

Patterns of prescription of antimicrobial agents in the department of otorhinolaryngology in a tertiary care teaching hospital

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This study was carried out to study the pattern of antimicrobial prescription in OPD and IPD of the department Otolaryngology in a tertiary care teaching hospital of North India. This was a prospective study conducted at the Teerthanker Mahaveer Medical College and Research Centre, over a period of 12 months. All the patients who attended the ENT OPD and IPD were included. Out of 4800 patients, only 2600 patients were included in the study, 60% (n=1560) were males and 40% (n=1040) were females. Maximum no. of patients were in the age group 16-35 years 60% (n=1560) while the geriatric group (76-85 years) comprised the lowest 1.9% (n=50). 55% (n=1430) of patients were diagnosed with ear, 30% (n=764) with throat and 15% (n=296) with nose disorders. The most frequently prescribed antibacterials were β -Lactams (75.68 %) followed by Aminoglycosides (9.43%). Among the penicillin group the commonest drug prescribed was a combination of amoxicillin and Clavulanic acid (9.58 %), in Cephalosporins was Cefixime (37.98%) and in Aminoglycosides was Gentamicin (6.25%). Further, 69.11% of the patients received single antibacterial drug and the average number of antibacterial agents prescribed per patient per course was found to be 1.38. It was also observed that 75.43% of the antibacterials were prescribed by oral route. In the concomitant medications antihistaminic were prescribed in 11.53%, Proton Pump Inhibitors in 20.38 % cases and NSAIDS in 7.26% cases. The average number of drugs used in each prescription was 2.70. All the drugs were prescribed with trade names. The average cost per prescription per day in OPD & IPD patients were Rs.45 and Rs.185 respectively. Out of 2600 patients; culture sensitivity tests were performed for only 71 patients (inclusive of OPD and IPD). Of which only 43 patients depicted a positive culture sensitivity tests. Our study showed that antimicrobials were mostly prescribed in patients of ear diseases while it was least in throat disorders. Proton Pump inhibitors was the most common concomitant drug used. The cost of treatment in IPD patients were 4.11 times more than the OPD patients.

Keywords: Antibacterial agents, drug utilization, ENT infections, prescribing pattern, pharmacoepidemiology

INTRODUCTION

Drug utilization research was defined by (WHO, 1977) as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" (WHO, 1977). The principal aim of drug utilization studies is to facilitate rational use of drugs in populations. The drug

utilization studies also relates to the effects of drug use, beneficial or adverse (Lunde, 1988; Strom, 2005). Inappropriate drug use may also lead to increased cost of medical care, antimicrobial resistance, adverse effects and patient mortality (Einarson, 2008). Hence in recent years studies on drug utilization have become a potential tool to be used in the evaluation of health systems (Laporte, 1983).

Diseases of the ear, nose and throat (ENT) affect the functioning of adults as well as children, often with

significant morbidity causing impairment of routine life of affected patients (Grace, 2006.). It has been envisaged that with increase in global population, infections remain the most important cause of disease, with upper respiratory tract infections (URTIs) causing hearing loss especially in children. In its World Health Report of 2004, the World Health Organization (WHO) estimated that respiratory infections generated 94.6 disability adjusted life years lost worldwide and were the fourth major cause of mortality, responsible for 4 million deaths or 6.9% of global number of deaths in 2002.

Acute respiratory infections accounts for 20-40% of outpatient and 12-35% of inpatient attendance in a general hospital (Jain *et al.*, 2001). URTIs including Otitis media (OM) constitute 87.5% of the total episodes of respiratory infections (Jain *et al.*, 2001) and are a major source of morbidity and absenteeism at work. The vast majorities of acute URTIs are caused by viruses and does not require antimicrobial agent unless it is complicated by acute OM (AOM) with effusion, tonsillitis, sinusitis and lower respiratory tract infection. A WHO study of antibiotic use in 13 low-middle and high-income countries revealed that antibiotics were wrongly prescribed for approximately 30% of cases of URTI (Gaash, 2008).

Despite several years of clinical use of antibiotics, little is known about the optimal use of these drugs in the clinic to minimize resistance development without compromising safety and efficacy. The International Network for the Rational Use of Drugs (INRUD) was established in 1989 to promote the rational use of drugs in developing countries. Various indicators were developed by INRUD in collaboration with WHO that provided objective indices to allow for assessment of drug use practices (Laporte *et al.*, 1983). Still, there is a need for data on both antibiotic use and its determinants from all the regions of the world. The study conducted by (Ranjeeta *et al.*, 2008; Salman *et al.*, 2008) showed that the pattern of prescription in terms of completeness and rationality was poor. The main problems encountered were unnecessary prescription of drugs, particularly antimicrobials and injections. Therefore there is an urgent need to improve the standards of drug prescription.

A similar study conducted by (Kumari *et al.*, 2008) showed that antimicrobial prescription rate was higher in Lucknow, North India. Therefore, it is imperative to evaluate and monitor the drug utilization patterns in other parts of north India to enable suitable modifications in prescribing patterns and thus increase the therapeutic benefit and decrease the adverse effects (Krishnaswamy *et al.*, 1985).

The present prospective study was undertaken with the aim to evaluate drug utilization pattern of antibacterials used in ENT infections in patients of outpatient (OPD) and inpatient (IPD) departments at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India.

MATERIALS AND METHODS

Setting

The study was carried out in the ENT OPD and IPD of Teerthanker Mahaveer Medical Hospital and Research Centre, a 550-bed teaching hospital situated in Moradabad, UP, India.

Study design

This was a prospective study and was based on a Medication Utilization Form, which has been designed on the basis of a WHO format. It included patient particulars, diagnosis, investigations, drug details and information regarding the indication for prescribing agents (both topical and oral), underlying infection, duration of therapy and details of any concomitant medications. Cost of the individual prescriptions was worked from prices as given in CIMS (current index of medical stores). The information was compiled and analyzed in consultation with ENT specialist.

Duration of study

The duration of study was 12 months (April 2010 to March 2011). The study was approved by the Institutional Ethical Committee. An oral and written consent was obtained from the patients before their participation in the study.

Study population

The present study was conducted on 4800 patients who visited the OPD and IPD of ENT department during the 12-month period. The subjects who had willingly participated were enrolled on the basis of inclusion and exclusion criteria. All the patients using antibacterials, irrespective of age and sex, including pregnant and lactating patients were studied. However, patients who were not treated with antibacterials or were unable to comply due to mental retardation or drug addiction etc. were excluded.

Outcome measures

The outcome measures included gender distribution, average age range of patients, types of infections, types of antibacterial prescribed, most commonly used agents of a particular class, average number of antibacterials per prescription, comparison of antibacterials prescribed in monotherapy versus fixed dose combination therapy, mode of administration, comparison of antibacterials

Table: 1 Antimicrobials prescribed (n=3599)

Class	Antibacterial agents	No. of agents prescribed	Consumption %
β-Lactams	Amoxicillin	125	3.47
	Ampicillin+ Cloxacillin	145	4.02
	Amoxicillin + Clavulanic acid	345	9.58
	Cefpodoxime	70	1.94
	Cefixime	1367	37.98
	Cefixime+ Clavulanic acid	350	9.72
	Ceftriaxone	287	7.97
	Cefuroxime	35	0.97
	Total	2724	75.68
Quinolones	Ciprofloxacin	73	2.02
	Ofloxacin	27	0.75
	Levofloxacin	70	1.94
	Total	170	4.72
Aminoglycosides	Neomycin	65	1.80
	Amikacin	50	1.38
	Gentamicin	225	6.25
	Total	340	9.43
Macrolide	Azithromycin	228	6.33
Nitroimidazoles	Metronidazole	117	3.25
	Ornidazole	20	0.55
	Total	137	3.80
	Grand Total	3599	100

prescribed by generic versus brand name, concomitant disease conditions, compliance or adherence (using weekly diary cards).

Data source

The sources of data were physicians prescribing records, patient's medication profile and weekly diary cards. Patient profile (age, sex, weight, height, patient's address), drugs prescribed (generic/brand name), doses and frequency were recorded. Patients were interviewed after their informed consent was obtained. Interviews were conducted by using structured questionnaire (open question method). Weekly diary cards were used to determine patient compliance. Non compliance was considered if there was <80% of recommended intake of prescribed drugs.

RESULTS

Of the 4800 patients who visited the ENT OPD and IPD, 2600 patients were selected for the study. Among the 2600 ENT patients, 1560 (60%) were male and 1040 (40%) were female. The highest numbers of patients

were in the age group of 16-35 years and the lowest percentage was in geriatric patients. During the study, it was observed that 1430 patients visited for ear disorders, 296 for nasal disorders, and 764 for throat infections and 110 for combined ENT infections. During the study, it was observed that the most commonly prescribed antibacterials were β-lactam (penicillins and cephalosporins)-n=2724, followed by aminoglycosides –n=340, macrolides-n=228, quinolones –n=170, [Table1]. The most commonly used agent of these classes, i.e., β-lactam was penicillins (amoxicillin with clavulanic acid-n=345) and Cephalosporins (Cefixime-n=1367) followed by aminoglycosides (gentamicin-n=225), quinolones (ciprofloxacin-n=73), macrolides (azithromycin-n=228), nitroimidazoles (metronidazole-n=117) [Table 1]. Antimicrobial therapy were most commonly instituted in ear diseases (67.93%), followed by nose (17.06%) and throat (15.00%) respectively [Table 2]. β-lactam antibiotics were most commonly used in ear disorders (57.51%) and least in throat (5.83%) [Table 2].

The prescription of patients showed that a total of 1797 patients received antibacterial monotherapy, whereas 803 patients were on multiple drug therapy [Table 3.1]. Among those on concomitant drug combinations, 398 received two drugs, 242 received three drugs and 163

Table: 2 Relationship between type of infection and Class of antimicrobial agent prescribed in Ear, Nose and Throat

Organ	Class	No. of agents prescribed	Consumption %
Ear	β -Lactams	2070	57.51
	Quinolones	55	1.52
	Aminoglycosides	250	6.94
	Macrolide	20	0.55
	Nitroimidazoles	50	1.38
	Grand Total	2445	67.93
Nose	β -Lactams	444	12.33
	Quinolones	25	0.69
	Aminoglycosides	70	1.94
	Macrolide	13	0.36
	Nitroimidazoles	62	1.72
	Grand Total	614	17.06
Throat	β -Lactams	210	5.83
	Quinolones	90	2.50
	Aminoglycosides	20	0.55
	Macrolide	195	5.41
	Nitroimidazoles	25	0.69
	Grand Total	540	15.00

Table: 3.1 Frequency of Antimicrobials used

Drugs Prescribed	No. of Prescription	% of Prescription
Single antibacterial agent (one drug)	1797	69.11
Multiple antibacterial agents	803	30.89
Total	2600	100

Table: 3.2 Multiple antibacterial agents

Drugs Prescribed	No. of Prescription	% of Prescription
Two drugs	398	49.56
Three drugs	242	30.13
Four drugs	163	20.31
Total	803	100

received four drug regimens. The average number of drugs used in each prescription was 2.70 [Table 3.2].

A total of 3599 antibacterials were prescribed. Their routes of administration were oral (n=2699), intravenous (n=715) and topical (n=185) [Table 4]. The average number of antibacterial agents prescribed per patient per course was found to be 1.38 [Table 4]. The average cost per prescription per day in OPD and IPD patients were Rs.45 and Rs.185 respectively. Out of 2600 patients; culture sensitivity tests were performed for 71 patients (inclusive of OPD and IPD). Of which only 43 patients

depicted a positive culture sensitivity tests. The common microbes isolated from the culture were staphylococcus aureus (58.2%). Streptococcus (9.8%), Enterobacteriaceae (8.1%), Pseudomonas mirabilis (16.2%). & Pseudomonas aeruginosa (7.7%). The most frequent comorbid condition of the study population was found to be Hypertension (6.1%) followed by Tuberculosis (5.8%) and Diabetes (4.4%) [Table 5.1]. All the antibacterial agents were prescribed by their brand names. In the concomitant medications antihistaminic were prescribed in 11.53 %, Proton Pump Inhibitors in

Table: 4 Prevalence & indication of antimicrobials

Indicators	No. of Patients
average number of drugs per prescription (encounter)	2.70
percentage of drugs prescribed by generic name;	0
percentage of encounters resulting in prescription of an injection;	715
percentage of drugs prescribed from essential drugs list or formulary, and	73
Prevalence of use	
Total No. of Prescription	2600
Total No. of AMAs prescribed	3599
Mean No. of AMAS	1.38
Routes of Drug administration	
Oral	2699
Parenteral (i.v)	715
Topical (ear drops)	185
Purpose of use of AMAs	
OPD patients	2198
IPD patients (Post operated and Conservatively managed)	402
Total No. of patients	2600

Table: 5.1 Concomitant Conditions:

Concomitant Conditions:	No. of Patients	Patient %
Diabetes	115	4.4
Hypertension	159	6.1
Hyperthyroidism	27	1.0
Tuberculosis	151	5.8
Depression	17	0.6
Hypothyroidism	26	1.0
Hypertension + Diabetes	21	0.80
Total	516	19.84

20.38 % cases and NSAIDS in 7.26% cases [Table 5.2].

Weekly diary cards were used for daily drug intake to monitor compliance. The standard criteria for noncompliance were <80% of the recommended intake of prescribed drugs. In the present study, 1593 of total patients showed good compliance. Adherence was found to be slightly better in females than in males.

DISCUSSION

There is much discrepancy regarding the prescription of antimicrobials in the past few decades especially with the advent of higher generation antibiotics. In our study

male/female ratio was 60/40%, probably males are more ambulatory and most of our subjects were occupational workers. Moradabad had enjoyed the privilege of being the brass capital of western UP, India and our patients who were workers formed the framework of diseases like rhinitis and eustachian tube dysfunctions. This is in concordance with the study conducted by (Yadav *et al.*, 2010; Ain *et al.*, 2010; Shankar *et al.*, 2006; Pradhan *et al.*, 2007) showing higher percentage of males suffering from ENT infections. Many other studies showed that females are more sensitive to ENT infections than males; the reason might be their exposure to kitchen smoke (Dhingra PL, 2004).

We observed dominance of otological diseases in our

Table 5.2: Concomitant drugs used

Class	Generic Name	No. of agents prescribed	Consumption %
Proton Pump Inhibitors	Pantaprazole	380	14.61
	Ranitidine	150	5.76
	Total	530	20.38
Antihistaminics	Levocetirizine	150	5.76
	Chlorpheniramine maleate	80	3.07
	Fexofenadine	70	2.69
	Total	300	11.53
NSAIDS	Diclofenac	189	7.26
Benzodiazepines	Alprazolam	93	3.57
Corticosteroids	Dexamethasone	60	2.30

study mainly CSOM, which may be attributed to inadequate medical management of eustachian tube dysfunctions at the peripheral level. Majority of the patients were from rural background. It may be an indicator of the inefficient health care delivery system, injudicious faith in the quacks and poor socioeconomic status. This is in concordance with the study conducted by (Yadav Pramila *et al*, 2010) showing higher incidence of ear infections 50.8%, followed by throat (31.37%) and least were nose 26.47%.

In our study, most commonly prescribed categories of antibacterials were β -lactam (75.68%), followed by aminoglycosides (9.43%), macrolide (6.33%). quinolones (4.72%). Among the individual antibiotic drugs, maximum patients received cefixime (37.98%), a combination of cefixime+ clavulanic acid (9.72%), amoxicillin with clavulanic acid (9.58%), followed by ceftriaxone (7.97%), azithromycin (6.33%), and gentamicin (6.25%). Our study contradicts the study conducted by (Das *et al.*, 2005) reported that ciprofloxacin (23.85%) was preferred, followed by amoxycillin (20.06%), a combination of ampicillin + cloxacillin (9.17%), doxycycline (5.96%), erythromycin (4.58%) and co-trimoxazole (4.58%). A similar study reported that β -lactam antibiotics (amoxicillin, amoxicillin-clavulanate, cefdinir, cefpodoxime proxetil and cefuroxime axetil) are all considered appropriate for the initial treatment of acute bacterial rhino sinusitis in children (Anon JB 2003). It is well known that indiscriminate use of broad spectrum antibiotics increases bacterial resistance (Stille *et al.*, 2004). So, azithromycin and clarithromycin should be used only when their broad coverage is required or when other antibiotic use is prohibited due to allergy, etc. However, a change in the prescribing patterns from a small spectrum penicillin to amoxicillin/clavulanate, as indicated in our study, could be due to an increase in antibiotic resistance which encourages physicians to choose a broader and safer option.

In our study, β -lactams (cefixime) was most commonly prescribed antibiotic. The reason for prescribing the third generation cephalosporin was the preponderant mixed

group of infections. This contradicts the study conducted by (Ain *et al.*, 2010) who documented amoxycillin as the most common antibiotic prescribed. Again this study was performed in both OPD & IPDs that included the post-operative patients, which demanded higher generation cephalosporins. Earlier studies were mainly based on OPDs, so this may be a strong reason for the difference of antibiotics preferred.

Few patients with non-specific throat complaints received antimicrobial therapy. We observed laryngopharyngeal reflux as the most common cause and these patients responded very well to the proton pump inhibitors. Good numbers of patients were with non-specific throat complaints and the fear psychosis of malignancy of throat drove them to OPD. These were treated with a combination of PPI & anxiolytics, PPI & decongestant with dramatic response. We infer that most of the antibiotics used in patients with sorethroat are an overcautious approach of most of our contemporaries. The reason for higher prescription of PPI's in sorethroat was a rationale evaluation by means of indirect laryngoscopy or video laryngoscopy in all patients above 30 years of age. Bogginess near posterior commissure was noticed in some patients thereby reflecting LPR (laryngopharyngeal reflux). Also patients with no evidence of tonsillitis and pharyngitis were subjected to PPI for 3 weeks with promising results.

Culture sensitivity was done in 71 patients only. Majority of the antibiotics were prescribed on grounds of presumption and clinical experience of the physicians. Patients of CSOM who didn't respond to prolonged antimicrobial therapy were taken for AFB staining. AFB bacilli were seen on Z.N staining in 5 patients who responded well to first line anti-tubercular therapy. It is our assessment to consider for AFB analysis in cases of non-respondents of discharging ear. Although patient had a good adherence but it would be more empirical to consider culture sensitivity before prescribing antimicrobials.

The mean number of antibacterial agents prescribed per patient per course was found to be 1.38. In a similar

study, (Das *et al.*, 2005) reported 1.4 antimicrobial agents per patient in outpatient services of ENT department in a tertiary care hospital of Eastern Nepal. It is an important indicator for assessing rationality of prescription. Hence, physicians should preferably keep the mean number of drugs per prescription as low as possible as higher figures always lead to increased risk of drug interaction, development of bacterial resistance and increased cost (Atanasova, 1955 ; Till *et al.*, 1991). Further, in our study 69.11% patients received antibacterial monotherapy; whereas 30.88% patients were on multiple drug therapy. This is in concordance with the study conducted by (Yadav *et al.*, 2010; Ain *et al.*, 2010) using higher percentage of single antimicrobial agent. (Das *et al.*, 2005) have reported that single drugs were prescribed the maximum (89.52%), followed by two drugs (9.94%) and three drugs (0.52%) in ENT patients'. In the present study, the routes of administration of antibacterials were found to be oral 75.43%, parenteral (i.v.) 19.86% and topical (via ear drop) 5.14%. (Shankar *et al.*, 2006) have carried out a prospective study where 48.9% antibacterial agents were prescribed by the parenteral route.^[8] So, we have used lesser no. of injectables than (Shankar *et al.*, 2006).

In our study, it was found that all the antibacterial agents were prescribed by their brand names only, which could be due to the influence of medicinal drug promotional activities. The trend of prescribing drugs under generic name is declining (Ryan HS 2003). Prescribing the brand name may undermine some of the goals of essential drug concept. On the other hand, prescribing by generic names may reduce overall expenditure on drugs, especially on newer antibiotics..

However, in spite of all these limitations, our study highlighted some rational prescribing practices. Continuing education on rational drug use and development of easy to use treatment guidelines for common diseases is suggested. In our future endeavors, we plan to study the effect of regulatory and educational interventions on drug use pattern in the management of ENT infection.

Summary

The present work is the maiden drug utilization study conducted in ENT department at our university hospital. It highlighted some rational prescription patterns including less utilization of antibiotics in ENT infections, good adherence by patients and prescription by brand names. The data presented here will be useful in future, long-term and more extensive drug utilization studies in the hospital and in promotion of rational prescribing and drug use in hospitals. We recommend Regular CMEs for the doctors at different levels to encourage prescribing by generic names and on correct writing of prescriptions. We also recommend framing strategies to make the

prescriptions cost effective.

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