

Efficacy of Monotherapy in the Treatment of *Pseudomonas* Ventilator-Associated Pneumonia in Patients With Trauma

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Background: Controversy persists regarding the optimal treatment regimen for *Pseudomonas* ventilator-associated pneumonia (VAP). Combination antibiotic therapy is used to broaden the spectrum of activity of empiric treatment and provide synergistic bactericidal activity. The relevance of such "synergy" is commonly supposed but poorly supported. The purpose of this study was to evaluate the efficacy of monotherapy in the treatment of *Pseudomonas* VAP as measured by microbiological resolution.

Methods: Patients admitted to the trauma intensive care unit during a 36-month period with gram-negative VAP diagnosed on initial bronchoalveolar lavage (BAL) ($\geq 10^5$ colony forming units [CFU]/mL) were evaluated. All patients received empiric antibiotic monotherapy based on

the duration of intensive care unit stay. Patients with *Pseudomonas* VAP were identified and appropriate monotherapy was selected. Repeat BAL was performed on day 4 of appropriate antibiotic therapy to determine efficacy. Microbiological resolution was defined as $\leq 10^3$ CFU/mL. Combination therapy with an aminoglycoside was reserved for patients with either persistent positive or increasing colony counts on repeat BAL. Recurrence was defined as $\geq 10^5$ CFU/mL on subsequent BAL after 2 weeks of appropriate therapy.

Results: One hundred ninety-six patients were identified with late gram-negative VAP. There were 84 patients with *Pseudomonas* VAP. Monotherapy achieved microbiological resolution in 79 patients (94.1%) with zero recurrence. Thirty-six isolates were completely eradicated at re-

peat BAL. Five patients (5.9%) required combination therapy to achieve resolution.

Conclusions: Monotherapy in the treatment of *Pseudomonas* VAP has an excellent success rate in patients with trauma. Empiric monotherapy therapy should be modified once susceptibility of the microorganism is documented (all isolates were sensitive to cefepime) and antibiotic choice should be based on local patterns of susceptibilities. The routine use of combination therapy for synergy is unnecessary. Combination therapy should be reserved for patients with persistent microbiological evidence of *Pseudomonas* VAP despite adequate therapy.

Key Words: Monotherapy, *Pseudomonas* ventilator-associated pneumonia, Trauma patients.

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Ventilator-associated pneumonia (VAP) is one of the most common causes of morbidity and mortality among critically ill patients. In fact, it is the most frequent nosocomial infection in the intensive care unit (ICU),^{1,2} a major determinant for increases in ICU length of stay and ventilator days,³ and is associated with a twofold increase in the mortality rate.⁴ The reported incidence in trauma patients ranges from 4% to 87%.^{5–7} Specific risk factors in patients with trauma for the development of pneumonia include emergent intubation, associated head injury, presence of shock on arrival, blunt trauma, and Injury Severity Score.⁷ Although these risk factors are difficult to control, the treatment of

pneumonia (including aggressive pulmonary toilet and appropriate antibiotic therapy) can be controlled.

In nearly all series, *Pseudomonas aeruginosa* is the most frequently isolated pathogen in VAP with a high mortality rate.⁸ Although mortality associated with VAP may differ depending on the patient population, the organism responsible, and the clinical management, it is clear that VAP secondary to multidrug resistant gram-negative (GN) bacilli (including *P. aeruginosa*) has a significantly higher mortality than episodes caused by other pathogens.⁹ In fact, the attributable mortality rate of VAP caused by *P. aeruginosa* has been estimated to be 13.5%, excluding episodes with inappropriate empiric treatment from the analysis.¹⁰ It has been proposed that the expression of certain virulence factors, high-level resistance to many antimicrobials, and the capacity to develop resistance during therapy may contribute to this increased mortality.¹¹ Nevertheless, selection of a proper antibiotic therapy is essential for the successful management of any *P. aeruginosa* pulmonary infection. Not surprisingly, controversy regarding the optimal treatment regimen for the management of *Pseudomonas* VAP persists. Combination antibiotic therapy is often used to broaden the spectrum of activity of empiric treatment and provides synergistic bactericidal activity. One of the most common regimens (the

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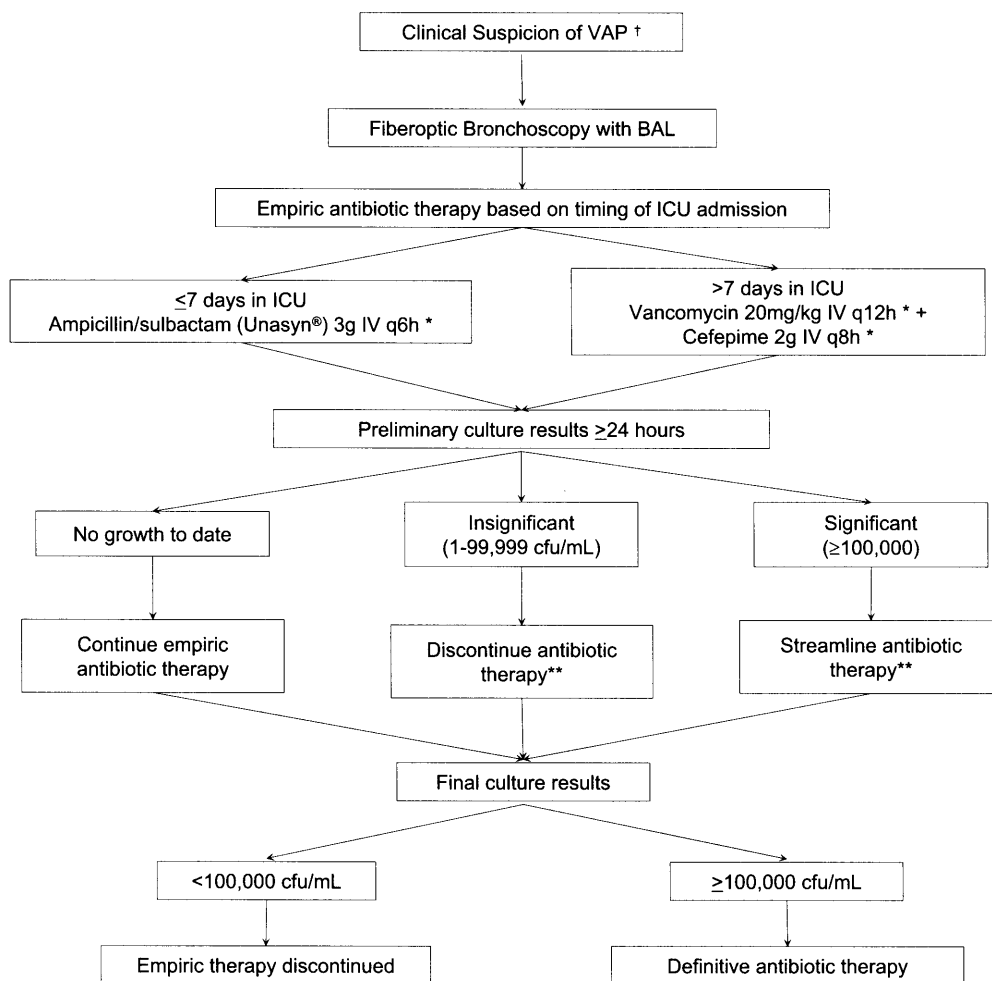


Fig. 1. Clinical pathway for the diagnosis and empiric management of ventilator-associated pneumonia. † Defined as any three of the following: (1) appearance of a new or changing infiltrate on chest radiograph; (2) abnormal temperature ($>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$); (3) abnormal white blood cell count ($>10,000$ cells/ mm^3 or $<4,000$ cells/ mm^3 or the presence of $>10\%$ immature bands); (4) macroscopically purulent sputum. If severe beta-lactam allergy, change: Unasyn to Moxifloxacin 400 mg IV Q24H, Cefepime to Ciprofloxacin 400 mg IV Q8H; dosage adjustment may be necessary based on renal function. ** Continue to monitor for changes in final culture results.

combination of a β -lactam antibiotic with an aminoglycoside) allows different mechanisms for bacterial killing, specifically the β -lactam enhancing intracellular uptake of the aminoglycoside, leading to cell death.¹² There is also evidence that aminoglycoside-mediated alteration of the outer cell envelope of GN bacilli may facilitate passage of β -lactams into the periplasmic space.¹³ This synergistic action occurs in vitro.^{14,15} However, clinical data to support this are sparse and conflicting. In fact, the relevance of such “synergy” is commonly supposed but poorly supported. In a recent meta-analysis of septic patients, no benefit was found for combination therapy over monotherapy in terms of mortality or prevention of resistant pathogens.¹⁶ It is our contention, then, that monotherapy is sufficient for the treatment of *Pseudomonas* VAP in patients with trauma. The purpose of this study was to evaluate the efficacy of monotherapy in the treatment of *Pseudomonas* VAP as

measured by microbiological resolution after repeat bronchoalveolar lavage (BAL).

PATIENTS AND METHODS

Identification of Patients

In a retrospective study, patients admitted to the trauma ICU at the Presley Regional Trauma Center in Memphis, TN over a 36-month period with late GN VAP diagnosed on initial BAL ($\geq 10^5$ colony forming units [CFU]/mL in the effluent) were identified from the VAP database. Only patients with isolated *Pseudomonas* VAP diagnosed on initial BAL were evaluated. Data were merged with additional patient information in the trauma registry (NTRACS version 3.5, Digital) to compile the database for this study.

Diagnosis and Management of VAP

The diagnosis of VAP was made by quantitative culture of BAL effluent obtained by fiberoptic bronchoscopy (Fig.

1). The clinical triggers for bronchoscopy with BAL included any three of the following: abnormal temperature ($>101^{\circ}\text{F}$ or $<96^{\circ}\text{F}$), abnormal blood leukocyte count ($>10,000\text{ mm}^3$ or $<4,000\text{ mm}^3$), macroscopically purulent sputum, and new or changing infiltrate on chest radiograph. BAL was only performed in the presence of clinical triggers and the diagnosis of VAP established by quantitative culture (no episodes of VAP were diagnosed in the absence of BAL). After recognition of clinical signs of VAP,^{17,18} all patients underwent diagnostic fiberoptic bronchoscopy with BAL culture. All BAL procedures were performed in a uniform manner by the treating surgeon as described previously.^{17,19,20} Briefly, after blind endotracheal suctioning through the ventilator circuit, the bronchoscope was advanced into the lung segment wherein radiographic changes were seen, or into the left lower lobe of patients who had diffuse bilateral infiltrates. With the bronchoscope wedged into the appropriate lung segment, 100 mL of sterile, nonbacteriostatic saline was instilled into the lung in five 20-mL aliquots. The effluent was pooled and sent to the microbiology laboratory for Gram's stain, and quantitative aerobic and anaerobic culture. Generally, results of Gram's stain were reported within 30 minutes of effluent arrival to the microbiology department, whereas preliminary quantitative results were reported within 24 hours to 36 hours and final results between 48 hours to 96 hours. VAP was confirmed using a BAL threshold of $\geq 100,000\text{ CFU/mL}$.^{17,19–21} All patients received empiric antibiotic therapy based on the duration of ICU stay.^{19,22} Patients in the ICU for 7 days or less (early) received 3 g ampicillin/sulbactam intravenously every 6 hours (or equivalent alternative in penicillin allergic patients), whereas patients in the ICU greater than 7 days (late) received 2 g cefepime intravenously every 8 hours and vancomycin 20 mg/kg intravenously every 12 hours (dose adjusted to maintain steady-state peak serum vancomycin concentrations 35–45 mg/L and trough concentrations 15–20 mg/L). In the current study, all patients underwent BAL after 7 days in the ICU (no patient had a BAL before day 7). Empiric antibiotic therapy was considered adequate if at least one antibiotic included in the empiric regimen demonstrated in vitro activity against the identified pathogen(s).^{23–28} Empiric antibiotic therapy was deescalated based on final susceptibility results according to guideline recommendations.²⁹ Monotherapy using an agent with demonstrated efficacy (i.e., in vitro and published outcome data for VAP) was encouraged for all pathogens.^{16,29} The duration of definitive antibiotic therapy was directed according to the Clinical Pathway for the Definitive Management of VAP (Fig. 2).³⁰ Repeat BAL was performed on the fourth day of adequate antibiotic therapy defined as the presence of antibiotic therapy active against all pathogens on final culture and sensitivity. Microbiological resolution was defined as $\leq 10^3\text{ CFU/mL}$.³⁰ The threshold to discontinue antibiotic therapy of 10,000 CFU/mL (responding isolate) was chosen because it represented regression of bacterial growth below the diagnostic threshold of 100,000 CFU/mL and at least a 1–log₁₀

decrease in bacterial growth for all diagnostic culture magnitudes of growth. The duration of definitive antibiotic therapy was encouraged to adhere to local practice patterns and guideline recommendations.^{30,31} Combination therapy with an aminoglycoside (either intravenous or aerosolized)^{32,33} was reserved for patients with either persistently positive or increasing colony counts on repeat BAL and was chosen at the discretion of the attending trauma surgeon. Recurrence was defined as $\geq 10^5\text{ CFU/mL}$ on subsequent BAL after 2 weeks of appropriate therapy.

Ventilator Management

All patients were managed according to our standard protocol. Briefly, all intubated patients are placed on a standard sedation protocol, stress ulcer prophylaxis, and deep venous thrombosis prophylaxis. Once the spine has been cleared, the head of the bed is elevated $>30^{\circ}$ and patients are moved out of bed daily to chair. For those patients with traumatic brain injuries, all sedation is turned off daily to perform neurologic assessment. In other patients with non-traumatic brain injury, no true daily wake up is performed. However, sedation is adjusted (per protocol) to keep patients calm and comfortable but awake and assessable. A spontaneous breathing trial is performed in all appropriate patients daily.

Outcomes

The primary outcome measure was efficacy of monotherapy as determined by microbiological resolution (defined above). Secondary outcome measures included ventilator support days, ICU days, duration of hospital stay, in-hospital mortality, VAP recurrence (defined above), and superinfection (defined as a new bacterial organism causing infection within 10 days of discontinuation of definitive therapy for VAP).

RESULTS

During a 36-month period (January 2004 to December 2006), 196 patients were identified with late GN VAP as diagnosed on quantitative culture after BAL. Overall, there were 84 patients with *Pseudomonas* VAP (mean time to diagnosis = 10 days from admission). These patients ranged in age from 15 years to 85 years and included 59 men (70%) and 25 women (30%). Seventy-three patients (87%) sustained blunt injuries and 11 patients (13%) penetrating injuries. Eighteen patients had concomitant infection at the time of VAP diagnosis and were on appropriate antibiotics (based on culture data). More than 90% of patients had abnormal chest radiograph at the time of diagnostic BAL with mean temperature of 38.9°C and leukocyte count of 13.5. The characteristics of all study patients are listed in Table 1. Overall mortality was 10.7%.

All patients received initial monotherapy as per our protocol (defined above). Specifically, patients with late (>7 days from ICU admission) VAP were treated with cefepime

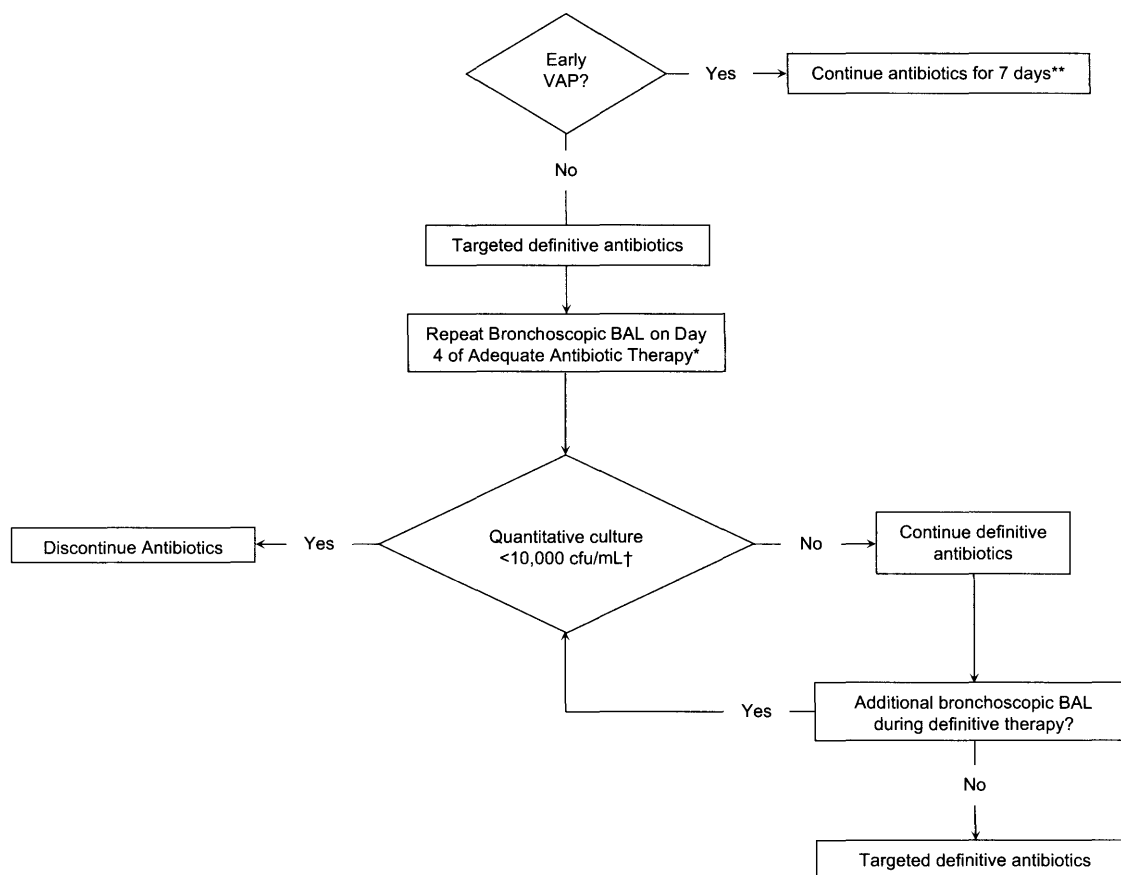


Fig. 2. Clinical pathway for the definitive management of ventilator-associated pneumonia. * Adequate antibiotic therapy is antibiotic therapy with in vitro activity against the pathogen. Patients extubated or not eligible for repeat BAL should be treated for 7 full days (consider 10–14 days if *Pseudomonas* or not responding clinically). † Use final culture result. ** *Pseudomonas* requires a follow-up BAL regardless of being early or late VAP.

Table 1 Characteristics of the Study Population

	All	Monotherapy	Combination
No.	84	79	5
Age (yr)	44	44	46
Male (%)	70	72	40
Blunt (%)	87	86	100
ISS	34	34	25
Chest AIS	2.5	2.5	1.8
GCS score	10	10	12
Base excess	−5.9	−5.9	−6.7
24-h transfusions	5.9	6.0	5.2
Concomitant Infection (%)	21	22	20
ARDS (%)	23	23	20

ISS, Injury Severity Score; AIS, Advanced Injury Scale; GCS, Glasgow Coma Scale; ARDS, adult respiratory distress syndrome.

(covers 95% of *Pseudomonas* isolates in our trauma ICU) 2 g intravenously every 8 hours. There were no patients with documented penicillin allergy during the study period. Most importantly, there were no episodes of inadequate empiric antibiotic therapy (with respect to *P. aeruginosa*) in these 84 patients (i.e., all *Pseudomonas* isolates were susceptible to cefepime) over the study period.

Table 2 Outcomes by Specific Treatments

	Monotherapy	Combination
Ventilator days	28	30
ICU days	35	38
Hospital days	47	49
Recurrence	0	0
Superinfection (%)	16	20
Mortality (%)	10	20

ICU, intensive care unit.

Monotherapy alone achieved microbiological resolution in 79 patients (94.1%). Thirty-six isolates were completely eradicated at repeat BAL. The remainder demonstrated decreasing colony counts at repeat BAL. There were no recurrent *Pseudomonas* VAPs in this group. The characteristics of those patients receiving only monotherapy are listed in Table 1. Secondary outcomes are described in Table 2.

Five patients (5.9%) required combination therapy to achieve microbiological resolution (two patients for persistently elevated colony counts and three patients for increasing colony counts on repeat BAL). Four patients received aerosolized tobramycin in addition to intravenous cefepime. The

Table 3 Distribution of Superinfection by Specific Pathogens

	Monotherapy	Combination
<i>Acinetobacter baumannii</i>	2	1
<i>Alcaligenes</i> sp.	3	0
Coagulase negative <i>Staphylococcus</i> sp.	1	0
<i>Enterobacter aerogenes</i>	1	0
<i>Stenotrophomonas maltophilia</i>	5	0
<i>Streptococcus viridans</i>	2	0

remaining patient was treated with intravenous tobramycin plus intravenous cefepime. All patients went on to microbiological resolution. Despite the need for combination therapy, once again there were no recurrent *Pseudomonas* VAPs in this group. The characteristics of those patients receiving combination therapy are listed in Table 1. Secondary outcomes are described in Table 2.

Overall, 14 patients developed superinfection. Thirteen patients (16%) undergoing monotherapy developed superinfection (one patient developed superinfection with two different pathogens) and one patient (20%) receiving combination therapy developed superinfection. The distribution of superinfection by specific pathogen is listed in Table 3. The organism most commonly associated with superinfection was *Stenotrophomonas maltophilia* (33% of all superinfections).

DISCUSSION

Despite adequate prospective data supporting the efficacy and safety of monotherapy in the empiric treatment of VAP, controversy still persists regarding the optimal treatment regimen for *Pseudomonas* VAP. Several earlier randomized trials comparing monotherapy with combination therapy in the treatment of pneumonia have demonstrated clinical responses ranging from 31% to 92%.^{34–39} No study found combination therapy to be superior in clinical efficacy.

In 1993, in a randomized prospective trial (foundation for our current empiric VAP management), Croce et al.⁴⁰ concluded that monotherapy had a higher cure rate compared with combination therapy for the empiric treatment of VAP in critically ill, trauma patients. This study compared an antipseudomonal cephalosporin (cefaperazone or ceftazidime) to the same agents in combination with gentamicin. Clinical response was higher for the monotherapy group (56% vs. 31%, $p = 0.04$) with no difference in mortality. Higher rates of superinfection with methicillin-resistant *Staphylococcus aureus* were seen in the combination group.

Subsequent prospective, randomized trials comparing monotherapy with combination therapy in patients with severe nosocomial infections including pneumonia corroborate these findings. In 1994, Cometta et al.⁴¹ compared imipenem to a combination of imipenem plus netilmicin in non-neutropenic hospitalized patients and found no difference with respect to clinical response or outcome in the subset of patients with pneumonia. In a similar trial comparing ceftazidime with

ceftriaxone plus tobramycin in patients with GN nosocomial infections, researchers again found no advantage to combination therapy in the subset with pneumonia.⁴² In a large, multicenter randomized trial comparing ciprofloxacin with imipenem as monotherapy in the treatment of severe pneumonia, there was excellent response to both drugs; ciprofloxacin had a slightly higher clinical response rate (69% vs. 56%, $p = 0.021$).⁴³ Isolation of *P. aeruginosa* was an independent predictor of treatment failure in both groups. In addition, *P. aeruginosa* was also associated with development of resistance in both groups occurring in 33% and 53%, respectively. These authors concluded that although empiric monotherapy for severe pneumonia was safe and effective, therapy may need to be altered if *P. aeruginosa* is recovered.

In nearly all series, *P. aeruginosa* is the most frequently isolated pathogen in VAP with a high mortality rate.⁸ In fact, the attributable mortality rate of VAP caused by *P. aeruginosa* has been estimated to be as high as 13.5%.^{10,44,45} Not surprisingly, controversy regarding the optimal treatment regimen for the management of *Pseudomonas* VAP persists. In this context, then, the allure of using combination therapy in VAP episodes with the theoretical intent of de-escalating based on in vitro susceptibilities remain a matter of debate, and many propose continuing with a combined regimen to avoid the appearance of resistance and recurrent infections.^{8,46,47}

The impact of monotherapy versus combination therapy on outcome in patients with *P. aeruginosa* bloodstream infection has generated conflicting results.^{48–50} A recent study concluded that empiric combination therapy reduces the risk of death compared with monotherapy.⁵¹ In contrast, the beneficial effects of combination therapy were not demonstrated in another recent series of *P. aeruginosa* bacteremia.⁵² In two recent meta-analyses, combination therapy with a β -lactam plus an aminoglycoside had no advantage over β -lactam monotherapy.^{16,53} In a recent study of 126 bacteremic VAP patients, the subset analysis of the 28 episodes caused by *P. aeruginosa* revealed that survival rates were not statistically different in patients treated with monotherapy versus combination therapy.⁴⁵

The results of this observational study demonstrate that monotherapy has an excellent success rate in the treatment of *Pseudomonas* VAP in patients with trauma. In fact, monotherapy alone achieved microbiological resolution in >90% of patients with *Pseudomonas* VAP. Combination therapy was reserved for only those patients with persistent microbiological evidence of *Pseudomonas* VAP despite adequate therapy (as determined by in vitro sensitivity patterns). The overall mortality for this specific patient cohort (only *Pseudomonas* VAP) of 10.7% was not different from what we have previously reported.⁵⁴ This finding that combination therapy is not associated with clinical benefit compared with broad-spectrum monotherapy in patients with VAP is consistent with our previous work⁴⁰ and others.^{55,56} In a recent multi-

center study, researchers demonstrated that monotherapy alone with one active antibiotic achieves equal outcomes compared with combination therapy with two active antimicrobials and therefore concluded that the prolonged use of two agents is not of proven efficacy, and once the susceptibility of *P. aeruginosa* is documented can be safely administered in this serious pulmonary infection.⁵⁷

We also examined the rate of VAP recurrence, a common and serious sequellae of *P. aeruginosa* infection. In a recent study, the mere presence of GN bacilli, such as *P. aeruginosa*, was identified as an independent risk factor for VAP recurrence in patients with appropriate empirical therapy.⁵⁸ After a single episode of *P. aeruginosa* VAP, the rate of recurrence ranges from 2.6% to 16%^{55,59} and is believed to be secondary to persistence of the same strain present in the previous infection.⁵⁹ Theoretically, the use of two active antibiotics may reduce the incidence of recurrent pulmonary infections, although this is not confirmed by our findings. In fact, there were no recurrent infections in the present study. Our results are in agreement with a previous study concluding that the use of combined therapy did not reduce the risk of recurrence.⁴¹

Despite the large amount of available data concerning management of VAP, controversies surrounding treatment remain. It does seem that the disease is associated with excess mortality, and that the appropriate application of empiric antimicrobials affects outcome. The balance of prospective data concerning the use of empiric monotherapy points to the safety and efficacy of this approach in VAP.

Our findings have important clinical implications for the optimal management strategy for critically ill patients with a clinical suspicion of VAP. Our data indicate that the judicious use of monotherapy even in the face of *Pseudomonas* VAP is likely to result in less microbiological failure and improved survival, as a consequence of reducing the likelihood of inappropriate treatment. Nevertheless, it must be stressed that therapy should be modified once susceptibility of the microorganism is documented and antibiotic choice should be based on local patterns of susceptibilities. In fact, combination GN therapy could be required if pathogen resistance patterns (within a given ICU) mandate multiple agents to achieve a high likelihood of appropriate coverage. Thus, monotherapy is predicated on knowledge of unit-specific resistance patterns. This approach will reduce the use of unnecessary antibiotics, avoiding adverse side effects and achieving substantial cost savings.

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DISCUSSION

Dr. Ellen Omi (Maywood, Illinois): Dr. Magnotti, thanks for a great presentation and I enjoyed reading your paper. *Pseudomonas* ventilator-associated pneumonia is something that

plagues all of our ICUs and a particular challenge is to determine a therapy that balances adequate treatment for an appropriate duration with the avoidance of breeding resistance.

You wonder if there's something that has to do with the flora and fauna of each of our ICUs that contributes to this. The multi-drug resistant strains of *pseudomonas aeruginosa* is a real and serious threat and it tends to be sensitive to only the most toxic and most unfamiliar antibiotics and so I think that this is an important topic to address.

Dr. Magnotti and his group have a very nice model for looking at this disease and have shown that the effectiveness of monotherapy in the trauma population with late *pseudomonas* VAP, using microbiologic endpoints. I have a few questions.

First of all, did the patients with complete and partial resolution of the bacterial counts at day four have clinical resolution also and did the patients who did have resolution have signs of ongoing infection? That has just to see whether there's clinical applicability in this model.

Secondly, what is the average duration of the antibiotics with the patients that had microbial resolution and of them, how many of them were still intubated and had actually received a repeat BAL?

Third, how do you explain your lack of recurrence of *pseudomonas* pneumonia?

Next, did the patients with superinfection in the microbial resolution group all have some evidence of bacteria in the day four BAL? In other words, did the thirty-six patients that completely resolved on the second BAL have superinfections and how many of them compared to the group that had decreasing colony counts?

Finally, how long after treatment was the superinfection identified, on average, and were the organisms resistant to cefepime? Kind of going with that, what was the rate of your superinfection in the patients with late VAP that did not have *pseudomonas*?

Dr. Deborah Kuhls (Las Vegas, Nevada): I had a question about your BAL results. Did your BAL results isolated *pseudomonas* only and did they all have the same MICs? What impact do you feel the MICs had on either lack of resolution or on superinfection?

Dr. Louis Magnotti (Memphis, Tennessee): First, I would like to thank Dr. Omi for her comments and thoughtful review of the manuscript. She had a lot of helpful suggestions and they were greatly appreciated.

For those patients that had complete and partial resolution, in terms of the clinical parameters, on that day of repeat BAL, the average Tmax across the entire patient cohort was thirty-eight degrees, about 38.2. White count was 13.6 and P to F ratio and was 251.

Really, there was not much difference between the two groups, but it's really difficult to make comparisons, since the one group had seventy-nine patients and the other group had five patients. What can be said is that these clinical parameters, although they trended downward throughout the treatment course, tended to remain abnormal throughout.

The average duration of antibiotic use over the entire cohort was 9.8 days. For those with responding isolates, that is those that either resolved completely or had decreasing colony counts, the average duration was about 8.8 days.

I would like to think that our lack of recurrence was due to our judicious use of antibiotics, with following the colony counts and stopping antibiotics when the colony counts were negative, but I'm not sure that's the explanation and I don't think there was a really good explanation as to why we didn't see any recurrence. The rate of recurrence in patients with even just a single episode of *pseudomonas* VAP has been reported anywhere from 2.6 to 16 percent, depending on the series that has looked at. Maybe we just had good luck.

In the patients that developed superinfection, there were thirteen patients in the monotherapy group. Three of those patients were part of the thirty-six that had eradicated colony counts at repeat BAL. Of those three, two of them had evidence of gram-negative rods, which were unidentified on the repeat BAL because the counts were insignificant and our micro lab doesn't typically identify insignificant counts.

The organisms that comprised the superinfections primarily were *Stenotrophomonas*. Again, our micro lab doesn't really test that against all antibiotics, because we typically treat that, once that shows up, with Bactrim. Another organism that was part of the superinfections was *Acinetobacter*. Again, when that comes up, we typically treat that with imipenem and so even if it is sensitive to cefepime at the time, we won't use that for treatment. In a previous study, the rate of superinfection in the non-*pseudomonas* patients was approximately 30%, although that was not specifically looked at for this study.

DISCUSSION OF PAPER NUMBER 11

Title of Paper: Efficacy of Monotherapy in the Treatment of *Pseudomonas* Ventilator-Associated Pneumonia in Trauma Patients.

CLOSING DISCUSSANT

Dr. Louis Magnotti (Memphis, Tennessee): The BALs did have just *pseudomonas* in them. The MICs were not significantly different among the different isolates and we typically use cefepime as our empiric therapy and unless it's resistant, we continue with the cefepime for the treatment.