

Prevalence of antimicrobial chemotherapy in hospitalized patients in the department of internal medicine in a tertiary care center

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ABSTRACT

Use of antimicrobial agents (AMAs) is associated with significant reduction in morbidity and mortality. However, indiscriminate and injudicious use of AMAs leads to the ineffective treatment, increased adverse effects, exacerbation or prolongation of illness, emergence of bacterial resistance and an additional burden of an expensive medical cost to the patients. So controlled use of AMAs at right dose, right interval and right duration is of utmost importance. In this retrospective study, prevalence and prescription patterns, and cost of the prescribed AMAs in the hospitalized patients in the department of internal medicine in a tertiary care center were analyzed. A total of 428 hospitalized patients were included in the study. Out of 428 patients, 274 (64.0%, $P < 0.01$) patients received AMAs for therapeutic (66.4%) and prophylactic (24.1%) purposes. In 9.5% patients AMA prescription was inappropriate. Use of intravenous route was significantly higher (55.48, $P < 0.01$) than the oral route. COPD with acute exacerbation was most frequent condition for AMA prescription. Majority (90.42%) of AMA prescriptions were based on empirical basis. Mean number of AMA per patient was 2.12 (minimum 1 and maximum 8). Most frequently prescribed AMA was Ceftriaxone (30.2%) from cephalosporin group (33.9%, $P < 0.05$). Patients received AMAs for the duration of 1-31 days and total cost of single AMA dosage regimen was as high as \$ 482.3. As most of the hospitalized patients were prescribed AMA empirically, strategic AMA prescription guidelines and AMA prescription monitoring systems are extremely necessary in the hospitals to prevent emergence of microbial resistance and to expedite the cost effectiveness of medical treatment.

Keywords: Antimicrobial, chemotherapy, prescription, prevalence.

INTRODUCTION

Appropriate antimicrobial treatment greatly improves the prognosis of infectious diseases. There has been a very significant reduction in morbidity and mortality associated with the use of antimicrobial agents (AMAs) since they were first introduced.¹ However, the overuse of AMAs may increase the risks of drug resistant pathogens, side effects and costs of medical care. The right agent at the right dose and dosing interval, and right duration can achieve both a favorable clinical outcome and prevent the selection of resistance. Almost 20.0–50.0% of antimicrobial use has been found to be questionable or inappropriate.^{1,2} Accurate information about prescribing patterns in hospitals is valuable in improving the quality of antimicrobial prescriptions.

Recently it has been an alarming concern over injudicious use of antimicrobials world- wide. This practice of indiscriminate prescribing of antimicrobials has led to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient as well as an additional burden of an expensive medical cost to the patients.³ Non-selective and widespread use of antimicrobials leads to development of bacterial resistance and is a serious concern in the medical field

because we may land in a post- antibiotic era or a worldwide bacterial resistance to the most of the available antimicrobials in the very near future. The epidemiological trend of antibiotic resistance observed so far; tend to indicate that we will continue to move in the opposite direction, towards an environment with ever-growing number of new infectious diseases and of more common bacteria developing antibiotic resistance, more bacteria becoming resistant from hospital setting to the community. The net result could be even higher morbidity, higher mortality, higher costs, and the potential for rapid spread of these bacteria and overall a decreasing number of useful AMAs to combat the infections they cause.⁴

For the above reasons, AMAs should be used very cautiously and should be prescribed only to those individuals in whom their use is clearly justified and when it clearly outweighs the potential risks, including the risk of the development of resistance. Unfortunately, in today's healthcare system where physicians have only a few minutes to fully evaluate a patient, make a diagnosis and prescribe a drug, they frequently find themselves under tremendous pressure to prescribe an AMA even when this may not be appropriate.⁴ Because

of the rising costs in the health care system, lack of uniformity in the prescribing attitudes and the emergence of antimicrobial resistance, monitoring and controlling antimicrobial use is of growing concern.⁵ This study analyzed prevalence of utilization of antimicrobials in hospitalized patients in the department of internal medicine in a tertiary care center, with special regard to antimicrobial prescription attitudes and patterns (generic class, route, frequency, dose, duration, indication, sensitivity patterns and costs).

METHODS

This is a retrospective study. It was carried out at BP Koirala Institute of Health Sciences (BPKIHS), Dharan located in the eastern region of Nepal. It is the only tertiary referral center in this region of Nepal. Hospital record sheets of the admitted patients in the year of 2006 were randomly selected and were analyzed for antimicrobial use. Data were recorded in customized proforma and were analyzed by using discharge letters and in-patient daily record sheets and reports. Medical and nursing records were analyzed for patient

characteristics (e.g. age, gender and number of days of hospital stay), number of antibiotics for each patient, generic or trade names, route, dose and duration of each AMA. Cost of each AMA was calculated by referring to Current Index of Medical Specialities (CIMS) and pharmacies. Bacteriological culture and drug sensitivity patterns were recorded based on the microbiological laboratory reports. Medical files of the patients were used to obtain information on the indications for the antimicrobial prescription to find out whether the prescription was therapeutic or prophylactic or inappropriate/questionable based on the final diagnosis, provisional diagnosis and investigations (e.g. positive blood culture, inflammatory infiltrate on the x-rays) with systemic signs of infection and microbiological proof. Antimicrobial therapy was considered when there were definite signs and symptoms of infection with investigational and/or microbiological proof. Prophylaxis was defined as the use of antimicrobials in immunocompromised patients susceptible to the infections or in patients with clinical features suggestive of infection but absence of definitive localizing signs or focus or microbiological confirmation. Inappropriate or questionable therapy was defined as the use of AMAs without clinical or microbiological proof of infection or prophylaxis.⁶ To assess statistical significance between data Chi Square test with Yates correction was used where appropriate. P value less than 0.05 was considered significant.

RESULTS

Out of 428 hospitalized patients enrolled in this study, 274 (64.0%) received 584 AMAs. Antimicrobial prescriptions were made empirically in 248 (90.1%) patients and according to microbiological data in 26 (9.5%) patients. One patient received 2.13 AMAs on an average with minimum 1 and maximum 8. 57.5% (336) AMAs were prescribed by generic names (P<0.05) and

Table-1: Number of patients hospitalized, number of patients who received antimicrobials, generic and trade names, routes of administration and number of antimicrobials prescribed.

Title	Number (percentage)
Total patients	428
Male	240* (56.1%)
Female	188 (43.9%)
Patients who received AMAs	274* (64.0%)
Total no. of AMAs prescribed	584
Mean no. of AMAs per patient	2.13 (lowest 1-highest 8)
AMAs prescribed by generic name	366* (57.5%)
AMAs prescribed by trade name	248 (42.5%)
No. of patients in whom culture and sensitivity test was done	26 (9.5%)
AMAs used via intravenous route	324* (55.5%)
AMAs used via oral route	260 (44.5%)
Patients who received one AMA	72 (26.3%)
Patients who received two AMAs	118* (43.0%)
Patients who received three or more AMAs	84 (30.7%)

* P<0.01, AMAs- antimicrobial agents.

Table-2: Descriptions of hospitalized patients and duration of hospital stay for those patients who received antimicrobials.

Title	Number (percentage)
Patients	428
Cured or improved	396 (92.5%)
Left the hospital against medical advice	6 (1.4%)
Shifted to ICU	4 (0.9%)
Expired	22 (5.2%)
Average days of hospital stay	5.65 days (lowest 1day-highest 31days)

ICU- Intensive Care Unit

Table-3: Purpose of use (therapeutic or prophylactic or inappropriate) of antimicrobials with corresponding diseases or conditions (n=274)

Therapeutic n=182 (66.4%)		Prophylactic n=66 (24.1%)		Inappropriate n=26 (9.5%)	
Disease	No. of patients (%)	Disease	No. of patients (%)	Disease	No. of patients (%)
COPD with acute exacerbation	46 (25.2%)	Liver	26 (39.4%)	Cardiovascular	14 (53.9%)
Community acquired pneumonia	26 (14.2%)	Renal	20 (30.3%)	Cerebrovascular accident with hemiparesis	8 (30.8%)
Post TB complications	22 (12.0%)	Blood disorders	4 (6.0%)	OP poisoning	4 (15.3%)
Diabetes mellitus with febrile illness	20 (10.9%)	Others	16 (24.3%)		
Bronchiectasis	8 (4.4%)				
Rheumatic heart disease	8 (4.4%)				
Urinary tract infection	8 (4.4%)				
Sepsis	6 (3.2%)				
Enteric fever	4 (2.2%)				
Rickettsial fever	4 (2.2%)				
Acute pyelonephritis	4 (2.2%)				
Others	26 (14.2%)				

COPD- Chronic Obstructive Pulmonary Disease, TB- Tuberculosis.

324 (55.5%) AMAs were used through intravenous route (Table-1). Average hospital stay of patients receiving antimicrobials was 5.65 days per patient (minimum 1 and maximum 31) (Table-2). 66.4% patients received the antimicrobials for therapeutic purpose. COPD with acute exacerbation (25.2%) was the most frequent clinical condition for AMA prescription followed by community acquired pneumonia (14.2%) and post TB complications (12%) (Table-3). 24.09% patients received AMA prophylactically and 9.5% patients received AMA inappropriately (Table-3). Different antimicrobial groups and agents, and their frequencies, doses and durations of prescription have been given in table 4 and 5. Out of 584 antimicrobials prescribed, 198 (33.9%) (P<0.05), 92 (15.7%) and 84 (14.0%) were from cephalosporin, nitroimidazole and macrolide groups respectively. Ceftriaxone (30.2%) was the most frequently prescribed antimicrobial agent followed by metronidazole (15.7%), azithromycin (13.4%) and doxycycline (4.5%). Duration of AMA prescription was ranging from 1-31 days and cost of single AMA therapy was found to be as high as \$ 482.3 (Table-5).

Table-4: Generic classes of antimicrobials prescribed for the hospitalized patients in the department of internal medicine with their corresponding numbers and percentages.

Generic classes of AMAs	Number (percentage) n=292
Cephalosporin	198* (33.9%)
Nitroimidazole	92 (15.7%)
Macrolide	84 (14.0%)
Penicillin	60 (10.2%)
Antitubercular drugs#	50 (8.6%)
Aminoglycoside	28 (4.8%)
Fluoroquinolone	28 (4.8%)
Tetracycline	26 (4.5%)
Vancomycin	12 (2.0%)
Antifungal	4 (0.7%)
Monobactam	2 (0.3%)

One case of TB hip fracture stage II in which isoniazid, rifampin and ethambutol were prescribed for 12 months with pyrazinamide for 3 months, which is not included in this study, * P<0.05.

Table-5: The variations in the dose, frequency, duration and cost of antimicrobials prescribed in the department of internal medicine in a tertiary care center.

Antimicrobial agent	No of prescriptions (%), n=584	Dose	Frequency	Duration (days)	Cost (\$) range
Ceftriaxone	176 (30.2%)	400mg, 1gm, 2gm	stat, bid, tid	2-31	9.6-170
Metronidazole	92 (15.7%)	125 mg, 250mg, 400mg, 500mg, 800mg 1 gm	stat, tid	2-14	1.4-14.4
Azithromycin	78 (13.4%)	500mg	od	2-10	0.7-5.9
Doxycycline	26 (4.5%)	100mg	od, bid	1-7	0.07-2.3
Cloxacillin	24 (4.1%)	500mg, 1gm	qid	3-17	3-56
Ciprofloxacin	16 (2.7%)	200mg, 500mg	bid	3-9	1.4-25.4
Amikacin	14 (2.4%)	250mg, 500mg	od, bid	2-10	5.2-56.4
Ethambutol	14 (2.4%)	600mg, 800mg	od	3-7	1.4-1.6
Isoniazid	14 (2.4%)	225mg, 300mg, 450mg	od	3-7	1.4-1.6
Pyrazinamide	14 (2.4%)	100mg, 800mg, 1200mg, 1400mg	od	3-7	1.3-1.6
Ampicillin	12 (2.0%)	500mg, 1gm	stat, qid bid	2-6	1-19.8
Gentamicin	12 (2.0%)	5mg,40mg, 60mg, 300mg, 500mg, 600mg, 1gm	stat, od, bid, tid	2-15	0.14-26.5
Vancomycin	12 (2.0%)	1gm, 2gm	stat, every 48 hrs, od, bid	2-10	28.2-353
Cefepime10 (1.7%)	1gm, 2gm	bid	2-15	14.1-482.3	
Amoxicillin	8 (1.4%)	500mg, 1 gm	qid, bid	5-10	2.4-9.4
Amoxicillin +clavulanate	8 (1.4%)	625mg, 1.2 gm	bid, tid	3 -12	1.4-17
Rifampin8 (1.4%)	450mg, 600mg	od	3-7	1.4-1.6	
Clarithromycin	6 (1.0%)	500mg	bid	2 -5	3.7-17.6
Ofloxacin	6 (1.0%)	200mg, 400mg	bid	3-6	0.3-3
Ampicillin+cloxacillin	4 (0.7%)	250mg+250mg	qid	3-5	0.8-3.3
Cefuroxime	4 (0.7%)	300mg, 500mg, 600mg	od, bid	2-5	0.8-4.7
Fluconazole	4 (0.7%)	150mg	od	5	1.2-3.5
Norfloxacin	4 (0.7%)	400mg	bid	5-7	2.3-8.2
Nitrofurantoin	4 (0.7%)	100mg	bid	2-5	1-5.8
Aminopenicillin	2 (0.3%)	250mg	od	1	0.1-0.2
Aztreonam	2 (0.3%)	1gm	tid	6	193
Benzathine penicillin	2 (0.3%)	1.2 MU	od	1	0.3
Cefotaxime	2 (0.3%)	250mg	tid	6	6-11.8
Ceftazidime	2 (0.3%)	1gm	tid	3	53-65.6
Levofloxacin	2 (0.3%)	500mg	od	8	0.5-1.3
Tobramycin	2 (0.3%)	60mg	tid	5	15.8-32

stat- at once, od- once a day, bid- twice a day, tid- thrice a day, qid- four times a day, MU- million unit, \$- US dollar.

DISCUSSION

In this present study, significantly higher (66.4%, $P < 0.05$) number of hospitalized patients in the department of internal medicine received AMAs. This finding is higher than the previous similar studies which showed the prevalence of AMA use to be 30.6%,⁷ 36.0%⁶ and 37.0%⁸ in different age groups of hospitalized patients in different departments. Among the patients who received AMAs, only 9.5% patients received AMAs on the basis of microbiological reports. Similarly, 11.5%⁷ and 59%⁸ patients were prescribed AMAs on the basis of culture reports in the previous studies. More than 2/3rd of hospitalized patients (73.7%) received two or more AMAs during their hospital stay. 24.1% patients received AMAs for prophylaxis whereas use of AMAs in 9.5% patients was unjustifiable or inappropriate. Similarly, data in the literature have been reported that 20.0–50.0% of antimicrobial use was questionable or inappropriate.^{1,2} These variations in the prescribing patterns show that although the principles of rational antimicrobial usage have been well defined for many years, inappropriate and injudicious use of AMAs remains wide spread.⁷ Number of AMAs received by a patient was as high as eight. As average 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 figures always lead to increased risk of drug interactions and increased cost.^{9,10}

Use of extensive AMAs limits the affordability of our community as patient compliance is primarily dependent on the cost of treatment.¹¹ Moreover, the emergence and spread of drug resistant pathogens have already become a very serious problem internationally due to indiscriminate and overuse of AMAs. It was reported that 14.0–43.0% of all courses of antimicrobial chemotherapy were deemed unnecessary because there was no evidence of infection.^{2,12}

Present study showed large variations in doses, frequencies and durations of all AMAs prescribed. Though individualization of the AMAs based on the patient factors (e.g. liver disease, renal disease and old age), severity and nature of infection, and purpose of use (therapeutic or prophylactic) is needed, AMAs should be prescribed at the correct frequency, dose and duration as far as possible so that the minimum inhibitory concentration (MIC) is exceeded, and side effects and selection of resistant bacteria are prevented.¹³ However, AMAs such as aminoglycosides which have postantibiotic effect may be effective even in the concentration below MIC after large single dose. So all these pharmacokinetic and microbial pharmacodynamic factors should be considered while prescribing any AMA.¹⁴

In conclusion, this study showed more than half of the hospitalized patients in the departments of internal medicine received AMAs for any of the therapeutic, prophylactic or injudicious reasons. In order to improve AMA prescription in a hospital, a stricter and a more uniform policy is deemed necessary to prevent many problems such as rising health care costs and emergence of antibiotic resistance associated with indiscriminate use of AMAs. Clear cut guidelines and educational initiatives on prescribing of AMAs based on microbial sensitivity patterns are highly recommended. Moreover, continuous systematic monitoring based on the specific clinical guidelines for the control of AMA use is strongly advocated.

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