PREScribing PATTERN AND USE OF ANTIBIOTICS AND COMBINATION OF ANTIBIOTICS IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT
Antibiotics are most extensively used drugs in hospitals. The approach of the study is to decrease the adverse drug reactions, compare cost effectiveness of the drugs, to decrease drug resistance of the drugs and to reduce the medication errors in the prescriptions. The major antibiotic group which were used to treat the antibiotics are mentioned. Wide ranges of antibiotics are available to treat various types of infections. Though the choice of antibiotics prescribed depends upon the clinical interest, culture sensitivity, age and gender, their extensive use, may lead to the poor therapeutic outcome in terms both health and economic conditions. The present study was conducted over a period of 8 months i.e. from July 2013 to February 2014 in tertiary care teaching hospital. The research summarized a total of 250 cases were reviewed to evaluate the prescribing pattern of antibiotics in the treatment of various types of infection. The result was found that majority of the patients were treated with Quinolones (36.55%), the major route of drug administration employed was oral route. Excessive and inappropriate use of antibiotics contributes to the development of bacterial resistance. This study was carried out to collect relevant demographic information and antibiotics prescribing patterns. 250 patients were prescribed antibiotics; 128 were male (51.2%) and 122 were females (48.8%). Median duration of hospitalization was 10 days. 390 antibiotics were prescribed. The most common were ciprofloxacin, amoxicillin, metronidazole, ampicillin, aminoglycosides, macrolide antibiotics, cephalosporin and sulphonamides. Antibiotic resistance is becoming a problem in the general medicine ward. The strategies required to prevent antibiotic resistance are as follows: Formulation of a policy for hospital antibiotic use, educational programmes should be conducted for patients and health care providers. Patient counseling is required for proper use of antibiotics, culture sensitivity tests should be conducted before prescribing antibiotics.

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INTRODUCTION
Infections are very common and responsible for a large number of diseases adversely affecting human health. Most of the infectious diseases are caused by bacteria can be prevented, managed and treated through anti-bacterial group of compounds known as antibiotics. The most common use of cephalosporins and metronidazole seems to be effective in reducing the surgical site infection and other complications.1

DEFINITION
Antibiotics can be defined as the variety of substances produced by or derived from certain fungi, bacteria, and other organisms, that can destroy or inhibit the growth of other microorganisms. Antibiotics are widely used in the prevention and treatment of infectious diseases.

HISTORY OF ANTIBIOTICS
During ancient times:
• Greeks and Indians used moulds and other plants to treat infections.
• In Greece and Serbia, mouldy bread was traditionally used to treat wounds and infections.
• Warm soil was used in Russia to cure infected wounds.
• Sumerian doctors gave patients beer soup mixed with turtle shells and snake skins to their sick patients.
• Babylonian doctors healed the eyes using a mixture of frog bile and sour milk.
• Sri Lankan army used oil cake (sweet meat) to server both as desiccant and antibacterial.
(www.experiment-resources .com)

SIR ALEXANDER FLEMING
Sir Alexander Fleming, a Scottish biologist, defined new horizons for modern antibiotics with his discoveries of enzyme lysozyme (1921) and the antibiotic substance penicillin (1928). The discovery of penicillin from the fungus Penicillium notatum perfected the treatment of bacterial infections such as syphilis, gangrene and tuberculosis. He also contributed immensely towards medical sciences with his writings on the subjects of bacteriology, immunology and chemotherapy.

CLASSIFICATION OF ANTIBIOTICS
Most classes of antibiotics, including the β-lactam antibiotics, tetracycline’s, amino glycosides, and macrolides were originally derived from natural sources, and are now further chemically modified to confer better properties on the drug.

However, some important classes of antibiotics (including the sulpha antibiotics, the quinolones, and the oxazolidinones) are derived from synthetic chemical sources(Greenwood .D et al., 2002).

CLASSIFICATION OF ANTIBIOTICS

<table>
<thead>
<tr>
<th>S.No</th>
<th>CLASSES</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>β-Lactam antibiotics</td>
<td>Penicillin (e.g. Amoxicillin), cephalosporin, monobactams, etc.</td>
</tr>
<tr>
<td>2</td>
<td>Tetracyclines</td>
<td>Tetracycline, etc.</td>
</tr>
<tr>
<td>3</td>
<td>Macrolide antibiotics</td>
<td>Erythromycin, etc.</td>
</tr>
<tr>
<td>4</td>
<td>Aminoglycosides</td>
<td>Gentamycin, Tobramycin, Amikacin</td>
</tr>
<tr>
<td>5</td>
<td>Quinolones</td>
<td>Ciprofloxacin, levofloxacin</td>
</tr>
<tr>
<td>6</td>
<td>Cyclic peptides</td>
<td>Vancomycin, Streptogramins, Polymyxins</td>
</tr>
<tr>
<td>7</td>
<td>Lincosamides</td>
<td>Clindamycin, etc.</td>
</tr>
<tr>
<td>8</td>
<td>Oxazolidinones</td>
<td>Linezolid (Zyvox), etc.</td>
</tr>
<tr>
<td>9</td>
<td>Sulpha antibiotics</td>
<td>Sulfisoxazole, etc.</td>
</tr>
</tbody>
</table>

(Antibiotics by V.K Ahluwalia., 2009)

LIST OF COMMON CAUSATIVE MICRO-ORGANISMS

❖ E.coli.
❖ Klebsiella.
❖ Staphylococcus auerus.
❖ Pseudomonas.
### COMMON LIST OF ANTIBIOTICS:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of administration</th>
<th>Dose and frequency of administration</th>
<th>Contra indications/caution</th>
<th>Interactions</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Intramuscular, Intravenous</td>
<td>10-20 L Units every 2 to 6 hrs.</td>
<td>Hypersensitivity</td>
<td>None significant</td>
<td>Hypersensitivity- rashes, anaphylaxis, fever, joint pains, angioedema, serum sickness like reaction, blood disorders, CNS toxicity in high doses; colitis and diarrhoea; ampicillin rashes are more common in infectious mononucleosis, chronic lymphatic leukemia and HIV infection.</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>Oral</td>
<td>400-800 mg every 6-8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Oral, intravenous</td>
<td>New born (&lt;1 wk): 25-50 mg/kg 12 hrly1-4 wks: 100-200 mg/kg/day 8-hrly Older children: Same dose 6 hourly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>Oral, intravenous</td>
<td>Intravenous Children: 50-100 mg/kg in 3-4 doses.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cephalexin (1\textsuperscript{st} gen.)</td>
<td>Oral</td>
<td>250mg-1 g every 6 hours</td>
<td>Hypersensitivity, renal failure, porphyria</td>
<td>Hypersensitivity rashes, joint pains, rarely anaphylaxis; abdominal discomfort; colitis; erythema multiforme; reversible interstitial nephritis; transient hepatitis; blood disorders; dizziness etc.</td>
<td></td>
</tr>
<tr>
<td>Cefazolin (1\textsuperscript{st} gen.)</td>
<td>Intravenous</td>
<td>1-1.5 g every 6 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefuroxime (2\textsuperscript{nd} gen)</td>
<td>Oral, Intravenous, oral (axetil)</td>
<td>1 g every 12 hours Up to 3 g every 8 hours i.v. 250-500 mg 12 hourly oral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime (3\textsuperscript{rd} gen.)</td>
<td>Intravenous</td>
<td>1-2 g every 4-8 hours.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone (3\textsuperscript{rd} gen.)</td>
<td>Intravenous</td>
<td>1-2 g every 12-24 hours.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftazidime (3\textsuperscript{rd} gen., anti pseudomonal)</td>
<td>Intravenous</td>
<td>1-2 g every 8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Intramuscular, intravenous</td>
<td>Adults: 2 mg/kg loading dose, then 3-5 mg/kg per day, every 8 hours Age &lt; 2 yrs: 2-2.5 mg/kg every 8 hrs.</td>
<td>Renal failure; myasthenia gravis;</td>
<td>Ototoxicity may worsen with potentially ototoxic diuretics like furescemide</td>
<td>Ototoxicity, nephrotoxicity, more common in the elderly and in renal failure; may impair neuromuscular transmission and may cause transient myasthenia</td>
</tr>
<tr>
<td>Amikacin</td>
<td>Intramuscular, intravenous</td>
<td>15 mg/kg/day in 2-3 equally divided doses</td>
<td></td>
<td>Antacids reduce</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Oral</td>
<td>Children &gt;8 years: 25-</td>
<td>Pregnancy,</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>Oral: 50 mg/kg/day in 2-4 doses. Adults: 1-2 g/day in 2-4 doses.</td>
<td>Lactation; renal impairment; children below 8 years. Absorption; anticonvulsants increase metabolism of doxycycline, calcium salts, oral iron and zinc reduce absorption; sucralfate and bismuth salts reduce absorption</td>
<td>Nausea, vomiting, diarrhea; erythema (discontinue); benign intracranial hypertension; colitis</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Oral: 100 mg twice daily on the first day, then 100 mg once or twice a day depending on the severity of infection</td>
<td>Hepatic and renal impairment; prolonged QT interval; porphyria; estolate in liver disease</td>
<td>Avoid use with astemizole, terfenadine, pimozide, midazolam, cisapride, cimapride; increases theophylline levels</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>Oral: 400 mg twice daily for 3-7 days for UTI; Age less than 18 years; pregnancy and lactation; epilepsy; hepatic and renal impairment</td>
<td>Increased risk of convulsions with NSAIDs; antacids reduce absorption; anticoagulant effects of coumarins enhanced; iron and zinc reduce absorption; increases levels of theophylline, avoid concomitant use.</td>
<td>Nausea, vomiting, diarrhea, headache, dizziness, sleep disorders, rash, pruritus, anaphylaxis, increase in urea, creatinine and liver enzymes, arthralgia and myalgia, blood disorders, restlessness, hallucinations, depression, tendon damage</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Oral: UTI: 250-500 mg twice daily; LRTI: 500-750 mg twice a day; Intravenous: 200-400 mg over 30-60 minutes, twice a day</td>
<td>Hepatic and renal impairment; blood disorders; G6PD deficiency; breast feeding</td>
<td>Enhanced effects of warfarin, sulfonylureas, phenytoin</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>Oral: Children: 120-480 mg 12 hourly</td>
<td>Hepatic and renal impairment; blood disorders; G6PD deficiency; breast feeding</td>
<td>Enhanced effects of warfarin, sulfonylureas, phenytoin</td>
</tr>
</tbody>
</table>

**ANTIBIOTICS RESISTANCE**

Antimicrobial resistance (AMR) - the ability of micro-organisms to find ways to evade the action of the drugs used to cure the infections they cause and is increasingly recognised as a global public health issue which could hamper the control of many infectious diseases. Some bacteria have developed mechanisms which render them resistant to many of the antibiotics normally used for their treatment (multi-drug resistant bacteria), so pose particular difficulties, as there may be few or no alternative options for therapy. They constitute a growing and global public health problem. WHO suggests that countries should be prepared to implement hospital infection control measures to limit the spread of multi-drug resistant strains and to reinforce national policy on prudent use of antibiotics, reducing the generation of antibiotic resistant bacteria.

An article published in The Lancet Infectious Diseases on 11 August 2010 identified a new gene that enables some types of bacteria to be highly resistant to almost all antibiotics. The article has drawn attention to the issue of AMR and in particular, has raised awareness of infections caused by multi-drug resistant bacteria.

WHO strongly recommends that governments focus control and prevention efforts in four main areas:

- Surveillance for antimicrobial resistance;
- Rational antibiotic use, including education of healthcare workers and the public in the appropriate use of antibiotics;
- Introducing or enforcing legislation related to stopping the selling of antibiotics without prescription; and
- Strict adherence to infection prevention and control measures, including the use of hand-washing measures, particularly in healthcare facilities.
CULTURE SENSITIVITY TEST

Bacteria are a common cause of infection in both community and hospital setting, and can cause infection in patients with normal or suppressed immune systems. In case of suspected infection, appropriate culture specimen should be obtained for laboratory testing (if possible) from the suspected site of infection before antibiotics are initiated in an attempt to isolate and identify the causative pathogen. Special attention should be placed on specimen collection and timely transport to the laboratory since the accuracy of the result will be limited by the quality and condition of the submitted specimen. Identification of bacteria includes direct microscopic examination using specialized stains (Gram staining) and growth of the micro-organism using culture techniques. Once bacteria grow in culture, the organism is identified and antimicrobial susceptibility testing methods are performed to determine the susceptibility of the infecting organism to various antibiotics.

IMPORTANCE OF RATIONAL USE OF ANTIBIOTICS

The aim of any medicine management system is to deliver the right medicine to the patient who needs the medicine. The steps of selection, procurement, and distribution are necessary precursors to the rational use of medicines.

The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational use as follows:

“The rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.”

The requirements of the rational use of medicines can be fulfilled only if the process of both prescribing and dispensing is appropriately followed. This includes steps concerned with proper diagnosis, correct prescribing, dispensing, and giving proper information to the patient. In this module, we shall focus on the role of a pharmacist in promoting the rational use of medicines.

Study methodology:

Objectives:
To assess the prescribing habits of antibiotics used in a tertiary care teaching hospital.

Specific objectives:
(a) To enhance the quality use of antibiotics.
(b) To promote the cost effective use of antibiotics
(c) To minimize the risk of adverse drug reactions.
(d) To improve the patient care.
(e) To reduce the drug resistance.
(f) Obtain information on the antibiotic prescribing pattern and the disease conditions for which antibiotics were prescribed.

Study site:
The study was conducted in a tertiary teaching hospital.

Source of data:
Prescriptions and treatment charts of patients admitted in various wards of tertiary teaching hospital.

Method of collection:
The study includes both retrospective and prospective treatment chart review. It was conducted over a period of 8 months (July 2013 to February 2014).

Those patients who met study criteria were identified from inpatients wards and outpatient departments. Data of the patients were collected from medical record section and medicine department.

A suitable data collection form was designed for the data collection. A total of 250 cases with a diagnosis of infections were reviewed for data collection. The Antibiotics data collected from the period of JULY 2013 to FEBRUARY 2014. Data is collected from various infections of inpatients and out patient’s diagnosis.

Patient’s demographic characters:

A total of 250 patients were treated with antibiotics for various types of infections. The mean age of the patient was found to be 34.25±20.16 years ranging from 1 to 60 years. The number of patients were maximum from middle aged group(16-35years) which accounts for 49.6% of patients ,the 250 of patients 36-58 (31.6%) and 59(5.6%) were male and female patients respectively. Male patients 128(51.2% and females 122(48.8%) including children.

The patients demographic data, different types of infections, classes, subclasses of antibiotics used in infections, mode of administration, patient receiving parenteral, oral, both parenteral and oral antibiotic therapy, patients receiving mono therapy and combination therapy.
PERCENTAGE NO. OF PRESCRIPTIONS BASED ON TYPE OF DIAGNOSIS:
The total 250 patients were treated with antibiotics for various types of infections. From that diseases data major number of patients suffered from viral fever (25.2%) and respiratory tract infections (9.6%). In this data collection diseases are mainly seasonal disease or infections.

Figure-1: Patients Demographic Characters Based On Age.

Figure-2: Percentage number of prescriptions based on type of diagnosis.

Figure-3: Number of antibiotics prescribed in each prescription and number of patients.

Number of antibiotics prescribed in each prescription:
In this survey single antibiotics (50.4%) is prescribed in more prescriptions, medium number of prescriptions have two (28.8%), Three (16.8%) types of antibiotics and five types of antibiotics (8%) are prescribed in very less number of prescriptions based on diseased state of patient.

### Table-2: Different Combinations of Antibiotics Used.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Type of combination</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aminoglycosides+Nitroimidazoles</td>
<td>1(0.9)</td>
</tr>
<tr>
<td>2</td>
<td>Quinolones +Nitroimidazoles</td>
<td>12(11.1)</td>
</tr>
<tr>
<td>3</td>
<td>Quinolones + Amino glycosides</td>
<td>12(11.1)</td>
</tr>
<tr>
<td>4</td>
<td>β-lactams + Quinolones</td>
<td>14(12.9)</td>
</tr>
<tr>
<td>5</td>
<td>Sulphonamides + Quinolones</td>
<td>7(6.5)</td>
</tr>
<tr>
<td>6</td>
<td>Nitroimidazoles + Quinolones</td>
<td>12(11.1)</td>
</tr>
<tr>
<td>7</td>
<td>Amino glycosides + Sulphonamides</td>
<td>4(3.7)</td>
</tr>
<tr>
<td>8</td>
<td>β-lactams + Sulphonamides</td>
<td>4(3.7)</td>
</tr>
<tr>
<td>9</td>
<td>β-lactams + Nitroimidazoles</td>
<td>3(2.8)</td>
</tr>
<tr>
<td>10</td>
<td>Nitroimidazoles + Nitrofurans</td>
<td>6(5.5)</td>
</tr>
<tr>
<td>11</td>
<td>Quinolones + Nitrobenzenes</td>
<td>2(1.8)</td>
</tr>
<tr>
<td>12</td>
<td>β-lactams + Macrolides</td>
<td>1(0.9)</td>
</tr>
<tr>
<td>13</td>
<td>Macrolides + Lincosamides + Amides</td>
<td>1(0.9)</td>
</tr>
<tr>
<td>14</td>
<td>β-lactams + Sulphonamides + Quinolones</td>
<td>9(8.3)</td>
</tr>
<tr>
<td>15</td>
<td>Nitroimidazoles + Quinolones + Aminoglycosides</td>
<td>14(12.9)</td>
</tr>
<tr>
<td>16</td>
<td>Nitroimidazoles + Quinolones + β-Lactams</td>
<td>4(3.7)</td>
</tr>
<tr>
<td>17</td>
<td>Macrolides + Lincosamides + Amides + Sulphonamides</td>
<td>2(1.8)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>108(100%)</strong></td>
</tr>
</tbody>
</table>

**Antibiotics used:**

Majority (36.55%) of the patients were treated with Quinolones of the 250 patients. Ampicillin 250mg prescribed in such doses not achieved required therapeutic concentrations hence it would be a better choice to use either of these drugs alone containing 500mg.

The majority of infections were treated with Quinolones. Quinolones were used in patients below 13 years of age since these classes of drugs are contraindicated to the paediatric population as they may cause musculoskeletal disorders. Combination therapy also used to cure the infections. Quinolones are widely used in combination therapy.

**Combination of Quinolones:**

Quinolones - Amino glycosides (12.9%), Quinolone-sulphonamides (12.9%), Quinolones - Nitroimidazoles (11.1%), Quinolones - β-lactam antibiotics (12.9%) and Quinolones - Nitrobenzene (1.8%). Data collected for treatment of infections contains mostly the drug combination, but also three drug combinations and four drug combinations are used.

![Figure-6: Mode Of Drug Administration Based On Diseases](image)

**Mode of administration:**

Mainly the drugs are administered by Oral route and parenteral routes. Oral route of administration is more preferable route of administration. But in children’s and unconscious patients this route of administration is difficult. Parenteral route of administration is less preferred when compared to oral route of administration. As the parental formulations of antibiotics are less stable. They are prepared in powder form and converted into liquid fousing water for injection at the time of administration. Total number of drugs...
administration through oral route of administration is 69% and parenteral route of administration is 28%. Some times both oral and parenteral therapy is used (2.8%) but this type of administration is less observed.

Mode of administration is based on infections:

In majority of the infections, Oral route is major route and parenteral route is minor route. Fever- oral route (51%), parenteral route (19.6%), Respiratory infection- oral route- (85%) Parenteral route- (8.5%), GI infection- oral route- (63%), parenteral route- (10.56%). In some cases only oral route is used

- Urinary tract infection,
- Toothache.

Only parenteral route of administration is used in treatment of Tubectomy. In some cases, oral and parenteral route are used together for the treatment of infection.

Summary and Conclusion:

Development of microbial resistance to antibiotics is inevitable. However, it can be delayed through their appropriate use. Overuse, underuse and unnecessary use of antibiotics often results in development of resistance towards antibiotics. There are various factors contributing towards inappropriate use of antibiotics. The factors may be related to patients, health care persons as well as society. The appropriate use of antibiotics delays the development of drug resistance by microorganisms. Antibiotics are overused, particularly for minor infections, misused for self-limiting viral infections and underused due to financial concerns.

In this project an attempt was made to study the antibiotics prescribing pattern in tertiary teaching Hospital. The study was conducted for a period of eight months. A thorough literature survey was done on the area of project to review the past work. Past knowledge was utilized in designing the present study and compare the results of the present studies with those of the past studies. The study methodology involved the following steps – i). Data collection form, ii). Prescription analysis, iii). Culture sensitivity test, iv). Disease pattern. In this study, majority of prescriptions were collected from out patients 175(70%) when compared to in patients 75(30%).When prescriptions of male patients were compared with female patients, it showed that male’s prescriptions contained more antibiotics, than female patients. Majority of patients were treated with Quinolones. In combination therapy too, Quinolones were widely used when compared to other combinations of antibiotics. From the diseases data, major number of patients suffered from viral fever (25.2%) and respiratory tract infections (9.6%). In majority of the infections, Oral route is major route and parenteral route is minor route.

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