotaxime Cefoxitin Clindamycin + gentamicin		Mean 5 Mean 4 Mean 6	N/A N/A 108	$ 382.77 $ 404.95 $ 594.55
Reed RL 2d	1992	The pharmacokinetics of prophylactic antibiotics in trauma. *J Trauma 32:21-7*	II	Clindamycin + amikacin (Uniform Dose) Clindamycin + amikacin (Adjusted Dose)	16 12	3 3	None Peak and Trough	Variations in volume of distribution cause non-therapeutic levels with standard doses.
Rosemurgy AS 2d	1995	Ceftizoxime use in trauma celiotomy: Pharmacokinetics and patient outcomes. *J Clin Pharmacol 35:1046-51*	II	Ceftizoxime	53	2	11% developed infections. All had significant-ly less volume distribution.	N/A

Author	Year	Reference	Class	Conclusions
Hooker KD	1991	Aminoglycoside combinations versus beta-lactams alone for penetrating abdominal trauma: A meta-analysis. *J Trauma 31:1155-60*	III	Meta-analysis of 17 randomized studies to assess effectiveness of single vs. combinations containing aminoglycoside used for penetrating abdominal wounds. Concluded single beta-lactam antimicrobials are as effective as traditional combinations including aminoglycoside.

PROPHYLACTIC ANTIBIOTICS IN PENETRATING ABDOMINAL TRAUMA: EVIDENTIARY TABLE
CLASS I DATA - COMBINATION VERSUS SINGLE AGENT

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Fabian TC	1982	Use of antibiotic prophylaxis in penetrating abdominal trauma. *Clin Ther 5:38-47*	I	Cefotaxime Cefotaxime Cefazolin	117 127 116	< 1 1 1	colon 19/hv 45 colon 19/hv 41 colon 16/hv 32	17 10 9
Oreskovich MR	1982	Duration of preventive antibiotic administration for penetrating abdominal trauma. *Arch Surg 117:200-5*	I	Penicillin G + Doxycycline	42 39	12 hrs 5	colon 9/hv 17 colon 9/hv 12	26 15
Nichols RL	1984	Risk of infection after penetrating abdominal trauma. *N Engl J Med 311:1065-70*	I	Cefoxitin + placebo Clindamycin + Gentamycin	70 75	5	colon 40/sb 30 colon 35/sb 40	24 24
Jones RC	1985	Evaluation of antibiotic therapy following penetrating abdominal trauma. *Ann Surg 201:576-85*	I	Tobramycin + Clindamycin Cefamandole Cefoxitin	85 78 94	2 2 2	colon 39/hv 61 colon 26/ hv 55 colon 31/hv 64	29 36 18
Heseltine PN	1986	The efficacy of cefoxitin vs. clindamycin/ gentamicin in surgically treated stab wounds of the bowel. *J Trauma 26:241-5*	I	Gentamicin + Clindamycin Cefoxitin	41 34	? ? 3	colon 14 /hv 27 colon 7/hv 27	7 3
Nelson RM	1986	Single-antibiotic use for penetrating abdominal trauma. *Arch Surg 121:153-6*	I	Tobramycin + Clindamycin Moxalactam	85 78	5 5	colon 26/hv 54 colon 30/hv 50	11 16
Fabian TC	1992	Duration of antibiotic therapy for penetrating abdominal trauma: A prospective trial. *Surgery 112:788-95*	I	Cefoxitin Cefotetan Cefoxitin Cefotetan	135 130 117 133	1 1 5 5	colon 28 colon 28 colon 26 colon 29	11 6 7 13
Griswold JA	1993	Injury severity dictates individualized antibiotic therapy in penetrating abdominal trauma. *Am Surg 59:34-9*	I	Cefoxitin Ceftizoxime Mezlocillin Cefoxitin Ceftizoxime Mezlocillin	25 53 20 6 13 15	6 or 12 hrs Primary repair, no shock, ? 3 organs 6 or 12 hrs Colostomy, shock, ? 3 organs	colon 5 colon 3 colon 3 colon 5 colon 3 colon 5	12 8.7 10 50 15 53

* hv = hollow viscus injuries
sb = small bowel injuries

Author	Year	Reference	Class	Antibiotics	# Pts	Duration (days)	Organs*	% Infected
Fabian TC	1994	Superiority of aztreonam/clindamycin compared with gentamicin/clindamycin in patients with penetrating abdominal trauma. *Am J Surg 167:291-6*	I	Gentamicin + Clindamycin Aztreonam + Clindamycin	36 37	4/1 4/1	colon 9/hv 27 colon 8/hv 29	13 3
Sims EH	1997	How many antibiotics are necessary to treat abdominal trauma victims? *Am Surg 63:525-35*	I	Cefoperazone Ceftriaxone + Metronidazole Ampicillin + Gentamicin + Metronidazole	101 95 95	 All ? 5	colon 29/hv 53 colon 25/hv 53 colon 37/hv 69	8 2 5

* hv = hollow viscus injuries
sb = small bowel injuries