Prescription Patterns of Antimicrobial Drugs in Hospitalized Patients in Tertiary Care Hospital of Kathmandu

Binod Raut[1], Anjan Khadka[2], Robrindra Nath Borah[1]

[1]Department of Pharmacology, Kathmandu Medical College, Duwakot, Bhaktapur. [2]Department of Pharmacology, Nepalese Army Institute of Health Sciences, Sanobharyang, Kathmandu, Nepal.

ABSTRACT

Introduction: Antimicrobial drugs are one of the most commonly prescribed drugs in hospital. Overuse and irrational use of antimicrobials is a key factor behind rapidly spreading antimicrobial resistance in microorganisms. Use of irrational and unnecessary antimicrobials remains common in the developing countries. This study was conducted to analyze the prescription pattern of antimicrobials in the department of internal medicine of tertiary care hospital. **Methods:** Antimicrobials are among the most commonly prescribed drugs in hospital. Overuse and irrational use of antimicrobials is a key factor behind rapidly spreading antimicrobial resistance in microorganisms. Use of irrational and unnecessary antimicrobials remains common in the developing countries. This study was conducted to analyze the prescription pattern of antimicrobials in the department of internal medicine of tertiary care hospital. **Results:** The mean duration of hospitalization among the study population was 5 days. Of the 460 medicines prescribed, mostly indicated for respiratory infections, and the most common antibiotic was from the group cephalosporin 209 (69.7 %). 55 % of prescriptions include only one drug, 39 % with two drugs and 6% with three or more than three drugs. **Conclusion:** The mean duration of hospitalization among the study population was 5 days. Of the 460 medicines prescribed, mostly indicated for respiratory infections, and the most common antibiotic was from the group cephalosporin 209 (69.7 %). 55 % of prescriptions include only one drug, 39 % with two drugs and 6% with three or more than three drugs.

Keywords: antimicrobial drugs; culture sensitivity; prescription; resistance; rational therapy

INTRODUCTION

Antimicrobial drugs are substances or compounds which are used to treat infections which are caused by microorganisms including bacteria, fungi, protozoa and viruses. Antimicrobials are classified on the basis of their modes of action, spectrum of activity and chemical structure [1]. The ultimate objective of antimicrobial chemotherapy is to cure the infections. With the establishment of the efficacy and safety of the antimicrobials, selection of empirical monotherapy or combination therapy is made. Another approach is to use definitive antimicrobial therapy once the sensitivity of the microorganism is known [2, 3]. The purpose of

Correspondence: Binod Raut, Department of Pharmacology, Kathmandu Medical College and Teaching Hospital, Duwakot, Bhaktapur, Nepal.E-mail: binod14raut@gmail.com

treating infections is to prevent complications like sepsis and to improve patient survival. The selection of the antimicrobials should be based on their sensitivity pattern, toxicity profile and their resistance status. The use of antimicrobials have significantly brought down mortality and morbidity from infectious diseases [3, 4]. At the same time inappropriate use of antimicrobials is widespread all over the world even for trivial infection of viral etiology. Antimicrobial agents are the most commonly used and misused of all the drugs and they had been used in excess for decades [5, 6]. Antimicrobials if not used prudently, will lead to toxicity and resistance among microorganism [7].

The problems raised with irrational antimicrobial chemotherapy include systemic toxicity, drug resistance, super-infection and economic burden to the patient [8]. There is increasing trend in the use of combinations of broad spectrum as well as newer generation antimicrobials which poses serious concern on antimicrobial resistance. Antimicrobial resistance elicits negative impact in health as well as economic burden in low economic countries where infectious diseases behold a major health challenge [9].

The study of a prescription pattern includes drug audit involving monitoring and evaluation of various prescriptions of medical practitioners to ensure rationality in medical care [10-13]. The indiscriminate and injudicious use of antimicrobials has led to ineffective treatment or treatment failure with prolongation or exacerbation of illness, toxicity, drug resistance, psychological impact and additional cost to the patient. The issue of antimicrobial resistance and treatment failure in hospitals cannot be addressed without the knowledge of the pattern of antimicrobial prescription in hospitals. In the view of this, the study was planned and conducted to analyse the prescription pattern of antimicrobial drugs in hospitalized patient in tertiary care hospital.

METHODS

The hospital based cross-sectional study involving prescriptions of 300 patient was conducted in the Department of Internal Medicine of tertiary care hospital from May 2015 to December 2015 after obtaining ethical approval from institutional ethics committee.. The study was carried out among patients admitted in the department of internal medicine at tertiary care hospital who were prescribed antimicrobials during their hospital stay. Data has been recorded in customized proforma from the daily case sheets and reports. Records were analyzed for various characteristics of patients and prescriptions such as age, gender, types of antimicrobials used based on generic or trade names, number of antimicrobials for each patient and duration of hospital stay and course of each antimicrobials. The informations regarding the indication and objectives of antimicrobial chemotherapy were also collected from the records. SPSS package version 20 was used for analysis.

RESULTS

During the study period, total of 300 prescriptions of patients for infectious diseases were assessed. More numbers of elderly patients were prescribed antimicrobials. The demographic variables of patients are expressed in table 1.

Out of 300 prescriptions, it was found that 270 (90 %) got cured or improved during the period of treatment, 8 (2.6 %) didn't complete the

Table 1: Demographic variables of patients. For age: median= 61 years; range= 14 to 92 years, standard deviation = 19.17 years.

Title	Number	Percentage
Age		
Less than 20 years	13	4.3
21- 40 years	59	19.7
41- 60 years	76	25.3
More than 60 years	152	50.7
Children/ Adults (≤ 65 years)	186	62
Elderly (>65 years)	114	38
Sex		
Male	155	51.7
Female	145	48.3

Table 2: Indications for use of antimicrobials

Indications	Number of antimicrobials (%)
COPD	94 (31.3)
Pleural Effusion	30 (10)
Hypertension with Diabetes Mellitus	48 (16)
Enteric Fever	26 (8.7)
Pneumonia	42 (14)
Bronchial Asthma	14 (4.7)
Post TB	27 (9)
RHD	13 (4.3)
UTI	28 (9.3)
Sepsis	23 (7.7)
Others	55 (18.3)

course of treatment, 10 (3.4 %) shifted to ICU for further treatment, and 12 (4 %) died during the treatment. 71% and 15.5 % of the drugs were prescribed for the therapeutic purposes and prophylactic purposes respectively as a treatment and prevention strategy for infectious diseases. 14.5 % drugs were found to be prescribed inappropriately. The infectious or associated comorbid conditions for which antimicrobials used were found to be acute exacerbation of chronic obstructive pulmonary disease, urinary tract infections, enteric fever, sepsis, post tuberculosis, etc (Table 2). 55 % of prescriptions include only one drug, 39 % with two drugs and 6 % with three or more than three drugs**.** Among all 300 prescriptions, only 59 (19.7 %) were prescribed with culture and sensitivity test and remaining 241 (80.3%) were prescribed without culture and sensitivity test as empirical therapy. Only 27 of 59 prescriptions had positive report on culture and sensitivity test which advocates for definitive antimicrobial therapy for infectious diseases.

Among the total prescribed antimicrobials, cephalosporin (209) are the most commonly prescribed drugs followed by fluoroquinolones (91), both with median duration of 7 days. The commonly prescribed drugs and their duration are shown in table 2. Aminoglycosides (5), vancomycin (4) and carbapenems (2) are least prescribed drugs and those prescribed were all in generic name.

Among the total number of 466 antimicrobial drugs prescribed, 117 (25.1 %) were prescribed on the basis of generic name and 349 (74.8 %) were prescribed on the basis of trade name (Figure 1).

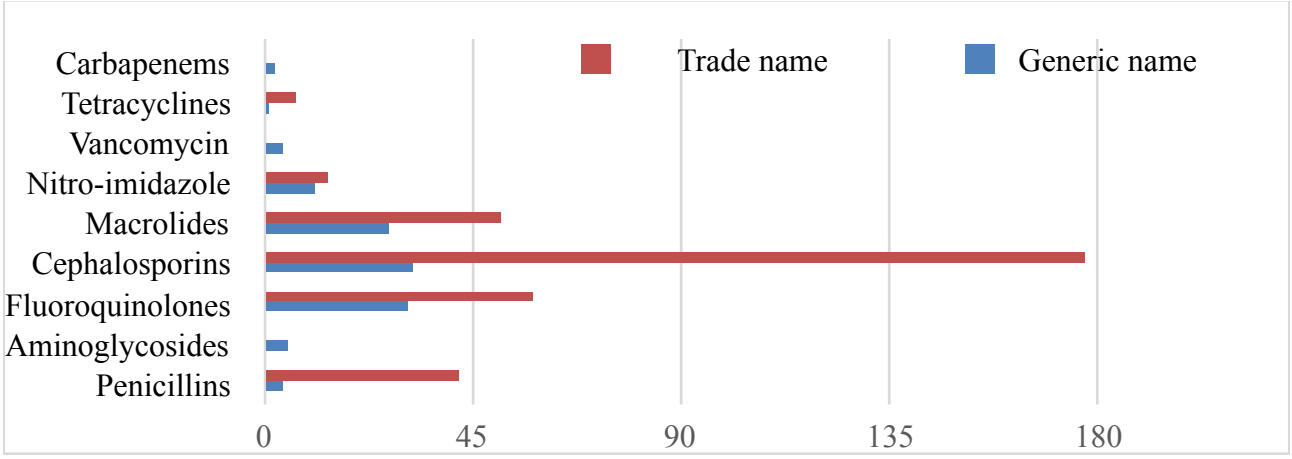
DISCUSSION

The prescription-based study provides information to the prescribers, researchers, policy makers and the drug and therapeutics committee members to determine the drug use

Table 3: Types of antimicrobials prescribed with the duration in days.

Drug Group	No. (%)	Duration in days		
		Median	Range	SD
Penicillins (Amoxicillin, Amoxicillin + Clavulanic acid, Amoxicillin + Cloxacillin)	46 (9.8 %)	7	3-21	3.17
Aminoglycoside (Amikacin)	5 (1.1 %)	7	3-10	2.49
Fluoroquinolones (Ciprofloxacin, Levofloxacin, Ofloxacin)	91 (19.5 %)	7	3-21	3.87
Cephalosporins (Cefadroxil, Cefepime, Cefixime, Cefpodoxime, Ceftriaxone)	209 (44.8 %)	5	1-21	2.97
Macrolides (Azithromycin, Clarithromycin)	76 (16.3 %)	5	3-14	2.52
Nitro imidazole (Metronidazole)	25 (5.4 %)	5	3-7	1.08
Tetracycline	8 (1.7 %)	2	5-30	7.86

Figure 1: Pattern of individual group of antimicrobials prescribed under generic and trade name



pattern [14, 15]. In our study, antimicrobials prescriptions was prescribed more to the patients aging 60 years and above. The trends on antimicrobial prescription increases with increasing age of the patient which might be due to the high prevalence of infectious diseases in elderly due to low immunity towards microorganisms. The gender analysis showed that male patients are more than female patient. The majority of the patient suffered from respiratory diseases followed by 20 % with sepsis and enteric fever as in the similar types of previous study [16]. The comorbidities were found to be hypertension with diabetes, post tubercular fibrosis, alcoholic liver diseases, cerebrovascular accident, etc. which are common problems in elderly population. The average number of drugs per prescription in the present study was found 1.53 which is comparable with the results of Jordan (2.3), Brazil (2.4), and India (2.7) [17-19]. The variation in results may be due to difference in health care delivery system, socioeconomic profile, and morbidity and mortality characteristics in the population. The larger number of drugs were prescribed by trade name. The generic name prescription in our study (25.1 %) is less than that reported in

studies conducted in Cambodia (99.8 %), India (73.4 %) and Brazil (30.6 %) [20, 21]. In similar type of studies conducted in Nepal, generic name prescription rate were 63.5 % and 59 % [22, 23]. The factor contributing to lesser prescription of generic drug might be the low production and lack of adequate promotion of generic drugs in Nepal. The use of generic names is recommended by WHO as a part of rational use of medicines. The use of generic name contributes to cost reduction and provides more alternatives for drug purchases [24].

In our study, more than half of the prescriptions include single drug prescription which include broad spectrum antibiotics with low toxicity profile like cephalosporins, fluoroquinolones and macrolides. The maximum number of drugs prescribed were ceftriaxone from the group cephalosporin which support the previously published literature [25]. The beta-lactam antibiotics (cephalosporins) were found to be commonly used as there is strong evidence of their effectiveness in the respiratory infections [26]. Poly pharmacy was not the issue among all prescriptions as two antimicrobial drugs combination were higher than three or more than three drugs combination. Combinations of cephalosporins with aminoglycosides, and penicillins with beta-lactamase inhibitors were commonly prescribed and it might be due to their proven synergistic activity, broader coverage of organisms for several serious gram negative infections and low risk of developing resistance [27].

Most of the drugs were prescribed for the therapeutic purpose. Antimicrobials were also prescribed for prophylactic purpose in few patients who are at high risk of developing infections due to exposure to infectious conditions, low immunity and lack of proper care. Among all 300 prescriptions, only few prescriptions were based on reports of culture and sensitivity test. Few drugs were found to be prescribed inappropriately which might be due to the lack of proper guidelines or the confusion in choosing the antimicrobial drugs as empiric therapy[28]. Majority of the antimicrobials were prescribed on grounds of presumption and clinical experience of the physicians[29]. The study conducted in Saudi Arabia observed that a high proportion of patients received antimicrobial agents prior to the availability of the results of blood culture tests[30]. This may lead to the risk of toxicity and possibility of emergence of drug resistance. However, in India, it was observed that empirical use of antimicrobial agents in primary care centre was 100% and 78% in tertiary care centre although culture and sensitivity was done after initiation of therapy in 80% cases of the tertiary care centre[24]. Above studies indicates that empirical use of antimicrobial agents are common in developing countries. Though culture and sensitivity testing is easy and cost effective to perform, it is not always feasible in developing countries due to lack of trained personnel, facilities and high chance of contamination. Sometimes, this pattern may also be due to lack of interest and unwillingness of physician or patients[31]. In some instance sufficient time is not available for culture and sensitivity and empirical antimicrobials are prescribed to avoid complications of severe bacterial infections. These variations in the prescribing patterns show that although the principles of rational antimicrobial usage have been well defined and recommended for many years,

inappropriate and injudicious use of AMAs remains wide spread as a global problem[32].

The number of drugs is important indicator for assessing rationality of prescription. It is preferable to keep the mean number of drugs per prescription as low as possible since higher number always lead to increased risk of drug interactions and increased cost which will result in poor patient compliance[33-35]. In similar type of study, it was found that 14 % - 43 % of antimicrobial chemotherapy were unnecessary because of no evidence of infection[36]. The studies done in Nigeria and Israel demonstrated that the antimicrobial prescription habits of doctors become prime concern[37]. Low economic burden for antimicrobial therapy can be achieved without compromising the quality of treatment. Focus should be on promoting expenses and infectious control with the rational prescription of antimicrobials and utilization being aimed at reducing the future emergence of resistance against bacteria[26, 37]. There is dire need of antibiotics guideline and stewardship based on local epidemiological data of potential pathogens and their pattern of antibiotics susceptibility. Our study being single centered study, there is possibility of selection bias and referral bias. Similarly, the present study on prescription patterns on antimicrobials may not completely reflect the general population of Nepal.

CONCLUSION

The number of drug prescribed per patient is quite low compare to other studies. Poly pharmacy is not the problem in our settings but antimicrobials prescribed on trade name and without culture sensitivity report is the prime problem. Prescriptions on antimicrobial drugs does not follow the protocol of rational drug therapy. However, there is further need of multicentre analytical studies to link the prescription pattern analysis to figures on morbidity, outcome of treatment, quality of care, and ultimately assess the rationality of drug therapy.

REFERENCES

1. Neu HC, Gootz TD. Antimicrobial Chemotherapy. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 11. Available from:http://www.ncbi.nlm.nih.gov/books/NBK7986/

2. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care-associated pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep. 2004;53:1–36.

3. Rotstein C, Evans G, Born A, Grossman R, Light RB, Magder S, et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. The Canadian Journal of Infectious Diseases & Medical Microbiology. 2008;19(1):19-53.

4. Laxminarayan R, Bhutta Z, Duse A, et al. Drug Resistance. In: Jamison DT, Breman JG, Measham AR, et al., editors. Disease Control Priorities in Developing Countries. 2nd edition. Washington (DC): World Bank; 2006. Chapter Available from: http://www.ncbi.nlm.nih.gov/books/NBK11774/

5. Gonzales R, Maselli J, Sande MA. Trends in antimicrobial treatment of acute respiratory tract infections by United States primary

care physicians, 1994-1999. J Gen Intern Med. 2001; 16(suppl): 196-7.

6. Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. Clin Infect Dis. 2001; 33: 757-62.

7. Odonkor ST, Addo KK. Bacteria Resistance to Antibiotics: Recent Trends and Challenges. Int J Biol Med Res. 2011; 2(4): 1204 -10.

8. Rafii F, Sutherland JB, Cerniglia CE. Effects of treatment with antimicrobial agents on the human colonic microflora. Therapeutics and Clinical Risk Management. 2008;4(6): 1343-1358.

9. Alsan M, Schoemaker L, Eggleston K, Kammili N, Kolli P, Bhattacharya J. Out-of-pocket health expenditures and antimicrobial resistance in low-income and middle-income countries: an economic analysis. Lancet Infect Dis. 2015 Oct; 15(10):1203-10. doi: 10.1016/S1473-3099(15)00149-8. Epub 2015 Jul 9

10. Kale A, Maniyar YA. Prescribing Patterns of Antihypertensive Drugs in A Tertiary Care Hospital. Sch. Acad. J. Pharm., 2013; 2(5):416-8.

11. Das BP, Sethi A, Nutan K, Gunjan. Teaching Exercise of Drug Utilization by Medical Students. J Nep Med Assoc 2005; 44: 160-4.

12. Hutchinson JM, Patrick DM, Marra F, Helen Ng, Bowie WR, Heule L, et al. Measurement of antibiotic consumption: A practical guide to the use of the Anatomical Thgerapeutic Chemical classification and Defined Daily Dose system methodology in Canada. Can J Infect Dis. 2004 Jan-Feb; 15(1): 29–35.

13. Bachhav SS, Kshirsagar NA. Systematic review of drug utilization studies & the use of the drug classification system in the WHO-SEARO Region. Indian J Med Res. 2015;142(2):120-9.

14. Cole CP, James PB, Kargbo AT. An evaluation of the prescribing patterns for under-five patients at a tertiary paediatric hospital in Sierra Leone. Journal of basic and clinical pharmacy. 2015; 6(4):109-14.

15. Upadhyay DK, Palaian S, Ravi Shankar P, Mishra P, Sah AK. Prescribing pattern in diabetic outpatients in tertiary care teaching hospital in Nepal. Journal of Clinical and Diagnostic Research 2007; 1(4):248-55.

16. Pradhan S, Jauhari AC. A study of antibiotics used in adult respiratory disorders in Kathmandu and Bhaktapur. Nepal Med Coll Journal 2007; 9: 120-4.

17. Otoom S, Batieha A, Hadidi H, Hasan M, Al- Saudi K. Evaluation of drug use in Jordan using WHO prescribing indicators. . East Mediterr Health J 2002; 8: 537-43.

18. Acurcio FA, Perini E, Magalhaes SM, Terceiro LG, Vieira Filho JM, Coutinho KE, et al. Analysis of medical prescriptions dispensed at health centers in Belo Horizonte, Minas Gerais, Brazil. Cad Saude Publica. 2004 Jan-Feb;20(1):72-9. Epub 2004 Mar 8.

19. Mhetre NA, Bodhankar SL, Pandit VA, Zambare GN. Study of pattern of drug usage in an urban area. Indian J Pharmacol 2003; 35: 316-317.

20. Karande S, Sankhe P, Kulkarni M. Patterns of prescription and drug dispensing. Indian J Pediatr 2005; 72: 117-22.

21. Pereira JC, Baltan VT, deMello DL. National Health Innovation System relations between scientific fields are economic sectors. Rev Saude Publica 2004; 38: 1- 7.

22. Shanker PR, Dubey AK, Rana MS, Mishra P, Subish P, Vijaya Bhaskar P. P. Drug utilization with special reference to antimicrobials in a subhealth post in western Nepal. Journal of Nepal Health Research Council 2005; 3: 65-69.

23. Ghimire S, Nepal S, Bhandari S, Nepal P, Palaian S. A prospective surveillance of drug prescribing and dispensing in a teaching hospital in Western Nepal. J Pak Med Assoc. 2009; 59(10): 726-31.

24. Till B, Williams L, Till B, Williams L, Oliver SP, PI. P. A survey of inpatient antibiotic use in a teaching hospital. S Afr Med J 1991; 8: 7-10.

25. Paudel KR, Sharma M, Das BP. Prevalence of antimicrobial chemotherapy in hospitalized patients in the department of internal medicine in a tertiary care center. Nepal Med Coll J 2008; 10: 91-95.

26. Krivoy N, El-Ahal WA, Bar-Lavie Y, Haddad S. Antibiotic prescription and cost patterns in a general intensive care unit. Pharmacy Practice 2007; 5(2):67-73. doi: 10.4321/S1886-36552007000200003

27. Arason VA , Sigurdsson JA, Stefánsdóttir G, Mölstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin resistant pneumococci in children? Cross sectional prevalence study. BMJ. 1996 Aug 17;313(7054):387–391.

28. Leekha S, Terrell CL, Edson RS. General Principles of Antimicrobial Therapy. Mayo Clin Proc. 2011 Feb; 86(2): 156–67.

29. Khan FA, Nizamuddin S, Salman M. Pattern of prescription of antimicrobials agent in the Department of Otorhinolaryngology in a tertiary care teaching hospital. Int. Research Journal of pharmacy and pharmacology 2011;1(5): 79-85.

30. Shimemeri AA, Ghadeer HA, Memish Z. Antibiotic utilization pattern in a general medical ward of a tertiary medical center in Saudi Arabia. Avicenna J Med. 2011 Jul-Sep; 1(1): 8–11.

31. Williams JD. Beta-lactam antibiotics in respiratory tract infections. Int J Antimicrob Agents 1993; 3: S21-30.

32. Kulkarni RA, Dargude VA, Kochhar PH, Rajadhyakshya SS, Thattle UM. Patterns of antimicrobial use by surgeons in India. Ind J Surg 2005;67:308-15.

33. Borg MA, Zarb P, Ferech M, Goossens H. Antibiotic consumption in southern and eastern Mediterranean hospitals: results from the ARMed project. J Antimicrob Chemother, 2008; 62: 830–6.

34. Belongia EA, Schwartz B.Strategies for promoting judicious use of antibiotics by doctors and patients. Br Med J 1998; 317: 668-71.

35. Dumpis U, Gulbinovic J, Struwe J, Lagergren A, Griskevicius L, Bergman U. Differences in antibiotic prescribing in three university hospitals in the Baltic region revealed by a simple protocol for quality assessment of therapeutic indications. Int J Clin Pharmacol Ther, 2007; 45: 568–76.

36. Das BP, Sethi A, Rauniar GP, Sharma SK. Antimicrobial utilization pattern in outpatient services of ENT department of tertiary care hospital of Eastern Nepal. Kathmandu Univ. Med. J. 2005; 3: 370-5.

37. Akande TM, Ologe M, Medubi GF. Antibiotic prescription pattern and cost at University of Ilorin Teaching Hospital, Ilorin, Nigeria. International Journal of Tropical Medicine 2009; 4(2): 50-4.