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Shocking Levels of Antimicrobial Resistance in Burn Infections in Bestian Hospital, Seoul, South Korea

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ABSTRACT

Studies of microbial species and antimicrobial resistance in burn wound infections are rare in Korea. This study investigated the microbial species and antimicrobial resistance present in 630 patients with burns admitted to Bestian Hospital, a specialized burns clinic in Korea, between 2011 and 2013.

Bacterial species were identified using the Vitek system and antimicrobial resistance was assessed using both disk diffusion method and the Vitek 2 system. Acinetobacter baumannii (37.3%) was the most frequently isolated organism in burn wound infections. Methicillin-resistant Staphylococcus aureus (MRSA), Pseudomonas aeruginosa, coagulase-negative Staphylococci, Enterococcus faecalis, and Escherichia coli were also isolated. Pandrug-resistant strains were present in 91.8% of A. baumannii samples. They were also carbapenem-resistant. However, no colistin-resistant strains were isolated. Care is needed when administering antibiotics for burn infections as most microbial strains are multidrug-resistant.

Keywords: *burn, A. baumannii, pandrug-resistance*

INTRODUCTION

Patients with burns are prone to infection due to the destruction of the skin barrier, functional disorders of the immune system, long-term hospitalization, invasive diagnostic and therapeutic procedures, and massive antimicrobial therapy (1,2). Many pathophysiological mechanisms of burn infection are known, and despite strict infection control measures and progress in therapeutic methods, infection is still the most common cause of death in patients with burns (1,2). Microorganisms can invade easily through the destroyed skin barrier, and proliferate around eschar. Moreover, injured vessels may restrict the transportation of antibiotics or immune cells (3). Changes that occur in the immune system of patients with burn include functional disorders of segmented neutrophils, inverted number of T-helper and T-suppressor cells, and decreased number of lymphocytes and levels of interleukin-2 (4-6).

However, the study of burn wound infections is rare in Korea (7-9). A. baumannii, P. aeruginosa, and Enterococcus spp. were isolated in decreasing order in 137 patients at Bestian Hospital in 2008 (8). However, the number of patients was too small to analyze the microbial species and antimicrobial resistance.

The study of microbial species and antibiotic resistance in burn wound infections assists in a priori choice of an antimicrobial regimen before culture results, which in turn improves therapeutic effects and reduces mortality (2). The authors evaluated the microbial species and antimicrobial resistance in patients with burn wound infections who were admitted to Bestian Hospital, the largest specialized burns clinic in Korea.

MATERIAL AND METHODS

There were 630 patients with burns admitted to the intensive care unit of Bestian Hospital between 2011 and 2013. All of them underwent a microbiological study. The wound region was sterilized with 2% povidone iodine because of the possibility of colonization in a wound culture. After debridement, necrotic tissue was removed, and then a tissue sample was placed in a screw cap sample jar, transported to the microbiological laboratory, and refrigerated at 4℃ for 24 hrs. Culture mediums included blood agar, MacConkey agar, and phenylethyl alcohol (PEA) blood agar for anaerobes. An anaerobic

culture was performed for Clostridium or Bacteroides in deep wounds. The incubation time was 24–48 hrs. The strain that was isolated repeatedly was excluded. The isolates were identified by using the Vitek 2 (Biomerieux) system.

The antimicrobial resistance testing was performed using both the disk diffusion method and the Vitek 2 system. For gram-negative organisms, the antimicrobial susceptibility test profile included ampicillin (10 µg), ampicillin/ sulbactam (10/10 µg), cefepime (30 µg), ceftazidime (30 µg), imipenem(10 µg), meropenem (10 µg), gentamicin (10 µg), amikacin (30 µg), aztreonam (30 µg), ciprofloxacin (5 µg), tobramycin (10 µg), piperacillin (100 µg), piperacillin / tazobactam (100/10 µg), and colistin (10 µg). For gram-positive organisms, the antimicrobial susceptibility test profile included penicillin (10U), ampicillin (10 µg), gentamicin (10 µg), teicoplanin (30 µg), vancomycin, ciprofloxacin (5 µg), clindamycin (2 µg), erythromycin (15 µg), and tetracycline (30 µg). The organism was classified as multidrug-resistant if it was resistant to the three major classes of antimicrobials (10). The organism was classified as pandrug-resistant when it was resistant to all classes of antimicrobial drugs except colistin. The antimicrobial tests were interpreted according to the 2011 revision of the Clinical and Laboratory Standards Institute guideline (11). A control group was selected from the data at the Research Institute of Bacterial Resistance at Yonsei University. The antimicrobial resistance data for the control group is shown in Table 1, 2 (12). Pearson's chi-square test was used for statistical analysis. This study was approved by the Institutional Review Board of Bestian Hospital (BEST 2012-03-001).

Table1. *Antimicrobial resistance of gram negative bacteria in burn wound patients*

	A. baumannii			P.aeruginosa			E. coli		
Antibiotics	**Pt.**	**Cont.**	**p**	**Pt.**	**Cont.**	**p**	**Pt.**	**Cont.**	**p**
AMP	100						86	67	0.374
AMP/SUL	100	39	0.009				75	37	0.043
CFP	100	70	0.031	50	9	0.007	50	8	0.007
CAZ	99.3	64	0.028	53	13	0.015	40	11	0.029
IPM	98			53	28	0.029	0		
MEP	99.3	68	0.030	47	19	0.030			
GEN	99.3	59	0.019	50	12	0.012	43	26	0.041
AMK	98.7	55	0.021	44	5	0.017	0	1	1.000
ATM	99.2			50	17	0.019	29	15	0.056
CIP	100			47	22	0.033	57		
PIP	100			62.5	21	0.024			
PIP/TAZ	100	70	0.031	56.3	26	0.027			
COL	0	1	0.875	0	0	1.000			

Abbreviations; Pt.: patient, Cont.: control, p: p-value, AMP: ampicillin, AMP/SUL: ampicillin/sulbactam, CFP: cefepime, CAZ: ceftazidime, IPM: imipenem, MEP: meropenem, GEN: gentamicin, AMK: amikacin, ATM: aztreonam, CIP: ciprofloxacin, TOB: tobramycin, PIP: piperacillin, PIP/TAZ: piperacillin/tazobactam, COL: colistin

Table2. *Antimicrobial resistance of gram positive bacteria in burn patients.*

Antibiotics	**S. aureus**			**E. faecalis**		
	Pt.	**Cont.**	***p***	**Pt.**	**Cont.**	***p***
PC	100	94	0.824			
AMP				0	0	1.000
GEN	89.5					
TEI	0	0	1.000	0	2	0.910
VA	0	0	1.000	0	2	0.910
CIP	84.2	39	0.023	20	29	0.573
CLI	76.3	50	0.048			
ERY	83.8	51	0.032			
TET	84.2	39	0.023	56	87	0.078

Abbreviations; PC: penicillin, AMP: ampicillin, GEN: gentamicin, TEI: teicoplanin, VA: vancomycin, CIP: ciprofloxacin, CLI: clindamycin, ERY: erythromycin, TET: tetracycline

RESULTS

We collected data on patient characteristics. The mean age was 45 ± 15.8 years, and the male to female ratio was 4:1. The mean burn surface area was 43% (range 5–65%, +/-19%). Causative organisms were isolated in 69.8% of patients. Single organisms were isolated in 57.7% of patients and multiple organisms in 12.1%. The total number of isolated organisms was 536. The mean time since admission was 42 days (range 3–98 days, +/- 25 days). Mortality was 34% according to the chart reviews. No anaerobic organisms were isolated.

A. baumannii was the most frequently isolated organism. It was isolated in 37.3% of patients, and most strains were pandrug-resistant. Other isolated organisms, in decreasing order of occurrence, were methicillin-resistant Staphylococcus aureus (MRSA) (21%), P. aeruginosa (17.8%), coagulase-negative Staphylococci (13.9%), E. faecalis (5%), and E. coli (3.9%) (Fig 1). Most gram-negative bacteria were non-fermenting organisms such as A. baumannii or P. aeruginosa. E. coli species, which are frequently isolated in wound infections, were isolated in only 3.9% of patients, and no K. pneumoniae was isolated in our sample.

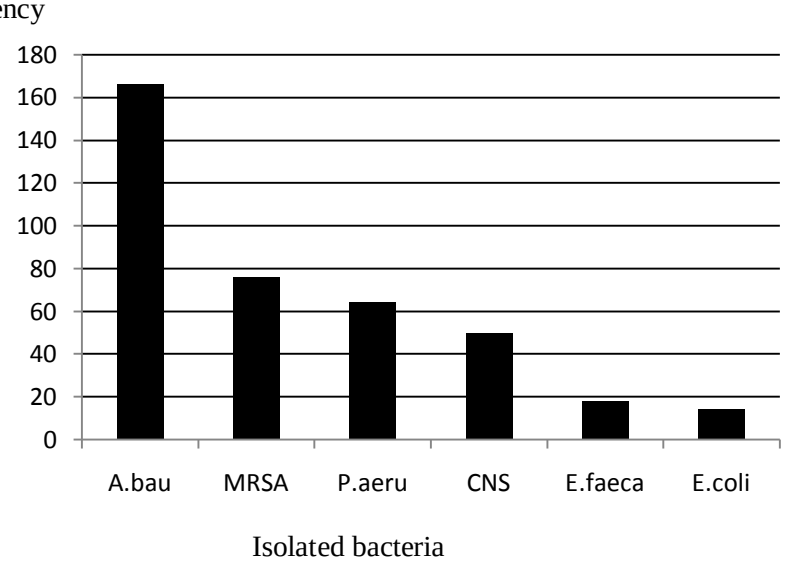

Fig1. *The bacterial frequency in burn patients (total N=447).*

Abbreviations; A.bau: A.baumannii, MRSA: methicillin resistant S.aureus, P.aeru: P.aeruginosa, CNS: coagulase negative S.aureus, E.faeca: E.faecalis.

Antimicrobial resistance of A. baumannii was 100% to ampicillin, ampicillin / sulbactam, cefepime, ciprofloxacin, tobramycin, piperacillin, and piperacillin / tazobactam; 99.3% to ceftazidime, meropenem, and gentamicin; 99.2% to aztreonam; 98.7% to amikacin; 98% to imipenem; and 0% to colistin. Pandrug-resistant isolates were identified in 91.8% of patients (Table 1). Antimicrobial resistance to imipenem and meropenem was 98% and 99.3%, respectively for A. baumannii, showing that most of the isolated organisms were resistant to carbapenems. Moreover, most isolates showed resistance to extended – spectrum cephalosporins, aminoglycosides, and quinolones (Table 1). There were no colistin-resistant isolates. In patients with burns, antimicrobial resistance of P. aeruginosa was 62.5% to piperacillin; 56.3% to piperacillin / tazobactam; 53% to ceftazidime and imipenem; 50% to cefepime, gentamicin, and aztreonam; 47% to meropenem, ciprofloxacin, tobramycin; 44% to amikacin; and 0% to colistin, indicating about 40–60% resistance. Although both A. baumannii and P. aeruginosa are non-fermenting organisms, pandrug resistance was evident in 91.8% of patients with A. baumannii but only 33.2% of patients with P. aeruginosa. However, high resistance rates to extended - spectrum cephalosporins, aminoglycosides, and carbapenem were observed in P. aeruginosa ($p<0.05$) (Table 1). Resistance to quinolone in patients with burns was similar to that in the control group. There were no colistin-resistant organisms.

The antimicrobial resistance of E. coli was 86% to ampicillin, 75% to ampicillin / sulbactam, 57% to ciprofloxacin, 50% to cefepime, 43% to gentamicin, 40% to ceftazidime, 29% in

aztreonam, and 0% to imipenem and amikacin. The E. coli species showed higher resistance rates to extended spectrum cephalosporins, gentamicin, and quinolones in patients with burns compared to the control group ($p<0.05$). No colistin-resistant E. coli were isolated (Table 1).

All isolates of S. aureus were MRSA (100%). In patients with burns, the antimicrobial resistance of S. aureus was 100% to penicillin and cefoxitin, 89.5% to gentamicin, 84.2% to ciprofloxacin and tetracycline, 83.8% to erythromycin, 76.3% to clindamycin, and 0% to teicoplanin and vancomycin. Resistance to aminoglycosides, quinolones, and MLSbs was higher in patients with burns than in the control group ($p<0.05$). However, glycopeptide-resistant S. aureus was not isolated (Table 2). Resistance patterns of E. faecalis were similar in the burns group and the control group and no vancomycin-resistant enterococci (VRE) were detected (Table 2).

DISCUSSION

The survival rate of patients with severe burns has increased remarkably in the last decade due to fluid replacement therapy, nutritional therapy, management of the respiratory system, burn wound care, and active infection control. Despite the mortality rate for burns decreasing by 50% over the last four decades, Trottier reported that the mortality rate for burn wound infection was 30% (13), showing the significance of wound infection in patients with burns (2, 13-15).

The most frequently isolated organism in patients with burns in this study was A. baumannii, with a frequency of 37.3%. Lari et al. reported that the most frequent organism they found in burn wound infections was P. aeruginosa (16). According to burn wound infection reports prior to 2010, P. aeruginosa and S. aureus were the most frequently isolated organisms, and A. baumannii was less frequently isolated (16, 17). However, the significance of A. baumannii has increased recently. Nasrolahei et al. (18) warned that multidrug-resistant A. baumannii is a rapidly increasing hospital-acquired infection in patients with burns. A report comparing bacterial species in an intensive care unit (ICU) and a general ward, found that A. baumannii was the most common organism in the ICU, and S. aureus and P. aeruginosa were the most common organisms in a general ward (19-22). Enterobacteriaceae, which has been considered an important organism in wound infection, was not detected in this study except a low frequency of E. coli, which is similar to other reports (16, 17).

Lee et al. reported that 95.3% of A. baumannii isolated from patients with burns showed resistance to carbapenem, which is similar to our results (2). In another study, the resistance rate of A. baumannii to imipenem was 87%, which was considered very high (13). Carbapenem resistance in burn infections is mainly due to OXA-type enzymes (18, 23). Colistin may be effective for treating A. baumannii infection in patients with burns because colistin-resistant A. baumannii was not detected in the patients enrolled in this study. Amikacin and imipenem may also be effective. We monitored the patients in this study, and they were mainly treated with imipenem; however, the prognosis was poor, and the mortality rate was 34%.

The pandrug resistance rate of P. aeruginosa was lower than that of A. baumannii, at 33.2% and 91.8%, respectively. The resistance rates of P. aeruginosa to imipenem and meropenem were 53% and 47%, respectively, showing moderate-level resistance. In one burns study, they reported that 95.9% of P. aeruginosa showed carbapenem resistance on blood culture (2), which is a higher rate than the resistance rate (40-60%) found in our study. However, another study showed similar resistance rates to this study (24). Resistance to extended-spectrum cephalosporins and aminoglycosides was higher in the burns group than in the control group, suggesting the need to restrict treatment with these drugs in patients with burns.

In the E. coli species, resistance to extended-spectrum cephalosporins, gentamicin, and quinolones was higher in the burns group than in the control group. Imipenem-resistant carbapenem-resistant Enterobacteriaceae (CRE) was not detected. However, CRE is increasing worldwide and may become more prevalent in burn injury infections.

All S. aureus isolated in patients with burns were MRSA (100%), which was similar to the finding of another Korean study where the proportion was 96.3% (2). Resistance to aminoglycosides, ciprofloxacin, and MLSbs was higher in the burns group than in the control group. Glycopeptide-resistant organisms were not detected. This result suggests that glycopeptides, such as vancomycin and teicoplanin, would be effective in treating burn wound infections. VRE was not detected, although this result may be due to the small sample size. In another study, they reported

VRE in 36.2% of blood cultures (2).

In conclusion, A. baumannii is now thought to be the most significant organism in burn wound infections. Moreover, because 91.8% of patients with burns in our study showed pandrug-resistant organisms, we should be cautious about this and infection control should be performed thoroughly. Because no colistin-resistant A. baumannii was isolated (13), colistin could be considered the main treatment regimen for patients with infected burns. However, because MRSA and P. aeruginosa showed higher resistance in the burns group than in the control group, and many multidrug-resistant organisms were isolated, it is thought that significant limitations are present when treating burn wound infections. Most organisms are antimicrobial-resistant, so we need to be careful when prescribing antimicrobial treatment for patients with burns.

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