

Original Article

Laboratory-based evaluation of MDR strains of *Pseudomonas* in patients with acute burn injuries

Hong-Tu Zhang¹, Hui Liu²

¹Department of Burn and Plastic, Jining Number 1 People's Hospital, Jining 272100, China; ²Medical Laboratory Center, Jining Number 1 People's Hospital, Jining 272100, China

Received June 7, 2015; Accepted July 28, 2015; Epub September 15, 2015; Published September 30, 2015

Abstract: Localization of burn was variable: head and face in 76 patients (29%), trunk in 58 (49%), upper limb in 37 (52%), lower limbs in 44 (41%), hands in 16 (15%), perineal area in 26 (5.5%) and whole body except perineal area in 10 (9%) patients. Inhalation syndrome was present in 56 (44%) patients. Ninety patients (82%) had indwelling venous catheters, 83 (75.5%) patients' arterial catheter and 86 (78%) patients' urinary catheters. By multivariate analysis: age ≤ 4 years, Garses 4, colistin use in documented multiresistant infections, and mechanical ventilation were independent variables related with mortality and graft requirement was a protective factor for mortality. Despite advances in care, gram negative bacterial infections and infection with *Pseudomonas aeruginosa* remain the most common cause of bacteria related mortality early in the hospital course. Viral infections are also associated with mortality and numbers have remained stable when compared to data from prior years.

Keywords: *Pseudomonas*, acute burn injury, gram positive bacteria, fungi

Introduction

Serious infections caused by *Pseudomonas aeruginosa* remain a common complication in thermally injured patients contributing substantially to burn morbidity and death rate. In a study of 176 burn care centres in North America; *Pseudomonas* species (sp.) was seen the most dangerous cause of life threatening infections in the thermally injured patients [1]. *P. aeruginosa* is an opportunistic gram-negative pathogen which produces many exoproducts including elastase, alkaline protease, hemolysin, exotoxin A, exoenzyme S and together with its heterogeneous lipopolysaccharide mediate much of its virulence [2]. Colistin was initially used therapeutically in Japan and in Europe during the 1950s and in the United States in the form of colistimethate sodium in 1959 [3]. During the past two decades, the intravenous use of colistin was mainly restricted during the past two decades for the treatment of lung infections due to multi-drug-resistant (MDR), Gram-negative bacteria in patients with cystic fibrosis [4].

According to the American Burn Association (ABA), close to 500,000 patients with burn injuries

seek medical attention in the US each year. Some 40,000 of those who seek medical care require hospitalization and over 60% of those hospitalized, require intensive maintenance in a specialized burn centre [5]. The immune-compromising effects of burns, hospital stay; diagnostic and therapeutic procedures put these patients at increased risk of morbidity and death rate. In the final few years in patients who held out to burn injury has increased, but despite improvements in the management of burn patients, infections remain the most usual causal agent of morbidity and mortality following burn injury [6, 7]. Infections caused by *P. aeruginosa* are often severe and life threatening and are difficult to treat because of the limited susceptibility to antimicrobial agents and the high frequency of an emergence of antibiotic resistance during therapy [8, 9], thus resulting in severe adverse outcomes [10]. Historically, bacterial pathogens have been the most common cause of infections in burn patients and wound infections a common clinical manifestation. Nevertheless, the widespread usage of topical antimicrobials has resulted in the descent, though not the elimination; of bacterial wound infections [11]. Early surgical debridement and skin grafting, widespread usage of

systemic antimicrobials and enhanced infection control practices have replaced β -hemolytic streptococci with *S. aureus* and Gram-negative pathogens such as *P. aeruginosa*, *K. pneumoniae* and *A. baumannii* [12-14].

The evolution of antibiotic resistance, especially aminoglycoside resistance, is plasmid mediated and renders the organism much more difficult to handle. Transmission of aminoglycoside resistance from one species of *Pseudomonas* to another and more importantly to other gram-negative organisms, including *Enterobacter* sp., *Acinetobacter* sp., *Escherichia coli* and others has been demonstrated and recognised in the burn population [15, 16]. Despite frequent reports of multiply resistant *P. aeruginosa* infections in burn units and the predilection of this organism for the equipment used to care for the wounds of burn patients, most burn centres continue to employ this form of wound care routinely and examine equipment and its water supply for bacterial contamination infrequently [1, 17]. Antimicrobial resistance is a great problem in infectious disease. In burn units, because of the wide usage of antibiotics and particularly the empirical administration of broad-spectrum antimicrobials, this trouble is worse than in other hospital departments [18].

Materials and methods

Patients and methods

All kids with acute burns admitted to the Department of Burn and Plastic, Jining Number 1 People's Hospital, Jining, between January 2014 and August 2014 were recruited.

Type of study: prospective and observational work. Patients were followed prospectively during hospitalization and data collection was made through discharge or end.

Definitions

Independent variables: (1) Gender: male and female. (2) Age in months. (3) Type of burn: superficial (A), intermediate (AB) and "full-thickness" or (B). (4) Mechanisms of burns: classified as: flame, scalds, inflammable liquids; explosion and others mechanisms. (5) Burn surface: Defined as percentage of body according Lund and Bowder chart [19]. (6) Garcés's

Index: It is an index of prediction of mortality and is computed according to the formula [20]: (i). 40-age of patients + the percentage of burn body surfaces for 1 (burn type A), for 2 (AB) or for 3 (B). (ii). 0-60 points: first degree (low danger). (iii). 61-90: second level (moderate hazard). (iv). 91-120: third degree (severe risk). (v). ≥ 121 : fourth degree (critical). (7) Invasive procedures: Use of mechanical ventilation, central venous line, arterial and urinary catheters. (8) Inhalation syndrome: suspected in facial burns, stridor, and/or vulnerability to heavy smoke and confirmed by endoscopic examination. (9) Type of infections was defined according to the American Burn Association 7 and based on clinical and/or microbiological parameters. (10) Positive blood culture. (11) Type of microorganisms isolated in sterile material. (12) Use of colistin: In patients with documented infections by multiple-resistant microorganisms only susceptible to colistin or, in some cases the use was empirical, pending culture results.

Statistical analysis

Data were summarized in frequencies and percentages for categorical variables and as means and ranges (for continuous variables). The Mann-Whitney Rank Sum test was applied to evaluate differences between groups for two continuous variables. Dichotomous variables were analysed using the Chi-square test (with Yates correction). To estimate the multivariate predictive value of independent covariates for mortality stepwise multiple logistic regression models were employed (software at <http://statpages.org/logistic.html>) including all important variables in univariate analysis. The predictive value for each covariant was expressed as the relative risk (RR) and 95% confidence interval. A *p*-value of ≤ 0.05 was considered significant for both positions. This work was sanctioned by the Ethics committee of the Hospital, Jining Number 1 People's Hospital, Jining, China.

Results

Clinical and microbiological characteristics

Median burn surface affected was 24.2% (range 1-90%). Garcés' index was 1 in 15 patients (15%), 3 in 39 (35%), 4 in 24 (22%) and 5 in 33 (30%). Type of burn was: An in 33 patients (36%), AB in 22 (15%) and B in 52

Pseudomonasin acute burn injuries

Table 1. Characteristics and exposure of patients with *P. aeruginosa* and their matched control

Characteristic	Cases (n=82)	Controls (n=82)	OR (95% CI)	P value
Emographics				
Age (yr) ^a (mean ± SD)	62 ± 17	65 ± 20	1.2 (0.9-1.02)	0.5
Male gender [no. (%)]	50 (60)	41 (50)	1.5 (0.8-2.9)	0.16
No. of comorbidity [mean (SD)]	1.2 (0.9)	1.3 (0.8)	0.8 (0.6-1.2)	0.5
Exposures prior to MDR <i>P. aeruginosa</i> isolation^b				
Transfer from institution [no. (%)]	11 (13)	1 (1)	11.1 (1.4-85)	0.02
Home antibiotic Rx [no. (%)]	14 (15)	6 (6)	2.1 (0.9-7.2)	0.03
ICU stay [no. (%)]	31 (39)	16 (19)	14 (2.3-127)	0.005
Surgery [no. (%)]	47 (52)	26 (45)	1.1 (0.7-3.2)	0.2
Immunosuppressive therapy [no. (%)] ^c	7 (8)	11 (13)	0.5 (0.1-1.6)	0.2
Foley catheter [no. (%)]	64 (76)	42 (50)	5.5 (2.2-18.6)	<0.001
Central venous line [no. (%)]	34 (47)	28 (31)	3.8 (1.4-10.1)	0.008
Dialysis [no. (%)]	4 (4)	5 (6)	0.7 (0.1-3.3)	0.7
Mechanical ventilation [no. (%)]	44 (51)	15 (20)	25 (3.6-198.6)	0.001
Severity of illness^d				
Vasopressor treatment [no. (%)]	23 (28)	11 (13)	4.0 (1.3-11.9)	0.01
Bedridden [no. (%)]	56 (68)	38 (46)	3.4 (1.4-7.9)	0.004
Antibiotic treatment				
No. of patients treated ^e (%)	64 (76)	53 (64)	3.2 (1.3-7.9)	0.014
No. of antibiotics (mean ± SD)	2.3 ± 1.6	1.7 ± 1.5	1.4 (1.1-1.9)	0.006
Agent [no. (%)]^d				
Pencillin	63 (76)	50 (60)	3.1 (1.3-7.9)	0.01
Cephalosporin (narrow spectrum)	3 (3)	2 (2)	1.5 (0.2-8.9)	0.6
Cephalosporin (fourth generation) ^f	3 (3)	3 (3)	1.8 (0.2-4.9)	1.0
Quinolones	11 (13)	6 (7)	1.8 (0.6-4.9)	0.2
Antipseudomonal drugs	48 (58)	31 (37)	5.2 (1.8-15.2)	0.002
Carbapenems	6 (7)	6 (7)	1.0 (0.2-3.9)	1.0
Aminoglycosides	30 (36)	18 (21)	2.7 (1.1-6.4)	0.02
Vancomycin	6 (7)	7 (8)	0.8 (0.2-2.7)	0.7
Macrolides	6 (7)	4 (4)	1.5 (0.4-5.3)	0.5
Chloramphenicol	5 (6)	3 (3)	1.6 (0.3-6.9)	0.4
Metronidazole	6 (7)	9 (10)	0.5 (0.1-1.9)	0.3
Sulfamides	2 (2)	0		1.0

^aContinuous variable. ^bExposures that occurred between hospital admission and inclusion in the study. ^cImmunosuppressive therapy referred to chemotherapy within 3 weeks of study entry or treatment with at least 20 mg of prednisone daily for at least 2 weeks before study entry (16). ^dSeverity of illness 48 hours before inclusion in the study. ^eMatched univariate analysis. CI, confidence interval; Rx, prescription. ^fFourth generation refers to cefepime.

(47%). Localization of burn was variable: Head and face in 76 patients (29%), trunk in 58 (49%), upper limb in 37 (52%), lower limbs in 44 (41%), hands in 16 (15%), perineal area in 26 (5.5%) and whole body except perineal area in 10 (9%) patients. Inhalation syndrome was present in 56 (44%) patients. Ninety patients (82%) had indwelling venous catheters, 83 (75.5%) patient's arterial catheter and 86 (78%) patients urinary catheters. Seventy-five

patients (69%) required mechanical ventilation. We documented 134 infections in 84 patients being sepsis related to burn injury the most vulgar. Stock cultures were positive in 49 infections. Multiresistant *Pseudomonas aeruginosa* and *Acinetobacter* spp. were isolated most frequently. Colistin was used in 62% patients: Empirical use in 41% and with multiresistant documented infection in 40 (59%) patients. Antifungal was used in 40 (36%) patients.

Pseudomonasin acute burn injuries

Table 2. Matched univariate analysis for risk factors for mortality and increased length of hospital stay

Variable	Mortality		Length of hospitalization	
	OR (95% CI)	P value	HR (95% CI)	P value
Demographics				
Age	1.1 (0.9-1.09)	0.07	1	0.4
Underlying conditions				
No. of comorbidities	1.8 (0.8-4.2)	0.1	1	0.3
Diabetes	NA ^a		1	0.3
Cardiovascular	NA ^a		1	0.5
Organ transplant	NA ^a		1.25	0.5
Exposures before MDR <i>P. aeruginosa</i> isolation				
Home antibiotic prescription	1 (0.2-4.9)	1	0.6	0.005
Transfer from institution	NA		0.8	0.4
ICU stay	1 (0.2-4.9)	1	2.1	<0.001
Surgery	0.8 (0.2-2.9)	0.7	1.6	0.01
Immunosuppressive therapy	1.5 (0.2-8.9")	0.4	1.4	0.1
Invasive devices				
Devices score	2.5 (0.4-12.8)	0.2	2.6	<0.001
Foley catheter	5 (0.5-42.7)	0.1	3.0	<0.001
Mechanical ventilation	3.5 (0.7-16.8)	0.1	3.0	<0.001
Central line	1.2 (0.3-4.6)	0.7	2.5	<0.001
Dialysis	NA ^a		2.1	0.1
Severity of illness				
Vasopressor prescription	1.6 (0.3-6.9)	0.4	1.8	0.003
ADL, bedridden	NA ^a		2.5	<0.001
McCabe score	5.2 (1.1-20.1)	0.01	1.3	0.07
No. of antibiotics	1.5 (0.8-2.8)	0.1	1.5	<0.001
MDR <i>P. aeruginosa</i> isolation	2.4 (0.8-4.0)	0.05	2 (3.0-1.4)	<0.001

^aNA, not available; ADL, activities of daily living.

Table 3. Impact of multidrug resistant *P. aeruginosa* on study patient outcomes compared to their matcher controls

Outcome	% of cases (n=82)	% of controls (n=82)	Univariate analysis		Multivariate analysis	
			RR ^f (95% CI)	P value	OR (95% CI)	P value
Mortality ^a	24	14	2.5 (0.8-6.0)	0.05	4.7	0.03
Length of stay ^b	22 ^c	11 ^c	2.6 (1.4-3.0)	<0.001	2.0	0.002
Surgery ^d	32	15	2.4 (1.0-6.4)	0.05	2.5 (1.0-6.4)	0.05
Procedures ^d	38	11	5.4 (2.0-14.0)	0.001	5.4 (2.0-14.0)	0.001
Chronic care ^e	53	24	5.0 (1.3-26.8)	0.01	6.0 (1.34-26.8)	0.02
Full activity at discharge ^e	34	59	6.7 (2.0-22.4)	0.002	4.7 (1.3-16.2)	0.015

^aMultivariate model adjusted for McCabe score. ^bMultivariate survival analysis model adjusted for male gender, being bedridden, and invasive device score. RR and OR denote the hazard ratio. ^cMedian length of stay after inclusion in the study. ^dNo other variable was retained in the multivariate model. ^eMultivariate analysis for surviving patients admitted from home. ^fRR, relative risk.

Scarectomy was required in 90 (82%) patients and graft in 82 (74.5%) (Tables 1 and 2). Independent risk factors for mortality were: Age ≤4 years, Garcés 4, full thickness burn, ≥40%

burn surface, inhalation syndrome, venous catheter, arterial catheters, urinary catheter, mechanical ventilation, positive blood cultures, colistin use in documenting multiresistant

Pseudomonasin acute burn injuries

Table 4. Microbiologic features and foci (n=128 foci in 86 patients)

Focus	N (%)	Micro organisms	N
Sepsis burn related	48 (37)	Gram negative bacterial species	
		<i>Pseudomonas aeruginosa</i> resistant strain	24
		<i>Acinetobacter</i> sp resistant strain	17
		<i>Stenotrophomonas maltophilia</i>	4
		<i>Enterobacter agglomerans</i>	5
		<i>Escherichia coli</i>	7
		<i>Serratia</i>	2
		<i>Klebsiella pneumonia</i>	1
		<i>Burkholderia</i>	7
		Non-fermenting (non typeable)	2
		Gram positive bacterial species	
		Meticilin resistant <i>staphylococcus.aureus</i>	8
		Meticilin sensitive <i>S.aureus</i>	5
		<i>Enterococcus faecium</i>	
		<i>Bacillus</i> spp.	6
Wound Infections	21 (25)	Gram negative bacterial species	
		MR- <i>Pseudomona aeruginosa</i>	9
		MR- <i>Acinetobacter</i> spp.	5
		<i>Klebsiella</i> spp.	2
		<i>Enterobacter agglomerans</i>	1
		Gram positive bacterial species	
		Meticilin R <i>Staphylococcus aureus</i>	4
		Meticilin <i>S.aureus</i>	2
		<i>Bacillus</i> sp.	3
		<i>Corynebacterium</i> sp.	2
Catheter related infections	12 (7.5)	<i>Enterococcus</i> sp.	1
		<i>S.pyogens</i>	1
		Gram negative bacterial species	
		Methicillin resistant <i>pseudomonas aeruginosa</i>	3
		Methicillin resistant <i>actinetobacter</i> sp.	
		<i>Klebsiella pneumonia</i>	1
		<i>Serratia marcescens</i>	1
		<i>Alcaligenes xylosoxidans</i>	1
		Gram positive bacterial species	
		Meticilin sensitive <i>S.aureus</i>	1
Urinary tract infections	13 (13)	<i>Enterococcus faecium</i>	1
		<i>Bacillus</i> sp.	1
		Gram negative	
		<i>Pseudomonas aeruginosa</i>	7
		<i>Enterobacter agglomerans</i>	2
		<i>Klebsiella pneumoniae</i>	1
		<i>Actinobacter</i> spp.	
Ventilator associated pneumonia	1 (5)	Fungi species	
		<i>Candida albicans</i>	5
		<i>Candida tropicalis</i>	2
		Gram negative bacterial species	
		<i>Pseudomonas aeruginosa</i> MR	6

Pseudomonasin acute burn injuries

		<i>Actinobacter</i> sp. MR	2
		<i>Klebsiella pneumonia</i>	1
		<i>Alcaligenes xylosoxidans</i>	1
		Gram positives	
		Meticillin R-S. <i>aureus</i>	1
		Fungi species	
		<i>Candida albicans</i>	2
Pneumonia	4 (3)	<i>Streptococcus pneumonia</i>	1
		Negative cultures	3
Corneal abscess	3 (2)	MR- <i>Pseudomonas aeruginosa</i>	3
Chondritis	2 (1.5)	MR- <i>Pseudomonas aeruginosa</i>	2
Toxic shock	1 (1)	<i>Streptococcus pyogenes</i>	1
Endocarditis	1 (1)	MR- <i>Actinobacter</i> spp.	1
Zoster	1 (1)	<i>Varicella zoster</i> virus	1

infections, antifungal use and graft requirement. By multivariate analysis: Age ≤ 4 years, Garcés 4, colistin use in documenting multiresistant infections, and mechanical ventilation were independent variables related to mortality and graft requirement was a protective factor for mortality in **Table 3**. A comparison between survivors and non-survivors by univariate and multivariate analysis is demonstrated in the microorganism variations are shown in the **Table 4**.

Discussion

Research to advance burn care is an ongoing process which is contemplated in the published literature from year to year. Many research labs throughout the Earth, both clinical and basic, are active in investigating the science of burns and testing treatments; all of this is done in an attempt to ameliorate the lot of patients with this trauma. The risk for acquiring MDR organisms may be related to temporospatial factors (extrinsic, ecological characteristics) such as the number of carriers in the same ward, the nurse to patient ratio, and compliance with infection control standards as well as to individual risk factors, such as patient characteristics and in-hospital events, including treatment with antibiotics [21]. It limits therapeutic options and leads to increased death rate and morbidity. Resistance to antimicrobial agents is an increasing public health threat [22]. MDR *P. aeruginosa* was isolated from various sites and often from more than one site in the same patient. A sum of 74% of the patients was identified as being infected at the time of the first

closing off and virtually all the others got an active infection with MDR *P. aeruginosa* later during their hospitalization. The individual risk factors identified in this work included a halt at an ICU, being bedridden and the purpose of invasive devices. These factors portray a severely ill patient who requires intensive contact with caregivers and for whom the disease, treatment and invasive devices compromise protective barriers. ICU stay had been established in previous studies to be an important risk factor for acquisition of resistant organisms and the SCENIC study reported that half of the patients hospitalized in ICUs acquired a nosocomial infection [23-25]. Pediatric burn patients are susceptible to a broad spectrum of infections which represent the most common and severe complication in this population [26, 27]. In-depth knowledge of the bacteria frequently causing fatal infectious complications as well as of their antibiotic susceptibilities is a requirement for all healthcare professionals involved in treating thermally injured patients.

In accession to the preconditions, a development of antibiotic resistance has been indicated to rise rapidly in the bacteria colonising individual patients. Preventing this potentially fatal process is of prime importance and is based on adequate topical burn wound care, aggressive surgical wound closure and proper intensive care. However, judicious use of antibiotics is very important.

The present study shows and further confirms not only that there are breaks in the microbial spectrum and their antibiogram, but besides

that there are considerable local differences. Moved over the increasing resistance rates in *P. aeruginosa*, multidrug resistance can be expected to become more predominant in many hospitals. We carried this study to better read the individual risk factors for having MDR *P. aeruginosa* and to probe the issues of its happening.

In conclusion, a high endemic incidence rate of MDR *P. aeruginosa* was observed at our medical centre. We planned this study in order to examine its occurrence, the individual risk factors in affected patients, and the clinical impact of infection with these beings. In closing, this analytic study highlights the complex epidemiology of MDR *P. aeruginosa* in hospitals. These infections are likely to affect critically ill patients who call for intensive attention and treatment with multiple antibiotic agents. Infection with *P. aeruginosa* is associated with adverse clinical outcome and strict isolation of patients infected with MDR microorganisms and judicious use of antibiotics should be emphasized in order to prevent the spread of MDR *P. aeruginosa*.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hong-Tu Zhang, Department of Burn and Plastic, Jining Number 1 People's Hospital, No. 6 Jiankang Road, Shizhong District, Jining 272100, Shandong, China. Tel: 0086-537-2253431; Fax: 0086-537-2253431; E-mail: zhanght9953@gmail.com

References

- [1] Shankowsky HA, Callioux LS, Tredget EE. North American survey of hydrotherapy in modern burn care. *J Burn Care Res* 1994; 15: 143-146.
- [2] Vasil ML, Ochsner UA. The response of *Pseudomonas aeruginosa* to iron: genetics, biochemistry and virulence. *Mol Microbiol* 1999; 34: 399-413.
- [3] Reed MD, Stern RC, O'Riordan MA, Blumer JL. The pharmacokinetics of colistin in patients with cystic fibrosis. *J Clin Pharmacol* 2001; 41: 645-654.
- [4] Conway S, Pond M, Watson A, Etherington C, Robey H, Goldman M. Intravenous colistin sulphomethate in acute respiratory exacerbations in adult patients with cystic fibrosis. *Thorax* 1997; 52: 987-993.
- [5] D'Avignon LC, Hogan BK, Murray CK, Loo FL, Hospenthal DR, Cancio LC, Kim SH, Renz EM, Barillo D, Holcomb JB. Contribution of bacterial and viral infections to attributable mortality in patients with severe burns: an autopsy series. *Burns* 2010; 36: 773-779.
- [6] Macedo JL Sd, Santos JB. Predictive factors of mortality in burn patients. *Rev Inst Med Trop Sao Paulo* 2007; 49: 365-370.
- [7] Alp E, Coruh A, Gunay GK, Yontar Y, Doganay M. Risk factors for nosocomial infection and mortality in burn patients: 10 years of experience at a university hospital. *J Burn Care Res* 2012; 33: 379-385.
- [8] Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control* 1988; 16: 128-140.
- [9] Carmeli Y, Troillet N, Eliopoulos GM, Samore MH. Emergence of antibiotic-resistant *Pseudomonas aeruginosa*: comparison of risks associated with different antipseudomonal agents. *Antimicrob Agent Chemother* 1999; 43: 1379-1382.
- [10] Carmeli Y, Troillet N, Karchmer AW, Samore MH. Health and economic outcomes of antibiotic resistance in *Pseudomonas aeruginosa*. *Arch Intern Med* 1999; 159: 1127-1132.
- [11] Weinstein RA, Mayhall CG. The epidemiology of burn wound infections: then and now. *Clin Infect Dis* 2003; 37: 543-550.
- [12] Agnihotri N, Gupta V, Joshi R. Aerobic bacterial isolates from burn wound infections and their antibiograms-a five-year study. *Burns* 2004; 30: 241-243.
- [13] Albrecht MA, Griffith ME, Murray CK, Chung KK, Horvath EE, Ward JA, Hospenthal DR, Holcomb JB, Wolf SE. Impact of *Acinetobacter* Infection on the Mortality of Burn Patients. *J Am Coll Surg* 2006; 203: 546-550.
- [14] Altoparlak U, Erol S, Akcay MN, Celebi F, Kadanali A. The time-related changes of antimicrobial resistance patterns and predominant bacterial profiles of burn wounds and body flora of burned patients. *Burns* 2004; 30: 660-664.
- [15] Nicas TI, Iglewski BH. Isolation and characterization of transposon-induced mutants of *Pseudomonas aeruginosa* deficient in production of exoenzyme S. *Infect Immun* 1984; 45: 470-474.
- [16] Vasishta R, Saxena M, Chhibber S. Contribution of silver ion resistance to the pathogenicity of *Pseudomonas aeruginosa* with special reference to burn wound sepsis. *Folia Microbiol (Praha)* 1991; 36: 498-501.
- [17] Insler MS, Gore H. *Pseudomonas* keratitis and folliculitis from whirlpool exposure. *Am J Ophthalmol* 1986; 101: 41-43.

- [18] Vrankova J, Adamkova V. Bacteriological monitoring after burn injury. *Acta Chir Plast* 2003; 46: 48-50.
- [19] Demirdjian G. Adjusting a prognostic score for burned children with logistic regression. *J Burn Care Res* 1997; 18: 313-316.
- [20] Garcés M, Tapia L, Hoecher F. Clasificación y pronóstico de los quemados. *Asistencia Pública* 1971; 1: 5-9.
- [21] Samore MH, Carmeli Y, Eliopoulos GM. Antecedent treatment with different antibiotic agents as a risk factor for vancomycin-resistant *Enterococcus*. *Emerg Infect Dis* 2002; 8: 802-7.
- [22] Eliopoulos GM, Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis* 2003; 36: 1433-1437.
- [23] Haley RW, Shachtman RH. The emergence of infection surveillance and control programs in US hospitals: an assessment, 1976. *Am J Epidemiol* 1980; 111: 574-591.
- [24] Haley RW, Meade Morgan W, Culver DH, White JW, Grace Emori T, Mosser J, Hughes JM. Update from the SENIC Project: hospital infection control: recent progress and opportunities under prospective payment. *Am J Infect Control* 1985; 13: 97-108.
- [25] Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Infect Dis* 2004; 39: 309-317.
- [26] Geyik MF, Aldemir M, Hosoglu S, Tacyildiz HI. Epidemiology of burn unit infections in children. *Am J Infect Control* 2003; 31: 342-346.
- [27] Santucci S, Gobara S, Santos C, Fontana C, Levin A. Infections in a burn intensive care unit: experience of seven years. *J Hosp Infect* 2003; 53: 6-13.