International Journal of Medicine and Medical Sciences Vol. 2(5), pp. 148-152, May 2010
Available online http://www.academicjournals.org/ijmms
ISSN 2006-9723 © 2010 Academic Journals

Full Length Research paper

De-escalation of antibiotics in nosocomial pneumonia in an Indian intensive care unit

Smrati Bajpai* and D. R. Karnad

Department of General Medicine, Seth G. S. Medical College and K. E. M. Hospital, Parel, Mumbai.

Accepted 22 February, 2010

In India, there have been reports of high prevalence of antibiotic resistance in intensive care units but very little data regarding the attempt to de-escalate. While de-escalation is gaining usage in west, in Indian patients, it is not studied enough leading to skepticism which made us to carry out this study. Consecutive patients with nosocomial pneumonia in the ICU were prospectively studied. All patients underwent mini-BAL for qualitative assessment of tracheobronchial secretions. After culture and antibiotic susceptibility report was available, if the organism was sensitive to a narrower spectrum, the treatment was de-escalated. Results: A total of 248 patients admitted in the study period in ICU, 19% (49) developed nosocomial pneumonia. Of the 49, culture was positive in 25, of these de-escalation was possible in 68% of patients (18). Our study showed that despite high prevalence of antibiotic resistance, de-escalation was still possible in 68% patients where organisms could be isolated.

Key words: Ventilator associated pneumonia, antibiotic sensitivity pattern, ESBL, de-escalation, multi-drug – resistant pathogen.

INTRODUCTION

Studies have shown that early appropriate antibiotic therapy significantly decreases mortality in nosocomial pneumonia. Therefore, initial therapy with broad spectrum antibiotics was started as soon as the diagnosis was made to cover all possible organisms. Choice of antibiotics initially is empiric, guided by time of onset of infection and the antibiotic susceptibility pattern of local microbes.

Once culture and antibiotic susceptibility reports were available, it was recommended to modify the empirical therapy and to use antibiotics with narrower spectrum. This so-called de-escalation of antibiotic therapy is done to limit the emergence of multi-drug – resistant pathogens related to overuse of antimicrobial agents and to avoid the risk of super-infection with resistant micro-organisms (Wunderink 1993; Sandiumenge et al., 2003).

There were limited studies on the role of de – escalation in Indian patients while de-escalation is gaining widespread usage in the western countries. Previous studies have shown that microbial resistance to antibiotics is much more prevalent in India than in Europe and North America (Peter, 1996; Mohanty et al., 2005). As a result, many Indian physicians are skeptical about the feasibility of de-escalation in Indian scenario. This study thus aimed to assess the feasibility of de-escalation in an Indian Intensive Care Unit (ICU).

*Corresponding author. E-mail: smrati.bajpai@gmail.com. Tel: 02224137517 ext: 7410. Fax: 02224137517

MATERIALS AND METHODS

We prospectively studied consecutive patients with nosocomial pneumonia in the medical intensive care unit of a tertiary care centre in Mumbai for a period of three years from March, 2004 - 2007.

All patients with nosocomial pneumonia underwent mini-bronchoalveolar lavage (mini-BAL) technique for qualitative and quantitative estimation of tracheobronchial secretions for colonization and infection.

In this technique a suction catheter was passed through the endotracheal tube or tracheostomy and inserted as far as it could go, till it was wedged against the bronchus, 20 ml of saline was instilled through a syringe into the catheter. The saline was then aspirated back into the syringe and the fluid obtained was sent for the microbiological investigation.

Nosocomial pneumonia was diagnosed by the Centers for Disease Control and Prevention (CDC) criteria (Garner et al., 1988). After obtaining the specimens for bacterial culture, patients were started on empirical broad spectrum antibiotic therapy based upon

Table 1. The protocol of antibiotic de-escalation carried out in the ICU.

Level	*Staphylococci*	GPB other than *Staphylococci*	GNB other than *Pseudomonas*	*Pseudomonas* species
I	Cloxacillin Cefazolin	Crystalline penicillin Cefazolin Erythromycin Azithromycin Doxycycline Amoxycillin Cotrimoxazole	Ciprofloxacin Ofloxacin Amoxycillin Cotrimoxazole Gentamicin	Ceftazidime+Aminoglycoside Cefoperazone+Aminoglycoside Cefotaxime+Aminoglycoside Ceftriaxone+Aminoglycoside Piperacilin+Aminoglycoside
II	Coamoxyclav Clindamycin	Coamoxyclav Clindamycin Levofloxacin Gatifloxacin Amikacin Netilmicin	Gatifloxacin Levofloxacin Cefuroxime Coamoxyclav Cefotaxime Cefoperazone Amikacin Netilmicin Ceftizoxime	Cefprerazone-sulbactam+aminoglycoside Piperacilin tazobactam+aminoglycoside Ticarcillin-clavulanate+aminoglycoside Cefpirome+aminoglycoside Cefepime+aminoglycoside
III	Vancomycin	Vancomycin	Cefprerazone-sulbactam Piperacilin-tazobactam Ticarcillin-clavulanate Cefpirome Cefepime	Aztreonam+aminoglycoside Imipenem-cilastatin+aminoglycoside Meropenem+aminoglycoside
IV	Linezolid Teicoplanin	Linezolid Teicoplanin	Aztreonam Imipenem-cilastatin Meropenem	

GPB = gram positive bacteria, GNB= gram negative bacteria.

universal guidelines for the management of nosocomial pneumonia (American Thoracic Society Association Guidelines, 2005).

The ICU scores of Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment score (SOFA) and Clinical Pulmonary Infection Score (CPIS) were calculated of all patients within 24 h of their diagnosis of nosocomial pneumonia to determine their clinical status. Early onset nosocomial pneumonia was defined as occurring within the first 4 days of hospitalization and late-onset nosocomial pneumonia, occurring after 5 days or more of hospitalization. Once the antibiotic susceptibility report was available and if the causative organism was sensitive to a narrower spectrum, the treatment was de-escalated.

Table 1 shows the protocol of antibiotic de-escalation carried out in the ICU. A descriptive analysis was later performed and the data was expressed as percentages.

RESULTS

The total number of patients admitted into the study was 248. The rate of nosocomial pneumonia was 19% (n = 49). The commonest causative pathogen was *Pseudomonas aeruginosa* (27%, n = 13), *Acinetobacter spp* (18%, n = 9), *Staphyloccocus (*2.04%, n = 1) and *Candida* (2%, n = 1). In some samples of mini BAL more than one organism was grown (Table 2).

Beta lactam-betalactamase inhibitor combination of piperacillin and tazobactam along with aminoglycoside (Amikacin) was the most commonly used antibiotic combination for empirical therapy (Table 3). Culture of miniBAL was positive in 51.02% (n = 25) of the 49 patients, 44% (n = 11) with early onset ventilator associated pneumonia (VAP) and 56% (n = 14) with late-onset.

Among these, de-escalation to a narrower spectrum of antibiotic was possible in 68% (n = 18) patients (Table 3), including 50% (n = 9) each with early and late VAP.

The antibiotic sensitivity pattern is shown in Table 4. Table 5 shows the clinical status of the patients with nosocomial pneumonia while Table 6 shows the clinical status in patients where de-escalation was feasible

Table 2. Frequency of isolated pathogens in patients with nosocomial pneumonia (n =25).

Organisms (n = 49)	Frequency	Percentage (%)*
Pseudomonas aeruginosa	13	26.52
Acinetobacter spp.	09	18.36
Klebsiella spp.	03	06.12
Enterobacter spp.	03	06.12
E. coli	05	10.20
Proteus	05	10.20
MRSA	01	02.04
Candida	01	02.04
No growth	24	48.96

* Some samples had growth of more than one organism.

Table 3. Frequency of antimicrobial agents used for empirical management (n = 49).

Antibiotics	Total number of patients (n = 49)	Percentage
Amikacin	22	44.90
Piperacillin tazobactam	20	40.82
Ticarcillin clavulanate	09	18.37
Ampicillin clavulanate	05	10.20
Cefaperazone + sulbactam	09	18.37
Third generation cephalosporins*	11	22.45
Cefepime	04	08.16
Imipenem cilastatin	05	10.20
Aztreonam	04	08.16
Linezolid	05	10.20
Vancomycin	05	10.20
Amphotericin B	02	4.08
Fluconazole	02	04.08

*Third generation cephalosporins include cefotaxime, ceftriaxone and ceftazidime.

Table 4. Possibility of de-escalation as per antibiotic sensitivity.

Organisms	Total patients (n)	De-escalation possible (n) (%)
Pseudomonas aeruginosa	13	06 (46)
Acinetobacter spp.	09	07 (78)
Klebsiella spp.	03	003 (100)
Enterobacter spp.	03	02 (67)
E. coli	05	005 (100)
Proteus	05	04 (80)

compared to the ones where it was not (Table 7).

DISCUSSION

The incidence of nosocomial pneumonia in our ICU was 19%. *Pseudomonas aeruginosa* was the commonest organism isolated in patients followed by *Acinetobacter baumanii.* The pattern of organisms isolated was similar to most previous studies. (NNIS Report, 1995)) According to NNIS report of 1995, *Pseudomonas* was found responsible for 14% of nosocomial pneumonia and

Table 5. Antibiotic sensitivity patterns of gram negative organisms.

Antibiotics	Organisms				
	Pseudomonas aeruginosa **(n = 13) (%)**	***Acinetobacter baumanni*** **(n = 9) (%)**	***E. coli and Proteus*** **(n = 10) (%)**	***Enterobacter and Klebsiella*** **(n = 6) (%)**	**Gram- negative bacilli (n = 38) (%)**
Piperacillin-Tazobactam	7 (53.8)	9 (100)	6 (60)	(66.6)	26 (68.4)
Ticarcillin-Clavulanate	2 (15.3)	1 (11.1)	3 (30)	2 (33.3)	8 (21.0)
Imipenem -Cilastatin	7 (53.8)	9 (100)	7 (70)	4 (66.6)	27 (71.0)
Meropenem	6 (46.1)	7 (77.7)	8 (80)	4 (66.6)	25 (65.7)
Aztreonam	2 (15.3)	Not tested	2 (20)	2 (33.3)	6 (15.7)
Cefpirome	2 (15.3)	2 (22.2)	3 (30)	2 (33.3)	9 (23.6)
Cefepime	2 (15.3)	1 (11.1)	3 (30)	1 (16.6)	7 (18.4)
Cefaperazone-Sulbactam	4 (30.1)	6 (66.6)	3 (30)	3 (50.0)	16 (42.1)
Ceftazidime	3 (23.0)	1 (11.1)	4 (40)	Not tested	8 (21.0)
Ceftriaxone	3 (23.0)	1(11.1)	2 (20)	2 (33.3)	8 (21.0)
Cefotaxime	3 (23.0)	1 (11.1)	2 (20)	2 (33.3)	8 (21.0)
Amikacin	5 (38.4)	5 (55.5)	7 (70)	2 (33.3)	19 (50)
Netilmicin	3 (23.0)	6 (66.6)	5 (50)	1 (16.6)	15 (39.4)
Gentamicin	2 (15.3)	3 (33.3)	5 (50)	2 (33.3)	12 (31.5)
Levofloxacin	Not tested	3 (33.3)	1 (10)	2 (33.3)	6 (15.7)
Gatifloxacin	Not tested	5 (55.5)	2 (20)	3 (33.3)	10 (26.3)
Ofloxacin	Not tested	2 (22.2)	1 (10)	1 (16.6)	4 (10.5)
Ciprofloxacin	4 (30.1)	2 22.2)	1 (10)	2 (33.3)	9 (23.6)

Table 6. Mean clinical ICU scores of patients with nosocomial pneumonia.

ICU score	Mean value	Scale of score	Normalized scale
Mean APACHE II	11.67	0-71	0.16
Mean SAPS II	18.42	0-163	0.11
Mean SOFA	7.14	0-24	0.29

APACHE: Acute Physiology and Chronic Health Evaluation
SAPS: Simplified Acute Physiology Score
SOFA: Sequential Organ Failure Assessment score.

Table 7. Clinical status and outcome of patients with positive culture using mini-BAL growth.

Mean ICU scores	Patients in which de-escalation was feasible as per microbiology (n = 18)	Patients in which de-escalation not feasible (n =7)
Mean APACHE score	10.3	14.2
Mean SAPS score	07.07	22.0
Mean SOFA score	10.90	22.4
Total patients survived	08.00	02.0

APACHE: Acute physiology and chronic health evaluation
SAPS: Simplified acute physiology score
SOFA: Sequential organ failure assessment score.

Western data (NNIS report 1995).

Previous studies had shown that resistance of Gram negative bacterial isolates from Indian hospitals to antibiotics was much higher than that reported in other parts of the world.(Peter 1996;Mohanty etal. 2005) We too found that 71% of organisms were sensitive to imipenem-cilastatin, 68.4% sensitive to piperacillin -tazobactam, 50% to amikacin and 42% to cefaperazone- sulbactam.

The prevalence of ESBL-producing Gram negative bacilli in India was reported to be high (Mohanty et al., 2005; Kaul et al., 2007; Sinha et al., 2007; Rodrigues et al., 2004). It was found in 20 - 50% of isolates from patients in a hospital in Vellore (Kaul et al., 2007) 28% in Bangalore (Sinha et al., 2007) and 53% in Mumbai (Rodrigues et al., 2004).

Although not supported by bacteriological data, many Indian physicians believe that de-escalation would probably be feasible in very few cases, given the high rate of antibiotic resistance in India. Our study showed that despite the high prevalence of antibiotic resistance, de-escalation was still possible in 68% patients where the organism could be isolated. Michael Niederman's article analysed the study of Ibrahim et al and stated that he could discontinue one antibiotic in 36.5% of patients receiving initial empiric broad-spectrum antibiotics in an American ICU, and two antibiotics in about 61.5% patients (Neiderman, 2006).

A Greek study found that de-escalation was possible in 40.5% patients while Rello et al in a Spanish study could de-escalate antibiotics in 31.4% of patients (Giantsou et al., 2007; Rello et al., 2004).

On examining the relationship between de-escalation attempt and isolated organism, it was found that de-escalation was possible in 80 - 100% of patients when *Proteus, E. coli* or *Klebsiella* were isolated, while it was possible in 46% - 67% cases when non-fermenting bacteria like *Pseudomonas* and *Acinetobacter* were isolated.

De-escalation was possible in 64% of late onset VAP where non-fermenters were isolated compared to 82% with early onset VAP in our study; this was also observed by Rello et al. (2004). On the other hand, Leone et al reported that de-escalation was possible in 72% of late-onset and 26% of early-onset VAP showing a higher de-escalation in late onset as compared to early VAP. They attributed this to their practice of using monotherapy with narrow spectrum antibiotics for early onset VAP (Leone et al., 2007).

It is observed as shown in Table 7 that the clinical profile of the patients where the de-escalation is feasible was better, for they had better ICU scores as compared to the ones where de-escalation was not feasible.

A major factor preventing de-escalation is the inability to grow the causative organisms from respiratory specimens which was negative in 30% of the cases as reported by Depuydt (2007). In our patients the culture was negative in 48% of the cases.

Nevertheless, our study showed that even in countries with relatively high prevalence of antibiotic resistance, de-escalation was still feasible in about 68% of nosocomial pneumonia if the causative organisms could be isolated. The feasibility of de-escalation might be higher if greater care is taken in collection and processing of respiratory samples to increase the yield of organisms.

REFERENCES

American Thoracic Society Association. (2005) Guideline for the management of adults with hospital acquired, ventilator associated and health care associated pneumonia. Am. J. Respir. Crit. Care Med., 176: 388-416

Depuydt P (2007): Editorial; Antibiotic therapy for ventilator-associated pneumonia: De-escalation in the real world; Crit. Care Med., 35(2): 632,633

Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM (1988). CDC definitions for nosocomial infections, Am. J. Infect. Control, Jun; 16(3): 128-40.

Giantsou E, Liratzopoulos N, Efraimidou E (2007). De-escalation therapy rates are significantly higher by bronchoalveolar lavage than by tracheal aspirate; Intensive Care Med., 33: 1533-1540

Kaul S, Brahmadathan KN, Jagannati M etal (2007): One year trends in the gram negative bacterial antibiotic susceptibility patterns in a medical intensive care unit in south India, Indian J. Med. Microbiol., 25(3): 230-5

Leone M, Garcin F, Bouvenotetal J (2007). Ventilator-associated pneumonia: Breaking the vicious circle of antibiotic overuse; Crit. Care Med., 35(2): 379-385

Mohanty S, Singhal R, Sood S (2005). Comparative in vitro activity of beta-lactam/beta-lactamase inhibitor combinations against Gram negative bacteria; Indian J. Med. Res., 122: 425-428

Niederman M (2006). De-escalation therapy in ventilator-associated pneumonia. Curr. Opin. Crit. Care Oct 12: 452-457.

Peter JB (1996): Antimicrobial resistance in India and the United States. Clin. Infect. Dis., 23: 1315-6.

Rello J, Vidaur L, Sandiumenge A (2004). Deescalation therapy in ventilator associated pneumonia; Crit. Care Med. Nov., 32(11): 2183-90

Rodrigues C, Joshi P, Jani SH (2004). Detection of β-lactamases in nosocomial gram negative clinical isolates; Indian J. Med. Microbiol., 22(4): 247-250

Sandiumenge A, Diaz E, Bodi M (2003). Therapy of ventilator-associated pneumonia. A patient-based approach based on the ten rules of "The Tarragona Strategy." IntensiveCare Med., 29: 876-883

Sinha M, Srinivasa H, Macaden R (2007). Antibiotic resistance profile and extended spectrum beta-lactamase (ESBL) production in Acinetobacter species; Indian J. Med. Res., July 126: 63-67

Wunderink RG (1993). Mortality and ventilator associated pneumonia. The best antibiotics may be the least antibiotics. Chest, 104: 993-995