Antimicrobial Susceptibilities of Respiratory Pathogens in the Surgical/Trauma Intensive Care Unit Compared with the Hospital-Wide Respiratory Antibigram in a Level I Trauma Center

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Abstract

Background: Unit-specific antibiograms have developed to guide clinicians to appropriate antibiotic choices for subsets of patients. The additional level of a unit- and respiratory-specific antibiogram for surgical and trauma patients defines key differences in susceptibility information for treating hospital-acquired pneumonia.

Methods: This was a three-year, retrospective single-center study. A total of 729 positive respiratory specimens from 612 patients were analyzed using Quality Compass Pathfinder[®], the antibiotic-reporting software. Culture and susceptibility reports were compared for the surgical/trauma intensive care unit (S/TICU) and the general hospital (excluding the S/TICU but including the medical ICU [MICU]). Data were filtered to include those genera and organisms with a high association with hospital-acquired pneumonia: *Acinetobacter*, *Citrobacter*, *Enterobacter*, *Escherichia coli*, *Haemophilus*, *Klebsiella*, *Neisseria*, *Pseudomonas*, *Staphylococcus*, *Stenotrophomonas*, *Streptococcus*, and *Serratia*.

Results: For gram-negative organisms, susceptibility differences were noted for *Acinetobacter* and *Pseudomonas* between the S/TICU and the rest of the hospital. In particular, *Acinetobacter* was significantly more susceptible to ciprofloxacin (86% vs. 43%; $p < 0.001$), gentamicin (86% vs. 54%; $p = 0.001$), imipenem-cilastatin (93% vs. 55%; $p < 0.001$), trimethoprim-sulfamethoxazole (88% vs. 54%; $p = 0.001$), and tobramycin (50% vs. 0; $p = 0.012$). *Pseudomonas* isolates from the S/TICU were significantly more susceptible to aztreonam (83% vs. 68%; $p = 0.037$), ciprofloxacin (86% vs. 69%; $p = 0.019$), and imipenem-cilastatin (94% vs. 79%; $p = 0.01$). For gram-positive organisms, *Staphylococcus* isolates from the S/TICU were significantly more susceptible to erythromycin (81% vs. 57%; $p = 0.007$) and trimethoprim-sulfamethoxazole (98% vs. 91%; $p = 0.034$) than were the hospital isolates.

Conclusions: For key respiratory pathogens, such as *Pseudomonas*, *Acinetobacter*, and *Staphylococcus*, surgical and trauma patients present greater susceptibility to several antibiotics. Although this information cannot be extrapolated to other institutions, it does provide a basis for comparable institutions to consider developing unit- and collection-site-specific antibiograms for infections that affect surgical/trauma patients commonly.

HOSPITAL ANTIBIOGRAMS are used routinely to select empiric therapy for suspected infections in hospitalized patients. Trending patterns of susceptibility also guide clinicians and infectious diseases teams to appropriate choices for antibiotic preservation programs such as antibiotic cycling and mixing [1–3]. Local susceptibility patterns serve as a resource, guided by antibiograms, in providing adequate empiric therapy until the appropriate culture and susceptibility reports are finalized to confirm a causative organism.

Inappropriate selection of antimicrobial therapy is a substantial contributor to poor clinical outcomes [4,5].

Whereas institution-specific antibiograms serve clinicians who provide patient care in a variety of care units, unit-specific antibiograms have emerged as a useful tool for institutions with units devoted to a homogeneous patient population [6–8]. Unit-specific antibiograms can guide initial antibiotic choices for different populations within the same institution [7,9]. Evidence has begun to indicate that susceptibility patterns can

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differ significantly between the entire hospital and specific units, such as the intensive care unit (ICU), within the same institution [9–13]. Unit- and disease-specific antibiograms have been pursued only on a limited basis as options for guiding clinicians to antibiotic choices.

Hospitals that provide care for victims of trauma have an additional, a unique demographic. Trauma patients tend to be younger and have fewer co-morbidities, neither do they have an extensive pre-admission hospitalization history [14]. Thus, trauma patients may be less likely to be infected with multi-drug-resistant organisms (MDROs). There is a need for institution-, unit-, and patient-specific evidence to guide adequate empiric antimicrobial therapy early for these critically ill patients.

The management of hospital-acquired pneumonia (HAP) accounts for more than one-half of all antibiotics prescribed in the hospital, and is responsible for as many as 25% of all ICU infections [15]. There is evidence that the number of MDROs that cause HAP and ventilator-associated pneumonia (VAP) differ between surgical/trauma ICUs (S/TICUs) and general surgery ICUs [16].

Patients admitted to the S/TICU tend to differ considerably from other critically ill patients with regard to age, co-morbidities, and severity of illness [17]. Considering the variability in these patient populations, infectious processes such as pneumonia may have to be treated with different antibiotics. Furthermore, research that focuses specifically on antibiotic susceptibilities of respiratory isolates in surgical and trauma patients remains limited.

The purpose of this study was to evaluate antibiotic susceptibility patterns in the S/TICU compared with the entire hospital for pathogens causative of pneumonia. The working hypothesis was that respiratory cultures among surgical/trauma patients will exhibit greater susceptibility to antimicrobial agents than respiratory isolates from the general hospital population.

Patients and Methods

Study Design/Methodology

Our S/TICU is a 20-bed unit in a 283-bed acute-care academic hospital that serves primarily the uninsured and underinsured population of a large metropolitan area. The S/TICU is the only level I trauma center in the southeastern Louisiana area. In addition to trauma admissions, the surgical teams service general, vascular, neurologic, orthopedic, otolaryngologic, obstetric-gynecologic, urologic, and plastic surgery patients. The surgical/trauma care team consists of two trauma/critical care surgical fellows, surgical residents, emergency department residents, medical students, a trauma attending, a respiratory therapist faculty member, and clinical pharmacists with pharmacy residents and pharmacy students. In addition, weekly rounding of a multi-disciplinary team consisting of one trauma/critical care fellow, nutritionist, respiratory therapist, charge nurse, social worker, and rehabilitation physician occurs on all patients admitted to the S/TICU.

There were 12,400 admissions and 370 admissions to the hospital and S/TICU, respectively, for the fiscal year 2011 (Table 1). A 5% cross-over of patients from the medical ICU to the S/TICU occurs monthly.

As part of larger national multi-disciplinary initiatives, a cross-disciplinary group of healthcare professionals devel-

TABLE 1. HOSPITAL AND UNIT ADMISSION DATA DURING PERIOD OF STUDY

	2009	2010	2011
Adult admissions ^a	13,702	14,161	12,400
S/TICU admissions	346	367	370

^aAll hospital admissions, including the surgical/trauma intensive care unit (S/TICU), are included in these figures.

oped the Antimicrobial Stewardship Program (ASP) in January of 2011. The mission was to “optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms (such as *Clostridium difficile*), and the emergence of resistance” and to “reduce healthcare costs without adversely impacting quality of care.” The ASP is a multi-disciplinary team consisting of clinical pharmacists, infectious disease physicians, and representatives from infection control and the microbiology laboratory. The ASP meets all of the evidence-based recommendations for institutional antimicrobial stewardship programs set by the Infectious Diseases Society of America and the Society of Healthcare Epidemiologists of America. The surgical/trauma critical care pharmacist was a member of the team and served the goals of the initiative among the surgical/trauma patients.

Participation

Antibiotic susceptibility of all respiratory isolates collected from January 2009 to December 2011 was reviewed retrospectively. Respiratory isolates included bronchoalveolar lavage, sputum cultures, tracheal aspirates, and bronchial washings (Table 1). A total of 729 positive specimens from 612 patients was collected and analyzed. Institutional Review Board approval was gained prior to initiation of the study.

Quality Compass Pathfinder[®] (Vecna Technologies, Cambridge, MA), the antibiotic reporting software that integrates demographic and microbiologic data with pharmacy orders, was used to retrieve the data on the culture and susceptibility reports for all respiratory isolates. The data were then filtered to include those organisms with a high association with HAP. The isolates reported were of the genera *Acinetobacter*, *Citrobacter*, *Enterobacter*, *Escherichia*, *Haemophilus*, *Klebsiella*, *Neisseria*, *Pseudomonas*, *Staphylococcus*, *Stenotrophomonas*, *Streptococcus*, and *Serratia*. To eliminate duplicate data, the program was set to delete duplicate isolates collected from the same patient within a 365-d window. If the secondary isolate had a different susceptibility pattern from the first isolate despite being the same bacterium, both isolates were included in the data.

Outcome Measurements

Antibiotic susceptibility data of all isolates were collected using MicroScan[®] (Siemens Medical Solutions USA, Inc., Malvern, PA) according to manufacturer-provided panels. Interpretation of all results was based on Clinical and Laboratory Standards Institute (CLSI) or SHEA guidelines. Results reported as intermediate were considered resistant for the purpose of this study. All antibiogram results are reported as a percentage of isolates. Statistical comparisons between the S/TICU and hospital-wide (excluding S/TICU, but including

TABLE 2. ALL RESPIRATORY SPECIMEN CULTURES 2009–2011^a

Culture Source	S/TICU	Hospital	Total
Sputum ^b	375	266	641
Bronchioalveolar lavage	11	29	40
Bronchial washing	6	12	18
Tracheal aspirate	6	24	30
Total	398	331	729

^aA second specimen from a patient within a 365-day window was excluded if the two isolates were identical.

^bIncludes sputum and induced sputum.

MICU) antibiograms and prevalence data were carried out using the Fisher exact test. The a priori significance level was set at $p < 0.05$. All data were analyzed using SPSS version 19[®] (IBM, Inc., Armonk, NY).

Results

Organisms Recovered

A total of 899 isolates were collected over the three-year study period from a total of 729 specimens representing 612 patients. The initial results of the study demonstrated that the majority of positive respiratory specimens were being collected from the S/TICU compared with the hospital, which includes the MICU and all other in-patient beds (54.6% vs 45.4%), whereas the S/TICU accounts for only 7% of total hospital beds and 0.6% of total hospital admissions (Table 1). The majority of respiratory isolates were sputum isolates for both the S/TICU and the hospital (94% and 80%, respectively).

The bacterium reported most often was *Staphylococcus aureus* (234 isolates; 26.03%), followed by *Pseudomonas aeruginosa* (129; 14.3%), *Haemophilus influenzae* (95; 10.57%), and *Acinetobacter baumannii* (87; 9.68%) (Table 2). Of note, *Acinetobacter* (58 from the S/TICU, 29 from the hospital) and *Enterobacter* (37 from S/TICU, six from the hospital) had a disproportionately greater prevalence in the S/TICU than in the rest of the hospital ($p = 0.0406$ and $p < 0.0001$, respectively) (Table 3).

Tables 4 and 5 represent the antibiogram data for gram-negative and gram-positive organisms, respectively, for the

S/TICU vs. the hospital. Absent from the antibiograms are culture and sensitivity data for *H. influenzae* and *Neisseria* spp. This is a result of the fact that the clinical significance of *N. meningitidis* resistant to penicillin has been established. Also, susceptibility testing for *N. meningitidis* is difficult because no consensus has been reached regarding the best techniques or their standardization [18,19]. Routine antimicrobial susceptibility testing for *H. influenzae* is not usually because the β -lactamase observed usually in *H. influenzae* inactivates only a few β -lactam drugs such as penicillin, ampicillin, and amoxicillin; and rapid tests such as β -lactamase assays yield relevant clinical information earlier than the results of antimicrobial susceptibility testing [20].

For gram-negative organisms, several susceptibility differences were noted for key species such as *Acinetobacter* and *Pseudomonas*. *Acinetobacter* was significantly more sensitive to ciprofloxacin (86% vs. 43%; $p = 0.000$), gentamicin (86% vs. 54%; $p = 0.001$), imipenem-cilastatin (93% vs. 55%; $p < 0.001$), trimethoprim/sulfamethoxazole (88% vs. 54%; $p = 0.001$), and tobramycin (50% vs. 0; $p = 0.012$) than organisms isolated from the rest of the hospital. *Pseudomonas* isolates from the S/TICU were significantly more sensitive to aztreonam (83% vs. 68%; $p = 0.037$), ciprofloxacin (86% vs. 69%; $p = 0.019$), and imipenem-cilastatin (94% vs. 79%; $p = 0.01$). No significant differences were noted among the other gram-negative species. Despite the considerably greater prevalence of *Enterobacter* among S/TICU respiratory isolates, there was no significant difference in susceptibility patterns. This absence of significance may be attributable to the fact that fewer than ten isolates were collected from the hospital outside the S/TICU.

For gram-positive organisms, *Staphylococcus* isolates from the S/TICU were significantly more sensitive to erythromycin (81% vs. 57%; $p = 0.007$) and trimethoprim-sulfamethoxazole (98% vs. 91%; $p = 0.034$) than organisms from the rest of the hospital. *Staphylococcus* susceptibility to oxacillin and vancomycin was similar in the S/TICU and the hospital. There was no significant difference noted for *Streptococcus pneumoniae*.

Discussion

The results of this study are consistent with previous findings in surgical vs. medical ICUs, with organisms from surgical ICUs showing greater susceptibility in several key

TABLE 3. PREVALENCE (NUMBER [%]) OF PATHOGENS IN RESPIRATORY SPECIMEN BY SPECIES, 2009–2011^a

	S/TICU	Hospital ^b	Total	p
<i>Acinetobacter</i> spp.	58 (11.51)	29 (7.34)	87 (9.68)	0.0406*
<i>Citrobacter koseri</i>	11 (2.18)	3 (0.08)	14 (1.56)	0.1067
<i>Enterobacter cloacae</i>	37 (7.34)	6 (1.52)	43 (4.78)	<0.0001*
<i>Escherichia coli</i>	20 (3.97)	21 (5.32)	41 (4.56)	0.3396
<i>Haemophilus influenzae</i>	53 (10.52)	42 (10.63)	95 (10.57)	1.00
<i>Klebsiella pneumoniae</i>	53 (10.52)	38 (9.62)	91 (10.12)	0.7380
<i>Neisseria meningitidis</i>	6 (1.19)	4 (1.01)	10 (1.11)	1.00
<i>Pseudomonas aeruginosa</i>	64 (12.69)	65 (16.46)	129 (14.35)	0.1251
<i>Serratia marcescens</i>	13 (2.58)	20 (5.06)	33 (3.67)	0.0724
<i>Staphylococcus aureus</i>	126 (25.0)	108 (27.34)	234 (26.03)	0.4443
<i>Stenotrophomonas maltophilia</i>	28 (5.56)	27 (6.84)	55 (6.12)	0.4838
<i>Streptococcus pneumoniae</i>	35 (6.94)	32 (8.10)	67 (7.45)	0.5247
Total	504	395	899	

^aA second specimen from a patient within a 365-d window was excluded if the two isolates were identical.

^bHospital includes medical intensive care unit (ICU) but excludes the surgical/trauma ICU (S/TICU).

*Significance $p < 0.05$.

TABLE 4. SURGICAL/TRAUMA INTENSIVE CARE UNIT VS. HOSPITAL RESPIRATORY ANTI BIOGRAM FOR GRAM-NEGATIVE ORGANISMS, 2009–2011^{a,b}

	No. of Isolates	Amikacin	Ampicillin	Aztreonam	Cefazolin	Cefepime	Cefotaxime	Ceftazoxime	Ciprofloxacin	Gentamicin	Imipenem-cilastatin	Piperacillin-Tazobactam	Trimethoprim-Sulfamethoxazole	Tobramycin
ACINETOBACTER SPP.	58	25	—	—	—	—	—	—	86	86	93	—	88	50
Acinetobacter spp	29	15	—	—	—	—	—	—	43	54	55	—	54	0
p ^c		0.579	—	—	—	—	—	—	0.000	0.001	0.000	—	0.001*	0.012
CITROBACTER KOSERI	11	—	40	100	100	—	—	—	100	100	100	100	100	—
C. koseri	3	—	33	100	100	—	—	—	100	100	100	100	100	—
p		—	0.685	1.00	1.00	—	—	—	1.00	1.00	1.00	1.00	1.00	—
ESCHERICHIA COLI	95	100	40	90	55	100	66	66	60	90	100	75	65	0
E. coli	21	100	19	95	57	0	89	0	52	86	100	75	48	33
p		1.00	0.129	0.481	0.57	0.50	0.288	0.50	0.43	0.524	1.00	0.642	0.21	0.60
ENTEROBACTER CLOACAE	37	100	2.7	70	2.7	76	18	59	95	97	100	76	97	97
E. cloacae	6	—	0	50	0	75	17	20	100	100	100	67	100	100
p		—	0.86	0.295	0.86	0.70	0.721	0.133	0.738	0.86	1.00	0.488	0.86	1.00
KLEBSIELLA PNEUMONIAE	53	100	100	91	79	20	27	38	89	96	100	92	94	0
K. pneumonia	38	50	100	84	79	0	11	14	84	92	100	94	82	0
p		0.238	1.00	0.275	0.586	0.455	0.375	0.338	0.375	0.345	1	0.555	0.058	1.00
PSEUDOMONAS AERUGINOSA	64	1.6	—	83	—	88	—	—	86	88	94	94	—	11
P. aeruginosa	65	1.5	—	68	—	77	—	—	69	77	79	89	—	14
p		0.748	—	0.037	—	0.09	—	—	0.019	0.09	0.011	0.274	—	0.401
SERRATIA MARCESCENS	13	100	0	85	0	92	0	92	85	100	100	92	92	100
S. marcescens	20	57	0	95	0	50	0	95	75	95	100	70	65	100
p		0.625	1.00	0.338	1.00	0.667	1.00	0.64	0.419	0.606	1.00	0.136	0.082	1.00
STENOTROPHOMONAS MALTOPHILIA	28	8	0	0	—	0	—	0	14	7	0	—	100	0
S. maltophilia	27	0	0	0	—	0	—	0	28	28	0	—	96	0
p		1.00	1.00	1.00	—	1.00	—	1.00	0.660	0.345	1.00	—	1.00	1.00

^aData from surgical trauma intensive care unit (ICU) are presented in all capitals; data from hospital including medical ICU are presented in capitals and lower case. Statistically significant differences are in boldface type.

^bResults reported as percent susceptible= number of isolates susceptible to antibiotic divided by total number of isolates.

^cResults may not be statistically significant when fewer than 30 isolates are tested.

TABLE 5. SURGICAL/TRAUMA INTENSIVE CARE UNIT VS. HOSPITAL RESPIRATORY ANTIBIOGRAM FOR GRAM-POSITIVE ORGANISMS, 2009–2011

	Number of Isolates	Ceftriaxone (Meningitis)	Ceftriaxone-Non (meningitis)	Clindamycin	Erythromycin	Gentamicin	Linezolid	Oxacillin	Penicillin G	Rifampin	Trimethoprim-sulfamethoxazole	Vancomycin
<i>STAPHYLOCOCCUS AUREUS</i> ^a	126	–	–	96	81	99	100	53	7	98	98	99
<i>S. aureus</i>	108	–	–	87	57	99	100	45	15	99	91	96
p		–	–	0.116	0.007	0.454	1.00	0.155	0.186	0.569	0.034	0.546
<i>STREPTOCOCCUS PNEUMONIAE</i>	35	74	83	–	100	20	86	20	20	–	–	–
<i>S. pneumoniae</i>	32	81	69	–	97	31	75	31	31	–	–	–
p		0.854	0.7099	–	1.00	0.588	0.8546	0.588	0.588	–	–	–

^aData from surgical/trauma intensive care unit (ICU) are presented in all capitals; data from hospital including medical ICU are presented in capitals and lower case. Statistically significant results are in boldface type.

pathologic organisms. Variations within specific pathogens such *S. aureus*, *A. baumannii* complex, and *P. aeruginosa* in this study are consistent with the results found by Namias et al. in 2000 [21]. Unlike the findings by Kaufman et al. in 1998 [17], S/TICU patients had organisms with greater susceptibility to key antibiotics. Becher et al. found that trauma patients have a more favorable susceptibility profile for respiratory isolates than do surgical patients [22].

In addition, key differences were noted for species with MDRO susceptibility profiles. Of most significance are the key differences in the common pathogens *Acinetobacter* and *Pseudomonas*. Given the prevalence of these organisms in the units, with a disproportionate representation of *Acinetobacter* in the S/TICU, the results provide information appropriate for antibiotic choices for these two organisms. For this institution, *Klebsiella* isolates, also associated with MDRO profiles, had favorable sensitivity profiles for both the S/TICU and the hospital.

Unit- and disease-specific antibiograms will be a useful tool for hospitals to develop antibiotic preservation programs such as restricted antibiotic formularies, antibiotic cycling, and antibiotic heterogeneity within a single unit [23]. Unit-specific antibiograms also may reduce the likelihood of inappropriate prescribing of empiric therapy, which correlates with poor clinical outcomes [24]. In our S/TICU, the unit-specific antibiogram led to changes in empiric antimicrobial choices for patients with suspected HAP/VAP. In addition, a unit-specific antibiogram has been generated in each subsequent year after this study was completed to guide antimicrobial choices by practitioners. A dedicated antimicrobial stewardship pharmacist in the unit ensures compliance with guidelines and use of the antibiogram to inform prescribing habits.

The major limitation of this study is the potential misidentification of tracheal and bronchial specimens as sputum cultures in both the S/TICU and the hospital. This is primarily a laboratory system's labeling concern and does not impact

the results, although the validity of true sputum cultures in providing clinically meaningful respiratory isolates is controversial. Respiratory specimens in both the hospital and the S/TICU were collected from patients who presented with signs and symptoms consistent with pneumonia (see Table 2). An additional limitation is the occasional cross-over of patients between the S/TICU and the MICU. Data were analyzed based on the unit where the specimen was collected, not the admission diagnosis. This cross-over affected fewer than 5% of the patients.

Given that the hospital data included the MICU, there may be misrepresentation of general antibiotic susceptibilities for non-critically ill patients. Unit-specific antibiograms for the medical and S/TICUs should be developed relative to the general hospital. This may not be feasible for smaller community hospitals, as there sometimes may be too few isolates collected to achieve statistical significance.

Additional limitations include the small number of isolates of some bacterial species. Reviewing respiratory specimens exclusively over a period of only three years impacted the number of isolates, especially for the less prevalent organisms such as *Citrobacter* and *Serratia* spp. It is possible the small number of isolates of the less prevalent organisms impacted susceptibility differences in the antibiogram data. This study did not evaluate antibiotic use after culture results became available. Furthermore, antimicrobial susceptibilities tends to change over time. Data in this study and similar antibiograms serve as a snapshot of susceptibilities over a specified period of time. A secondary analysis of the data proved that minimum inhibitory concentration trends differed between the antibiograms over the three-year period. These data, published in December 2012, demonstrated that although the S/TICU had a better susceptibility profile overall, key organisms such as *Acinetobacter* and *Pseudomonas* were developing resistance more rapidly within the S/TICU than in the hospital, coming to resemble MICU patterns [25].

This study adds to the growing evidence that unit- and disease state-specific antibiograms are important tools in optimizing antibiotic therapy. Additionally, the significant sensitivity differences among these isolates indicate the need for clinicians to have knowledge of antibiotic susceptibility patterns among surgical/trauma patients as a distinct critically ill population.

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The authors have no conflicts of interest to disclose.

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