Drug Utilization Pattern and Adverse Drug Reaction Monitoring of Antibiotics Use in Ear, Nose and Throat Infection at Tertiary Care Hospital, Lucknow, India

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Abstract

Objective: To investigate the ENT department's (OPD, IPD) antibiotic prescribing practices at a tertiary care hospital in Lucknow, India. Material and Methods A prospective, cross-sectional, non-experimental (observational) study was performed in (OPD, IPD) department of Ear, Nose and Throat (ENT) over a period of 6 months. Result In this study, 100 ENT patients (51 male, 49 female) were selected based on inclusion and exclusion criteria. Ear infections were the most common reason for visits (86 patients), followed by nose (7 patients) and throat infections (5 patients). The most commonly prescribed antibiotics were β-lactam antibiotics, with penicillin's (amoxicillin with clavulanic acid) and cephalosporin's (cefixime) being the most commonly used. Combination therapy was used in 117 patients, with an average of 1.9 antibiotics per patient per course. A total of 40 antibiotics were prescribed, with oral being the most common route of administration. Only one adverse drug reaction was reported, with a suspected link to cefixime causing an increase in rashes in one patient. The study population had comorbid conditions of anxiety, epilepsy, and anaemia. Conclusions To conclude, our study in the university teaching hospital (IIMSR) highlighted lesser utilization of antibiotics in ENT infections, as some of the ENT infections are not due to bacteria. The majority of ENT patients admitted to the hospital appear to have bacterial infections, and most of them reacted favourably to antibiotic treatment. Majority of the patients used the regimen in accordance with the current guidelines. Keywords: Antibiotic agents, drug utilization, adverse drug reaction, ENT infection.

Original Article Research Paper

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ABSTRACT

Objective : To investigate the ENT department's (OPD, IPD) antibiotic prescribing practices at a tertiary care hospital in Lucknow, India.

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A prospective, cross-sectional, non-experimental (observational) study was performed in (OPD, IPD) department of Ear, Nose and Throat (ENT) over a period of 6 months.

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Conclusions

To conclude, our study in the university teaching hospital (IIMSR) highlighted lesser utilization of antibiotics in ENT infections, as some of the ENT infections are not due to bacteria. The majority of ENT patients admitted to the hospital appear to have bacterial infections, and most of them reacted favourably to antibiotic treatment. Majority of the patients used the regimen in accordance with the current guidelines.

Keywords: Antibiotic agents, drug utilization, adverse drug reaction, ENT infection.

INTRODUCTION

Adults and children generally are affected by diseases of the ear, nose, and throat (ENT), which can cause severe impairment in patients' daily lives [1]. With the growing global population, infections are expected to remain the leading cause of disease, with upper respiratory tract infections (URTIs) causing hearing loss and learning disabilities. The World Health Organization (WHO) reported in its World Health Report that respiratory infections caused 94.6 disability adjusted life years lost worldwide and were the fourth leading cause of death, accounting for 4.0 million fatalities or 6.9% of all deaths.

In a general hospital, acute respiratory infections account for 20-40% of outpatient visits and 12-35 percent of inpatient stays. URTIs, which include nasopharyngitis, pharyngitis, tonsillitis, and otitis media (OM), account for 87.5 percent of all respiratory infection episodes. They are a major cause of morbidity and workplace absenteeism. Viruses cause the great majority of acute URTIs. In most cases, a common cold is caused by viruses and does not require the use of antimicrobials unless it is accompanied by acute OM with effusion, tonsillitis, sinusitis, or a lower respiratory tract infection. Because most occurrences of rhino sinusitis are viral, they recover on their own without the need for antibiotics [2]. Antibiotics were mostly administered for respiratory and ENT diseases having a viral aetiology, like rhino-pharyngitis and severe bronchitis. Antibiotic prescriptions are written in around 40% of all consultations for rhino-pharyngitis and in about 80% of those for acute bronchitis, according to the findings of the various surveys. Antibiotics were administered in more than 90% of pharyngitis cases, regardless of the patient's age. In contrast, the frequency of consultations for acute middle ear infections has stayed essentially stable over the last ten years,

while antibiotic prescriptions have climbed dramatically, reaching 80 percent of consultations. Antibiotic prescription diversity is due to true variances in infecting organisms and antimicrobial susceptibility from country to country or even region to region, but other factors may also be at play, such as physician choice, local policy, costs, and a lack of local guidelines [3]. The current global rise in antibiotic-resistant bacteria, along with a lower trend in new antibiotic discovery, has major health and economic ramifications. Antibiotics are widely misused, including use based on false medical grounds, as well as misuse involving the improper agent, administration method, dose, and treatment duration. Antibiotic use results in the development of resistance as a natural biological process. "Poor patient adherence to dose regimens and the administration of substandard antibiotics result in suboptimal concentrations that fail to treat infection and may promote the formation of resistant bacterial populations; hence, underuse, irrational use, and overuse may both play a role in promoting resistance." At this time, there is no such thing as an ideal antibiotic, and the overuse of broad-spectrum antibiotics in respiratory infections leads to resistance development in pathogenic bacteria as well as the patient's normal bacterial reservoir [4]. Asia is one of the regions with the most serious resistance issues. The prevalence of resistant pneumococci in Asian countries, in particular, have been worrying. In India, bacteria resistant to ampicillin, trimethoprim, nalidixic acid, and chloramphenicol are found in nearly every healthy person [5]. Despite the fact that antibiotics have been used in clinical practice for many years, little is understood about how they should be used best in the clinic. How antibiotics should be delivered clinically to reduce resistance development while maintaining safety and efficacy is a crucial and largely unresolved subject. There is a need for data on both antibiotic use and determinants of use from all regions in the world. In too many countries there is no adequate surveillance of prescribing, of drug quality, or of the resistance problem. Through European surveillance of antimicrobial consumption (ESAC) project, significant improvements in the surveillance of antibiotic use in Europe have been achieved. However, a global approach is needed where comparable data are generated [6]. Therefore, studies reflecting drug utilization are required, as they assess the appropriateness of drug therapy. Drug use evaluation is an ongoing, authorized, and systemic quality improvement process that is designed to review the drugs that are prescribed to patients, provide appropriate feedback to clinicians/other relevant groups, develop criteria and standards that describe optimal drug use, and educate and counsel patients on appropriate drug use. Prospective drug utilization studies can directly influence patient treatment and outcome. Pharmacovigilance of antibiotics for its safer use is also essential; the overall purpose of pharmacovigilance is improvement in the safety of medicines (WHO, 2004). The estimation of the probability that a drug caused adverse clinical event is usually based on clinical judgment. Using the conventional categories and the criteria of definite, probable, possible and doubtful adverse drug reaction generates wide variability scales (Naranjo's and WHO's probability scale). The Naranjo's scale categorizes the reaction as highly probable, probable, possible and unlikely; this probability scale is based on simple questionnaire that can be answered rapidly [7], this scale is easier and time saving as compared to WHO's probability scale.

Hence, the present prospective study was aimed to evaluate drug utilization pattern and adverse drug reaction monitoring of antibiotics use in ear, nose and throat infections.

METHODOLOGY

Study design

It is a prospective study and it is based on a Medication Utilization Pattern that was designed on the basis of the WHO format.

Study site

Study was carried out in the IPD and OPD of a 500 bedded tertiary care and teaching hospital situated in Lucknow.

Study duration

The Study was carried out for 6 months.

Study Population

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Study was conducted on 100 patients during study period who shall willingly participate; subjects will be enrolled on the basis of inclusion and exclusion criteria.

Inclusion criteria

All the patients, of any age, irrespective of the sex attending the OPD and IPD will be included in the study.

All the patients who are prescribed at least one antibiotics.

Exclusion criteria

1. Patient who are not treated with ENT infection
2. Patient unable to comply.
3. Mentally retarded and unconscious patient.

Sources of data

Physician prescribing record

Patient medication profile

Method and Materials used

Medication Utilization and Suspected Adverse Drug Reaction Monitoring (MUADRM) form and CDSCO Suspected ADR Reporting Form. The data will be collected in a predesigned proforma from the medical record sheets, drug charts, and laboratory investigations of patients. The enrolled patients will be 100 observed from admission till discharge. Descriptive statistics will be applied to the collected data and analysed using Microsoft Excel software.

Data collection

The following data will be collected based on the questionnaire.

1. Patient profile (age, sex, weight, patient address, marital status).
2. Drugs prescribed (generic/brand name)
3. Drugs dose and frequency
4. Demographics, current diagnosis, medical history

Evaluation of parameters

The following parameters will be evaluated:

- Types of antibiotics prescribed
- Average number of antibiotics per prescription
- Average age range of patients utilizing antibiotics
- Comparison of antibiotics prescribed in monotherapy vs. fixed dose combination therapy
- Comparison of antibiotics prescribing by generic vs. brand name
- Compliance or adherence (using Weekly Diary Cards). A criterion for noncompliance is < 80% of recommended intake of prescribed drugs.
- Mode of administration of drugs
- Concomitant diseased conditions
- Most commonly used agents of a particular class
- Most common diagnosis
- Average cost of drug per prescription
- Occurrence and severity of adverse drug reactions due to antibiotics.
- Following are the example of suspected adverse drug reactions due to antibiotics mentioned in the table given below:

Table

Class	Drugs	Drugs	Adverse reaction
Beta - Lactams	**Beta - Lactams**	**Beta - Lactams**	**Beta - Lactams**
Penicillins	Amoxicillin, Amoxicillin + Clavulanic acid Piperacillin +Tazobactum	Amoxicillin, Amoxicillin + Clavulanic acid Piperacillin +Tazobactum	Nausea, vomiting, diarrhoea, erythematous maculopapular rashes, erythema multiforme, hypersensitivity vasculitis, urticaria, Anaphylaxis, Stevens-Johnson syndrome, Diarrhoea/loose stools, skin rashes, urticaria, vaginitis
Cephalosporins	Cefadroxil , Cefpodoxime, Cefixime, Cefixime , Ceftriaxone, cefoperazone + salbactum, cefepime + Tazobactum	Cefadroxil , Cefpodoxime, Cefixime, Cefixime , Ceftriaxone, cefoperazone + salbactum, cefepime + Tazobactum	Nausea, vomiting, diarrhea, rash, urticaria, angioedema, pruritus, erythema multiforme, Stevens-Johnson syndrome, Anaphylactic reaction, Diarrhoea, nausea, abdominal pain, vomiting, diaper and skin rash, headache, pruritus, Anaphylactic reaction
Carbapenems	Meropenem, Imipenem, Doripenem	Meropenem, Imipenem, Doripenem	Gastrointestinal upset and diarrhea, Nausea, Seizures, Headache, Rash and allergic reactions, Hypokalemia
Glycopeptides	Vancomycine , Teicoplanin	Hypersensitivity reactions (eg. Anaphylaxis, redman syndrome), AKI, hearing loss, vertigo, fever, chills.	Hypersensitivity reactions (eg. Anaphylaxis, redman syndrome), AKI, hearing loss, vertigo, fever, chills.
Aminoglycoside	Amikacin, Gentamycin, Streptomycin	Ototoxicity, Nephrotoxicity, Vertigo	Ototoxicity, Nephrotoxicity, Vertigo
Quinolones	Ciprofloxacin Norfloxacin Ofloxacin Levofloxacin Moxifloxacin	Nausea (rare), irreversible damage to central nervous system (uncommon), tendinosis (rare)	Nausea (rare), irreversible damage to central nervous system (uncommon), tendinosis (rare)
Macrolides	Azithromycin, Clarithromycin	Nausea, vomiting, and diarrhea (especially at higher doses), Jaundice	Nausea, vomiting, and diarrhea (especially at higher doses), Jaundice

Statistical analysis

· Descriptive statistics were applied to the collected data using Microsoft Excel software. Results are expressed in percentages and mean-standard deviation (SD). · ANOVA / Student's T- test was applied

on the collected data to evaluate the statistical significance.

Ethical considerations

The study was complied fully with the WHO guidelines and done after obtaining approval from Institutional Research and Ethics Committee with approval no IEC/IIMS&R/2021/58.

Informed Consent Form

An oral and written consent was obtained from the patient before participation of subject in the study.

RESULT

Demographic Character of Study Population

A total of around 700 patients visited the ENT OPD and IPD, over a period of 6 months. On the basis of inclusion and exclusion criteria, 100 patients were selected for the present study. Among the 100 ENT patients, 51 were male and 49 were female. The highest numbers of patients were in the age group 16–25 years and the lowest percentage was geriatric patients (Table 1, Graph 1).

Type of ENT Infection

During the study, it was observed that 87 patients visited for treating ear infection, 7 for nose infections, 5 for throat infections and 1 for combination of ENT infections (Table 2, Graph 2).

Average Number of Antibiotics Per Prescription

During the study, it was observed that the most commonly prescribed antibiotics were β-Lactam (penicillin's and cephalosporin's)–107, followed by Quinolones- 2, Macrolides- 2, Chloramphenicol – 43, Tetracycline – 2 and Aminoglycosides -43 (Table 3, graph 3).

Most Commonly Used Agents

The most commonly used agent of these classes, i.e., β-lactam was penicillin's (amoxicillin with clavulanic acid-50) and cephalosporin's (cefixime-49) followed by quinolones (chloramphenicol-43), macrolides (azithromycin-3), tetracycline's (doxycycline-1) and aminoglycoside (amikacin- 43) (Table 4, Graph 4).

Comparison of Antibiotics Prescribed in Monotherapy VS Fixed-Dose Combination Therapy

The prescription of patients showed that a total of 8 patients received antibiotics as monotherapy, whereas 12 patients were on multiple drug therapy. Among those who were treated with drug combinations, 25 received two drugs, 43 received three drugs and 17 received four drug regimens (Table 5, Graph 5). The average number of antibiotics agents prescribed per patient per course was found to be 19.894%

Mode of Administration of Drugs

A total of 40 antibiotics (this calculation is from both IPD and OPD and post- operative and pre-operative medications from day 1 to date of discharge of 100 patients) were prescribed. Their routes of administration were oral (30), intravenous (6) and ear drop (4) (Table 6, Graph 6).

Concomitant Disease Conditions

The comorbid condition of the study population was found was anxiety, epilepsy, anaemia (Table 7, Graph 7).

Occurrence and Severity of ADR due to Antibiotics

Overall 1 ADRs were reported during the study. Increase in no. of rashes in 1 patients due to suspected drug cefixime.(Table 8, Graph 8)

Discussion

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Prescription by a doctor may be taken as a reflection of physician's attitude to the disease and role of the drug in treatment. It also provides an insight into the nature of health care delivery system. Little information exists about the prescriptive behaviour of physicians and the misuse of antibiotics in the management of outpatient and inpatient with ENT infections.

In general practice, the therapeutic approach for ENT infections is nearly empirical and the main aim of physicians is to treat as specifically as possible, while covering the most likely pathogens. The present descriptive study indicates general trends of prescribing in the OPD and IPD of ENT department

Demographic characteristics showed that percentage of males suffering from ENT infections was more than females. Many other studies showed that females are more sensitive to ENT infections than males; the reason might be their exposure to kitchen smoke. In our study, the observed percentage of males was predominant which might be due to the occupational reasons.

Further, it was found that a majority of the patients were in the age group of 16–25 years and the lowest percentages were in geriatric group. It indicates that ENT infections are more prevalent in young adults. Few studies have reported that majority of patients fell in different age groups like 35 - 55 years.

Patients suffering from various acute and chronic ENT infections were treated with different antibacterial agents. In our study, the number of patients with OM was maximum, however the cases of acute and chronic suppurative OM (ASOM and CSOM) observed. The cases sinusitis , DNS (DEVIATED NASAL SPETUM) ,allergic rhinitis predominate in nose-infected patients , Thyroglossal Fistula and Chronic Rhinosinusitis Polyposis. However, sore throat, acute pharyngitis were the maximum cases of throat-infected patients. It was an interesting observation that a significant number of patients with combination of ENT patients suffered from URTIs alone or along with OM and other infections.

Most commonly prescribed categories of antibiotics were found to be β-lactam (32.05%),followed by cephalosporins (36.53%) , Aminoglycosides (27.56%) and macrolides (1.92%). The chloramphenicol and tetracyclines constituted only 1.28 and 0.64%, respectively. Among the individual antibiotic drugs, maximum patients received a combination of amoxicillin with clavulanic acid (25%), followed by Cefixime (28.84%), amikacin (27.56) chloramphenicol (1.28%), azithromycin (2.56%), clarithromycin (1.92%) ceftriaxone (3.84%) and doxycycline (0.64%). So, the use of azithromycin and clarithromycin should be indicated 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 to penicillin to amoxicillin/clavulanate, as indicative in our study, could be due to an increase in antibiotic resistance which encourages physicians to choose a broader and safer option. Further, 7.61 %patients received antibacterial monotherapy; whereas 91.8 % patients were on multiple drug therapy.

Limitation

Our study has many limitations. The study was carried out over a six month period, and the seasonal variations in disease pattern and drug utilization were not considered. Furthermore, the no of patients was low and the study was restricted only one hospital, hence the result cannot be considered representatives of the whole country. 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 disease suggested. In our future endeavours, we plan to study the effect of regulatory and educational interventions on drug use patterns in the management of Ear, Nose and Throat Infections.

Conclusion

To conclude, our study in the university teaching hospital (IIMSR) highlighted lesser utilization of antibiotics in ENT infections, as some of the ENT infections are not due to bacteria. It appears that majority of the ENT patients visiting the hospital have infections primarily due to bacteria and most of the patients responded well to the use of antibiotics. Majority of the patients used the regimen in accordance with the current guidelines.

Confidentiality of data

The data identifying each subject by name was kept confidential and accessible to the study personnel.

Data Availability

The patient's data have not been made public. They are kept with all the authors. If anyone need this data then request to corresponding author via e-mail.

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