

Prevalent Nosocomial Gram Negative Aerobic Bacilli and their Antimicrobial Susceptibility Pattern in Intensive Care Unit

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Abstract

Objective: To determine the type of prevalent aerobic gram-negative bacilli and their sensitivity pattern among nosocomial isolates.

Design: Prospective collection of clinically significant nosocomial gram negative bacilli.

Setting: Tertiary care hospital in Karachi.

Method: One hundred isolates were identified by standard methods and minimum inhibitory concentration was checked by epsilometer test.

Results: The most frequent isolates were *Escherichia coli* (43%) followed by *Klebsiella pneumoniae* (18%) *Acinetobacter* spp. (7%) *Enterobacter* spp. (7%) and *Klebsiella* spp. other than *pneumoniae* (7%). Most of the isolates of dominant species (*E.coli* and *Klebsiella pneumoniae*) were multiresistant including third generation cephalosporins.

Conclusion: This study indicates that most effective antibiotics imipenem and amikacin inhibited most of the isolates. Imipenem alone or amikacin in combination with one broad spectrum B-lactam drug should be used in initial empiric therapy in any life threatening nosocomial infection. UPMA 49:169, 1999).

Introduction

Infection is one of the principal hazards to which patients in intensive care units ICU are exposed¹. Aerobic gram negative bacilli (AGNB) are a major cause of nosocomial infection (NI) among the patients admitted in ICU. Isolates from patients in ICU are more likely to be associated with antimicrobial resistance than those in other wards². The prevalent microorganisms and the pattern of antimicrobial susceptibility in ICU patients differ widely from one hospital to another in the same geographical region. Indiscriminate use of broad spectrum antibiotics in hospital and community contributes to the emergence of infection with multi resistant organisms seen frequently in ICU's³. This study was designed to know the prevalent AGNB and antimicrobial susceptibility pattern of these ICU isolates against commonly used antibiotics.

Material and Method

A prospective study was designed and carried out in the department of Microbiology at Dr. Ziauddin Hospital Karachi which is a tertiary referral unit. Isolates included in this study were from the patients admitted in intensive and neonatal care unit (ICU, NCU) and developed temperature > 38oF after 48-72 hours of admission. Bacterial isolates were obtained from blood, urine, tracheal aspirate/sputum, pus and deep wounds. Any aerobic gram-negative rod considered clinically, significant was processed and identified on the basis of morphological characters and biochemical reactions by using API 20E and API 20NE galleries (Biomérieux, France). Minimum inhibitory concentrations were checked by E test (AB Biodisk Sweden). The E test was performed according to manufacturer's instruction. After overnight growth on brain heart infusion agar, the organisms were suspended in saline to a turbidity equal to that of a 0.5 Mc Farland.

The suspension was used to inoculate unsupplemented Muller Hinton agar plates by swabbing them with a cotton swab. F strips were placed on sensitivity plates and those plates were incubated for 18 hours aerobically at 35-37°C. The MIC's were interpreted as the point of intersection of the inhibition ellipse with the E test strips edge. Control strains of E.coli (ATCC 25922, ATCC 3512) and Pseudomonas aeruginosa ATCC 27853 were used. Results were analysed in accordance with published guidelines of the National committee for clinical laboratory standard⁴. Antibiotics included in this study were Penicillin (piperacillin-tazobactam, co-amoxyclave), cephalosporins (cefuroxime, cefotaxime, ceftriaxone, ceftazidime) Aminoglycosides (gentamicin, amikacin) Fluoroquinolone (ciprofloxacin) Monobactam (azactam) and Carbapenem (meropenem).

Results

The isolates were obtained from blood (35), urine (39), tracheal aspirate/sputum (7), pus (8) and deep wounds (7). The most frequent isolates were E.coli & Klebsiella pneumoniae (Table). Drug utilization data showed that all of the patients were on at least one antibiotic at the time of sampling. Ceftazidime, cefotaxime and aztreonam were the most commonly used drugs followed by ciprofloxacin and meropenem. Aminoglycosides were used only in few cases. Table shows the minimum inhibitory concentration of E.coli, Klebsiella pneumoniae and other isolates to different antibiotics used in this study. Out of 100 isolates only a quarter of them were sensitive to amoxyclave and cefuroxime (Table).

Table . Percentage of Susceptibility (NCCLS break point).

Species	No. of Isolates	Antibiotics used in study mic mg/l										
		Imipenem 4mg/l	Amikacin 16mg/l	Gentamicin 4mg/l	Ciprofloxacin 1mg/l	Pip-tazo 16mg/l	Amx-clave 8mg/l	Cefuroxime 8mg/l	Cefoxitin 8mg/l	Cefotaxime 8mg/l	Ceftriaxone 8mg/l	Ceftazidime 8mg/l
Escherichia coli	43	43 (100)	35 (81)	23 (53)	18 (41)	23 (53)	7 (16)	14 (32)	24 (55)	27 (62)	27 (62)	25 (58)
Klebsiella pneumoniae	18	18 (100)	15 (83)	6 (33)	13 (72)	7 (36)	2 (11)	2 (11)	14 (78)	10 (55)	7 (38)	7 (38)
Klebsiella spp (other than spp)	7	7 (100)	6 (85)	6 (85)	6 (85)	4 (57)	1 (14)	1 (14)	6 (85)	5 (71)	5 (71)	2 (28)
Enterobacter spp	7	7 (100)	5 (71)	4 (57)	7 (100)	2 (28)	2 (28)	2 (28)	5 (71)	2 (28)	3 (42)	2 (28)
Acinetobacter spp.	7	7 (100)	7 (100)	3 (42)	4 (57)	2 (28)	3 (42)	0 (0)	4 (57)	2 (28)	3 (42)	2 (28)
Others	18	18 (100)	16 (88)	11 (61)	14 (77)	12 (66)	9 (50)	3 (16)	6 (33)	14 (77)	2 (11)	11 (61)

Others include:- Citrobacter freundii, Pseudomonas aeruginosa, Serratia marcescens, Escherichia spp, Hafnia spp, Protus spp and Salmonella spp.
() = Percentage

63% of E.coli were resistant to third generation cephalosporins and same strains were found to be multi-resistant (isolates were resistant to three or more classes of antibiotics). Klebsiella pneumoniae showed moderate degree of resistance. 41% of E.coli were resistant to 4 - fluoroquinolones.

Almost all ciprofloxacin resistant strains of E.coli showed high level resistance MIC of >32 mg /l. On the other hand most of Klebsiella pneumoniae were sensitive to ciprofloxacin (MIC of 0.13 - 0.50 mg/l). Only low level of resistance was observed (MIC 1mg). Similar finding was observed with Enterobacter, Citrobacter, Serratia and other spp. of Klebsiella. HLR was also observed among different species of Acinetobacter.

Two aminoglycosides gentamicin and amikacin were tested. Out of 100 isolates, 47 were resistant to gentamicin and 16 to amikacin and again E.coli had the major contribution in resistance.

Discussion

Nosocomial infections (NI) are a frequent complication of hospitalization. ICU patients have 5-10 fold greater risk of developing NI with AGNB compared to those in general hospital wards⁵. Infections caused by the multiple resistant bacteria greatly influence the mortality rate in ICU. Prevalent AGNB differ between centres and in the present study it is clear that the prevalent AGNB in this setup was *E. coli* followed by *Klebsiella pneumoniae*.

The emergence of resistance to fluoroquinolone was recognized soon after their introduction for clinical use and was due to extensive and misuse of these compounds in both human and veterinary medicine. Resistance to fluoroquinolone is mainly chromosomally mediated but recently it has been reported that transferable resistance to fluoroquinolones and nalidixic acid has been found in a clinical isolate of *K. pneumoniae*⁶. High level resistance (HLR) to ciprofloxacin among *E. coli* and other members of enterobacteriaceae has been reported previously^{7,8}. This study also reports HLR to ciprofloxacin among *E. coli*. MICs of almost all resistant *E. coli* in this study was >32 mg/L. Other members of enterobacteriaceae were also resistant to ciprofloxacin but the level of resistance was low and highest MICs were 1 mg/L. This level of difference in MICs may be due to the repeated exposure of fluoroquinolone to the prevalent endemic flora of hospital or plasmid mediated as reported recently⁶. Analysis of antibiogram shows that most of the isolates were extended spectrum B-lactamase (ESBL) producers⁹. It has been shown in other studies that ESBL producing strains were multi resistant¹⁰. Findings are the same in this study and majority of ESBL producing nosocomial isolates of *E. coli* and *Klebsiella* were resistant to aminoglycoside and quinolones as well. Outbreaks of nosocomial infection due to ESBL producing AGNB were initially reported by investigators in Europe and other countries occurring specially in the ICU setting^{11,12}. It is a cause of concern that ESBL strains are endemic in our ICUs particularly when there is no control on use of antibiotics in this part of the world. Among all isolates, 47% and 16% were resistant to gentamicin and amikacin respectively. This finding is similar to another local study¹³. High frequency of resistance is probably due to the prolonged excessive use of systemic and topical gentamicin.

All isolates included in this study were sensitive to imipenem. Carbapenemase producing clinical isolates of *E. coli*, *Klebsiella pneumoniae* and other species have been reported¹⁴⁻¹⁶ which is a cause of concern; because there is no potent broad spectrum, B-lactamase stable antimicrobial drug available.

• Amikacin with one broad spectrum B-lactam drug or only imipenem should be considered as drugs of choice for initial empiric therapy in NI until microbiologic data is available. However, use of appropriate antibiotic can control the infection in a sick patient only but to stop the transmission of such pathogens careful hand washing, use of appropriate barrier precautions and isolation of colonized or infected patients are crucial.

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