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Full Length Research Paper

Patterns of prescription of antimicrobial agents in the Department of Otorhinolaryngology in a tertiary care teaching hospital

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The objective of this research is to study the pattern of antimicrobial prescription in outpatient (OPD) and inpatient (IPD) of the Department of 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 Ear Nose and Throat (ENT) OPD and IPD were included. The results show that out of 4800 patients, only 54% (n=2600) of patients were included in the study on the basis of inclusion and exclusion criteria and 31.25 % (n=1500) were defaulters. Majority of the patients were male 60% (n = 1560). Majority of the patients had suffered from ear disorders, 55% (n=1430). 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%). 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 and 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 were the most common concomitant drug used. The cost of treatment in IPD patients were 4.11 times more than the OPD patients.

Key words: Antibacterial agents, drug utilization, ear nose and throat (ENT) infections, prescribing pattern, pharmacoepidemiology.

INTRODUCTION

Drug utilization research was defined by World Health Organization (WHO) in 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 Expert Committee, 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 and Baksaas, 1988; Strom, 2005). Inappropriate drug use may also lead to increased effects and patient mortality (Einarson, 2008). Hence, in recent years, studies drug utilization has become a potential tool to be used in the evaluation of health systems (Laporte et al., 1983).

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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 and Bussmann, 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 2004) 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 to 40% of outpatient and 12 to 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-Indira 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

This prospective study was conducted on 4800 patients who visited the OPD and IPD of ENT department of Teerthanker Mahaveer Medical Hospital and Research Centre during the 12-month period.

The patient's details were obtained from the treatment cards which include 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 medical store of the hospital. The information was compiled and analyzed in consultation with ENT specialist.

We enroll only those patients in our study which were on antibacterial, irrespective of age and sex, including pregnant and lactating patients also. However, patients who were not treated with antibacterials or were unable to comply due to mental retardation or drug addiction etc. were excluded.

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

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 to 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, (Table 1). The most commonly used agent of these classes that is, 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 3a). Among those on concomitant drug combinations, 398 received two drugs, 242 received three drugs and163 received four drug regimens. The average number of drugs used in each prescription was 2.70 (Table 3b).

Table 1. Antimicrobials prescribed (n = 3599).

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

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), Enterobacteriacae (8.1), *Pseudomonas mirabilis* (16.2) and *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 5a). All the antibacterial agents were prescribed by their brand names. In the concomitant medications, antihistaminic were prescribed in 11.53, proton pump inhibitors in 20.38 cases and NSAIDS in 7.26% cases (Table 5b). Weekly diary cards were used for daily drug intake to monitor compliance. The standard criteria for non-compliance 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) and Pradhan and Jauhari, (2007) showing higher percentage of males suffering from ENT infections. Many other

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 3a. 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 3b. 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

studies showed that females are more sensitive to ENT infections than males; the reason might be their exposure to kitchen smoke (Dhingra, 2004).

We observed dominance of otological diseases in our 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 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) and quinolones (4.72%). Among the individual antibiotic drugs, maximum patients received cefixime (37.98%), a combination of cefixime + clavulanic acid (9.72%), amoxicillin with

Table 4. Prevalence and indication of antimicrobials.

Indicator	No. of patient
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,	73
Prevalence of use	
Total number of prescription	2600
Total number of AMAs prescribed	3599
Mean number 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 number of patients	2600

Table 5a. 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

Table 5b. 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	Levocetrizine	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

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, 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 and 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 laryngo=pharyngeal 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 and anxiolytics, PPI and 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 did not 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 anti-microbials. 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 (Atanasoval, 1955; Williams 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) and 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 were 48.9% antibacterial agents were prescribed by the parenteral route (http//www.jpbsonline.org/article.asp?). So, we have used lesser number 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, 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.

Conclusion

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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