Original article

Antimicrobial utilization study in the patient setting of tertiary care teaching hospital in western Maharashtra, India

Rajendra B. Pawade[1], Rahul R. Kunkulol,[2] Nilam S. Kute[3]

[1]Assistant Professor, [2]Associate Professor, Dept. of Pharmacology, [3]Tutor, Dept. of Biochemistry, Rural Medical college of Pravara Institute of Medical Sciences (Deemed University), Loni, Maharashtra, India

Correspondence author: Dr. Rajendra B. Pawade

Abstract:

Objectives: The study was done to find out antibiotic use in common infective diseases.

Methods: The data for this retrospective study was collected from record department of patients suffered from common infections which were admitted in medicine ward of Pravara Rural Hospital, Loni, India from period January 2003 to December 2006. The data was collected and analyzed for use of antimicrobial agents before and after culture and sensitivity test. Collected data was tabulated for common infective diseases, causative microorganisms, number of antibiotics given per patient, percentage number of antibiotic prescription before culture and sensitivity test and percentage number of antibiotics prescription changed after culture and sensitivity test and 'P' value detected by applying 'Z' test.

Results: The most common infective illness found were septicemia, UTI, acute gastroenteritis, enteric fever. Antibiotic prescription before and after culture and sensitivity test showed, 57% of antibiotic prescriptions were changed after availabity of culture and sensitivity report, in septicemia patients, 28% in UTI, 33% in acute gastroenteritis, 11% enteric fever. The difference in empirical therapy before culture and sensitivity test and changes in antibiotic prescription after culture and sensitivity were nonsignificant after applying 'Z' test.

Key words: Antimicrobial agents, Antibiotic prescription, Drug resistance

Introduction:

Quality of life can be improved by enhancing the standards of medical treatment at all levels of health are delivery system. "Survival of the fittest" holds good for human beings and animals as also for bacteria. A majority of bacteria in nature are nonpathogenic, a large number of them, live as commensals on our body leading a symbiotic existence. A limited population of bacteria which has become pathogenic was also sensitive to antibiotics to begin with. It is the man made antibiotic pressure, which has led to the emergence and spread of resistant genes amongst bacteria. Despite the availability of large arsenal of antibiotics, the ability of bacteria to become resistant to antibacterial agents is amazing. This is more evident in the hospital settings where the antibiotic usage is maximum. The major reasons for inappropriate use of antibiotics are due to lack of uniform policy and disregard to hospital infection control practices. Despite advancement in medical technology for diagnosis and patient care, a person can still die of infection caused by multi-drug resistant bacteria. It is time to think, plan and formulate a strong antibiotic policy to address the burgeoning hospital infection[1]

More than 90 percent of the deaths from infectious diseases worldwide are caused by only a handful of infectious diseases. These diseases - lower respiratory infections, HIV/AIDS, diarrheal diseases, tuberculosis, malaria and measles, and, while not major killers, a number of the world's 'neglected' infectious diseases such as lymphatic filariasis, trachoma, intestinal parasites, leprosy and

onchocerciasis cause chronic disability and stigma for millions.[2]

Illness and death from infectious diseases are particularly tragic because they are largely preventable and treatable. 10 % of world's population accounted for more than 40% of deaths to infectious deaths due to infectious diseases.[2]

Ideally, before beginning antibiotic therapy, the suspected areas of infection should be cultured to identify the causative organism and potential antibiotic susceptibities. Antibiotics are used in two general ways as empirical therapy and as definitive therapy. When used as empirical therapy, or initial, therapy, the antibiotic must "Cover" all of the likely pathogens, since the infecting organism(s) has not yet been defined .Combination therapy or treatment with a single broad-spectrum agent often is employed. However, once the infecting microorganism is identified, definitive antimicrobial therapy should be instituted – a narrow spectrum, low – toxicity regimen to complete the course of treatment.[3]

Optimal and judicious selection of antimicrobial agents for the therapy of infectious diseases requires clinical judgment and detailed knowledge of pharmacological and microbiological factors. Unfortunately, the decision to use antibiotics frequently is made lightly, without regard to the potential infecting microorganism or to the pharmacological features of the drug.[3]

Excessive & inappropriate use of antibiotics contributes to development of bacterial resistance.[4] However, there are also reports of an irrational use of antibiotics which may even lead to infections that are worse than the originally diagnosed ones.[5,6] A vast majority of physicians (97%) believed that widespread and inappropriate use of antimicrobials was an important cause of resistance.[7] The rising incidence of bacterial resistance to common antibiotics has prompted the need to use the antibiotics judiciously in the practice.[8] The main challenges in prescription of antibiotics are to achieve a rational choice and appropriate use of antibiotics and to recognize their potential problems.[8] The main challenges in prescription of antibiotics are to achieve a rational choice and appropriate use of antibiotics and to recognize their potential problems.[9]

Misuses of Antibiotics[10]

Organizations such as the Centers for Disease Control and Prevention have outlined a number of steps to optimize the use of antimicrobial agents and to prevent drug resistance and the transmission ofinfections.

Treatment of Nonresponsive Infections- A common misuse of these agents is in infections that have been proved by experimental and clinical observation to be nonresponsive to treatment with antimicrobial agents. Most of the diseases caused by viruses are self-limited and do not respond to any of the currently available anti-infective compounds. Thus, antimicrobial therapy of measles, mumps, and at least 90% of infections of the upper respiratory tract and many GI infections is ineffective and therefore useless.

Therapy of Fever of Unknown Origin- Fever of undetermined cause may persist for only a few days to a week or for a longer period. Both of these are treated frequently and inappropriately with empirical antimicrobial agents. Fever of short duration, in the absence of localizing signs, probably is associated with undefined viral infections. Antimicrobial therapy is unnecessary, and resolution of fever occurs spontaneously within a week or less. Fever persisting for 2 or more weeks, commonly referred to as fever of unknown origin, has a variety of causes, of which only about one-quarter are infections. Some of these infections (e.g., tuberculosis or disseminated fungal infections) may require treatment with

antimicrobial agents that are not used commonly for bacterial infections. Others, such as occult abscesses, may require surgical drainage or prolonged courses of pathogen-specific therapy, as in the case of bacterial endocarditis. Inappropriately administered antimicrobial therapy may mask an underlying infection, delay the diagnosis, and by rendering cultures negative, prevent identification of the infectious pathogen. Noninfectious causes, including regional enteritis, lymphoma, renal cell carcinoma, hepatitis, collagen-vascular disorders, and drug fever, do not respond to antimicrobial agents at all. Rather than embarking on a course of empirical antimicrobial therapy for fever of unknown origin, the physician should search for its cause.

Improper Dosage - Dosing errors, which can be the wrong frequency of administration or the use of either an excessive or a sub therapeutic dose, are common. Although antimicrobial drugs are among the safest and least toxic of drugs used in medical practice, excessive amounts can result in significant toxicities, including seizures (e.g., penicillin), vestibular damage (e.g., aminoglycosides), and renal failure (e.g., aminoglycosides), especially in patients with impaired drug excretion or metabolism.

Inappropriate Reliance on Chemotherapy Alone- Infections complicated by abscess formation, the presence of necrotic tissue, or the presence of a foreign body often cannot be cured by antimicrobial therapy alone. Drainage, debridement, and removal of the foreign body are at least as important as the choice of antimicrobial agent. For example, the patient with pneumonia and emphysema often fails to be cured even with administration of large doses of an effective drug unless the infected pleural fluid is drained. The patient with S. aureus bacteremia owing to an intravascular device will continue to have fevers and positive blood cultures and is at risk of dying unless the device is removed. As a general rule, when an appreciable quantity of pus, necrotic tissue, or a foreign body is present, the most effective treatment is an antimicrobial agent given in adequate dose plus a properly performed surgical procedure.

Lack of Adequate Bacteriological Information- Antimicrobial therapy administered to hospitalized patients too often is given in the absence of supporting microbiological data. Bacterial cultures and Gram stains of infected material are obtained too infrequently, and the results, when available, often are disregarded in the selection and application of drug therapy. Frequent use of drug combinations or drugs with the broadest spectra is a cover for diagnostic imprecision. The agents are selected more likely by habit than for specific indications, and the dosages employed are routine rather than individualized on the basis of the clinical situation, microbiological information, and the pharmacological considerations presented in this and subsequent chapters of this section.

Objectives:

The objectives of the study were to evaluate-

- Selection of antibiotic/s prior to culture and sensitivity testing.
- Change in antibiotic prescription after availability of culture and sensitivity report.
- To find out the rationale (or lack of it) of antibiotic usage in Pravara Rural Hospital, Loni.

Material and Methods:

The data of patients suffering from common infective illness (i.e. disease occurrence more than 3% in total collected data.) admitted under Medicine Dept. of Pravara Rural Hospital, Loni, Maharashtra, India during the period between January 2003 to December 2006 was collected for this retrospective study. It was found that 1667 patients of infective illness were admitted whose

antibiotic sensitivity test was done. Out of 1667 patients 1197 patients suffered from common infective illness.

Inclusion criteria-

1. All patients of either sex suffering from infective illness.
2. Patients irrespective of antibiotic/s prescribed before culture & sensitivity test.
3. Patients with infective illness irrespective of nature of illness (i.e. mild, moderate or severe).
4. Diseases caused by only bacterial infections, confirmed on the basis of organisms isolated in culture &sensitivity test.

Exclusion criteria-

1. Patients suffering from other concomitant illness with infective disease.
2. Infective diseases caused by viruses, fungi, parasites.
3. Infective illness occurring less than 3% of total samples.
4. Pregnant women suffering from infective illness.

The data was collected in following protocol format.

1. Patient's serial no.
2. Age in years / months.
3. Sex.
4. Clinical diagnosis.
5. Nature of illness –Mild, Moderate and Severe
6. Nature of sample for culture and sensitivity.
7. Name, dose, route of administration, frequency, duration of antibiotic prescribed, and administered before sending the sample for culture and sensitivity test.
8. Culture and sensitivity report. - Organism/s present in culture.
   Sensitivity pattern- Sensitive
   -Resistant. (Intermediate sensitive included in resistant)
9. Any change in clinical diagnosis.
10. Name, dose, route of administration, frequency, duration of antibiotic prescribed and administered after receiving the culture and sensitivity test report.

'Z' test of difference between two proportions was applied to analyze the data scientifically. The data was also be subjected to evaluation regarding selection of antibiotic prior to culture and sensitivity testing, change in the antibiotic prescription after the availability of culture and sensitivity report.

Results:

Table 1: Disease pattern of patients of infective illness admitted under medicine department during period of January 2003 to December 2006 (Whose antibiotic sensitivity test/s done)

Diseases	Number of patients
Septicemia	372
Urinary tract infection	247
Acute gastroenteritis	217
Enteric fever	160
Bronchopneumonia	98
Rheumatic heart disease	56
Meningities	47
Other diseases	470

(Tuberculosis, Upper respiratory tract infection, etc.)	
Total	1667
Therefore total sample size was 1197 i.e. excluding other diseases.	

Table 2: Abbreviations used for antimicrobials used in patients

Ca-ceftazidime	A-ampicillin	Cj-cefaclor	Nx- norfloxacine
Cf- ciprofloxacin	G-gentamycine	Cp-cephalexine	E-erythromycin
Co-cotrimoxazole	P-penicillin	C-choramphenicol	--
Cx-cloxacillin	Ce-cephotaxime	Ak-amikacin	--

Table 3: shows frequency (%) of individual antibiotic for specific diagnosis before culture and sensitivity test

Diagnosis	**Cf.**	**Nx.**	**C.**	**Ca.**	**G./Ak.**	**Cp.**	**A+Cx**	**Cx**	**P**	**Ce.**	**Others**
Septicemia	11	12	09	09	10	08	08	07	10	09	08
U.T. I.	08	09	12	07	11	09	10	08	09	10	08
Acute GE	10	11	09	11	09	10	09	09	10	06	06
Enteric fever	08	10	06	08	12	13	10	07	07	12	07
Bronchopneumonia	05	12	11	09	11	10	10	07	10	12	03
RHD	06	12	12	06	10	09	11	09	09	10	06
Meningitis	09	11	07	07	14	10	07	09	07	15	05

Table 4: shows frequency (%) of individual antibiotic for specific diagnosis after culture and sensitivity test

Diagnosis	**Cf.**	**Nx.**	**C.**	**Ca.**	**G./Ak.**	**Cp.**	**A+Cx**	**Cx**	**P**	**Ce.**	**Others**
Septicemia	18	14	18	15	05	05	05	05	05	05	05
U.T. I.	12	25	12	14	05	06	04	07	04	07	05
Acute GE	15	17	12	07	15	14	06	05	05	02	02
Enteric fever	10	20	10	08	05	04	04	15	15	04	05
Bronchopneumonia	09	08	09	16	05	05	20	15	02	02	08
RHD	10	03	03	10	07	16	27	15	03	03	03
Meningitis	07	03	06	08	05	20	15	20	06	05	05

Table 5: Antibiotic prescription pattern before & after culture and sensitivity test

Diseases	% of antibiotic prescriptions		
	Before culture & sensitivity report (Empirical antibiotic therapy)	unchanged after culture & sensitivity report 3	Changed after culture & sensitivity report
Septicemia	97	68	29
UTI	92	64	28
Acute gastroenteritis	87	54	33
Enteric fever	89	78	11
Bronchopneumonia	91	62	29
RHD	83	66	17
Meningitis	63	29	38

Table 6: Antibiotics prescribed during hospital stay

Name of antibiotics	No. of prescriptions (%)
Ampicillin	86 (24.8)
Amoxicillin	58 (16.7)
Metronidazole	46 (13.2)
Ciprofloxacin	40 (11.5)
Crystalline penicillin	28 (8.1)
Others	89 (25.7)
Total	345 (100)

Table 7: No of antimicrobials per patient

No. of antimicrobials	No. of patients who received antimicrobials	Percentage
1-2	843	70.42
3-5	305	25.52
>5	49	04.06

Table 8: Duration of Hospital stay

Duration of hospital stay in days	No. of patients	Percentage
1-5	473	39.47
6-10	582	48.58
11-15	102	08.63
>15	40	03.32

Discussion:

In the present study, 1197 patients suffered from infective illness whose incidence was more than 3%. The most common infective illness in Pravara Rural Hospital was septicemia (31.05%). The other common infective diseases were urinary tract infection (20.63%), acute gastroenteritis (18.12%), and enteric fever (13.36%). Whereas bronchopneumonia (8.18%), rheumatic heart disease (4.67%) and meningitis (3.99%) were less common among 1197 patients as shown in table no. 1.

The percentage of antibiotic agent/s prescribed for specific diagnosis before and after culture and sensitivity test and after culture and sensitivity test are shown in table number 3 and 4. Thus from these table it was found that there were increased frequency of use of antibiotic prescriptions of ciprofloxacin, norfloxacin, choramphenicol and aminoglycosides and decrease frequency for penicillin group of antibiotics after culture and sensitivity test for septicemia, urinary tract infection and acute gastroenteritis. While after culture and sensitivity test frequency of antibiotic prescriptions were increased for penicillin group and decreased for fluroqunolones, cephalosporin and aminoglycosides for bronchopneumonia, rheumatic heart disease, meningitis.

Antibiotic prescription before and after culture and sensitivity test showed, 29% of antibiotic prescriptions (out of 97% of antibiotic prescriptions given before culture and sensitivity report availability) were changed after availability of culture & sensitivity report, either addition of newer or change in group was done for septicemic patients. The percentage of antibiotics prescription changed after culture & sensitivity in urinary tract infection was 28% (out of 92%), acute gastroenteritis 33% (out of 87%), enteric fever 11% (out of 89%) bronchopneumonia 29% (out of 91%), rheumatic heart disease 17% (out of 83%), meningitis 38% (out of 63%). It was found that only 63% of antibiotic prescriptions given empirical for patients of meningitis, out of this 38% prescription further were changed after culture and sensitivity while 29% remained unchanged as shown in table 5. Table 6 and 7 shows number of antimicrobials prescribed per patient. Table 8 shows duration of hospital stay per percentage patient. In this study, the most frequently prescribed antimicrobial agents were penicillins, cephalosporins, aminoglycosides, fluroquinolones among which amikacin, ciprofloxacin, cefotaxime and cloxacillin were most preferred drugs. In all the disease the prescription given empirically before culture and sensitivity test were on the basis of prevalence of the common pathogens causing disease and its antibiotic sensitivity pattern. Overall the difference in empirical therapy before culture & sensitivity test & the changes in prescription after culture and sensitivity test were not significant after applying Z test.

Conclusion:

The study was undertaken to find out the antimicrobial utilization before and after culture & sensitivity report. Overall are the differences in empirical therapy before after culture and sensitivity test and the changes in prescription were not significant suggesting appropriate use of antimicrobial agents. The changes in prescription made reveal appropriate selection of antimicrobial agents for therapy of infective illness. Attempt had been made to evaluate the quality of prescribing antibiotics. It is an effort to provide continuing education in therapeutics to physicians and to develop systems for surveillance of drug utilization.

References:

1. Arti Kapil. The challenge of antibiotic resistance-need to contemplate -Review article. Indian J Medicine Research. 2005;121: 83-91.

2. Kunin C., Strand R. The impact of infections on medical care in the united the United states Ann. Inter. Med. 1987; 89: 737-866.

3. Goodman and Gillman's "The Pharmacological Basis of Therapeutics" –Tenth Edition. Page no. 1030-1032, and 1044-1055.

4. Ravi Pathiyil Shankar, Praveen Partha, Nagesh Kumar Shenoy, Joshy maducolil Easow, Koffullur N., Prescribing patterns of antibiotics& sensitivity patterns of common microorganisms in the Internal medicine ward of teaching Hospital in western Nepal : A prospective study. Annals of clinical microbiology & Antimicrobiotic 2001;2:1-13.

5. Principi N et al. Control of antibiotic therapy in paediatric patients. Developmental pharmacology and therapeutics 1981;2:145-55.

6. Schollenberg E and Albritton WL. Antibiotic misuse in a paediatric teaching hospital. Can Med Assoc J 1980;122:49-52.

7. M. Ipp Reduced antibiotic use in pediatrics practice: Practical office strategies based on current evidence. 2000:55-67.

8. Wester CW, Durairaj L, Evans AT, Schwartz DN, Husain S, Marinez E: Antibiotic resistance. Areh Intern Med 2002;162: 2210-16.

9. Srshyla M V, Naga Rani M A, Venkataram B V: Drug utilization of antimicrobial in the patient setting of tertiary Hospital: Indian J. Pharmacology 1994; 26:282-287.

10. Goodman and Gillman's "The Pharmacological Basis of Therapeutics" –Eleventh Edition. Page no. 1030-1032, 1044-1055.