CAUSATIVE AGENTS OF NOSOCOMIAL BLOODSTREAM INFECTIONS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERNS

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Abstract. The aim of this study was to retrospectively investigate nosocomial bloodstream infections (NBI) and their antimicrobial susceptibility patterns at Afyon Kocatepe University (AKU) Hospital, Turkey, from January 2006 to December 2011 and to determine the risk factors for nosocomial BSI. Subjects were aged ≥18 years. The data were obtained from patient files. Five hundred seventy-nine nosocomial infections in 461 patients were included in the study. Eighty-four point six percent was primary and 15.4% were secondary infections. Gram-positive cocci were the most common organisms. When compared year by year there was an increasing trend in antibacterial resistant gram-negative bacilli. The most common infection risk factors were H2 histamine receptor blocker use and blood transfusions. Regular surveillance of BSI is important to monitor changes in the types of microorganisms and their resistance patterns.

Keywords: nosocomial bloodstream infections, etiology, surveillance, risk factors

INTRODUCTION

Nosocomial bloodstream infections (BSI) are an important cause of morbidity and mortality in hospitals. Until the 1970s, the Enterobacteriaceae family members were the dominant BSI causative agents; however, gram-positive cocci bacteremias have become more frequent (Rupp, 2004). The course of BSI with gram-negative bacilli may be severe and results in a higher mortality rate (Harbarth *et al*, 1999). Improper empiric antibiotic treatment is another cause of mortality: studies have found a higher mortality risk among patients with BSI who have received improper initial empiric treatment (Kollef, 2000; Harbarth *et al*, 2002).

In all nosocomial infections, surveillance of trends in microorganisms and their resistance patterns risk factors is important (Liu, 2010). The aim of this study was to retrospectively investigate the types of organisms and their antimicrobial susceptibility patterns among patients with BSI at Afyon Kocatepe University (AKU) Hospital from January 2006 to December 2011.

MATERIALS AND METHODS

Study subjects in this retrospective study were patients aged ≥18 years who presented to AKU Hospital between

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January 2006 and December 2011 and developed a BSI. Data were obtained from the patient files archived at the Infection Control Committee (ICC) Department. Nosocomial BSI were diagnosed based on the Centers for Disease Control and Prevention (CDC) criteria (Rupp, 2004). Information obtained from patient charts included demographic characteristics, possible risk factors for BSI (history of diabetes mellitus, histamine receptor blocker usage, malignancy, blood transfusion, general body trauma, acute or chronic renal insufficiency or presence of a foreign body), history of having an invasive intervention (urinary catheter placement, central venous catheter placement, mechanical ventilation, intubation, tracheostomy, peripheral vascular catheter or hemodialysis), the causative microorganism(s) and their antibiotic susceptibilities, whether the infection was primary or secondary and the outcome of the patient.

The total number of nosocomial infections per year and hospitalized patients per year were recorded. The rate of BSI among nosocomial infections, the most frequently observed causative microorganisms each year and the most common risk factors were determined.

The prognosis of a nosocomial BSI was determined. The relationship between invasive interventions and other risk factors on the prognosis were calculated.

Statistical analyses

Statistical analyses were performed using SPSS 20.0 (Statistical Packages for Social Sciens, SPSS, Chicago, IL). Data were expressed as means ± standard deviation and a p-value <0.05 was considered significant. The Student's t-test and ANOVA test were used to compare groups.

RESULTS

Five hundred seventy-nine nosocomial BSI were seen among 461 patients; 264 males and 197 females. The mean ±SD age was 61±71 years. The age, gender and department contracting disease are shown in Table 1.

The total number of nosocomial infections, BSI infections and hospitalized patients per year are shown in Table 2.

The most common isolated organism was *Staphylococcus* (40.4% of total cases). Methicillin resistance was found in 89.3% of isolated staphylococci. The organisms isolated per year are shown in Table 3.

The susceptibilities of isolated *Escherichia coli, Klebsiella, Pseudomonas* and *Acinetobacter* against carbapenem group antibiotics (ertapenem, meropenem and imipenem) are shown in Table 4.

One risk factor was found in 163 cases (28.2%), two risk factors were found in 268 cases (46.3%) and three or more risk factors were found in 128 cases (22.1%). No risk factors were found in 20 cases (3.4%). The most frequent risk factors found were H_2 histamine receptor blocker use and having had a blood transfusion, seen in 507 (87,6%) and 335 (57.9%) cases, respectively.

At least one invasive intervention had been performed in 30 cases (5.2%), two interventions had been performed in 112 cases (19.3%) and three or more interventions had been performed in 392 cases (75.3%). There was only one patient (0.2%) with no history of an intervention (Table 5).

Two hundred ninety-seven patients (51.3%) died and the rest (282, 48.7%) survived. The greater the number of risk factors or invasive interventions the greater the risk of mortality. Patients with ≥3

Table 1
Distribution of nosocomial bloodstream infections by hospital unit.

Services	Number of infections *n* (%)	Number of patients *n* (%)	Gender (M/F)	Mean age
Reanimation unit	164 (28.3)	107 (23.2)	60/47	61±19
Internal medicine intensive care unit	116 (20)	104 (22.6)	64/40	63±17
General surgery intensive care unit	106 (18.3)	83 (18)	39/44	65±15
Internal medicine service	56 (9.7)	48 (10.4)	30/18	60±16
General surgery service	37 (6.4)	34 (7.4)	22/12	59±13
Neurosurgery service	36 (6.2)	30 (6.5)	23/7	52±20
Cardiovascular surgery service	23 (4)	17 (3.7)	9/8	65±8
Neurology	16 (2.8)	14 (3)	7/7	64±18
Chest disease service	12 (2.1)	11 (2.4)	1/9	67±8
Orthopedics service	7 (1.2)	7 (1.5)	4/3	55±25
Cardiology service	5 (0.9)	5 (1.1)	4/1	67±12
Urology service	1 (0.2)	1 (0.2)	0/1	35±0
Total	579 (100)	461 (100)	264/197	62±17

Table 2
Nosocomial bloodstream infections by year.

Years	Total inpatients	Number of nosocomial infections	The number of nosocomial blood stream infections	Percent[a]
2006	12,629	306	54	17.6
2007	14,063	445	86	19.3
2008	16,331	419	89	21.2
2009	15,595	502	113	22.5
2010	16,798	489	113	23.1
2011	14,557	483	124	25.7

[a]Percent of nosocomial bloodstream infections per total nosocomial infections.

invasive interventions had a significantly higher (p=0.0001) risk of mortality than patients with ≤2 invasive interventions. No correlations were observed between the number of risk factors or the causative organism and mortality.

Four hundred ninety nosocomial BSI (84.6%) were primary infections and 89 (15.4%) were secondary infections. The respiratory system was the most common system infected (73.12), followed by the urinary tract (14.6%), surgical site (10.1%), central nervous system (1.1%) and soft tussue (1.1%). Central and peripheral venous catheters had been presented in 390 (79.6%) and 42 (8.6%) cases, respectively. No intravenous catheter was presented in 58 cases (11.8%).

Table 3
Causative agents of nosocomial bloodstream infections by year.

Organism	Number of organisms isolated by year						Total
	2006	2007	2008	2009	2010	2011	
Gram-positive							
MRSA	11	18	25	27	27	34	142
MRCNS	5	16	14	20	6	6	67
E. faecium	1	2	8	6	13	10	40
E. faecalis	4	5	10	5	8	6	38
S. aureus	4	7	4	2	-	1	18
CNS	3	-	1	3	-	-	7
Total	28	48	62	63	54	57	312
Gram-nagative							
Acinetobacter spp	14	15	10	20	16	19	94
K. pneumoniae	2	4	2	8	12	14	42
P. aeruginosa	2	8	6	6	8	8	38
E. coli	6	3	4	4	11	9	37
E. cloacae	-	2	3	2	2	4	13
S. maltophilia	1	-	-	1	-	1	3
P. mirabilis	-	-	-	-	-	1	1
Total	25	32	25	41	49	56	228
Fungus							
C. albicans	1	6	2	9	10	11	39

MRSA, methicillin-resistant *Staphylococcus aureus*; MRCNS, Methicillin-resistant coagulase negative *Staphylococcus*; CNS, coagulase negative *Staphylococcus*.

DISCUSSION

Nosocomial infection is one of the most common complications in hospitalized patients (Simonetti *et al*, 2013). Nosocomial infections cause high morbidity and mortality rates; they may be prevented with proper precuations (NNIS, 2004). Regular surveillance at each hospital can determine the causative microorganisms and their susceptibilities to initial empiric treatment can be properly selected.

The percent of nosocomial BSI among all nosocomial infections has increased and there have been changes in antimicrobial resistance (Harbarth *et al*, 2002; NNIS, 2004; Liu *et al*, 2010). Over the duration of our study period the percent of the nosocomial BSI among all hospital-related infections had increased from 17.6% to 25.7%. The most frequently observed nosocomial BSI in our study was methicillin resistant *Staphylococcus aureus* (MRSA). *Candida* infections also increased. The number of *C. albicans*-related nosocomial BSI during the latter 3 years of our study was higher than in the first 3 years. Our findings are similar to other studies (Marchaim *et al*, 2008; Liu *et al*, 2010; Rosenthal *et al*, 2012). The increase in *Candida* infections might be due to the increased use of broad spectrum antimicrobials used to treat gram-negative bacilli (Boo *et al*, 2005; Yap *et al*, 2009).

Table 4
Carbapenem susceptibility among nonfermentative gram-negative bacilli isolates.

Organism	Ertapenem			Imipenem			Meropenem		
	A	B	C (%)	A	B	C (%)	A	B	C (%)
E. coli (n=37)	2	2	0 (0)	33	33	0 (0)	29	29	0 (0)
Klebsiella (n=42)	9	8	1 (11)	40	38	2 (5)	39	37	2 (5)
Pseudomonas (n=38)	-	-	-	36	25	11 (31)	33	23	10 (30)
Acinetobacter (n=94)	-	-	-	92	50	42 (46)	90	42	48 (53)

A, Number of strains evaluated for carbapenem susceptibility.
B, Number of strains sensitive to carbapenem.
C, Number of strains resistance to carbapenem.

Table 5
Risk factors and invasive procedures in nosocomial BSI attacks.

Risk factors	Number of infections (%)
H_2 receptor blocker usage	507 (87.6)
Blood transfusion	335 (57.9)
Diabetes mellitus	149 (25.7)
Acute renal insufficiency	54 (9.3)
Malignancy	26 (4.5)
Trauma	23 (3.9)
Foreign body	6 (1.0)
Chronic renal insufficiency	1 (0.2)
Invasive procedures	
Urinary catheter	533 (92.1)
Central venous catheter	479 (82.7)
Intubation	401 (69.3)
Mechanical ventilation	400 (69.1)
Tracheostomy	110 (18.9)
Peripheral vascular catheter	74 (12.8)
Hemodialysis	62 (10.7)

More than half of nosocomial BSI in our study occurred in the intensive care unit (ICU). Infection rates in ICUs may be reduced by implementing proper precautions (Shorr and Jackson, 2005; Gastmeier *et al* 2006). H_2 histamine recepter blockers and blood transfusion were risk factors for nosocomial BSI. H_2 histamine receptor blockers have been previously reported as a risk factor for nosocomial infections (Singh-Naz *et al*, 1996). Gastmeier *et al* (2006) reported a link between the number of blood transfusions and nosocomial pneumonia and BSI.

No correlation was observed between the number of risk factors and mortality in our study. Since our study was retrospective and not controlled, it is not possible to determine causality. However, it seems reasonable to conclude that limiting the use of H_2 receptor blockers and blood transfusions, might reduce the risk of nosocomial BSI (Singh-Naz *et al*, 1996; Gastmeier *et al*, 2006).

The presence of an intravenous catheter is an important risk for developing nosocomial BSI. Central venous catheters are a particularly strong risk facter for developing nosocomial BSI (Crow, 1996). In our study, central and peripheral venous catheters were present in 82.7% and 12.8% of nosocomial BSI, respectively. Intravenous catheter replacement and paying attention to reducing the risk of nosocomial BSI is important. The number of nosocomial BSI has been shown to be

reduced by in-service education (Crow, 1996; Blake, 2008).

Nosocomial infections differ by hospital. The causative microorganisms and their antibiotic sensitivities differ by hospital. Therefore, hospital infection surveillance data are important for determining initial empiric treatment. Surveillance is also important due to high mortality rates with nosocomial BSI, which may be reduced by proper, early antimicrobial use (Liu *et al*, 2010).

No significant changes were observed in the frequency of gram-positive cocci infections over the 6-year study period, but, an increase was seen in gram-negative bacilli and Candida infections. Gram-positive microorganisms are the most frequent causative agents for nosocomial BSI; the incidence of gram-negative bacilli infections resistant to many antimicrobials has been progressively increasing (Biedenbach *et al,* 2004; Rupp, 2004; Wu *et al*, 2006; Trecarichi *et al*, 2012). The gram-negative bacteria isolated in our study were mostly *Acinetobacter, Pseudomonas, Escherichia coli* and *Klebsiella* strains. The *Acinetobacter* and *Pseudomonas* strains demonstrated high rates of carbapenem resistance. The resistance rates observed are consistent with the data in the literature and suggest these microorganisms could cause serious problems in the future (Kiratisin *et al*, 2012). Since antimicrobial treatment options are limited among carbapenem resistant organisms, infection control measures are becoming increasingly important (Thabet *et al*, 2013).

Regular surveillance of nosocomial infection is important to determine the types of organisms present and their antibiotic resistance patterns. Resistant bacteria cause important problems now and in the future. Knowing what surveillance data shows can help guide initial empiric therapy.

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