Available online at www.sciencedirect.com
ScienceDirect
Diagnostic Microbiology and Infectious Disease 60 (2008) 301–305
DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Antimicrobial resistance pattern of Gram-negative bacilli of nosocomial origin at 2 university hospitals in Iran

Azar Hadadi[a,*], Mehrnaz Rasoulinejad[b], Zohreh Maleki[c], Masoud Yonesian[d], Afsaneh Shirani[e], Zahra Kourorian[f]

[a]*Department of Infectious Diseases, Sina Hospital, Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*
[b]*Iranian Research Center for HIV/AIDS, Department of Infectious Diseases, Imam Hospital, Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*
[c]*Department of Pathology, Imam Hospital, Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*
[d]*Department of Epidemiology, Faculty of Health, Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*
[e]*Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*
[f]*The Iranian Research Center for HIV/AIDS, Imam Hospital, Medical Sciences/University of Tehran, Tehran 11367-46911, Iran*

Received 16 May 2007; accepted 10 October 2007

Abstract

The purpose of this study was to investigate the antimicrobial resistance pattern among common Gram-negative bacilli isolated from patients with nosocomial infection. A total of 200 samples of common Gram-negative bacilli (*Klebsiella*, *Pseudomonas*, *Acinetobacter*, and *Escherichia coli*) were collected from 2 university hospitals in Iran during a 1.5-year period from June 2004 to December 2005. All samples were examined for the antimicrobial activity of imipenem, cefepime, ciprofloxacin, ceftriaxone, and ceftazidime using E-test methods. The most frequent pathogens were *Klebsiella* spp. (38.5%) followed by *Pseudomonas aeruginosa* (28.5%), *Acinetobacter* spp. (20.5%), and *E. coli* (12.5%). The most active antibiotic was imipenem (84%). The susceptibility of the studied microorganisms was 25% for cefepime, 24% for ciprofloxacin, 20.5% for ceftazidime, and 11.8% for ceftriaxone. The susceptibility rates of *Klebsiella* to imipenem, cefepime, ciprofloxacin, ceftazidime, and ceftriaxone were 90.9%, 20.8%, 18.2%, 10.4%, and 5.2%, respectively. Likewise, these rates were 88%, 19%, 17%, 21%, and 21% for *E. coli*. Among *Acinetobacter* spp., the susceptibility rates were 77% for imipenem and 21% for ciprofloxacin. Among *Pseudomonas*, the rates were 75% for imipenem and 39% for ciprofloxacin. The antibiotics resistance among Gram-negative bacilli was widespread, so an antibiotic policy is urgently needed to delay the resistance development.

Keywords: Nosocomial infection; Antimicrobial resistance; Gram-negative bacteria; E-test

1. Introduction

The patient in the intensive care unit (ICU) has a 5- to 7-fold higher risk of nosocomial infection compared with the other patient. This is a consequence of impaired defense mechanism, applying invasive methods and monitoring devices, exposure to broad-spectrum antibiotics, and the colonization of resistant microorganisms. The frequent use of broad-spectrum antibiotics results in colonization with resistant Gram-negative bacteria and consequently in serious infections (Gunseren et al., 1999; Kucukates, 2005).

The prevalence of antimicrobial resistance varies in different studies. In a study on ICUs in Turkey, imipenem, which was the most active agent, had an overall susceptibility rate of 68% (Leblebicioglu et al., 2002). In a Belgian study, the frequency of resistance for Gram-negative isolates were 31% for ceftriaxone, 17% for ceftazidime, 10% for cefepime, 13% for imipenem, and 21% for ciprofloxacin (Glupczynski et al., 2001).

Having an awareness of antimicrobial resistance patterns, particularly in ICUs, is crucial for choosing an appropriate antimicrobial treatment and consequently minimizing the hospitalization period, morbidity, and mortality along with the economic burden of nosocomial infections. In an attempt to avoid the inappropriate use of new expensive antibiotics, we aimed at determining the resistance pattern of Gram-negative bacteria by using the E-test method on patients hospitalized in

* Corresponding author. Tel.: +98-21-66716546; fax: +98-21-66716546.
E-mail address: hadadiaz@sina.tums.ac.ir (A. Hadadi).

0732-8893/$ – see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.diagmicrobio.2007.10.010

Table 1
Frequency of Gram-negative isolates according to the origins of nosocomial infections in the present study; data are count (percentage)

Infection	*P. aeruginosa*	*E. coli*	*Acinetobacter* spp.	*Klebsiella* spp.	Total
Primary septicemia	13 (19.7)	5 (7.6)	13 (19.7)	35 (53.0)	66
Pneumonia	19 (32.2)	7 (11.9)	14 (23.7)	19 (32.2)	59
UTI	11 (32.4)	9 (26.5)	4 (11.8)	10 (29.4)	34
Surgical site infection	10 (45.5)	3 (13.6)	5 (22.7)	4 (18.2)	22
Central catheter infection	1 (10.0)	1 (10.0)	3 (30.0)	5 (50.0)	10
Tracheitis	1 (25.0)	0 (0.0)	2 (50.0)	1 (25.0)	4
Meningitis	1 (10.0)	0 (0.0)	0 (0.0)	2 (66.7)	3
Bed sore	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)	2
Total	57 (28.5)	25 (12.5)	41 (20.5)	77 (38.5)	200 (100.0)

2 major referral university hospitals of Tehran, which have the highest admission rates of infectious diseases.

2. Patients and methods

This is a cross-sectional study carried out in 2 university hospitals in Tehran, Iran (Sina and Imam-Khomeini Hospitals), during June 2004 to December 2005. The Gram-negative isolates common in nosocomial infections, including *Pseudomonas*, *Acinetobacter*, and *Klebsiella* spp., and *Escherichia coli*, were collected from patients in the ICUs, and only 1 isolate per patient was included. Patients eligible to be included in the study were free of infectious diseases at the time of admission and were not in the incubation period of any infection. They were diagnosed to have nosocomial infections within 48 to 72 h following their admission according to the definitions described by the Centers for Disease Control (Gaynes and Horan, 1997), which is also confirmed by an infectious diseases specialist.

The specimen sources included blood, urine, cerebrospinal fluid, respiratory tract (collected during bronchoscopy or endotracheal suction), tip of central venous catheters, bedsores, and surgical incision sites. The Mueller–Hinton agar was used as the growth medium, and the antibiogram determination was performed on positive culture isolates growing a Gram-negative organism. Susceptibility testing was performed by E-test (AB BIODISK, Solna, Sweden) in accordance with the manufacturer's instructions. The E-test was done for imipenem, cefepime, ceftazidime, ciprofloxacin, and ceftriaxone in *Klebsiella* spp. and *E. coli*. In *Pseudomonas aeruginosa* and *Acinetobacter* spp., the susceptibility testing was performed for all of the 5 above-mentioned antibiotics except ceftriaxone.

Quality control was assured by concurrent testing with the American Type Culture Collection (ATCC) strains including *E. coli* ATCC 25921 and *P. aeruginosa* ATCC 27852. After the incubation in the ambient air of 35 °C for 24 h, MIC was interpreted as the point at which the inhibition ellipse intersected with the E-test strip edge. Isolates resistant to 3 or all antibiotics were considered multidrug resistant. The testing procedures were validated in accordance with the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS, 2003).

Statistical analyses was done using SPSS software (ver. 11.5; SPSS, Chicago, IL). For nominal variables, frequencies were calculated, and relative frequencies with the estimated 95% confidence intervals (CIs) are reported. For continuous variables, mean and SD are presented. For investigating determinants of resistance to each antibiotic, we performed binary logistic regression considering the presence of resistance as the dichotomous outcome, and germ and history of antibiotic receptions prior to sampling as independent variables; the estimated odds ratios (OR) by this model is reported.

3. Results

A total of 200 samples were obtained. One hundred five (52.5%) samples were obtained from patients admitted to Sina Hospital and 95 (47.5%) samples from patients admitted to Imam-Khomeini Hospital. Among the studied patients, 60.5% (121 cases) were male. The mean age of the patients was 47 ± 22.2 years. The most common specimen sources were blood (38.5%) followed by the respiratory tract (26%), surgical site infection (11%), and urine (17%); other infection sites include 7.5% of the total.

The most frequent nosocomial infection was primary septicemia (66 patients, 33%) followed by pneumonia (59 patients, 29.5%), surgical site infection (22 patients, 11%), urinary tract infection (UTI) (34 patients, 17%), and central line catheter tip infection (10, 5%). The frequency of microbial agents in nosocomial infections in the present study was stated as *Klebsiella* spp. 77 isolates (38.5%; 95% CI, 32–46); *P. aeruginosa* 57 (28.5%; 95% CI, 22–35); *Acinetobacter* spp., 41 (20.5%; 95% CI, 15–27), and *E. coli* 25 isolates (12.5%; 95% CI, 8–18). The frequency of microorganisms in terms of the infection site is shown in Table 1.

Concerning the history of receiving antibiotics, in 77.5% of the patients, at least 1 antibiotic was administrated prior to the sampling. These antibiotics were ceftriaxone (55%), ceftazidime (42.5%), ciprofloxacin (20%), imipenem (7.5%),