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To Study the Pattern of Resistance, Demonstrated by Device Dwelling Nosocomial Microorganisms to Commonly Prescribed Antimicrobials, In the Absence of a Standard Antibiotic Policy, In an Intensive Care Unit of a Tertiary Care, Teaching Hospital: an Observational Trial

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Abstract

Introduction: Nosocomial infections are frequently encountered in ICU because of severity of underlying diseases, frequency of invasive interventions and frequent use of wide spectrum antibiotics. The incidence of nosocomial infections in ICUs is showing a rising trend, mainly because of increasing invasive procedures performed in the ICU, which has a greater impact on infection rates, risk factors and in further planning the preventive strategies to ensure a quality health care in any hospital, especially in the ICU. Antimicrobial (AM) resistance to both Gram negative bacteria and Gram-positive bacteria is an emerging clinical global problem in intensive care units (ICUs).

Materials and Methods: After approval from the Institution Ethical Commette (IEC), this observational study was carried out in AIMSR, a tertiary care teaching center by the Department of Anaesthesiology and Intensive Care in collaboration with Department of Microbiology by analysing the data, collected from the culture reports of sample tips taken from the various invasive devices from the critical ill patients admitted in Intensive care units over a period of 15 months from June 2014 to September 2015.

Results: Total of 250 cultures from 175 patients (115 males and 60 females) sent and microorganisms were isolated from 135 cultures taken from 105 patients (70 male and 35female). Out of the 135 cultures, 7 cultures were positive for Gram-positive bacteria (GPB) and 128 were positive for Gram-negative bacteria (GNB). The most frequently isolated organisms were Klebsiella pneumoniae (36.29%), Acinetobacter baumannii (23.70%) and Pseudomonas aeruginosa (17.77%) respectively and we also described the sensitivity pattern of AM agents for Gram-negative bacterias (GNB) and Gram-positive bacteria's (GMB).

Conclusion: We conclude that there is a typical microorganism pattern that dwell on various devices and flourish in the environment of the ICU and also there is a increasing trend of resistance toroutinely prescribed antibiotics, particularly and more rapidly, in the absence of a standard antibiotics policy.

Keywords: *Nosocomial infections; Antimicrobial (AM) resistance; Device dwelling microorganisms; Routinely prescribed antibiotics*

Abbreviations: Antimicrobial agents (AM); Gram-positive bacteria (GPB); Gram-negative bacteria (GNB)

Introduction

Nosocomial infections are important public health related problems in many developing countries, particularly in Intensive Care Units (ICUs) [1]. Nosocomial infections are frequently encountered in ICUs because of severity of underlying diseases, frequency of invasive interventions and frequent use of wide spectrum antibiotics [1,2]. The incidence of nosocomial infections in ICUs is showing a rising

trend, mainly because of increasing invasive procedures being performed in the ICUs such as insertions of, central venous catheter, endotracheal tubes, tracheostomy tubes, urinary catheters and chest & pelvic drains, which has a greater impact on infection rates, risk factors and in further planning the preventive strategies to ensure a quality health care in any hospital, especially in the ICU [3-5].

Anti-Microbial (AM) resistance to both Gram-Negative Bacteria (GNB) and Gram-Positive Bacteria (GPB) is an emerging clinical global problem in intensive care units (ICUs), because of frequent use of broad spectrum antimicrobial agents (AMs), crowding of patients, shortage of nursing and other supporting staff and prolonged hospitalization [6,7]. Indiscriminate, inadequately and prolonged use of AMs, prescribed prophylacticaly and empirically without carrying out sensitivity studies also leads to emergence and proliferation of resistant strains preferentially [8].

Appropriate antimicrobial stewardship that includes optimal selection, dose, duration of treatment and control of AM use, will prevent or slow down the emergence of resistance among microorganisms [9,10] Audit of AM sensitivity patterns in ICUs and Critical Care Units (CCUs) are crucial and far more important for giving effective treatment and decreasing the spread of resistance [11,12].

The present study was, therefore, designed to audit the AM sensitivity pattern of microbial isolates from critical ill patients admitted in ICUs of a tertiary care teaching hospital in Malwa region of Punjab in India.

Materials and Methods

After approval from the Institutional Ethical Commette (IEC), this observational study was carried out in Adesh Institute of Medical Sciences and Research (AIMSR), a tertiary care teaching center by the Department of Anaesthesiology and Intensive Care in collaboration with Department of Microbiology by analyzing the data from the culture reports of sample tips taken from the various invasive devices from the critical ill patients admitted in ICU over a period of 15 months from June 2014 to September 2015.

Data collection

In this study, patients of all age groups, both sexes, who were critically ill, admitted in the ICU and had either endotracheal intubation (with and without mechanical ventilation), tracheostomy tubes, central venous catheter, urinary catheter and chest and pelvic drains for more than 72 hours were included. The tips of endotracheal tube, tracheostomy tube, central venous catheter and urinary catheter were collected and sent for culture to the Microbiology department. The antibiogram provided by the Microbiology department were compared with the commonly prescribed anti-microbial drugs.

Data analysis

A standard proformas were filled from various culture samples taken from the invasive devices in ICU patients and required data was collected, over the 15 months. Descriptive statistics were used to present demographics, infection rate, isolation pattern of 250 cultures from 175 patients (115 males and 60 females) sent for laboratory tests. Out of these cultures, organisms, their antibiogram and prescription pattern of antimicrobials (AMs) were analyzed.

Results and Discussion

Over a period of 15 months, from the patients, who were critical ill and admitted in the ICUs, 250 cultures from 175 patients (115 males and 60 females) sent to Microbiology department for culture examination. Out of these cultures sent, microorganisms were isolated from 135 cultures taken from 105 patients (70 male and 35female). Out of the 135 cultures, 7 cultures were positive for Gram-positive bacteria (GPB) and 128 were positive for Gram-negative bacteria (GNB). The specimens assessed were: Endotracheal tube tip (35), urinary catheter tip (35), tracheostomy tube tip (44), Central line tip (14), thoracic and pelvic drain tip (7), accounted as each specimen.

The most frequently isolated organisms were Klebsiella pneumoniae (36.29%), Acinetobacter baumannii (23.70%) and Pseudomonas aeruginosa (17.77%) respectively and the infection pattern of organisms and number of different samples are mentioned in Table 1 & 2.

No.	Microorganism	Type	Frequency (No)
1	Klebsiella pneumoniae	GNB	36.29% (49)
2	Acinetobacter baumannii	GNB	23.70% (32)
3	Pseudomonas aeruginosa	GNB	17.77% (24)
4	*Eshcherichia coli*	GNB	11.85% (16)
5	Staphylococcus aureus	GMB	4.44% (6)
6	Klebsiellaspecieses	GNB	2.96% (4)
7	Citrobacterfreundii	GNB	1.48% (2)
8	Coaugulase negative staphulococci	GMB	0.74% (1)
9	Enterobacteriaceae spp.	GNB	0.74% (1)
		Total	100% (135)

Table 1: *Frequency of microorganism isolated from patients admitted in ICU.*

No.	Microorganism	Freq	Endo Trechal tip	Tracheo Stomy tip	Central Line catheter tip	Urinary Catheter tip	Thoracic & chest drain
1	Klebsiella pneumoniae	49	14	14	9	10	2
2	Acinetobacter baumannii	32	12	15	0	2	3
3	Pseudomonas aeruginosa	24	7	8	1	8	0
4	*Eshcherchia coli*	16	1	2	2	11	0
5	Staphylococcus aureus	6	1	2	1	0	2
6	Klebsiellaspecieses	4	0	1	0	3	0
7	Citrobacterfreundii	2	0	2	0	0	0
8	Coaugulase negative Staphylococci	1	0	0	1	0	0
9	Enterobacteriaceae	1	0	0	0	1	0
Total		135	35	44	14	35	7

Table 2: *Microorganism isolated from different Samples.*

The sensitivity pattern of AM agents for GNB and GPB isolates are presented in Table 3 & 4, In addition the pattern of antimicrobial agents prescribed by the various physicians, is shown in Table 5.

No.	Antibiotics	Kleb. pneum	Acin. brunii	Pseud Arug.	*E. coli*	Kleb Spp.	Citro feud	Entro bacter
1	Amikacin	56.5	54.4	52.6	48.6	40.4	42.8	54.6
2	Gentamycin	34.78	32.6	30.6	28.4	34.7	36.8	28.6
3	Amoxicillin + clavulanate	26.08	28.4	26.8	27.9	22.7	36.8	36.6
4	Piperacillin + TZ	52.17	56.8	58.2	64.7	48.5	46.9	50.5
5	Imipinem	69.56	72.8	68.6	64.5	48.6	56.8	72.0
6	Meropanem	52.17	64.6	68.8	72.5	56.6	62.6	70
7	Ertapenem	30.43	34.6	38.2	36.6	30	28.6	38.2

8	Doripenem	34.78	36.0	42.6	44.2	56.6	54.2	44.6
9	Polymyxin B	60.86	62.4	66.6	72.2	68.2	60	62
10	Colistin	78.26	78.2	74.4	68.2	64.9	62.7	64.8
11	Tigecyclin	73.91	78.8	80	79	74.8	70	69.9
12	Cefuroxime	1.25	4.5	5.5	6.2	4.4	6.2	3.6
13	Cefoxitine	3.55	5.6	8.9	5.4	6.2	7.4	9.2
14	Cefataxime	5.55	5.5	8.3	6.5	7.5	5.7	7
15	Ceftazidime	4.24	8.9	3.4	8.2	2.3	8.3	2.8
16	Cefaperazone	6.26	6.6	8.2	6.5	3.2	7.3	5
17	Cefixime	7.13	2.4	4.4	5.7	3.2	6.4	6.4
18	Cefipime	4.56	4.6	5.8	8.8	3.2	6.4	6.2
19	Ciprofloxacin	4.55	6.8	4.8	7.3	8,8	10	2.8
20	Levofloxacin	8.69	14.2	12.6	20	18.4	16.6	12.6
21	Aztreonam	30.43	36.6	40	46	42	38.8	40
22	Cotrimaxazole	2.6	3.4	5.8	8.2	6.2	8.2	6.6
23	Chloramphenicol	17.39	18	20	24	28.8	24.6	20

Table 3: *The sensitivity pattern of Anti- microbial agents for GNB in percentage.*

No.	Antibiotics	Staph. aureus	Coagulase neg Staph.aureus
1	Oxacillin	32	3
2	Cefoxitine	5	2
3	Doxycycline	16	20
4	Gentamycin	4	5
5	Cotrimoxazole	7	2
6	Erytromycin	16	6
7	Clindamycin	32	9
8	Ciprofloxacin	2	8
9	Cephalaxin	4	1
10	Cefuroxime	3	2
11	Ceffotaxime	6	2
12	Amoxycyclin + Clavulinic acid	32	44
13	Azitromycin	48	25
14	Chloramphenicol	3	2
15	Levoflox	16	25
16	Teicoplanin	32	60
17	Linezolid	80	65

Table 4: *The sensitivity pattern of AM agents for GPBs.*

No.	Anti microbials drug RX	Patients (%)
1	`Metronidazole	74
2	Amikacin	78
3	Gentamycin	54
4	Piperacillin + TZ	78
5	Amoxicillin + Clavulanate acid	60
6	Imipenam	36
7	Cilastin	42
8	Cefatrizone	40
9	Ceftazidime	56
10	Cefipime	42
11	Tigecyclin	32
12	Ciprofloxacin	34
13	Levoflaxacin	64
14	Chloramphenicol	28
15	clindamycin	34
16	Vancomycin	56
17	Cotrimoxazole	28

Table 5: *Prescription pattern of antimicrobial agents in the ICU.*

Discussion

Antimicrobial agents (AMs) are among the most commonly used drugs in critical ill patients. The emergence of AM resistance in ICU is of great concern as it increases the likelihood of drug interactions/side effects and cost of therapy due to use of newer antibiotics. Resistance may also be responsible for prolonged hospital stays and can affect prognosis. The problem of resistance in a hospital is difficult to understand without the knowledge of AM use pattern [11,12]. Monitoring the use of AM and review of sensitivity pattern are, therefore, important.

In our study, Microorganisms were isolated in 54% (135/250) out of cultures investigated, compared to 64.7 % in an Indonesian study and 36.8% in another Indian study [10,13].

The most common microorganism isolated from our study was Klebsiella pneumonia (36.29%), followed by Acinetobacter baumannii (23.70%), Pseudomonas aeruginosa (17.77%), Escherchia. Coli (11.85%) and Stapylococcus aureus (4.44%) respectively.

Whereas Klebsiella pneumonia was the predominant organism isolated from other studies too [10,13]. Thus the isolation pattern of organisms appears to vary with time and hospital settings. Our data showed that there were more Gram-negative bacteria than Gram-positive isolates. This is not surprising because the former are known to develop resistance more rapidly and extensively than the latter [14,15].

In our study, we found that to Gram negative microbes, Klebsiella pneumonia (36.29%), the most common isolate, which was found to be sensitive to Colistin, Tigecyclin, Imipenem, polymyxin B, Amikacin and Piperecillin-Tazobactum respectively and showed mostly resistant to all generation cephalosporines. Unfortunately Cephalosporines were the anti-microbial agents most perescribed to the patients in ICU.

Another unusual finding in our study was that the occurrence of Acinetobacter baumaniias the second most common microorganism (23.70%), which was ironically not as common in other studies (<10%) [10,13], the cause of this happening could not be explained rationally, so needs further investigations and this microorganism showed almost same pattern of sensitivity and resistance to commonly prescribed antibiotics in the ICU, as the pattern shown by the Klebsiella pneumonia was also a striking finding. Also we found that higher sensitivity of Pseudomonas aeruginosaas 3rd most common microorganism (17.77%) to Meropanam, Imipenam, Colistin andaminoglycosides, whereas anti-pseudomonasagents such as cefoperazone, ceftazidimeand cefipime, which are the most commonly, prescribed AMs but found largely ineffective in the study.

The mechanisms of resistance to third generation Cephalosporins, carbenicillins and ureidopenicillins are production of Amp C, β-lactamases, class A carbenicillin-hydrolysing β-lactamases, class A ESBL and DNA gyrases, active efflux pumps and diminished permeability of the outer membrane [16,17].

Comparison of the sensitivity pattern for next common (11.85%) Gram negative microbe, *E. coli* in our study also showed the same pattern of resistance to commonly prescribed AMs as shown by K. pneumoniae.

For Gram positive microbes both Staphylococcus aureus and Coagulase negative Staphylococcishowed higher sensitivity to Linezolid, Clindamycin, Azithromycin, Amoxicillin- Clavulanic acid and Teicoplanin and showed resistant to Ciprofloxacin and Cephalosporinand Chloramphenicol, Unfortunately Cephalosporines and ciprofloxacin were the anti-microbial agents most commonly prescribed to the patients in ICU.

Also, third generation cephalosporins were very ineffective so their overuse must be restricted. Antibiotic cycling should be carried out to reduce selection pressure and further resistance to third generation cephalosporins [18]. Ongoing surveillance of AM susceptibility pattern helps in the preparation and regular review of local guidelines for the empirical selection of first-line AM agents [6,19]. Infection with resistant organisms can be associated with poor prognosis if the initial antibiotics used do not provide adequate coverage. Newly admitted patients should be screened for target organisms. AMs should be altered based on sensitivity results or stopped altogether if no organism has been isolated and the clinical picture of patients permit it [18,19].

Limitations of the study

This is a basically an observational study, so some biases and pitfalls may have crept in while designing and executing the study trial.

Conclusion

K. pneumoniae was the predominantly isolated organism in the ICU. Ceproflaxacin and Chloramphenicol resistant GPB, S.aureus and S. epidermidis and third generation cephalosporin-resistant GNB were predominant antimicrobial-resistant organisms found. The fluoroquinolones and gentamicin can be used as first-line drugs, with the carbapenams as second-line agents. Since the 3rd generation cephalosporins are very ineffective due, possibly, to their frequent use in the ICUs studied, their use should be restricted.

As per our observation, we found that there is a typical microorganism pattern that dwell on various devices and flourish in the environment of the ICU and also there is an increasing trend of resistance to routinely prescribed antibiotics, particularly and more rapidly, in the absence of a standard antibiotics policy. So after this observational trial, we want to propose a hypothesis that there would be a better control over these device dwelling microorganisms, if a standard antibiotics policy is being followed and also after searching the literature, we found that there are some studies already done by different authors, which also emphasize on this hypothesis that there should be a standard antibiotic policy to check over these microorganisms dwell in ICU as per their regions.

Conflict of interest

We confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. All authors have read and approved the final manuscript.

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