**Analysis of utilization pattern of antimicrobial agents—AMAs in ICU**

**Pravin. G. Dhone**  
Professor & Head, Department of Pharmacology, RSDKS GMC, Ambikapur

**Rimjhim Sahu**  
Associate Professor, Department of Pharmacology, People’s college of medical sciences & Research Centre, Bhopal

**Sabitri Beshra**  
Assistant professor, Department of Pharmacology, Bhima Bhoi Medical College and Hospital, Balangir

**Madhusmita Sahu**  
Associate Professor, Department Of Anaesthesiology and Critical Care, VIMSAR, Burla, Sambalpur  
*Corresponding author

**Abstract**---AMAs—Antimicrobial Agents are commonest used medicaments in all type of health faculty and specialty. To find out rationality of Anti-microbial use in different IPD wards such as ICUs of a tertiary care teaching hospital of eastern Odisha- SCB.MC & Hospital, Cuttack, Odisha. To start with AMAs prescribed empirically in 100% patients, at no response or decreased response, C/S is done in—21% of cases, and AMAs changed later on as per C/S report. Aim of empirical therapy is in a way that Early intervention will improve outcome, thus in prophylaxis group Single AMA 100%, Along with oral route. It is also proved that inadequate therapy for critically ill patients and serious hospitalized patients associated with poor outcomes with increased morbidity and mortality, as well as increased length of hospital stay.

**Keywords**---Prophylaxis, Antibiotics, Infections, Chemotherapy.

1. **Introduction**

AMAs — Antimicrobial Agents are commonest used medicaments in all type of health faculty and specialty. It will not be trustworthy if one will say that he or she has not used Antibiotics in his life time or cannot claim that will not use
antibiotics in future. [1,2]. It’s used in wide areas starting from nil infection—prophylaxis, from mild infection to severe life threatening situations, that often endangers life.[3,6] Not only used by doctors, but also used by quacks, as OTC drug by medicine shop keeper, often used by patients and relatives without any need or any advice, many times by a layman for his son or daughter and by medical and related staffs, leading in an increment of morbid condition in one hand and danger divesting drug resistant in other hand. By 1929-1941 as penicillin came to use, it was used in all infecting condition, quacks were already there but doctors did quackery in prescribing this to any fever, any sepsis and even to viral fevers, and other self-limiting infections. The cause was not only non-availability of any other magic bullet except sulfonamides but also ignorance, over enthusiasm and irrationality of use. [5,6,2]

During that latter half of the nineteenth century, scientists such as Koch were able to identify the microorganisms responsible for diseases such as tuberculosis, cholera, and typhoid. Methods such as vaccination for fighting infections were studied. Research was also carried out to try and find effective antibacterial agents or antibiotics. However, the scientist who can lay claim to be the father of chemotherapy—the use of chemicals against infection—was Paul Ehrlich. Ehrlich spent much of his career studying histology, then immunochemistry, and won a Nobel Prize for his contributions to immunology. However, in 1904 he switched direction and entered a field which he defined as chemotherapy. Ehrlich’s 'Principle of Chemotherapy' was that a chemical could directly interfere with the proliferation of microorganisms. [2,6,7,10,26]

Antimicrobial resistance is a naturally occurring biological phenomenon driven by Darwinian natural selection. Hence it is an inevitable accompaniment of appropriate antibiotic use. [18,19,41]. However, accumulated evidence points to misuse of antibacterial having further amplified the Emergence and spread of antibacterial resistance. The antimicrobial resistance crisis is heightened by the concomitant downward trend in the intent of pharmaceutical companies to develop novel antimicrobials. As a consequence, only a limited number of new antibacterial drugs have been introduced into the market in the last three decades. Systemic antibacterial new molecular entities approved by the United States Food and Drug Administration. [7,8,9]

2. Aims and Objectives

To find out rationality of Anti-microbial use in different IPD wards such as ICUs of a tertiary care teaching hospital of eastern ODISHA- SCB.MC & HOSPITAL, CUTTACK, ODISHA

- To find out the antibiotics commonly prescribed in various conditions.
- To determine average number of AMA use for patients.
- To find out judiciousness of combinations of AMAs.
- To find out judiciousness of AMAs use by determining antibiotics prescribed irrationally and whether they prescribed in accordance to standard treatment guide line.
- To compare antimicrobial prescriptions, to determine multiple antibiotic prescriptions and disease conditions in which they are prescribed.
- To collect C/S report and see sensitivity and resistant pattern.
• To locate AMAs change as per report,
• To find out whether laboratory investigation were done before or after prescription of AMAs.
• To find out supply chain management.
• To find out Govt. supply or private purchase
• To find out prescriptions in brand and generic name.
• To find out ADRs in AMAs use.
• To determine whether prescription was for treatment or for prophylaxis.

3. Material and Method

3.1 Methodology
Review of patient’s folders, Asses drug availability from stores and pharmacy records, informal interview with prescribers, scrutiny of laboratory records and observations.

3.2 Study Design
Observational and Retrospective survey of AMAs usage.

3.3 Place of Study
ICU ward of SCBMC & HOSPITAL, Cuttack. It is a 3-tier Medical College and Hospital, in eastern Odisha, providing wide variety of Diagnostics and Specialist OPD and IPD Services as well as Teaching faculty. More than half of Odisha state along with West-Bengal and Bihar, Jharkhand population depend on it.

3.4 Study Period----Sept.—2013--- Dec. 2015

3.5 Sampling
Data are collected from admitted patient’s case sheets from ICUs, surgery, orthopedics and burn indoor wards. Data's are collected by a self-prepared preformed proforma, which is prepared as per study design and includes Age, Sex, Disease, Unit, Ward, AMA or AMAs prescribed, Average no of AMAs, Dose, Frequency, Route of administration, along with Govt. supply or private purchase and supply chain.

Proforma

<table>
<thead>
<tr>
<th>Patients</th>
<th>Name, age, sex, address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Regd. No.</td>
<td></td>
</tr>
<tr>
<td>Ward, unit’ bed. No. unit head</td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>AMA used</td>
<td></td>
</tr>
<tr>
<td>Route, dose, Frequency, Duration</td>
<td></td>
</tr>
<tr>
<td>Ward supply</td>
<td></td>
</tr>
<tr>
<td>Yes or, no</td>
<td></td>
</tr>
<tr>
<td>Market purchase</td>
<td></td>
</tr>
<tr>
<td>Yes, or No</td>
<td></td>
</tr>
<tr>
<td>Availability in ward</td>
<td></td>
</tr>
<tr>
<td>Distribution point</td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>---</td>
</tr>
<tr>
<td>Availability in central store</td>
<td></td>
</tr>
<tr>
<td>Ware house</td>
<td></td>
</tr>
<tr>
<td>Availability in SDMU</td>
<td></td>
</tr>
<tr>
<td>Changed AMA After C/S</td>
<td></td>
</tr>
</tbody>
</table>

### 3.6 Inclusive Criteria
All Adult patients admitted to ICU-wards. All prescriptions single or combination of AMAs is included. No age, sex, race, residence, addictions and habituations, socio-economic state, co-morbid condition, height, weight not taken into account, except weight, age and co-morbid conditions such as liver and renal failure taken to determine type and dose of AMAs.

### 3.7 Exclusion Criteria
Topical antibiotics, ointments, combination of antibiotics with steroids for local applications, ATT, HAART, Antineoplastic drugs, Antifungal antibiotics are not taken into study.

### 3.8 Data Collection
By a special self-prepared PROFORMA given above and IPC ADR form. (Indian pharmacopeia commission)

### 3.9 Datas Belongs To
- Patients Demography, addictions, habits
- Patients ward; unit etc.
- Diagnosis and condition of patient.
- Whether Microbiologic investigations, were done and confirmed prior to prescription.
- Whether prescriptions were for treatment or preoperative treatment or for prophylaxis.
- Single or multiple AMAs use.
- Logic behind AMAs prescription and combination.
- AMAs change after C/S.
- Patient’s compliance and result of treatment.
- ADRs if any.
- Death if any.

### 4. Observations
In my study tenure, I have come across many types of cases; here I have included only some cases that may give an idea about broadness of the study.

#### 4.1 ICU CASES
- Intestinal perforation----Enteric fever and Acute abdomen
- Sigmoid colon perforation----stabbing
- Post Laparotomy Chole-cystoscopy
- Hepatic Abscess, Septicemia, Acute intestinal obstruction
- Acc. intestinal obstruction in low condition
• COPD, ALD in low condition
• CVA, Hemiplegia in low condition
• Penetrating injury Abdomen
• Appendicitis with Hypothyroidism
• Necrotic Ankle with large abscess
• Acute Abdomen in low condition
• Acute pancreatitis
• Acute on chr. pancreatitis
• Perforation GI and Acute abdomen -in low condition
• Post Laparotomy Fever
• Dermoid cyst in polycystic ovarian syndrome
• OP poisoning in low condition----in shock
• Post abortion septicemia with MODS –3 multiple organ Dysfunction syndrome
• Brain malaria in shock and low condition
• Eclampsia, IUD, venereal sepsis
• Acute very severe Asthma in low condition
• CVA in Carcinoma GB
• Type 2 DMC with CAD
• Severe MS, severe TR, PAH
• Periampulary Carcinoma, whipple'spancreo-Duendenostomy
• Anti partum shock
• OGS in shock
• Acute pancreatitis in shock
• GB carcinoma in shock
• Rapture GB in shock
• AKD and CKD in low condition
• Iliac fossa Adenocar. Mass
• Gall stone with Aortic valve disease, Mild AR, AS
• Extra Hepatic Bile duct obstruction with Deep jaundice
• Ventral Hernia with Burst out Abdomen contents
• Fracture neck of Right Femur, CVA let Hemiplegia, metabolic-Encephalopathy, Septicemia, and Bedsore
• Acute pancreatitis— Pseudo cyst in low condition
• PERIAMPPULLARY carcinoma with Whipple pancreatico-duodenostomy
• Acute int. obstruction Volvulus with Ilio-sigmoid noting
• Hollow Visceral perforation at low condition, Modified Graham’s closure-
• Squamous cell carcinoma and Maxilo Facial surgery
• HTN with CVA, left Hemiplegia
• Head injury in low condition
• RTA Head injury---HTN
• RTA with multiple organ injury with multiple fracture
• Sudden onset of altered Sensorium and vomiting
• CLD –chr. liver disease
• Attempted suicide, partial hanging, severe hanging
• Acute COPD with type 2 DM , Empyema---corpulmunale
• Shock / sepsis-in low condition
• Type 2 DM with OHA induced Hypoglycemia
- Type 1 IDM with DKA
- Uncontrolled type 2 DM with Gluteal abscess with Septicemia.
- Myxedema coma and Thyroid storm.
- Snake bite in low condition
- Snake bite in shock and coma
- Alcohol with drawl in coma

Table: 1 Types of ICU Cases

<table>
<thead>
<tr>
<th>SL No</th>
<th>System</th>
<th>Types of diseases</th>
<th>Total No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CVS</td>
<td>HTN, MI, CCF, CAD etc</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>Metabolic disorder</td>
<td>DM, THYROID, OBESITY, CUSHING SYNDROME</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>Surgical</td>
<td>GI, LIVER, PANCREA surgery</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>Orthopedic &amp; RTA</td>
<td>----</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>Respiratory</td>
<td>PNEUMONIA, ASTHMA, COPD, LUNG SABSES</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>Shock</td>
<td>Due to many cause</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>Others</td>
<td>SNAKE BITE, ANEMIA, POISONING</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>O&amp;G</td>
<td>Eclampsia, Hemorrhage, Post operative</td>
<td>31</td>
</tr>
<tr>
<td>9</td>
<td>Carcinoma</td>
<td>Different type, Post operative</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>Total</td>
<td></td>
<td>500</td>
</tr>
</tbody>
</table>

![Chart 1: Showing ICU Cases of Different Departments](chart.png)

Table-2 Demographic Patterns

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of ICU Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below 16 Yrs</td>
<td>77</td>
</tr>
<tr>
<td>Above 16 Yrs</td>
<td>399</td>
</tr>
<tr>
<td>Above 65 Yrs</td>
<td>22</td>
</tr>
<tr>
<td>Above 75 Yrs</td>
<td>2</td>
</tr>
</tbody>
</table>
Chart-2: Showing Age Distribution of ICU Cases

Table-3: Sex Distribution of ICU Cases

<table>
<thead>
<tr>
<th>SEX</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALE</td>
<td>297</td>
</tr>
<tr>
<td>FEMALE</td>
<td>203</td>
</tr>
</tbody>
</table>
Chart-4: bar diagram showing education

Chart-5: showing income

Chart-6: showing--addiction & habituation
Table-4: Showing--Amas Used In Icu, Dose, Duration, Frequency, Most Used

<table>
<thead>
<tr>
<th>SL No.</th>
<th>AMA</th>
<th>Dose &amp; Route</th>
<th>% of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inj.PIPTAZ—Piperacillin+Tazobactam</td>
<td>4.5gm/ IV / TID</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>Inj.Cefoperazone+Sulbactum</td>
<td>1gm / IV /BD</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>Inj.Cefotaxime + Sulbactam</td>
<td>1.5gm /IV /BD</td>
<td>10%</td>
</tr>
<tr>
<td>4</td>
<td>Inj.Metronidazole</td>
<td>500gm /IV /TID</td>
<td>100%</td>
</tr>
<tr>
<td>5</td>
<td>Inj.Mikacin</td>
<td>500mg /I V /IM /BD</td>
<td>56%</td>
</tr>
<tr>
<td>6</td>
<td>Inj.Meropenim</td>
<td>1gm /IV/ TDS / in 100ml NS</td>
<td>10%</td>
</tr>
<tr>
<td>7</td>
<td>Inj. Linezolid</td>
<td>600mg /IV/BD</td>
<td>88%</td>
</tr>
<tr>
<td>8</td>
<td>Inj.Imipenim+ cillastatin</td>
<td>1gm/IV/TDS / In 100ml NS</td>
<td>30%</td>
</tr>
<tr>
<td>9</td>
<td>Inj.Teicoplanin</td>
<td>400mg in 100 ml NS / BD / OD</td>
<td>10%</td>
</tr>
<tr>
<td>10</td>
<td>Inj.Ofloxacin</td>
<td>200mg / IV /BD</td>
<td>17%</td>
</tr>
<tr>
<td>11</td>
<td>Inj.Ciprofloxacin</td>
<td>500mg / IV /BD</td>
<td>11%</td>
</tr>
<tr>
<td>12</td>
<td>Inj. Levofloxacin</td>
<td>500mg/ IV/OD/BD</td>
<td>3%</td>
</tr>
<tr>
<td>13</td>
<td>Inj.Moxifloxacin</td>
<td>400mg /OD/BD</td>
<td>9%</td>
</tr>
<tr>
<td>14</td>
<td>Inj.Ceftrixone + sulbactam</td>
<td>1.5gm /IV/BD</td>
<td>23%</td>
</tr>
<tr>
<td>15</td>
<td>Inj.Amoxiclav</td>
<td>1.2gm /IV /TDS in 100ml NS</td>
<td>7%</td>
</tr>
<tr>
<td>16</td>
<td>Inj.Vancomycin</td>
<td>1gm / IV /BD</td>
<td>1.7%</td>
</tr>
</tbody>
</table>
Chart- 8: Showing AMA Used In ICU

Chart-9: Base Line AMA In ICU
Next Line Additions to base line

Chart-10: showing--next line / 2\textsuperscript{nd}, 3\textsuperscript{rd}, 4\textsuperscript{th} additions
Chart-11: Drug Combinations
Chart-12: pie diagram showing—amas combination.

Chart-13: showing common amas used
5. Discussion

Part-(1) ama utilization pattern

(i) Study Data

Total duration of this study is 3 years and total patients covered as follows-
1. Treatment of infections at ICU : 500
2. Different types of cases handled in the study, only very precise data is given to cut short the voluminous expansion
3. Out of 500 patients included in this study—60%--Male and 40% Female.
4. Age—Maximum patients within > 18 yrs. and < 65 yrs.—80%-85%
5. Education—<HSC and HSC caters maximum patients, maximum number—Cultivators and laborers
6. Age is a vital parameter. In old age reduced GFR, Creatinine clearance, kidney size and mass, decreased nephrons warrants reduced dose of AMAs. Amino glycosides—ototoxicity, vertigo, nephrotoxicity is a better examples.

(ii) Types of AMAs Used

From the jungle of AMAs—Only a few groups of AMA are used to combat multi variety of infections—Amino penicillin’s—cloxacillin, Ampicillin, Older penicillin’s—penicillin-G, penicillin-V, and procaine and longacillins, sulfonamides, chloramphenicol, tetracycline’s, erythromycins, Roxithromycins, cephalaxin, cephadroxyl and many other are not in use, where as 2nd, 3rd, 4th and 5th generations cephalosporin’s, piperacillin penicillin’s, carbapenims, monobactams, fluoroquinolones, linezolid’s along with metronidazole are frequently used. Most used AMA—Beta-lactams. Carbapenim and Fluoroquinolones followed by.
The mostly used AMA—Beta- lactam, along with linezolid and metrogyl. Then Amino glycosides—Mostly Mikacin, Followed by Fluor quinolones.

(ii) Number Of AMAs Used
Average no. of AMA per prescriptions—MAXM—3drugs—61-87%, 4 drugs—37.68%, and 5 drugs--0.45%(< ½ % )(C-45)
- No patients with 1 drugs. No patients were without any AMA
- Route---all IV

Type II Supply Chain Management

Every ward of a 3tire institution like Medical colleges of state, along with other peripheral PHC and CHC, daily consume as many as AMAs and other drugs, surgical, chemicals for treatment. The on-duty head-staff nurse prepare daily indent and brings and enriches local departmental store from central store via a ward attendant. Thus she is responsible for maintaining a good ward-store, avoiding any shortfall in the store, maintaining a continuous supply and continuous procurement through indent.

Central store in turn managed by an old experienced pharmacist, often by a promoted ward attendant, who prepare daily, weekly, monthly indents and procure medicines from ware-house. Ware-houses are many—ware house of medical college hospital, ware house of sisu-bhaban, ware house of Acharya Harihar cancer institute, ware house of psychiatric.

SCB Medical College & Hospital Ware house in turn supplies drugs as per weekly, monthly indents to SPM Dept., PP Centre, and All Medical dept. In a ware-house M/ O –IC, along with 4-5 pharmacists and other clerical staffs maintain the store. They procure drugs and chemicals from SDMU—State drug management unit, situated at Capital of Odisha, BBSR—Bhubaneswar, via a yearly indent, also via mid-emergency indents.

6. Summary

There is significant burden of infectious diseases in India, for which selection of AMAs to prescribe to fight the battle, is a scientific and technical maneuver. AMAs are thus prescribed as per
1. Clinical judgment and investigations.
2. Microbiological information.
3. Pharmacological knowledge.

Thus criteria for rational drug prescription is essential and is on basis of
1. Appropriateness
2. Efficacy
3. Safety
4. Cost of therapy
5. Less or nil ADRs.

AMAs are very precious, amongst drugs- ---so need of hour to rationalize use of AMAs, in interest of science, future community.
1. Limited resources of AMAs.
2. Only few drugs are in pipeline
3. TEIXOBACTIN—is the only AMA developed in last 3 decades.

**Conclusion**

This study highlighted the fact that poly pharmacy practice and multiple AMA combinations in prescription is notable higher in Tertiary care hospitals and use of these in Empirical way mostly. To prevent antimicrobial resistance, rationale use of antimicrobials is a must. The concept of antimicrobial for every patient should be eradicated. Antimicrobial policy should be developed and it must be ensured that it is implemented. Antimicrobial policy should be developed for every unit, ward, including ICU, operation theatre and regular monitoring should be done to ensure that antimicrobial policy is strictly implemented. Emphasis should be made on the use of drugs from the essential medicines list, and such list should be readily available in the ICU. Rotation therapy of antimicrobials should be followed to deal with the problem of resistance, restricting the drug formulary can also help in reducing antimicrobial resistance. Empirical therapy should be used only in an emergency and should be guided by the antimicrobial policy of the hospital, common causative organisms of nosocomial infection and local resistance pattern. These steps will ensure rational prescribing of antimicrobial agents and also decrease the risk of development of resistance to antimicrobial agents. The hospital staff should regularly be made aware of recent updates, changing patterns of resistance, and availability of new antimicrobials. The presence of a clinical pharmacologist in every ICU setup will ensure rational use of antimicrobials in a cost effective manner. The antimicrobial stewardship program is a must for every hospital and it should seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce the costs of health care for infections, and limit the selection for antimicrobial resistant strains.

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