PATTERN OF ANTIMICROBIAL USE IN PATIENTS ON VENTILATOR IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Excess and indiscriminate use of antibiotics has been described both in community and hospital settings particularly in developing countries, can lead to adverse affects complicating the therapy, emergence of drug resistance and increases the cost of health care. Antimicrobial(AMA) resistance in the intensive care unit (ICU) has emerged as an important problem. It is estimated that antibiotic consumption is approximately tenfold greater in ICU than in general hospital wards. Systematic studies to generate valid information regarding the utilization of AMAs in patients on ventilator may help in improving the quality of antimicrobial use and also in formulating effective infection control strategies in the management of such patients. There is limited data on antibiotic prescription pattern in patients on ventilator from India, hence the study was done with an objective to know the antibiotic prescription pattern in patients on ventilator and to analyze rationality among the prescriptions. This was an observational study conducted in the ICU of a tertiary care hospital in South India from March 2011 to June 2011. The prescribing pattern of AMAs in patients aged between 18-65 years was studied prospectively in patients of either sex, receiving antimicrobials. Total 34 AMAs preparations were used either single or in combination. In the present study, the commonly used AMAs were beta-lactam antibiotics, particularly piperacillin+tazobactam (extended-spectrum penicillins+β-lactamase inhibitor) and metronidazole followed by ceftriaxone (long-acting third-generation cephalosporin) as single or combination therapy. Combination of AMAs was used in 85% of patients. Out of
348 drugs in the National Essential Drug List 2011, 64 drugs are grouped under anti-infective agents. In our study, out of 34 AMAs preparation 17 (50%) drugs were essential drug list and study the average number of drugs prescribed in the ICU was 8.6±4.5. Rational empiric antimicrobial therapy is essential in achieving good outcomes. There is an urgent need to implement and monitor infection control committee, based on local AMAs prescription pattern and susceptibility patterns, which help in minimizing the irrational use of AMAs.

**Key words:** Antimicrobial agents, Intensive Care Unit, Rational use, Prescribing pattern.

**INTRODUCTION**

Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department.\(^1\) Worldwide, excess and indiscriminate use of antibiotics has been described both in community and hospital settings particularly in developing countries.\(^2\) Excess and indiscriminate antibiotic use can lead to adverse affects complicating the therapy, emergence of drug resistance and increases the cost of health care.\(^3,4\) Antimicrobial therapy in intensive care unit (ICU) patients requires special attention as these patients are often in debilitated physical condition, exposed to multiple invasive procedures, have deficiencies of the immune system, more prone to infectious complications and vulnerable to multidrug-resistant pathogens, requiring intense antibiotic therapy for long periods.

Antibiotic resistance in the ICU has emerged as an important problem. It is estimated that antibiotic consumption is approximately tenfold greater in ICU than in general hospital wards.\(^5\) There is a need of constant surveillance, strict implementation and monitoring of infection control practices and rational antibiotic prescription to combat the increasing multidrug resistance. The pattern of antimicrobial use may vary in different geographical regions, and from hospital to hospital, depending on the prevalent strains of pathogens, the susceptibility pattern, and cost and availability of antimicrobial agents (AMAs). Systematic studies to generate valid information regarding the utilization of AMAs in patients on ventilator may help in improving the quality of antimicrobial use and also in formulating effective infection control strategies in the management of such patients.

There is limited data on antibiotic prescription pattern in patients on ventilator from India, hence the study was done with an objective to know the antibiotic prescription pattern in patients on ventilators and to analyze rationality among the prescriptions.
MATERIALS AND METHODS

This was an observational study conducted in the ICU of a tertiary care hospital in South India from March 2011 to June 2011. The prescribing pattern of AMAs in patients aged between 18-65 years was studied prospectively in patients of either sex, receiving antimicrobials for prophylaxis or treatment. Ethical clearance from the institutional ethics committee was obtained before starting the study. Patients were excluded if they terminally ill patients (cancer), severely immunocompromised patients, HIV and HBsAg positive cases.

The demographic and treatment data of patients was collected in the following format:

- Age and sex of patient.
- Diagnosis/ Reasons for hospitalization in ICU
- Duration of Stay on ventilator
- Number and Percentage of AMAs
- Change in AMAs
- Dose and route of AMAs.
- Combination therapy used/Rationality

The appropriateness of antibiotic therapy was determined using the criteria described by Kunin and Jones.\cite{6,7} The universal guides were accepted as a reference for the diagnosis of infections and appropriate therapeutic recommendations in our study.\cite{8} Patients were followed up till discharge, referred for further management, transferred to the ward or discharged against medical advice. The data was analyzed using Microsoft Excel (2007 version) and the results are explained in number and percentage.

RESULTS

The AMAs administered to 100 consecutive patients admitted into the ICU were analyzed.

The age and gender distribution of the patients is shown in table 1.

Table 1: Age and gender distribution of patients.

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Male (n=60)</th>
<th>Female (n=40)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>18-25</td>
<td>18</td>
<td>30.00</td>
<td>15</td>
</tr>
<tr>
<td>26-35</td>
<td>10</td>
<td>16.7</td>
<td>12</td>
</tr>
</tbody>
</table>
Maximum patients were males and the most common age group was 18-25yrs followed by 56-65 yrs.

Table 2: Duration of stay on ventilation.

<table>
<thead>
<tr>
<th>Duration In days</th>
<th>Male</th>
<th></th>
<th></th>
<th>Female</th>
<th></th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td></td>
<td>%</td>
</tr>
<tr>
<td>0-1</td>
<td>2</td>
<td>3.3</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3</td>
<td>20</td>
<td>33.3</td>
<td>15</td>
<td>37.5</td>
<td>35</td>
<td>35.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td>23</td>
<td>38.4</td>
<td>11</td>
<td>27.5</td>
<td>34</td>
<td>34.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 days</td>
<td>15</td>
<td>25.0</td>
<td>14</td>
<td>35.0</td>
<td>29</td>
<td>29.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100.0</td>
<td>40</td>
<td>100.0</td>
<td>100</td>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Most common duration of stay on ventilator was 2-3 days, followed by 4-5 days.

Table 3: Reasons for hospitalization in Intensive care unit.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVA and Encephalopathy *</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>OP and other poisoning</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Respiratory tract infections</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>RTA and Head injury</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Hollow viscous perforation</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>CVS</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td><strong>100</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

CVA= Cerebro vascular Accident. *Meningitis, seizures, hemorrhage, stroke and cervical fracture.
OP= Organo phosphorous  
RTA= Road traffic accident  
Respiratory tract infections: Pneumonia, hemothorax, pulmonary edema, COPD.  
CVS: Cardiovascular system (Myocardial infection and cardiac arrest),  
Renal dysfunction: Acute renal failure, nephropathy.  
Others : Cellulitis, septicemia, DKA, anaphylactic shock, PPH, Snake bite, splenic rupture.  

Table 4: Antimicrobials used in patients on ventilator.

<table>
<thead>
<tr>
<th>Generic name and dose</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td><strong>Beta-lactams</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin+tazobactam 4.5-13.5 gm</td>
<td>37</td>
<td>61.7</td>
<td>30</td>
</tr>
<tr>
<td>Ceftriaxone+sulbactam 3-4.5 gm</td>
<td>4</td>
<td>6.7</td>
<td>2</td>
</tr>
<tr>
<td>Ceftriaxone +tazobactam 2.5-3.75 gm</td>
<td>3</td>
<td>5.0</td>
<td>1</td>
</tr>
<tr>
<td>Benzyl penicillin 6-8 megaunits</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>Meropenem 1-2 gm</td>
<td>9</td>
<td>15.0</td>
<td>8</td>
</tr>
<tr>
<td>Ceftriaxone 2 gm</td>
<td>5</td>
<td>8.3</td>
<td>6</td>
</tr>
<tr>
<td>Ticarcillin+Clavulanic acid 6.2 gm</td>
<td>2</td>
<td>3.3</td>
<td>0</td>
</tr>
<tr>
<td>Ceftazidime 2-3 gm</td>
<td>2</td>
<td>3.3</td>
<td>0</td>
</tr>
<tr>
<td>Imipenem+Cilastatin 1-1.5 gm</td>
<td>3</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Cefuroxime+sulbactam 3 gm</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td>Cefoperazone+sulbactam 3-4.5 gm</td>
<td>4</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Cefotaxime 2-3gm</td>
<td>1</td>
<td>1.7</td>
<td>1</td>
</tr>
<tr>
<td>Amoxicillin+clavulunate 2.4-3.6 gm</td>
<td>2</td>
<td>3.3</td>
<td>1</td>
</tr>
<tr>
<td>Meropenem+Suclactam 3-4.5 gm</td>
<td>1</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td>Cefuroxime+clavlunate 1.25-1.87 gm</td>
<td>1</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td><strong>Macrolides and lincosamides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin 0.5-1 gm</td>
<td>2</td>
<td>3.3</td>
<td>4</td>
</tr>
<tr>
<td>Clarithromycin 1 gm</td>
<td>1</td>
<td>1.7</td>
<td>3</td>
</tr>
<tr>
<td>Clindamycin 0.6-0.9 gm</td>
<td>2</td>
<td>3.5</td>
<td>4</td>
</tr>
<tr>
<td><strong>Aminoglycosides and glycopeptides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin 0.5-1 gm</td>
<td>11</td>
<td>18.3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Nitroimidazoles</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole 1-1.5 gm</td>
<td>34</td>
<td>56.7</td>
<td>20</td>
</tr>
<tr>
<td>Ornidazole+(ofloxacin) 1 gm</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Fluoroquinolones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxacin 0.5-1 gm</td>
<td>4</td>
<td>6.7</td>
<td>1</td>
</tr>
<tr>
<td>Ofloxacin+(ornidazole) 0.4 gm</td>
<td>1</td>
<td>1.7</td>
<td>1</td>
</tr>
<tr>
<td>Moxifloxacin 0.4 gm</td>
<td>3</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td><strong>Antitubercular drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard antitubercular drugs</td>
<td>1</td>
<td>1.7</td>
<td>0</td>
</tr>
<tr>
<td><strong>Antimalarial drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artesunate 60 mg</td>
<td>1</td>
<td>1.7</td>
<td>2</td>
</tr>
<tr>
<td>Primaquine 15mg</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
Most commonly used group was Beta lactam antibiotics

Table 5: Change in antimicrobial therapy.

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>Male (n = 60)</th>
<th>Female (n = 40)</th>
<th>Total (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Change / substituted</td>
<td>12</td>
<td>20.0</td>
<td>6</td>
</tr>
<tr>
<td>No change</td>
<td>48</td>
<td>80.0</td>
<td>34</td>
</tr>
</tbody>
</table>

An antimicrobial was changed in 18% of the patients

Table 6: Route of administration of antimicrobials.

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Male (n = 60)</th>
<th>Female (n = 40)</th>
<th>Total (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>IV</td>
<td>60</td>
<td>100.0</td>
<td>40</td>
</tr>
<tr>
<td>Oral</td>
<td>5</td>
<td>8.3</td>
<td>7</td>
</tr>
<tr>
<td>Topical (eye drops)</td>
<td>2</td>
<td>3.3</td>
<td>0</td>
</tr>
</tbody>
</table>

IV= intravenous.

Most commonly used route was intravenous

Table 7: Pattern of antimicrobial therapy.

<table>
<thead>
<tr>
<th>Pattern of antimicrobial use</th>
<th>Male (n = 60)</th>
<th>Female (n = 40)</th>
<th>Total (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Monotherapy(^5)</td>
<td>15</td>
<td>25.0</td>
<td>10</td>
</tr>
<tr>
<td>Combination therapy(^*)</td>
<td>45</td>
<td>75.0</td>
<td>30</td>
</tr>
</tbody>
</table>

\(^5\)Piperacillin+tazobactam, coamoxiclav, ceftriaxone+sulbactam, ceftriaxone+tazobactam, ticarcillin+clavulunate and ceftazidime+tazobactam were considered as single drug.

\(^*\)Concurrent use of two or more antimicrobial agents

In 75% of the patients combination therapy was used.
### Table 8: Antimicrobial combinations prescribed.

<table>
<thead>
<tr>
<th>Antimicrobial agents</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Piperacillin+Tazobactam)+Metronidazole</td>
<td>16</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Metronidazole+Amikacin</td>
<td>8</td>
</tr>
<tr>
<td>(Ceftriaxone+Sulbactam)+Metronidazole</td>
<td>4</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Amikacin</td>
<td>3</td>
</tr>
<tr>
<td>Meropenem+metronidazole</td>
<td>2</td>
</tr>
<tr>
<td>(Cefaperazone+Sulbactam)+Metronidazole</td>
<td>2</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Metronidazole +Clindamycin</td>
<td>2</td>
</tr>
<tr>
<td>Cefotaxime+metronidazole</td>
<td>2</td>
</tr>
<tr>
<td>Meropenem+Clarithromycin</td>
<td>2</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Meropenem</td>
<td>2</td>
</tr>
<tr>
<td>Linezolid+Meropenem+Metronidazole</td>
<td>2</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Levofloxacin</td>
<td>2</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Ceftriaxone</td>
<td>2</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Azithromycin +Levofloxacin + Oseltamivir</td>
<td>1</td>
</tr>
<tr>
<td>(Ceftriaxone+Tazobactam)+Metronidazole +Ofloxacin (eye drop)</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Clarithromycin+Benzy1 penicillin</td>
<td>1</td>
</tr>
<tr>
<td>Meropenem+Azithromycin</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Minocycline+Moxifloxacin+Oseltamivir</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+ Moxifloxacin</td>
<td>1</td>
</tr>
<tr>
<td>(Ticarcillin+Clavulanate)+Metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>Ceftriaxone+metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>Meropenem+Metronidazole +Azithromycin</td>
<td>1</td>
</tr>
<tr>
<td>Metronidazole+Linezolid+Ceftazidime</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 8: Antimicrobial combinations prescribed (continued)

<table>
<thead>
<tr>
<th>Antimicrobial agents</th>
<th>Patients (Number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Piperacillin+Tazobactam)+Ceftriaxone+Clarithromycin</td>
<td>1</td>
</tr>
<tr>
<td>Azithromycin+Linezolid+Meropenem</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Artesunate</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+metronidazole+meropenem</td>
<td>1</td>
</tr>
<tr>
<td>Clindamycin+Moxifloxacin+Meropenem</td>
<td>1</td>
</tr>
<tr>
<td>Meropenem+Metronidazole+doxycycline+Artesunate</td>
<td>1</td>
</tr>
<tr>
<td>(Ceftriaxone+sulbactam)+Metronidazole+Levofloxacin</td>
<td>1</td>
</tr>
<tr>
<td>Ceftriaxone+amikacin+Metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>Anti-TB+ceftazidime</td>
<td>1</td>
</tr>
<tr>
<td>Co-amoxiclav+Amikacin+(Cefoperazone+sulbactam)</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Imipenem+Linezolid</td>
<td>1</td>
</tr>
<tr>
<td>(Cefaperazone+ Sulbactam) +Amikacin</td>
<td>1</td>
</tr>
<tr>
<td>Imipenem+Metronidazole+Azithromycin</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Metronidazole+Meropenem+Linezolid</td>
<td>1</td>
</tr>
<tr>
<td>Co-amoxiclav+Metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Moxifloxacin+Penicillin +Primaquine</td>
<td>1</td>
</tr>
<tr>
<td>(Cefuroxime+Clavulnate) +Metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Artesunate+(Ofloxacin+Ornidazole)</td>
<td>1</td>
</tr>
<tr>
<td>Coamoxiclav+Metronidazole+Levofloxacin</td>
<td>1</td>
</tr>
<tr>
<td>(Piperacillin+Tazobactam)+Azithromycin+Oseltamivir</td>
<td>1</td>
</tr>
<tr>
<td>Imipenem+metronidazole</td>
<td>1</td>
</tr>
<tr>
<td>Meropenem+Metronidazole+Amikacin</td>
<td>1</td>
</tr>
<tr>
<td>Emipenem+Linezolid</td>
<td>1</td>
</tr>
</tbody>
</table>

Most common prescribed was (Piperacillin+Tazobactam)+Metronidazole, followed by (Piperacillin+Tazobactam)+Metronidazole+Amikacin
Table 9: Outcome of antimicrobial therapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Male (n = 60)</th>
<th>Female (n = 40)</th>
<th>Total (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Improved</td>
<td>34</td>
<td>56.7</td>
<td>21</td>
</tr>
<tr>
<td>Died</td>
<td>17</td>
<td>28.3</td>
<td>11</td>
</tr>
<tr>
<td>Discharge against medical advice (DAMA)</td>
<td>9</td>
<td>15.0</td>
<td>8</td>
</tr>
</tbody>
</table>

Maximum patients improved on antimicrobial therapy

Table 10: Evaluation of antimicrobial therapy

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>No. of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rational</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>Irrational</td>
<td>46</td>
<td>46</td>
</tr>
</tbody>
</table>

The number of rational prescriptions was 54.

DISCUSSION

Patients admitted in the ICU invariably suffer from chronic and critical illness. In majority of the cases, patients will be on polypharmacy ranging from anti ulcers, multivitamins and antimicrobials. The drug therapy should be rationale and knowledge of prescribing patterns will help in rational drug therapy. AMAs are the mainstay of treatment for life-threatening infections. But the selection of AMAs is dependent on the physicians personal choice. The lack of standardization in selection of AMs leads to widespread misuse.\[9\]

The demographic results of patients admitted to ICU is shown in table 1. The most common age group was 18-25yrs, which is different from a study in Nepal where the mean age was 50yrs.\[10\] The reasons for admission in the ICU is shown in table 3. The usual sites of infection include respiratory tract, intra-abdominal / GIT, bloodstream, and urinary tract. In the present study, the most commonly encountered infections were respiratory tract infections consistent with other studies.\[10\] However, the predominant system affected is the CNS with only 4 out of 34 cases having infection requiring AM therapy. In 13 subjects (13%), intra-abdominal infection was due to hollow viscus perforation. UTI was least common because of
prophylactic use of AMAs and aseptic precautions. Septicemia was seen in 8% of subjects, which was almost similar to other reported studies.\textsuperscript{11}

Total 34 AMAs preparations were used either single or FDC preparation. In the present study, the commonly used AMAs were beta-lactam antibiotics, particularly piperacillin+tazobactam (extended-spectrum penicillins+\(\beta\)-lactamase inhibitor) and metronidazole followed by ceftriaxone (long-acting third-generation cephalosporin) as single or fixed dose combination therapy. These were preferred because of their wider antimicrobial spectrum covering most of the common pathogens. A similar pattern of antimicrobial use has been reported in other studies.\textsuperscript{10,12} Metronidazole was commonly used as adjuvant to other AMAs for effective coverage on anaerobic organisms, as also reported in other studies.\textsuperscript{10,13}

The initial empirical antimicrobial therapy was continued in 82\% of subjects, but changed in 18\% of subjects by adding or substituting with other AMAs, based on laboratory report or inadequate clinical response or both. This data is not similar to the previous studies where there was more number of AMAs substituted based on culture and sensitivity but not possible in our study.

The route of administration of AMAs is generally determined by the site and severity of infection; parenteral route being preferred in ICU as the patients are critically ill.\textsuperscript{10} In our study, majority of antimicrobials were administered mostly IV and some of the AMAs like oseltamivir, clarithromycin, ornidazole along with ofloxacin, Tetracyclines like minocycline and doxycycline, antimalarial drug primaquine and anti-tubercular drugs were administered orally through nasogastric tube. AMAs which are used in topical application form are ofloxacin and sparflloxacin eye drops. AMAs were used for prophylaxis in 60\% of subjects which included both medical and surgical prophylaxis which was almost similar to an earlier reported study.\textsuperscript{14}
Combination of AMAs was used in 85% of patients (n = 85). Piperacillin or ceftriaxone-based combinations were most frequently used, often with metronidazole. Amikacin was added in case of Gram negative infections and to increase the synergistic prolongation of the post antibiotic effect of beta lactams. Other combinations involved, addition of specific antimicrobials as needed like anti-malarial, anti-viral and anti-tubercular agents.

However, the combined use of ceftriaxone with piperacillin in 3 patients, and piperacillin with carbapenems (meropenem & imipenem) in 5 patients and some other combinations like piperacillin with linezolid, carbapenems with linezolid and later combination with piperacillin may not be considered rational as there is no documented advantage with this combination. In other studies, the most frequently used combinations were ceftriaxone with metronidazole and penicillins with aminoglycosides such as gentamicin.[10]

Out of 348 drugs in the National Essential Drug List 2011, 64 drugs are grouped under anti-infective agents. In our study, out of 34 AMAs preparation 17 (50%) drugs were essential drug list. In the present study, the antimicrobial agents were used empirically in most of the cases (92%) and definitive therapy was possible only in 3% of patients, consistent with most of the other studies also.[15,16] The overall mortality rate in the study subjects was 28%, which was 10% more when compared to an international study of prevalence and outcomes of infection in ICU.[17]

In the present study the average number of drugs prescribed in the ICU was 8.6±4.5, in another study it was 12.1 ± 7.6.[18] Average number of drugs per person is an important index of prescription audit. It is preferable to keep the mean number of drugs per prescription as low as possible, since higher figures always lead to increased risk of drug interaction, development of bacterial resistance, increased hospital cost.[19]

**Limitations of the study**

The present study has certain limitations. This study was not an interventional study, which helps in reducing the mortality of the patients by appropriate AMAs therapy and the sample size was only 100 cases, requiring further studies in different hospitals with more knowledge about the management of severe infections. There were very few cases with culture and sensitivity reports for the definitive treatment of the patients. Defined Daily Dose was not calculated in this study.
CONCLUSION

The most frequently used AMAs were extended spectrum penicillins (piperacillin+tazobactum) along with metronidazole, followed by third-generation cephalosporins. Antibiotic resistance is increasing at an alarming rate leading to increased morbidity, mortality and treatment cost. Appropriate empiric antimicrobial therapy is essential for achieving good outcomes. There is an urgent need to formulate and implement antibiotic policy based on local AMAs prescription pattern and antibiograms, which will help in minimizing the irrational/inappropriate utilization of AMAs.

Conflict of interest: None

REFERENCES


