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PRESUMPTIVE ANTIBIOTICS FOR CHEST TUBE INSERTION

SUMMARY

There has been much debate regarding the role for prophylactic antibiotics following chest tube placement, particularly those placed in the setting of trauma. Attempts to study this question through randomized controlled trials have been plagued by insufficient power. There is currently insufficient evidence to support the routine use of prophylactic antibiotics following chest tube insertion. Consideration of additional risk factors for infection, such as mechanism of injury, hemothorax, retained hydrothorax, alcoholism, or presence of chronic disease, may provide guidance in determining which patients should receive presumptive antimicrobial therapy. When administered, antibiotics should have activity against the most likely causative pathogens (typically gram-positive bacteria).

RECOMMENDATIONS

- **Level 1**
 - **None**
- **Level 2**
 - **There is insufficient data to support the routine use of presumptive antibiotics for the prevention of infectious complications in patients who undergo tube thoracostomy for spontaneous pneumothorax.**
- **Level 3**
 - **Presumptive antibiotics should be considered for the prevention of infectious complications in patients who:**
 - **Undergo chest tube placement for traumatic pneumothorax / hemothorax AND have additional risk factors for infection**
 - Hemothorax**
 - Retained hydrothorax**
 - Contaminated hemothorax**
 - **When administered, cefazolin 1-2 gm every 8 hours should be given for 24 hours. The first dose should ideally be administered prior to insertion or within 1 hour of insertion in emergent situations. For patients with penicillin hypersensitivity, vancomycin or clindamycin are alternatives.**

INTRODUCTION

Although the use of peri-operative prophylactic antibiotic therapy is well established, the use of prophylactic antibiotics for chest tube placement remains controversial. The reported incidence of infectious complications following chest tube insertion for thoracic injuries ranges from 2 to 35 percent. The body of literature addressing this issue has yielded mixed results due to a number of factors such as differences in study design, sample size, choice of antimicrobial agent, duration of therapy, and

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

differences in patient population such as spontaneous pneumothorax, blunt trauma, penetrating trauma, and associated hollow viscus injury. The definition of an infectious complication has also varied between studies. As a result, there are currently no clear cut recommendations regarding antibiotic use in patients requiring thoracostomy to treat chest injury. Given the variable outcomes in the available literature, the potential benefit of presumptive antibiotics must be assessed in conjunction with the risks associated with this therapy.

LITERATURE REVIEW

Seventy-five patients with isolated penetrating chest wounds were randomized prospectively in a double-blind study to determine the efficacy of antibiotics in patients undergoing tube thoracostomy (1). Thirty eight patients were randomized to Group A and received 300 milligrams of clindamycin intravenously every 6 hours, beginning at admission and continuing until one day following chest tube removal, or for 5 days, whichever period was shorter. Thirty seven patients were randomized to receive placebo (Group B) on the same schedule. Evidence of pneumonia on chest X-ray was found in 10.5% of patients in Group A versus 35% in Group B ($p < 0.03$). Favorable trends were noted in length of stay, temperature elevation, white blood cell counts, incidence of empyema, wound infection, positive pleural and wound cultures, and surgical interventions in Group A, but none reached statistical significance. Empyema developed in 16.2% of patients in Group B, as compared to 2.6% in Group A ($p = 0.11$). The trial was terminated early due to reports of diarrhea and pseudomembranous colitis after clindamycin therapy. The authors concluded that many of the parameters measured may have reached statistical significance with a larger study population. (Class I)

Stone and colleagues conducted a randomized, double-blind trial involving 120 patients with isolated thoracic trauma to evaluate the efficacy of antibiotic therapy in the prevention of post-traumatic pulmonary and pleural related infections (2). Patients were randomized to placebo ($n = 60$) or cefamandole ($n = 60$) 1 gram IV/IM every 6 hours at the time of tube insertion and continued until the second day following tube removal. Infection was defined as gross purulent discharge from the pleural space or the development of purulent sputum with X-ray confirmation of the presence of an active pneumonia or an intrapulmonary abscess. A positive culture, fever, and leukocytosis were also required for the diagnosis of infection. Penetrating trauma resulting in hemothorax, pneumothorax or both was the indication for thoracostomy tube insertion in 46 patients. Thirty five patients experienced spontaneous pneumothorax. The remaining two patients developed a non-traumatic pneumothorax. There was no difference in average duration of tube placement, treatment with antibiotic or placebo, or length of hospital stay. There was a significant difference in infection rate between the placebo and cefamandole groups (13.3% versus 1.7%; $p < 0.05$). Infections consisted of empyema, lung abscess, and pneumonia. There was no difference, however, in infection rates in the subset of patients with spontaneous pneumothorax receiving either antibiotic therapy or placebo. No major adverse events were reported. (Class I)

Cant and colleagues conducted a randomized, double-blind, placebo controlled study in patients with stab wounds of the chest requiring drainage of the pleural space to determine whether short term antibiotics decreased the rate of infectious complications (3). The endpoints of the study were thoracotomy, significant pyrexia (Temp $> 38^{\circ} \text{C} \geq 2$ times during admission), positive cultures (from drain fluid or tip, or sputum) or an elevated WBC count ($> 11,000$). Patients were included if they sustained injury within 24 hours of admission, required placement of an intercostal tube drain for pneumothorax and/or hemothorax, did not have injuries or conditions requiring antimicrobial therapy, and were not allergic to penicillins or cephalosporins. Patients were excluded if they had gunshot wounds of the chest, blunt or multiple traumas, required immediate thoracotomy, or were less than 12 years of age. Patients were randomized to receive cefazolin 500 mg IV every 8 hours for 3 doses ($n = 57$) or placebo ($n = 56$). Intercostal drains were inserted in the emergency room. Thoracotomy rates were significantly greater in the placebo group regardless of whether all thoracotomies were considered or only those related to infectious complications. Sputum cultures from patients receiving placebo grew significantly more pathogens; the most common isolates were *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Klebsiella*. The incidence of pyrexia, volume and duration of chest drainage, WBC count and rate of positive cultures of initial drain fluid and tip were similar in both groups. Mean hospital stay was significantly shorter for patients receiving cefazolin, due mainly to patients undergoing thoracotomy. (Class I)

Nichols and colleagues conducted a double blind, randomized trial to evaluate the safety and efficacy of antibiotics in reducing infectious complications following closed tube thoracostomy for isolated chest trauma (4). Patients were excluded if they received antimicrobial therapy within 3 days prior to injury, had infections requiring antibiotic therapy or required surgical intervention. Patients were randomized to receive cefonicid 1 gram or placebo IV once daily. Drug administration was started as soon as possible, continued for the duration of chest tube placement, and stopped within 24 hours following removal. Chest tube placement was performed in the emergency department. Treatment failure was defined as wound infection requiring surgical intervention or additional antibiotic therapy, empyema requiring drainage, pneumonia as defined by the Center for Disease Control and Prevention or other presumed systemic infection. The majority of injuries were penetrating chest trauma (n=113) due to stab or gun shot wounds. The remaining patients (n=6) experienced blunt chest trauma. Antibiotic treatment was received by 63 patients and placebo by 56 patients. There was a statistically significant reduction in infectious complications in the group receiving antibiotics. The difference reached a higher level of significance if only culture-positive thoracic infections were considered. Thoracic infections seen in the placebo group included empyema, pneumonia, and empyema plus pneumonia. No difference was found in duration of treatment, days of chest tube placement, duration of hospitalization, peak WBC count or temperature, or adverse events. (Class I)

The efficacy of antibiotics for chest trauma patients with tube thoracostomy was assessed in a double-blind, randomized trial conducted by Gonzalez and colleagues (5). One hundred thirty nine patients with hemothorax and/or pneumothorax who suffered isolated chest injury secondary to blunt or penetrating trauma were enrolled. Patients were randomized to cefazolin 1 gram intravenously every 8 hours (Group A, n = 71) or placebo (Group B, n = 68). Antibiotics or placebo were administered before chest tube insertion and continued until the time of chest tube removal. No infectious complications occurred in Group A in comparison with 4 infectious complications in Group B (p = 0.05), including 2 empyemas and 2 pneumonias. Three of the complications occurred in patients with penetrating injury and one in a patient with blunt injury. The most common pathogen responsible for infectious complications was *S. aureus*. No significant difference was found in length of stay or average length of chest tube insertion. (Class I)

Maxwell and colleagues performed a prospective, randomized, double-blind study to determine whether presumptive antibiotics reduce the risk of empyema or pneumonia following tube thoracostomy for blunt or penetrating injuries resulting in hemothorax and/or pneumothorax (6). The first dose of study drug was given just before chest tube placement or within 1 hour of insertion. Dosing continued every 8 hours for the duration of chest tube insertion with one additional dose given after chest tube removal. Patients were randomized to one of three treatment groups: Group A (n = 77) received 1 gram of cefazolin for the duration of the study, Group B (n = 76) received cefazolin for the first 24 hours and then crossed over to placebo, and Group C (n = 71) received placebo for the entire duration of the study. Empyema developed in six (2.6%) of patients, none of which were in Group A; two (2.5%) were in Group B, and four (5.6%) were in Group C. These differences were not statistically significant. Fourteen (6.2%) patients developed pneumonia, five (6.5%) in Group A, six (7.8%) in Group B, and three (4.2%) in Group C, with no statistical differences between groups. Pneumonia occurred slightly more frequently in patients with blunt injuries as compared to penetrating injuries (p < 0.05). No differences were found in the average duration of tube placement, average duration of ICU stay, or total hospital stay. Logistic regression analysis showed that duration of tube placement and Thoracic Acute Injury Score were predictive of empyema (p < 0.05). Average duration of tube placement in those with empyema was 8.7 ± 7.4 days compared with 4.4 ± 3.2 days in those without empyema. Although there was a trend for patients with penetrating injury to develop empyema, statistical significance was not reached. While no significant difference in the incidence of empyema or pneumonia was found in patients randomized to short course or continuous course cefazolin versus placebo, a pre-study power analysis determined that 400-450 patients would need to be enrolled per treatment arm to demonstrate such a difference. A total of 224 patients were enrolled, leaving the possibility that these results reflect a Type II statistical error. One of the most striking findings noted by the authors was the emergence of nosocomial and resistant organisms in patients receiving antibiotics. (Class I)

LeBlanc and Tucker conducted a randomized trial involving 85 patients to determine the need for antibiotics in patients with isolated chest injuries resulting in pneumothorax (7). Injuries could be the result of penetrating or blunt trauma or spontaneous pneumothorax. Patients were randomized to receive no antibiotic therapy (n = 46) or cephapirin 1 gram IV q 6 hours (n = 39) starting with the insertion of the chest tube and ending 24 hours after the removal of the tube. No significant differences were found between the two groups in any of the study parameters, including length of time chest tube was in place, fever, leukocytosis, length of stay, or infectious complications. Both groups contained a fair number of spontaneous pneumothoraces (antibiotic group = 13, no antibiotic group = 20). A repeat analysis excluding patients with spontaneous pneumothorax did not result in any significant findings. (Class II)

Mandal and colleagues conducted a randomized trial in 80 patients admitted with isolated gunshot or knife injuries to the chest (8). Forty patients were randomized to receive doxycycline 200 mg IV once, followed by 100 mg IV twice daily until the chest tube was removed (Group A). The other forty patients were randomized to receive no antibiotics (Group B). Outcomes included infection, the need for surgical procedures, duration of chest tube drainage, and length of hospital stay. Infection was monitored by daily temperatures and peripheral total and differential leukocyte counts. If the patient was hospitalized for 5 days or more, or developed fever or pneumonia as seen on chest X-ray, bacterial cultures were obtained from deep expectorated sputum, urine, blood, and pleural fluid. All patients were evaluated for any infection or other complications for at least 3 months after discharge. There was no significant difference between Groups A and B in duration of chest tube placement (4.5 days and 3.8 days, respectively). Group A patients were hospitalized longer than those in Group B (6.2 days and 4.4 days, respectively). Five of forty patients (12.5%) in Group A required thoracotomy for either bleeding or persistent fistula. Two patients of forty (0.05%) in Group B required thoracotomy; one due to bleeding and the other due to infected hematoma (empyema due to *S. aureus*). The infection rate in Group A was 0% compared to 2.5% in Group B. This difference was not statistically significant. A separate analysis examining only the patients with gunshot wounds revealed no difference between the groups in any outcomes. The authors concluded that routine administration of antibiotics was unnecessary for isolated knife and gunshot wounds of the chest. (Class II)

A prospective randomized trial was undertaken by LoCurto and colleagues in patients requiring tube thoracostomy for pneumothorax and/or hemothorax due to blunt or penetrating chest trauma (9). Fifty eight patients were enrolled and assigned to no antibiotics (Group I, n = 28) or to cefoxitin 1 gram IV every six hours beginning before tube thoracostomy and ending 12 hours after removal (Group II, n = 30). The primary objective of the study was to determine the effects of antibiotic use upon the morbidity associated with tube thoracostomy in the setting of blunt or penetrating chest trauma. The criteria for treatment failure (i.e., the necessity to administer antibiotics Group I or alter antibiotics in Group II) were evidence of pneumonia and/or empyema. Statistically significant differences were demonstrated for peak temperature, duration of chest intubation, and length of hospitalization in favor of Group II. No significant difference was found in mean low systolic blood pressure, or maximum leukocytosis. Eighteen patients in Group I had negative initial pleural fluid cultures that were obtained at the time of chest tube insertion. Fifteen of those patients (83%) had positive cultures at day three. In Group II, 8 of the original 23 patients (35%) with negative cultures at chest tube insertion had positive cultures by day three. The conversion rate of negative to positive cultures between the two groups reached statistical significance ($p < 0.001$). The most frequently cultured organisms were Gram (+) cocci, however, mixed flora and/or Gram (-) bacilli were also encountered. There was a significant difference ($p < 0.001$) in treatment failures with a total of eight failures in Group I (29%) and one failure in Group II (3%). Treatment failures in Group I were due to pneumonia, empyema, or both. Five patients experiencing failure underwent thoracotomy. The single treatment failure in Group II required thoracotomy for pericarditis which may or may not have had an infectious etiology. (Class II)

Patients with isolated chest trauma due to blunt or penetrating injuries that resulted in hemothorax, pneumothorax, or hemopneumothorax and that required tube thoracostomy were enrolled in a prospective randomized trial conducted by Brunner and colleagues (10). The purpose of the study was to define the role of early antibiotic therapy in decreasing the risk of empyema in patients with isolated chest trauma. Ninety patients were randomized to no antibiotics (Group A, n = 46) or to cefazolin (Group B, n = 44), with IV administration beginning prior to chest tube insertion and then continuing every six hours until

tube removal. Treatment failure was defined as the need to institute antibiotic therapy in Group A or the need to change antibiotics in Group B. Nine patients in Group A experienced infectious complications, three of which were pneumonia. The remaining six developed empyema. Pneumonia accounted for the one infectious complication that occurred in Group B. A comparison of the rates of empyema demonstrates a significant reduction ($p=0.015$) in the group receiving antibiotic therapy. All of the empyema patients had chest trauma related to gunshot wounds and required surgery. Two additional patients in the antibiotic group who developed entrapment secondary to incompletely evacuated hemothorax also required surgery. These were both culture negative at the time of surgery. Culture results related to infectious complications demonstrated *S. aureus* in 8/10 of the cases and *Klebsiella pneumoniae* and *Pneumococcal sp.* in the other two cases. Both the duration of chest tube drainage and the length of stay in the non-antibiotic group were prolonged compared to those of the antibiotic group. No difference was found in the parameters of fever pattern or leukocytosis between the two groups. (Class II)

Demetriades and colleagues conducted a prospective randomized trial in which 188 patients with penetrating chest injuries (stab wound or gunshot wound) requiring a thoracostomy tube received ampicillin 1 gram IV prior to tube placement (11). Patients were randomized to receive either no further doses of antibiotic ($n = 95$) or to oral ampicillin 500 milligrams every 6 hours for as long as the tube remained in place ($n = 93$). Patients were assessed for a minimum of 10 days. The overall incidence of intrathoracic infection (pneumonia or empyema) was 3.2%. No significant differences were found in rates of pneumonia, empyema, or wound infection between the two groups. All cases of empyema were in patients who had a residual hemothorax after drain removal. The length of stay was similar in patients not undergoing an operation but for patients who developed intrathoracic infection length of stay was increased by approximately 11 days. The authors concluded that single dose prophylaxis is as effective as prolonged prophylaxis. The importance of chest physiotherapy immediately after drain insertion and of early removal of the drain was stressed as important steps in preventing intrathoracic infection. (Class II)

In an attempt to circumvent the problem of insufficient statistical power encountered in many of the previous studies, Sanabria et al. conducted a meta analysis of class I randomized controlled trials, including the Maxwell study (12). This study showed a significant reduction in both empyema [relative risk (RR) 0.19] and pneumonia (RR 0.44). Subgroup analysis showed no clear difference in empyema formation regardless of whether antibiotics were continued for 24 hrs or the entire duration of chest tube presence. The authors concluded that use of prophylactic antibiotics should be recommended for chest tubes placed in the setting of thoracic trauma.

A review of class I studies led the Clinical Practice Management Guidelines Committee of the Eastern Association for the Surgery of Trauma (EAST) led to a recommendation against prophylactic antibiotic use due to insufficient evidence (13).

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Author Year Class (n)	Mechanism of injury (n)	Antibiotic (duration after tube removal)	Empyema			Other infections* (All infections)**			Notes
			Rx	Control	p value	Rx	Control	p value	
Grover 1977 Class I (n = 75)	Penetrating (GSW, 24) (SW, 51)	Clindamycin (≤ 24 hr)	1/38	6/37	NS	4/38 ^Δ	13/37 ^Δ	SS	Trial stopped early due to diarrhea and pseudomembranous colitis
Stone 1981 Class I (n = 120)	Penetrating (46) Blunt (37) Spontaneous (35) Non-trauma (2)	Cefamandole (48 hr)	1/60	3/60	--	0/60 (1/60)	5/60 [◊] (8/60)	-- SS < 0.01	No difference in infection rates in patients with spontaneous pneumothorax
Cant 1993 Class I (n = 113)	Penetrating (SW, 113)	Cefazolin x 3 doses (0 hr)	0/57 [◊]	3/56 [◊]	--	0/57 ^{*K}	2/56 ^{*K}	--	Study endpoint was thoracotomy; Thoracotomy rates due to infectious complications were significantly greater in the control group (p < 0.05)
Nichols 1994 Class I (n = 119)	Penetrating (GSW, 40) (SW, 73) Blunt (6)	Cefonicid (≤ 24 hr)	0/63	4/56 [‡]	--	1/63 [‡] (1/63)	3/56 [‡] (6/56)	-- SS 0.0505	Significant difference found in study endpoint of infectious complications; when penetrating trauma analyzed alone, results remain significant
Gonzalez 1998 Class I (n = 139)	Penetrating (105) Blunt (34)	Cefazolin (0 hr)	0/71	2/68	--	0/71 (0/71)	2/68 [°] (4/68)	-- SS 0.05	Significant difference found in study endpoint of infectious complications
Maxwell 2004 Class I (n = 224 [◊])	Penetrating (86) Blunt (142) Unknown (1)	Cefazolin 1 gm x 1 (0 hr) 1 gm q8h (8 hr)	2/76 0/77	4/71	NS	6/76 [^] 5/77 [^]	3/71 [^]	NS	Possible Type II error; pneumonia occurred more frequently in patients w/blunt injuries (p<0.05); emergence of nosocomial and MDR bacteria noted in patients receiving antibiotics
LeBlanc 1985 Class II (n = 85)	Penetrating (GSW, 11) (SW, 25) Blunt (16) Spontaneous (33)	Cephapirin (24 hr)	0/39	1/46	NS	2/39 [†]	10/46 [†]	NS 0.29	No significant difference was found in the rate of infectious complications, even when spontaneous pneumothoraces were excluded
Mandal 1985 Class II (n = 80)	Penetrating (GSW, 29) (SW, 51)	Doxycycline (0 hr)	0/40	1/40	NS	0/40	0/40	NS	A separate analysis of patients with gunshot wounds of the chest showed no significant difference between treatment groups
LoCurto 1986 Class II (n = 58)	Penetrating (GSW, 8) (SW, 38) Blunt (5)	Cefoxitin (12 hr)	0/30	5/28 [◊]	--	1/30 1/30	4/28 [◊] 8/28 [◊]	-- SS < 0.001	
Brunner 1990 Class II (n = 90)	Penetrating (73) Blunt (17)	Cefazolin (0 hr)	0/44	6/46	SS 0.015	1/44 [°] 1/44 [°]	3/46 [°] 9/46 [°]	-- SS (?)	
Demetriades 1991 Class II (n = 188)	Penetrating (GSW, 14) (SW, 174)	Ampicillin x 1 (0 hr) Ampicillin q6h (0 hr)	0/95 1/93	--	--	3/95 [◊] (3/95) 2/93 [◊] (3/93)	--	NS NS	No patients randomized to receive placebo; Outcome showed no significant difference in infectious complications with single-dose vs antibiotic therapy for the duration of chest tube insertion.

*infections other than empyema; ** all infections, including empyema and other infections; NS Result were not found to be statistically significant; ^Δ infections other than empyema were pneumonia; SS Results are statistically significant; -- not a specific endpoint examined in the trial; [◊] infections other than empyema were pneumonia (3) and lung abscess (2); [◊] empyemas leading to thoracotomy; 2 empyemas, 1 empyema with subphrenic collection; ^{*K}infectious complications other than empyema leading to thoracotomy; included hemothorax growing a pathogen, and loculated collection secondary to pneumonia; [‡] infection was nonspecific, presumed due to fever (38.8° C) and increased WBC count (21.7 x 10⁹/L); pt improved with change of antibiotic; ^{‡‡} infections other than empyema were pneumonia; one patient in the placebo group developed empyema and pneumonia and is counted once in each category; [◊] 224 patients were enrolled, 5 patients received bilateral chest tubes, for a total of 229 chest tubes; [°] infections other than empyema were pneumonia; [^] infections other than empyema were pneumonia; [†] infections other than empyema included pneumonia and wound infections; [◊] infections other than empyema were pneumonia; one patient in the placebo group developed empyema and pneumonia and is counted once in each category (empyema and infections other than empyema) and twice in the all infections category; [°] infections other than empyema were pneumonia; [◊] infections other than empyema were pneumonia