BURN WOUND INFECTIONS AND ANTIMICROBIAL RESISTANCE IN TEHRAN, IRAN: AN INCREASING PROBLEM

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SUMMARY. Pseudomonas aeruginosa and Staphylococcus aureus remain the most important pathogens and are frequently the cause of burn wound infections in our centre. This is a particular problem in high-risk and long-stay patients and can lead to epidemics of infection in hospital settings. This study analysed P. aeruginosa and S. aureus infections in Tohid Burn Centre, Iran, in order to estimate their frequency and antibiotic susceptibilities. Out of 6704 strains examined, 4904 and 688 were found respectively to be P. aeruginosa and S. aureus in the period March 1995-September 1999, in burn patients hospitalized in this burn centre. Antimicrobial susceptibility was determined by the disk diffusion method outlined by the National Committee for Clinical Laboratory Standards. The overall frequencies of P. aeruginosa and S. aureus were respectively 73.1% and 10.3%; the remaining 16.6% consisted of other organisms. The frequency of P. aeruginosa resistance to ciprofloxacin, amikacin, and gentamicin was over 85%. The rate of S. aureus resistance to cloxacillin and cephalaxin was 90%. P. aeruginosa and S. aureus were thus the commonest organisms in this centre. High frequency rates of resistance to these micro-organisms were found in this study. It is necessary to limit the use of antimicrobial agents in our epidemiological setting. In 2000 the Burn Centre was closed.

Introduction

Burn injuries by fire and hot liquids and contact with hot surfaces have been recognized as a significant and major public health problem in economically developing countries like Iran. Unfortunately, most of the burn victims in Iran are children and women.1-7

Large open wound areas containing necrotic tissue make burn patients more susceptible to infection. In addition, a general state of immunosuppression is caused by the impaired functioning of neutrophils and the cellular and humoral immune system.8-11 In these conditions, micro-organisms can easily multiply and colonize wounds to high densities. Immunologically compromised patients are also obliged to stay in high-risk intensive care units for prolonged periods of time, during which they may be submitted to endotracheal intubation and/or catheterization of the blood vessels and bladder; also, in these units, both the air and environmental surfaces are heavily contaminated. That is why burn patients are high-risk groups for infection.12,13

Pseudomonas aeruginosa - particularly in economically developing countries - is one of the most important and most common causes of serious infection in burn patients.14-21 When infection caused by P. aeruginosa occurs in burn patients, treatment becomes very difficult and the mortality rate among infected patients is likely to reach up to 40-50%.6,7,14-16 Treatment of these infections is frequently complicated by antibiotic resistance, a problem that has been increasing over time.14-18 The emergence of multi-drug resistant strains in burns units, particularly in economically underdeveloped and developing countries like Iran, is an increasing infection control problem.14-16

The gains of established infection control measures are now being felt in the economically developed countries with purpose-built burns units.12,13 However, in economically developing countries, the establishment of such units is hindered by poverty, ignorance, poor management, and lack of personnel.17,23

This study of the bacteriological profile and antibiotic sensitivity patterns of isolates from a main referral burn centre in Tehran was carried out in order to highlight some of the problems faced by clinicians and to document burn wound infection patterns in this environment.

Materials and methods

This study was carried out during the period March 1995-September 1999 in Tohid Burn Centre, which is affiliated to the Iran University of Medical Sciences in Tehran, Iran. Tohid Burn Centre is one of two main referral burn centres in Tehran (the other is Motahari Burn Centre). In the present study, a total of 7132 samples of swabs and blood were processed from about 3864 admitted patients. Tohid Burn Center is located in the western part of Tehran and serves a population of 5.5 million peo-
people, most of them from the low and middle socio-economic classes. The inclusion criteria (admission policy) in our centre are:

1. children below 2 years
2. children with total body surface area (TBSA) ≥ 10%
3. adults with TBSA ≥ 15%
4. localized deep burns of 2% TBSA or greater
5. facial burns
6. burns of hands, feet, or perineum
7. suspected inhalation injury
8. chemical or electrical burns
9. associated fractures or chronic illness
10. suspected criminal or suicidal burns

The culture swabs from the burn wounds were taken on admission in all patients. Some patients were swabbed on day 3 and 7, depending on the clinical judgement of infection. Infection and sepsicaemia were suspected when a patient showed signs of disorientation, hyperpyrexia or hypothermia, circulatory embarrassment, petechial haemorrhages, black and dark discoloration in a previously clean appearing burn wound, early and rapid eschar separation, bleeding into the subcutaneous tissues, increasing oedema in surrounding areas, or leucocytosis in WBC counts.

For the isolation of \( P. \) \( aeruginosa \), sheep blood agar and eosin methylene blue were used. Subsequently, growth at 42 °C in brain heart infusion, the oxidative test, and the oxidative-fermentation test for carbohydrate utilization were used for identification of \( P. \) \( aeruginosa \). Also, antimicrobial susceptibility was determined by the disk diffusion method of Bauer-Kirby recommended by the American Society of Microbiology.

All the burn patients received first aid and dressing with silver sulphadiazine 1% in the reception room of the centre. Those who needed admission had an intravenous line established and secured respiration. Early excision and grafting is the rule in the centre. Cephalothin and amikacin were administered as prophylactic antibiotics from the first day of admission in patients with ≥ 20% TBSA burns (second and third degree). The wound was inspected daily during dressing changes.

Data were compared using analysis of variance and the \( \chi^2 \) test as appropriate. Two-tailed \( p \) values < 0.05 were considered significant. All statistical analyses were performed using Epi Info version 6.04 (CDC, USA, and WHO Geneva, Switzerland).

Results

During the 4.5-yr period March 1995-September 1999, 3864 patients were admitted to our burn centre. A total number of 7132 samples were processed. From these, 6704 bacterial strains were isolated. Of the 6704 isolates, \( P. \) \( aeruginosa \) (4904 strains) accounted for 73.2% (95% CI: 72.1-74.2%) of total isolates (Fig. 1). This was followed by \( S. \) \( aureus \) (688 strains; 10.3%) (95% CI: 9.5-11%) and other organisms (1112 strains, 16.5%), such as \( Acinetobacter \) spp. and \( Enterobacter \) spp.

The frequency rate of \( P. \) \( aeruginosa \) is shown in the different years of study in Fig. 2. The highest and lowest frequency rates of \( P. \) \( aeruginosa \) were found in 1997 (15.3%) and 1998 (5.7%). There were statistical significant differences between the frequency rates of \( P. \) \( aeruginosa \) during the period under review (\( p < 0.000001 \)). Fig. 3 shows the \( S. \) \( aureus \) frequency rate in the different years of study. The highest and lowest frequency rates of \( S. \) \( aureus \) were found in 1997 (15.3%) and 1998 (5.7%). There were statistical significant differences between the frequency rates of \( S. \) \( aureus \) during the period under review (\( p < 0.000001 \)).
were found in 1998 (77.7%) and 1997 (68.1%). There were statistically significant differences between the frequency rates of *S. aureus* during the period of study (*p* = 0.000001). There were also significant statistical differences between the frequency rates of *P. aeruginosa* and *S. aureus* over the period of study (*p* < 0.000001).

The resistance of the organisms to different antibiotics varied depending on the isolate. The frequency of *P. aeruginosa* resistant to carbenicillin, co-trimoxazole, ceftizoxime, and tetracycline was over 95% during the period of study. Eighty-five per cent of *P. aeruginosa* were resistant to ciprofloxacin. Also, *P. aeruginosa* was resistant to amikacin in 90% of the isolates tested and to gentamicin in 98% (Fig. 4). All *S. aureus* isolates were sensitive to vancomycin. *S. aureus* was resistant to cloxacillin and cephalexin in 57% and of the isolates and to co-trimoxazole in 50% (Fig. 5).

**Fig. 4** - Frequency rate of *Pseudomonas aeruginosa* resistant to antimicrobial agents.

**Fig. 5** - Frequency rate of antimicrobials resistant to *Staphylococcus aureus*.

Infection is one of the most serious complications in burn patients, and *Pseudomonas*, especially *P. aeruginosa*, is the most important, resistant, and dangerous organism in burn patient infections. *P. aeruginosa* thrives on the moist burn wound surface and is highly pathogenic in thermally injured immunosuppressed patients. These bacteria usually gain access to burn patients through cross-contamination of burn wounds. *Pseudomonas* infection is a common complication in burn patients and contributes to their morbidity and mortality. Despite advances in medical and surgical care, the prognosis remains poor, with a mortality rate of about 80% in such patients.

In this study, *P. aeruginosa* was found to be the commonest pathogen causing wound infection and bacteraemia in Tohid Burn Centre, which is comparable to earlier studies conducted in the same burn centre. Over the past 20 years, *P. aeruginosa* has reportedly been found to be the most prevalent bacteria in burn centres in Tehran. In a recent study undertaken in Motahari Burn Centre (the other referral burn centre in Tehran), *P. aeruginosa* was reported to be the most prevalent micro-organism. This suggests that *P. aeruginosa* is the “classic pathogen” in burn wound infections in the referral burn centres in the capital city of Tehran. A similar observation was reported in the referral burn centre in the province of Fars, in southwest Iran.

In many economically developing countries such as Zimbabwe, South Korea, Jordan, Libya, Nigeria, India, and Turkey, *P. aeruginosa* was reported to be the most commonest bacteria among burn patients. Although *P. aeruginosa* is not a classic pathogen of burn wound infections in the economically developed countries, a few burn centres in Canada and the USA, and Italy have reported *P. aeruginosa* as an important micro-organism in burn units.

The second most common isolate in this study was *S. aureus*, as in other studies from Iran and other economically developing countries. This contrasts however with some other studies, especially from economically developed countries, which report *S. aureus* as the most predominant organism in burn infection.

The time-related changes in the predominant flora of the burn wound from gram-positive to gram-negative recapitulate the history of burn wound infection. The predominance of gram-positive bacteria in the early phase switches to gram-negative species 4-10 days after injury. In this study, an inverse relationship between the frequencies of *P. aeruginosa* and *S. aureus* was found during the period of study (*p* < 0.000001). Also, previous studies in Tohid Burn Centre showed that the incidence of *S. aureus* decreased while that of *P. aeruginosa* increased during the first week of admission, compared to the day of admission. Similarly, Estahbanati et al. reported that in Motahari Burn Centre most burn wounds became infected with *P. aeruginosa* during the first week post-burn. We therefore strongly recommend that *P. aeruginosa* be seriously considered as the main nosocomial source of infection in Tehran referral burn centres. In addition, a study from Syria showed that in the first week of hospital stay the main organisms causing infection were *S. aureus*, *E. coli*, and other *Enterobacters*; in the second week *Pseudomonas* and *Candida* were the dominant organisms.
Several reports have documented environmental sources of burn wound infections from *P. aeruginosa*, and this organism thus continues to be a major cause of burn injury colonization and serious wound infections. Moisture is a critical factor in hospital reservoirs of *P. aeruginosa*, as for example in respiratory equipment, medicines, disinfectants, sinks, mops, food, and vegetables. We therefore believe that the following factors could be considered as possible reasons for the high percentage of *P. aeruginosa* infection in our centre:

- the centre was not built as a burn centre. However, two decades ago, officials declared that this substandard building should be used as a referral burn centre, because of the high number of burn patients and the limited burn care facilities;
- as several reports have shown that burn injury is a common and increasing problem in Iran, this referral burn centre, with its approximately 80 beds, cannot respond to the high demand. All the wards are usually overcrowded, and infection control measures and isolation policies are inadequate most of the time;
- as the number of patients admitted is higher than the centre’s capacity, the isolation of infected patients cannot be guaranteed - this is the key to the transmission of *P. aeruginosa* (the centre’s classic pathogen) from person to person or from environment to person (a patient or a health care worker).

The multi-drug resistance of *P. aeruginosa* is another problem, along with *Pseudomonas* infections. The pattern of antibiotic sensitivity is a source of serious concern as many of the isolates are resistant to antibiotics available in Iran, which in our earlier study was only 45.2% resistant to ciprofloxacin, 48.9% to amikacin, and 88.5% to gentamicin, showed 85% resistance to ciprofloxacin, 90% to amikacin, and 98% to gentamicin in the present report. In a microbiological study of burn wound infection in the other referral burn centre in Tehran, Motahari Burn Centre, *P. aeruginosa* resistance to ciprofloxacin, amikacin, and gentamicin was respectively 87.7%, 53.3%, and 90.7%, which shows high antibiotic resistance. In this study, the rate of *P. aeruginosa* resistant to carbenicillin, co-trimoxazole, cefizoxime, and tetracycline was over 95%. Estahbanati et al. reported that more than 90% of *P. aeruginosa* were resistant to cefizoxime, carbenicillin, and cefazidime in Motahari Burn Centre. The resistance rate of *P. aeruginosa* to the above-mentioned antibiotics in burn centres in Iran has increased dramatically in recent years and seems to be one of the highest in the literature. This problem could have the following explanations:

- consider absolute isolation seriously in contaminated patients, especially those with over 40% TBSA burns;
- improve barrier nursing, personnel hygiene, including hand washing before and after attending to a patient, and restriction of staff traffic;
- increase the number of intensive care unit beds so to be able to transfer patients at the most appropriate time;
- consider appropriate sterilization for all equipment;
- establish a new and effective antibiotic policy in order to revise and introduce prophylactic and therapeutic antibiotics, including the implementation of broad-spectrum antimicrobial agents in burn centres;
- avoid unnecessary use of antibiotics.

In this study, the present prophylactic antibiotics policy in Iranian Burn Centres has caused an increasing rate of *P. aeruginosa* resistance to commonly used antibiotics. In addition, the rate of development of resistance of *P. aeruginosa* to new antibiotics is much faster than the rate of invention and development of new antibiotics:

- there is overuse and abuse of available antibiotics such as gentamicin, amikacin, and ciprofloxacin, which in this centre are used as prophylactic or therapeutic measures;
- given that the Department of Health is in charge of importing and introducing new antibiotics (and new medications in general) into Iran, and given also that it has not yet considered or introduced broad-spectrum antimicrobial agents such as imipenem and aztreonam for use in burn centres, these antibiotics are not available. Consequently, in addition to the lack of preventive measures, broad-spectrum antibiotics that can be helpful in the treatment of burn patients with infections are not available either. It is also necessary to mention that as most burn victims come from the poorer economic classes they are unable to afford such expensive antibiotics on the black market.

### Conclusions

We would recommend that officials take into account the following guidelines in order to decrease the rate of infection and antibiotic resistance in burn centres in Iran:

- consider absolute isolation seriously in contaminated patients, especially those with over 40% TBSA burns;
- improve barrier nursing, personnel hygiene, including hand washing before and after attending to a patient, and restriction of staff traffic;
- increase the number of intensive care unit beds so to be able to transfer patients at the most appropriate time;
- consider appropriate sterilization for all equipment;
- establish a new and effective antibiotic policy in order to revise and introduce prophylactic and therapeutic antibiotics, including the implementation of broad-spectrum antimicrobial agents in burn centres;
- avoid unnecessary use of antibiotics.
RÉSUMÉ. Dans le centre des brûlés des Auteurs, *Pseudomonas aeruginosa* et *Staphylococcus aureus* continuent à être les pathogènes les plus importants et fréquemment ils causent des infections chez les patients brûlés hospitalisés, ce qui constitue un problème particulier pour les patients à haut risque destinés à une hospitalisation prolongée, pouvant mener à des épidémies d’infection dans un cadre hospitalier. Les Auteurs ont analysé les infections de *P. aeruginosa* et de *S. aureus* dans le Centre des Brûlés de Tohid, Iran, dans le but d’évaluer leur fréquence et leurs susceptibilités antibiotiques. Pendant la période mars 1995-septembre 1999, sur les 6704 souches examinées, 4904 et 688 se sont démontrées être respectivement *P. aeruginosa* et *S. aureus* chez les patients brûlés hospitalisés dans ce centre. La susceptibility antimicrobiens a été déterminée utilisant la méthode de la diffusion de disque décrite par le National Committee for Clinical Laboratory Standard. Les fréquences globales de *P. aeruginosa* et de *S. aureus* étaient respectivement 73,1% et 10,3%; les autres organismes (16,6%) étaient d’autres types. La fréquence de la résistance de *P. aeruginosa* à la ciprofloxacine, à l’amikacine et à la gentamicine était supérieure à 85%. Le taux de résistance de *S. aureus* à la cloxacilline et à la céphalexine était 90%. *P. aeruginosa* et *S. aureus* étaient donc les organismes les plus communs dans le centre. Les Auteurs ont trouvé dans cette étude des taux élevés de résistance à ces microorganismes, et il faudra limiter l’emploi des agents antimicrobiens dans ce cadre épidermiologique.

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