ORIGINAL ARTICLE

Antibiotic Susceptibility in the Surgical Intensive Care Unit Compared With the Hospital-Wide Antibiogram

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Objective: To compare the antibiotic susceptibility of bacterial isolates from patients in the sugical intensive care unit (SICU) with hospital-wide bacterial susceptibility.

Design: Retrospective cohort analytic study.

Setting: Eight-bed SICU in a university-affiliated teaching hospital.

Patients: All hospitalized patients with culture results positive for microorganisms.

Interventions: None.

Main Outcome Measures: Antibiotic susceptibility data were collected retrospectively for all bacterial isolates from SICU patients during July 1, 1994, to June 30, 1995. All duplicate and surveillance cultures were eliminated from the data set. Susceptibility testing was conducted using our standard laboratory methods. Results were compared with the hospital-wide antibiogram (HWA) for the same time period. Comparisons were made using the χ^2 test with Yates correction or the Fisher exact test, as appropriate. *Staphylococcus aureus* (HWA, n=494; SICU, n=71) was significantly less susceptible to oxacillin (51% vs 28%; $P<.001$), ciprofloxacin (50% vs 25%; $P<.001$), erythromycin (46% vs 23%; $P<.001$), and clindamycin (51% vs 27%; $P<.001$) in the SICU. Coagulase-negative staphylococci (HWA, n=339; SICU, n=37) were significantly less susceptible to oxacillin (33% vs 16%; $P=.04$) and clindamycin (57% vs 34%; $P=.02$). *Pseudomonas aeruginosa* (HWA, n=513; SICU, n=96) was less susceptible to imipenem (85% vs 74%, $P=.01$) and more susceptible to ticarcillin–clavulanic acid (88% vs 100%, $P<.001$) in the SICU. *Escherichia coli* (HWA, n=474; SICU, n=36) was more susceptible to most penicillin-derivative antibiotics in the SICU (ampicillin [68% vs 83%, $P=.06$], ticarcillin [65% vs 86%, $P=.01$], mezlocillin [76% vs 95%, $P=.01$], and ticarcillin–clavulanic acid [88% vs 100%, $P=.02$]).

Conclusions: The 2 most commonly isolated bacterial pathogens in the SICU (*S aureus* and *P aeruginosa*) had significantly different susceptibility patterns compared with the HWA. Surprisingly, *E coli* isolated in the SICU tended to be more susceptible to penicillin-derivative antibiotics. These data indicate that empiric antibiotic choices in the SICU may be better guided by unit-specific antibiograms.

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ANTIBIOTIC resistance is a substantial and growing problem, making the choice of empiric antibiotic therapy increasingly difficult. The potential differences in susceptibility between hospital-acquired and community-acquired infections is widely appreciated, and many clinicians choose initial empiric therapy based on this distinction. Susceptibility of microorganisms causing community-acquired infections is known to vary between geographic locales, while susceptibility of bacterial isolates causing hospital-acquired infections may vary widely among hospitals within the same geographic locale. The application of hospital-wide antibiograms to guide clinicians in the initial choice of antibiotics is a rational and recommended approach, given the differences in susceptibility patterns between hospitals.[1] However, susceptibility patterns may vary among individual hospital units. If more resistant organisms are isolated from patients in the intensive care unit (ICU) but not in other hospital units, then this important information could be masked by the use of a hospital-wide antibiogram.[2]

The emergence of resistance has paralleled the widespread use of antimicrobial agents. The classic example of staphylococci developing resistance within a few years of the introduction of penicillin has been repeated with many other antimicrobial agents throughout the antibiotic

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MATERIALS AND METHODS

The SICU is an 8-bed unit in a 535-bed acute care hospital that cares for general, vascular, neurologic, orthopedic, plastic, otolaryngologic, obstetric-gynecologic, and urologic surgery patients. It is 1 of 4 intensive care units in the institution. Antibiotic susceptibility data were collected for all bacterial isolates from SICU patients from July 1, 1994, to June 30, 1995. Hospital-wide antibiotic susceptibility data were also collected for the same period.

Antibiotic susceptibility data were provided for both the SICU and the hospital by the Vitek software package (bioMerieux Inc, Hazelwood, Mo), used routinely in our laboratory for archiving susceptibility data. In an attempt to minimize the effect of duplicate isolates, the program counts isolates according to the following algorithm. Successive isolates from the same anatomical site from a single patient are counted as a single isolate, provided the antibiotic susceptibility pattern is identical. Successive isolates for the same patient that have different susceptibility patterns are counted as separate isolates. The same organism isolated from different sites in a single patient is counted as separate isolates regardless of the antibiotic susceptibility patterns.

Surveillance cultures are not routinely performed in the SICU or elsewhere in the institution, with the exception of rectal swab cultures performed on ICU patients for the detection of vancomycin-resistant enterococci. Because rectal swab cultures are not routinely performed outside of the ICU, and the rectal cultures could not be easily separated from other wound cultures in the microbiology database, all data for enterococcal isolates were eliminated from this analysis.

Antibiotic susceptibility testing of all isolates was performed using our standard laboratory methods (Vitek), using commercially available panels provided by the manufacturer. Interpretations for susceptible and resistant tests were performed according to the National Committe for Clinical Laboratory Standards guidelines.[5] Test results interpreted as intermediate were considered resistant for the purposes of this study. All results are presented as percentage of isolates susceptible to the tested antibacterial agents.

Stastistical comparisons between the SICU and hospital-wide susceptibility results were completed using the χ^2 test with Yates correction or the Fisher exact test as appropriate for the available data. The a priori level of significance for all statistical tests was $P<.05$. All statistical tests were performed using Systat software, version 5.02 (Systat Inc, Evanston, Ill).

Percentage of Susceptible Bacterial Isolates*

Organism	No. of Isolates	AMP	TIC	CEPH	CFR	CFZ	MZL	GNT	TOB	TMP/SMX	CLD
											Surgical Intensive Care Unit
Gram-negative isolates											
Enterobacter aerogenes	15	0	33	17	33	17	100	100	100	100	ND
Enterobacter cloacae	20	0	67	0	68	0	89	100	100	100	ND
Escherichia coli	36	83†	88‡	88	91	92	95‡	100	100	97	ND
Klebsiella species	15	0	17	100	100	100	100	100	100	100	ND
Morganella morganii	7	0	100	0	71	0	100	100	100	100	ND
Proteus mirabilis	5	80	100	80	100	75	100	100	100	100	ND
Pseudomonas aeruginosa	96	ND	77	ND	ND	ND	69	92	99	ND	ND
Serratia marcescens	12	46	92	7	43	0	100	100	100	100	ND
Gram-positive isolates											
Staphylococcus aureus	71	ND	ND	ND	ND	ND	ND	ND	ND	92	27§
Staphylococcus species	37	ND	ND	16	ND	ND	ND	53	ND	37	34‖
											Hospital-Wide
Gram-negative isolates											
Enterobacter aerogenes	54	2	45	9	43	23	100	96	96	96	ND
Enterobacter cloacae	81	1	64	5	63	3	85	93	93	95	ND
Escherichia coli	474	68†	65‡	87	97	94	76‡	100	100	94	ND
Klebsiella species	201	1	10	92	97	97	90	100	100	94	ND
Morganella morganii	19	5	100	0	72	28	100	100	100	100	ND
Proteus mirabilis	96	89	86	93	94	84	95	98	98	88	ND
Pseudomonas aeruginosa	513	ND	77	ND	24	ND	76	87	92	ND	ND
Serratia marcescens	42	19	97	ND	ND	ND	100	98	98	100	ND
Gram-positive isolates											
Staphylococcus aureus	494	ND	ND	49	ND	ND	ND	59	ND	83	51§
Staphylococcus species	339	ND	ND	32	ND	ND	ND	58	ND	53	57‖

*AMP indicates ampicillin; TIC, ticarcillin; CEPH, cephalothin; CFR, cefuroxime; CFZ, cefazolin; MZL, mezlocillin; GNT, gentamicin; TOB, tobramycin; TMP/SMX, trimethoprim-sulfamethoxazole; CLD, clindamycin; ERY, erythromycin; VAN, vancomycin; OXA, oxacillin; AMK, amikacin; IMP, imipenem-cilastatin; CFT, ceftizoxime; CFX, ceftriaxone; CTZ, ceftazidime; TIM, ticarcillin–clavulanic acid; PIP, piperacillin; CIP, ciprofloxacin; AZT, aztreonam; and ND, not done. Except where noted otherwise, all values are expressed as percent susceptible.

†P = .06.

‡P = .01.

§P<.001.

‖P<.05.

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era.[3] The clinician must be aware of these developments given the high prevalence of nosocomial infections in the ICU compared with other hospital units.[4] More specifically, the critical care practitioner must be cognizant of the possibility that the appropriate choice of empiric antimicrobial agents hinges on the unique susceptibility patterns in a geographic locale. This locale may be as broad as a region of a country or as specific as a unit in a hospital.

This study was conducted to compare the susceptibility of bacterial isolates from patients in a surgical intensive care unit (SICU) with the hospital-wide antibiogram.

RESULTS

The **Table** presents susceptibility data for the bacterial isolates from the SICU and hospital, respectively. The method of identifying study isolates resulted in 314 bacterial isolates from 81 SICU patients among a total of 435 SICU admissions, and 2313 isolates from 1202 patients among a total of 20 855 hospital admissions during the study period. The most prevalent gram-negative and gram-positive organisms isolated from both the SICU and entire hospital were *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively. However, *P aeruginosa* was a significantly more prevalent gram-negative organism in the SICU as compared with the hospital-wide data (46.6% vs 25.9%; P=.001).

For the gram-positive isolates, *S aureus* was significantly less susceptible to oxacillin (51% vs 28%; P<.001), ciprofloxacin (50% vs 25%; P<.001), erythromycin (46% vs 23%; P<.001), and clindamycin (51% vs 27%; P<.001) in the SICU. Coagulase-negative staphylococci were significantly less susceptible to oxacillin (33% vs 16%, P=.04) and clindamycin (57% vs 34%; P<.02) in the SICU.

For the gram-negative isolates, *P aeruginosa* was significantly less susceptible to imipenem-cilastatin (85% vs 74%; P=.01) and more susceptible to ticarcillin–clavulanic acid (88% vs 100%; P<.001) in the SICU. *Escherichia coli* was more susceptible to most penicillin-derivative antibiotics in the SICU: ampicillin (68% vs 83%; P<.06), ticarcillin (65% vs 86%; P=.01), mezlocillin (76% vs 95%; P=.01), and ticarcillin–clavulanic acid (88% vs 100%; P=.02).

COMMENT

In 1988, the Infectious Disease Society of America made a series of recommendations to hospitals to improve the use of antimicrobial agents. The main purpose was to pro-

ERY	VAN	OXA	AMK	IMP	CFT	CFX	CTZ	TIM	PIP	CIP	AZT
ND	ND	ND	100	100	100	100	33	33	100	100	83
ND	ND	ND	100	94	68	67	68	67	83	100	67
ND	ND	ND	100	100	100	100	91	100‖	92	97	100
ND	ND	ND	100	100	100	100	100	100	100	100	100
ND	ND	ND	100	86	100	100	100	100	100	100	100
ND	ND	ND	100	100	100	100	100	100	100	100	100
ND	ND	ND	97	74‡	ND	ND	99	100§	97	76	72
ND	ND	ND	100	100	100	100	100	100	100	100	100
23§	100	28§	ND	28§	ND	ND	ND	ND	ND	25§	ND
26	100	16‖	ND	16‖	ND	ND	ND	ND	ND	34	ND
ND	ND	ND	95	95	84	96	52	49	91	95	74
ND	ND	ND	100	98	78	78	67	65	78	100	100
ND	ND	ND	100	100	100	100	98	88‖	68	100	100
ND	ND	ND	100	100	100	100	100	100	92	98	95
ND	ND	ND	100	94	100	100	100	100	94	100	100
ND	ND	ND	100	82	100	100	100	98	97	100	95
ND	ND	ND	96	85‡	71	62	96	88§	92	74	73
ND	ND	ND	100	100	100	100	100	100	100	98	100
46§	100	51§	ND	51§	ND	ND	ND	ND	ND	50§	ND
39	100	33‖	ND	33‖	ND	ND	ND	ND	ND	48	ND

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vide the patient with the safest and most effective antimicrobial agents. They suggested that each hospital establish a team concerned with the optimal use of antibiotics.[6] Despite the merits of this hospital-wide approach, it is necessary for clinical practitioners to have detailed knowledge of the specific antibiotic susceptibilty patterns in their individual ICU.[7]

SEVERAL INVESTIGATORS have compared hospital-wide antibiograms to unit-specific antibiograms, noting the trend toward increased resistance in ICUs.[8-12] Stratton et al[8,9] reported not only differences in ICU and hospital-wide susceptibility patterns, but also important differences in susceptibility patterns for *S aureus* and *P aeruginosa* among individual ICUs in the same hospital. Unfortunately, their publications provided no statistical analyses of the data, making it difficult to know the significance of the differences reported.

Bryce and Smith[10] compared the hospital-wide antibiogram with the ICU susceptibility pattern for gram-negative organisms. Resistance of *P aeruginosa* was considerably higher in the ICU, and this was not accurately reflected in the hospital-wide antibiogram. The susceptibility of the Enterobacteriaceae did not seem to be appreciably different between the ICU and the hospital-wide data. This study involved isolates from a combined ICU that housed medical, surgical, and burn patients, and therefore the results of this trial may not easily extrapolate to a specific ICU type such as the SICU.[8,9]

Gubbins et al[11] reported significantly greater antibiotic resistance for many gram-negative organisms isolated from ICU patients compared with isolates from non-ICU patients. However, this study combined data from multiple ICUs, which may mask important differences in susceptibility between ICUs. Also, this study did not compare ICU antibiotic susceptibility with the hospital-wide antiobiogram, but limited the comparison group to non-ICU patients. Because most institutions report antibiotic susceptibility profiles on a hospital-wide basis, we believed it was important to use the hospital-wide data as the comparator to illustrate the limitations of this profile in predicting susceptibility in a specific ICU environment. These authors also did not report the total number of isolates evaluated, making it difficult to know the clinical relevance of the reported statistically significant differences.

In our study, the 2 most commonly isolated bacterial pathogens in the SICU (*S aureus* and *P aeruginosa*) had significantly different susceptibility patterns compared with the hospital-wide antibiogram. *Staphylococcus aureus* was significantly more resistant to essentially all antistaphylococcal agents with the exception of vancomycin. Although the reason for the variability in staphylococcal resistance is not completely understood, it may be due to selection pressure arising from the common use of antistaphylococcal agents in the SICU.[13] The susceptibility of coagulase-negative staphylococci was similarly lower in the SICU; however, the difference did not reach statistical significance for several antibacterials, likely due to a lower level of susceptibility outside of the ICU combined with the smaller sample size.

The susceptibility of *P aeruginosa* was significantly less for imipenem-cilastatin and greater for ticarcillin–clavulanic acid. However, there were no differences in susceptibility for third-generation cephalosporins and antipseudomonal penicillins. This pattern is similar to the results reported by Stratton et al,[8] which did not demonstrate major differences in the susceptibility of *P aeruginosa* isolates comparing hospital-wide isolates with isolates from the SICU. The reason for this may be related to the fact that *P aeruginosa* infections are essentially all nosocomial infections, with many patients outside of the ICU developing infections from organisms that may have been originally acquired during an ICU stay earlier in their hospitalization.

Surprisingly, *E coli* isolated in our SICU were more susceptible to most penicillin-derivative antibiotics, and were highly susceptible to most other tested antibiotics for both the SICU and hospital-wide isolates. A possible explanation for this increased susceptibility in the SICU is that many isolates may come from patients who present to the SICU early in their hospital stay with intra-abdominal or other severe, life-threatening infections caused by their own community-acquired flora. However, for the hospital-wide isolates, *E coli* may more commonly represent a nosocomially acquired organism with a more resistant profile. Bryce and Smith[10] and Gubbins et al[11] reported greater resistance among gram-negative species from the ICU compared with non-ICU isolates; however, they did not report increased resistance for *E coli*. Other published studies[8,9] did not provide specific data for *E coli* isolates.

The major limitation of our study is the small number of isolates available from the SICU for the less prevalent gram-negative organisms. Because of this limited sample size we cannot draw any definitive conclusions concerning differences in susceptibility for these organisms. Also, the number of coagulase-negative staphylococci was relatively small, limiting the ability to detect statistically significant differences for some of the antibiotics. However, the overall susceptibility with most of these antibiotics was low enough that the results would not have affected empiric antibiotic choices.

An additional potential limitation of this study is that the method of data collection could not differentiate between isolates considered to be causing infection and those that represented colonization or contamination. It is possible that, if the data set had been limited to isolates causing infection and therefore requiring antimicrobial therapy, the resulting susceptibility patterns would be different. Once actual infections were determined, specific knowledge about the antibiotics chosen and the duration of therapy would likely explain many of the differences in antibiotic susceptibility. However, collection of this type of data would require extensive retrospective review of the medical records or prospective data collection, which would not be a practical or reasonable method to generate unit-specific antibiotic susceptibility data for routine use in

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the ICU. These limitations are significant in generating or supporting a theory of selection pressure on the development of antibiotic resistance. However, the practical reality is that the hospital-wide antibiogram is already generated and the unit-specific antibiogram can be easily queried from this database.

In conclusion, hospital-wide antibiograms may mask ICU susceptibility patterns. Unit-specific antibiograms are inexpensive tools that may help guide empiric therapy in the ICU. The results of this study are not intended to provide specific recommendations concerning empiric antibiotic selection in the SICU, because susceptibility will vary from hospital to hospital, but are intended to illustrate the importance of knowing unit-specific antibiotic susceptibility patterns.

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Alcohol and Breast Cancer in Women: A Pooled Analysis of Cohort Studies

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Objective.—To assess the risk of invasive breast cancer associated with total and beverage-specific alcohol consumption and to evaluate whether dietary and nondietary factors modify the association.
Data Sources.—We included in these analyses 6 prospective studies that had at least 200 incident breast cancer cases, assessed long-term intake of food and nutrients, and used a validated diet assessment instrument. The studies were conducted in Canada, the Netherlands, Sweden, and the United States. Alcohol intake was estimated by food frequency questionnaires in each study. The studies included a total of 322 647 women evaluated for up to 11 years, including 4335 participants with a diagnosis of incident invasive breast cancer.
Data Extraction.—Pooled analysis of primary data using analyses consistent with each study's original design and the random-effects model for the overall pooled analyses.
Data Synthesis.—For alcohol intakes less than 60 g/d (reported by >99% of participants), risk increased linearly with increasing intake; the pooled multivariate relative risk for an increment of 10 g/d of alcohol (about 0.75-1 drink) was 1.09 (95% confidence interval [CI], 1.04-1.13; *P* for heterogeneity among studies, .71). The multivariate-adjusted relative risk for total alcohol intakes of 30 to less than 60 g/d (about 2-5 drinks) vs nondrinkers was 1.41 (95% CI, 1.18-1.69). Limited data suggested that alcohol intakes of at least 60 g/d were not associated with further increased risk. The specific type of alcoholic beverage did not strongly influence risk estimates. The association between alcohol intake and breast cancer was not modified by other factors.
Conclusions.—Alcohol consumption is associated with a linear increase in breast cancer incidence in women over the range of consumption reported by most women. Among women who consume alcohol regularly, reducing alcohol consumption is a potential means to reduce breast cancer risk. (*1998;279:535-540*)

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