RESEARCH ARTICLE

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Rational Use of Antibiotics and Monitoring of Drug Interactions in Patients with Respiratory Tract Infection

Nahid Akbari¹, Ramakrishna Prudhivi^{2,*}, Shobha Naidu³

¹Department of Pharmacy Practice, Dayananda Sagar College of Pharmacy, Bengaluru- 560078, INDIA.

²Department of Pharmacy Practice, Faculty of Pharmacy, Dayananda Sagar University, Bengaluru- 560078, INDIA.

³Department of Chest, Consultant Physician, Sagar Hospitals, Kumaraswamy Layout, Bengaluru- 560078, INDIA.

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*Correspondence to:

Dr. Ramakrishna Prudhivi,

Assistant Professor, Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananda Sagar University, Bengaluru- 560078, INDIA.

Email: ramakrishna.prudhivi@gmail.com

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Abstract

Background: A respiratory tract infection (RTI) is considered as one of the commonest public health problem dealt with in primary care. **Objective:** To evaluate the prescribing pattern of antibiotics, drug interactions involved and their rationality in the management of respiratory tract infection. **Methods:** The study was conducted in 180 RTI patients admitted in Sagar Hospital, Bengaluru. The study was a prospective, observational study. The information collected was based on inpatient case record and documented in the predesigned patient profile form. The data was analyzed and assessed using Micromedex 2.0, Medscape and www.drugs.com. **Results:** A total of 180 patients were included as per inclusion and exclusion criteria, out of which 98(54.4%) were male and the mean (SD) age of the patients was 58(14.3) years. Majority of patients had hypertension 77(26.22%) as co-morbidity followed by diabetes mellitus 64(21.89%). Among 180 cases, 42(23.33%) cases were diagnosed with URTI in which 7(16.66%) patients had sinusitis, 5(11.9%) had tonsillitis, 8(19.04%) had common cold, 2(4.76%) had pharyngitis and 19(45.23%) had unspecified URTI. In study population 134(74.44%) cases were diagnosed with LRTI in which 7(5.22%) were acute bronchitis, 40(29.85%) were bronchitis, 2(1.49%) were broncholithiasis, 29(21.64%) were pneumonia and 56(41.80%) were unspecified LRTI. 4(2.23%) cases were diagnosed with both URTI and LRTI. In current study a total of 322 Antibiotics were prescribed among which most commonly used is Piperacillin+ Tazobactam 88(27.32%) followed by Clarithromycin 52(16.14%). The most offending drug in major, moderate and minor drug interactions was clarithromycin 111(79.28%), clarithromycin 65(51.58%) and Piperacillin + Tazobactam 23(56.09%) respectively. **Conclusion:** This study concluded the prudent use of antibiotics will diminish the burden of multi-drug resistance and thereby providing better patient management.

Key words: Respiratory tract infection, Prescribing pattern, Rational use of antibiotics, Drug interactions.

INTRODUCTION

A Respiratory Tract Infection (RTI) is an infection anywhere in the respiratory tract (i.e. nose, throat and lungs) and is the leading cause of morbidity and mortality in many developing countries.^[1] RTI is defined as any infectious disease of the upper and lower respiratory tract.^[2] Upper respiratory tract infection (URTI) is a common infectious disease which includes the common cold, laryngitis, pharyngitis/tonsillitis, acute rhinitis, acute rhino-sinusitis and acute otitis media. Lower respiratory tract infections (LRTIs) are the most common infectious disease which includes tracheitis, bronchitis, broncholithiasis and pneumonia.

Upper respiratory tract infections including nasopharyngitis, pharyngitis, tonsillitis and otitis media constitute 87.5% of the total episodes of respiratory infections. The vast majority of acute upper respiratory tract infections are caused by viruses.^[3] Lower respiratory tract infections (LRTI) are a major cause of morbidity and mortality in children aged <5 years in developing countries.^[4] Infections of LRTI are responsible for 4.4% of all hospital admissions and 6% of all general practitioner consultations.^[5] There is inadequate information from India on various lower respiratory tract bacterial pathogens and their resistance patterns in hospital settings.^[6] Globally more than 1.5 million deaths annually from respiratory infections are attributable to the environment, including at least 42% of lower respiratory infections and 24% of upper respiratory infections in developing countries.^[7]

Antibiotics are the substances produced by microorganisms, which selectively suppress the growth or kill other microorganisms at very low concentrations.^[8] According to the current literature, before prescribing an antibiotic for these infections, a precise diagnosis must precede; such diagnosis shall establish its bacterial origin to prevent the null clinical utility of the drug and a potential risk of increasing bacterial resistance.^[9] Inappropriate use of antibiotics, particularly for RTIs, has contributed to the major public health problem of antibiotic resistance in the community.^[10] Antibiotic resistance is a global health problem and a major cause for concern. It is associated with the inappropriate, as well as frequent, use of antibiotics.^[11] Antibiotics experienced some adverse reactions to the drugs of which 20% required treatment.^[12]

The prescribing pattern deals with monitoring, evaluating and suggesting modifications in the prescribing pattern, so as to make patient care safe, effective and cost effective.^[13] The identification of antibiotic-prescribing practices should be the first part of a strategy that would reduce its unnecessary usage and consequences.^[14] Irrational prescribing pattern has been widely reported from both developed as well as developing countries.^[15]

A drug interaction occurs when a patient's response to a drug is modified by food, nutritional supplements, formulation excipients, environmental factors, other drugs or disease. Interactions between drugs (drug-drug interactions)

may be beneficial or harmful. Harmful drug–drug interactions are important as they cause 10–20% of the adverse drug reactions requiring hospitalization and they can be avoided. Knowing how drug–drug interactions occur and how to manage them is an important part of clinical practice.^[16,17] However, clinicians should recognize that patient satisfaction is not compromised by the absence of an antibiotic prescription provided that patients understand the reasons.^[18]

Here, we explore the prescribing pattern of antibiotics in the management of respiratory tract infection and assessment of the drug interactions associated with antibiotics used in respiratory tract infections.

METHODOLOGY

Study design and settings: This was a prospective, observational study of RTI patients registered in Medicine Department at Sagar Hospitals, Bengaluru, India from September 2016 to February 2017 (six months). **Ethics approval and consent to participate:** All participants gave written informed consent to participate. Permission to conduct the study was obtained from Institutional ethics committee, Dayananda Sagar College of Pharmacy, Bengaluru. **Sources of data:** The sources of data used for this study includes, personnel interviews of patients and their representatives and patient's treatment files. **Inclusion criteria:** All patients either sex who diagnosed with respiratory tract infection, patients prescribed with antibiotics. **Exclusion criteria:** Patients who were not willing to participate in the study, patients having tuberculosis and other infections, patients suffering with other than RTI's and Immuno-suppressed patients. **Study procedure:** RTI patients visiting medicine department were identified and consented. Patients were enrolled in the study based on inclusion and exclusion criteria. Informed consent was obtained from the patient at the time of enrollment. During the study, the inpatient case records were reviewed which included patient demographics, antimicrobials use such as names of antimicrobials, their dosage schedule, route of administration, date of discontinuation, generic name and bacteriological investigation. Antibiotics were subsequently categorized into classes, informed by British National Formulary subcategories.^[19] The information collected was documented in the predesigned patient profile form. The rationality of antibiotics was analyzed with the help of guidelines prepared from Micromedex and ACP. The dose, indication, route and duration of antibiotics were verified from Micromedex. The drug interactions were assessed using Micromedex 2.0, Medscape and www.drugs.com. **Statistical analysis:** Categorical variables were reported as frequency and percentage frequency. Chi square test was performed to determine the strength of association between gender and variables P-value less than 0.05 were considered as statistically significant. Data was analyzed using a statistical tool Graph Pad Prism software version 5.0.

RESULTS

Patient characteristics: A total of 180 patients were included as per inclusion and exclusion criteria, out of which 98(54.4%) were male and 82(45.6%) were female. The mean (SD) age of the patients was 58(14.3) years. The majority 95(52.77%) of the patients belonged to age group >60 years. 163(90.55%) patients were married. There were 124(68.89%) cases of nonsmokers where 22(12.21%) were occasional smoker, 11(6.11%) were ex-smoker and 23(12.79%) were smokers. Out of 180 patients, 4 (2.22%) patients were having alcohol consumption in which 51(28.34%) were occasional alcoholic, 9(5%) were ex-alcoholic and 116(64.44%) were nonalcoholic patients (Table 1). Table 2 showed analysis of socio-demographic characteristic of patients. There is a significant difference between male and female in smoking habit and alcohol consumption.

Table 1: Socio-demographic and clinical characteristics of tuberculosis patients.

VARIABLES	N (%)
GENDER	98(54.4)
Male	82(45.6)
Female	
AGE (YEARS)	
0-10	5(2.77)
11-20	3(1.66)
21-30	17(9.44)
31-40	18(10)
41-50	11(6.11)
51-60	31(17.22)
>60	95(52.77)
MARITAL STATUS	
Married	163(90.55)
Unmarried	17(9.44)
SMOKING	
Non Smoker	124(68.89)
Ex-smoker	11(6.11)
Occasional smoker	22(12.21)
smoker	23(12.79)
ALCOHOL	
Non alcoholic	116(64.44)
Ex-alcoholic	9(5)
Occasional alcoholic	51(28.34)
Alcoholic	4(2.22)

Table 2: Analysis of socio-demographic characteristic of patients.

VARIABLE		MALE 98(54.4%)	FEMALE 82(45.5%)	CHI - SQUARE VALUE	P -VALUE
Age	≤65	53(52.47)	48(47.53)	0.3598, df = 1	0.5486
	>65	45(56.96)	34(43.04)		
Marital status	Married	87(53.37)	76(46.63)	1.832, df = 1	0.1758
	Unmarried	12(70.58)	5(29.41)		
Smoking status	Non Smoker	44(35.48)	80(64.51)	58, df=3	< 0.0001
	Ex-smoker	10(90.9)	1(9.09)		
	Occasional smoker	21(95.45)	1(4.54)		
	Smoker	23(100)	0		
Alcohol status	Non alcoholic	47(28.31)	69(59.49)	53, df=3	< 0.0001
	Ex-alcoholic	9(100)	0		
	Occasional alcoholic	38(74.5)	13(25.5)		
	alcoholic	4(100)	0		

Values are significant If P-value <0.05

Table 3: Distribution of the study population according to co-morbidities.

CO-MORBIDITY	NO. OF CASES	PERCENTAGE
Hypertension	77	26.22
Diabetes mellitus	64	21.89
Asthma	33	11.36
IHD	29	9.86
Hypothyroidism	22	7.48
Kidney disease	21	7.14
COPD	11	3.74
UTI	7	2.38
Anemia	6	2.04
Hyperlipidemia	5	1.70
Seizure	5	1.70
Methabolic acidosis	3	1.02
Sepsis	3	1.02
Dehydration	2	0.68
Obesity	2	0.68
Parkinsonism	2	0.68
Gout	1	0.34
Hypoglycemia	1	0.34

Table 4: Classification of respiratory tract infections.

TYPE OF RTI	NO. OF PATIENTS	PERCENTAGE
URTI	42	23.33
Sinusitis	7	16.66
Tonsillitis	5	11.9
Common cold	8	19.04
Pharyngitis	2	4.76
Unspecified	19	45.23
LRTI	134	74.44
Acute bronchitis	7	5.22
Chronic bronchitis	40	29.85
Bronchiolitis	2	1.49
Pneumonia	29	21.64
Unspecified	56	41.80
BOTH	4	2.23

Co-morbidities: Majority of patients had hypertension 77(26.22%) as co-morbidity followed by diabetes mellitus 64(21.89%). Highest number of co-morbidities seen in one patient was found to be four (Table 3).

Culture sensitivity test and TLC: In this study 130(72.22%) patients were undergone culture sensitivity test. Other diagnostic test like TLC was also performed. All patients were undergone TLC test and most of the patients 131(72.78%) had total leukocyte count more than 10000 cells/cmm.

Classification of RTI: Among 180 cases, 42(23.33%) cases were diagnosed with URTI in which 7(16.66%) patients had sinusitis, 5(11.90%) had tonsillitis, 8(19.04%) had common cold, 2(4.76%) had pharyngitis and 20(47.64%) had unspecified URTI. In study population 134(74.45%) cases were diagnosed with LRTI in which 7(5.22%) were acute bronchitis, 40(29.85%) were bronchitis, 2(1.49%) were bronchiolitis, 29(21.64%) were pneumonia and 56(41.80%) were unspecified LRTI. 4(2.23%) cases were diagnosed with both URTI and LRTI (Table 4).

Hospital Duration: The maximum number of patients 16.11% stayed in the hospital for duration of 5 days and the mean average stay of hospitalization were found to be 6.4 ± 3.22 days.

Major antibiotics prescribed: Among our 180 patients the maximum number of drugs prescribed was 20 drugs per prescription and least was 2 drugs per prescription. In the current study a total of 322 Antibiotics were prescribed among which most commonly used is Piperacillin+ Tazobactam 88(27.32%) followed by Clarithromycin 52(16.14%) (Figure 1).

Figure 1: Distribution of antibiotics used in RTI treatment. **Figure 2: Reasons for irrational use of antibiotics.**

- A= Inappropriate duration of treatment
- B= Culture sensitivity test not advised
- C= Inappropriate selection of Antibiotics for continue in discharge medication chart.
- D= Dose adjustment for kidney failure didn't consider
- E= Dose adjustment for elderly didn't consider
- F= Inappropriate duration of treatment and not dose adjustment for kidney failure
- G= Inappropriate duration of treatment and culture sensitivity test didn't advised
- H= Culture sensitivity test didn't advised and dose adjustment for kidney failure patients didn't consider
- I= Dose adjustment for elderly didn't consider and dose adjustment for kidney failure patients didn't consider
- J= Inappropriate duration of treatment and not dose adjustment for elderly
- K= Culture sensitivity test didn't advised and not dose adjustment for children
- L= Culture sensitivity test didn't advised and dose adjustment for elderly didn't consider

Figure 3: Distribution of antibiotics with major drug interactions.

Figure 4: Distribution of problems identified in prescriptions.

Rationality: It was found that 55.55% of prescriptions were rationally prescribed and 44.45% were irrational prescription of antibiotics out of which maximum number 28(35%) was for this reason that culture sensitivity test was not advised which lead to inappropriate choice of antibiotics (Figure 2).

Drug interactions: Out of 180 prescriptions, 129(71.67%) were found to have possible drug interactions among which 45.60% were major, 41.04% were moderate, 13.36% were minor drug interactions. The most offending drug in major, moderate and minor were clarithromycin 111(79.28%) (Figure 3), clarithromycin 65(51.58%) and Piperacillin + Tazobactam 23(56.09%) respectively.

Problems identified: As shown in Figure 4 there were some cases of problems occurred in prescriptions which included duplication (14.86%), Untreated indication (17.63%), Spelling of drug (8.76%), inappropriate use of letter in prescription (capital/small) (14.43%), completion of prescription (dose, frequency, route of administrations) (44.32%).

DISCUSSION

The present study includes a total of 180 patients, as per the inclusion and exclusion criteria and there were 54.4% males and 45.6% females which was found to be similar as study conducted by Divia *et al.* and concluded that there was no much variation between males and females.^[20] As per the study population the greatest number of patients was in the age group of above 60 years with the mean (SD) age of 58(14.3). This was similar to the

study conducted by Rosman *et al.* where it was found that greatest number of patients were in the age group of more than 60 years with the mean age of 56.2 ± 17.7 years.^[22] Majority of patients were nonsmokers and non-alcoholics which was similar to study.^[23]

Among 180 patients studied, there were a total of 294 co-existing illness such as HTN 26.22%, DM 21.89%, Asthma 11.36% which was similar to Harish *et al.*, study where it found that HTN 38.2%, DM 36.2%, Asthma 13.3%.^[24]

In this study 72.22% patients were undergone culture sensitivity test which helps in providing accurate antibiotic therapy. Other diagnostic test like TLC was also performed for all patients. In a study done by Harish GN *et al.* showed that culture sensitivity was done in 33.33%. The decrease in the percentage of culture might be based on the clinical presentation at the time of admission or patient might have consumed the antibiotic prior to admission.^[24]

In current study patients were categorized based on the type of RTI such as LRTI and URTI. Among 180 patients 75.45% of them were diagnosed with LRTI which was further categorized as acute bronchitis 5.22%, chronic bronchitis 29.85%, bronchiolitis 1.49%, pneumonia 21.64%, unspecified 41.80%. In a study carried out by Divya *et al.* out of 67 patients 46.55% were acute bronchitis 27.58% were pneumonia 20.68% were bronchopneumonia, 3.44% patients had COPD and 1.72% was chronic bronchitis.^[20]

In this study 23.33% of the cases were diagnosed with URTI. Out of which 19.04% had common cold, 4.76% had pharyngitis, 16.66% patients had sinusitis, 11.90% had tonsillitis and 47.64% had unspecified URTI. In another study conducted by Harish *et al.* diagnosis of URTI accounted for nonspecific URTI 56.5%, sinusitis 28%, pharyngitis 12% and CSOM 3.5%.^[21]

In present study the maximum number of patients 16.11% stayed in the hospital for duration of 5 days and the mean average stay of hospitalization was found to be 6.4 ± 3.22 days which was similar to the study conducted by Rosman *et al.* where the mean average stay of hospitalization was found to be 6.9 ± 5.33 days.^[22]

An audit of antibiotic prescribing patterns is an important indicator of the quality and standard of clinical practice. The most commonly prescribed antibiotics according their classes were combination of Penicillin + Beta lactamase inhibitors 33.84% followed by Cephalosporins 16.75 %. In other study conducted by Rajalingam R *et al.* the most commonly prescribed antibiotics were Cephalosporins 15.38%, followed by Quinolones 6.76%.^[25] The study of prescribing patterns is a part of medical audit and seeks to monitor, evaluate and if necessary, suggest modification in prescribing practice to make medical care rational.

When rationality was checked for overall appropriateness of antibiotics prescribed were analyzed and it was found to be 55.55%. In a study conducted by Rajalingam *et al.* the assessment of rationality was performed by collecting evidences from published literature about individual antibiotics. The results showed that rationality was found to be 57.85%.^[25]

In the current study prescriptions were subjected to drug interactions. The results revealed that out of 180 prescriptions, 71.67% were found to have drug interactions. The results of drug interactions between drugs prescribed with antibiotics was found to have 307 drug interactions, among which 45.60% were major, 41.04% were moderate, 13.36% were minor drug interactions. The most offending drug in major, moderate and minor was clarithromycin 79.28%, clarithromycin 51.58% and Piperacillin + Tazobactam

56.09% respectively. In study conducted by Divia *et al.* revealed that 67.5% prescriptions had at least 1 interaction and remaining 32.5% did not have any drug interactions at all. The number of drug interactions from these 135 prescriptions was counted to be 148. Out of 200 prescriptions, 25.42% of interactions were caused by antibiotics. Incidence of drug interactions was major 31.75%, moderate 42.56% and minor 25.67%.^[20]

Prevention of medication errors is a priority for health services. Pharmacists routinely screen prescriptions for potential problems, including prescribing errors. This study identified presence of some of problems with prescriptions of our population of study. In the analysis of prescriptions, the results showed there were some cases of problems occurred in prescriptions which included duplication, Untreated indication, Spelling of drug, Inappropriate use of letter in prescription (capital/small), Completion of prescription (dose, frequency, route of administrations). Out of 180 prescriptions, 14.86% prescriptions were found to have drug duplications. The most common drug duplication was with injection or tablet Lasix (Furosemide) with tablet Lasilactone (Furosemide+ Spironolactone) and nebulizer Asthalin (Salbutamol) with nebulizer Duolin (Salbutamol+ Ipratropium). Other problems identified include untreated indications 17.63%, spelling of drug 8.76%, inappropriate use of letter in prescription (capital/small) 14.43%, Completion of prescription 44.32% (dose 59.30%, frequency 27.91% and route of administrations 12.79%). No literature was available to compare the variables for the present study.

CONCLUSION

This study concluded the prudent use of antibiotics which will diminish the burden of multi-drug resistance and thereby providing better patient management and limiting the outcome morbidity and mortality arising from respiratory tract infections. There is essential need for microbiological investigation before treatment of infections. The result of this study distinctly illustrated the majority of antibiotics were not complying with the WHO and ACP guidelines used for the assessment of rationality.

Most potential drug interactions can be detected by applying principles of clinical pharmacology and good clinical care. Increased awareness by clinicians at the time of choosing of drug decreases the unwanted drug interactions before they cause significant harm. The addition of clinical pharmacist services in the care of in patients with respiratory tract infections resulted in better care team, assessing rational use of drug, detecting possible drug interaction, interacting with physicians which leads to improved outcomes.

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CONFLICT OF INTEREST

The authors declare no conflict of interest

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