ORIGINAL ARTICLE

Analysis of Pattern of Antimicrobial use in Respiratory Tract Infections in a Tertiary Care Hospital of Central India- A Drug Utilization Study

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Abstract

Background**: Respiratory tract infection (RTI) is leading infection among all the infections and antimicrobial agents (AMAs) are prescribed for the same more commonly. It is well known fact that, most common mechanism of antimicrobial resistance is irrational use.* ***Aims and Objectives: *To analyze the prescribing pattern of antimicrobial drugs used in respiratory tract infections for rational use, in a tertiary care hospital of central India.* ***Materials and Methods:*** *It was a six months observational, retrospective study, carried out on total of 400 records, obtained from Medical Record Department. WHO drug utilization indicators- ATC/DDD was used.* ***Results:*** *Upper RTI (URTI) and Lower RTI (LRTI) were found in 240 & 160 patients, respectively with non-specific RTI (viral fever) topping the list. Most common AMA prescribed was Azithromycin (23.9%), while Amoxicillin+Clavulanic acid, was most commonly used fixed dose combination-FDC (14.9%). Maximum cost was shared by Penicillins, Cephalosporins and Azithromycin. 9 out of 15 AMAs used (60%) were prescribed from WHO-essential drug list. No generic drug was prescribed. Culture/sensitivity was done only in 20 cases.* ***Conclusion:*** *Some irrationality seen can be corrected by continuous medical education (CME) for physicians. Prescription indicators should be used to evaluate the prescriptions from time to time, for improving quality of health care with minimal expenses.*

Key words: *Antimicrobial agents, upper respiratory tract infection, lower respiratory tract infections*

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Introduction

Respiratory tract infections (RTI), comprising of upper respiratory tract infection (URTI) and lower respiratory tract infection (LRTI) are one of the most common infections, and are associated with considerable expenditure of currency of the nation. RTI's have been identified as major cause for restriction of activity and loss of attendance at school and work. URTI includes infection ranging from nose to trachea. LRTI includes infection of lung parenchyma, bronchus, bronchiole.[1,2] Since RTI is one of the major reasons of antimicrobial agent/s (AMA/s) use on a large scale and because changes in AMA resistance pattern are a threat to its effective treatment, there is increasing concern about such unnecessary AMA prescription in the community.[3] Better drugs are available currently, patients are better educated, have greater expectations from health care systems and they use multiple health care systems, still drugs are not used properly according to the guidelines. Irrational use of AMAs has given rise to rapid emergence of resistance amongst microbes.[4] In the present scenario, AMAs are among the most common irrationally prescribed drugs.

The quality of health care depends on fulfillments of five properties of prescription- judicious, appropriate, safe, effective and economically feasible.[5] Inappropriate drug use includes misuse, overuse or underuse of a drug, either of which may lead to increased cost of health care, adverse effects or less therapeutic effect. There is mounting apprehension about ever increasing cost of health care, lack of rationality and homogeny in prescribing AMAs and finally, lack of monitoring and control over use of the same. Therefore, it is dire need of the hour, to promote rational use of AMAs,[6] which is tested lately by Drug Utilization (DU) studies. WHO defines DU as marketing, distribution, prescription and use of drugs in society, with special emphasis on the resulting medical, social and economical consequences.[7,8] For DU, WHO laid down guidelines of ATC/DDD (Anatomical and Therapeutic Classification, Defined Daily Dose) which are used as drug utilization indicators. DDD was formulated as a means of study of drug sales, to serve as a proxy for drug consumption/utilization. The objective of ATC/DDD system is to serve as a tool for DU research, to favor improvement in drug use. [9,10]

Present study was conducted to analyze the prescribing pattern of antimicrobial drugs used in respiratory tract infections for rational use, in a tertiary care hospital of central India using combination of latest WHO DU indicators (ATC/DDD, PDD- Prescribed Daily Dose) and conventional method of comparing actually prescribed AMAs with WHO essential drug list. Such studies are useful improving quality of health care with minimal expenses.

Materials and Methods

It was an observational, retrospective, record based study, which was carried out from September 2013 to March 2014 at NKPS Institute of Medical Sciences and Research Centre, Nagpur, India. Permission for the study was obtained from Institutional Ethics Committee. WHO recommendations for DU were avidly taken into account and were strictly and consistently followed throughout the study.[11] After filtering numerous records through inclusion criteria, and exclusion criteria, a total of 400 records were finally analyzed. Inclusion criteria were patients with diagnosis of RTI and age above 15 years, irrespective of sex. Exclusion was Pregnancy, Age below 15 years, Inadequate clinical records/ data, Tuberculosis and Malignancy.

All the records were retrieved from Medical Records Department (MRD), and all data was collected using a specially designed data collection sheet, which included important demographic characteristics like name, age, sex, occupation, diagnosis and prescription details including type of antibiotic, number of antibiotic per patient, route of administration, average hospital stay, culture and sensitivity reports, status of patient. Data was presented as n (%).Total AMAs prescribed were compared with WHO essential drug list and latest DDD values were substituted.[12,13] Drugs were classified according to ATC system proposed by WHO. Drugs are systematically classified at 5 levels- 1st level is anatomical i.e. system on which it acts, 2nd level is therapeutic subgroup, 3rd level is pharmacological subgroup, 4th level is chemical subgroup (its chemical nature) and 5th level is chemical substance i.e. specific drug name. For combinations, if 2 active drugs are at same level 4, they are classified in 5th level codes-20 to 30 and they don't belong to same 4th level, then they are classified using 50 series. DDD is defined as assumed average maintenance dose per day for a drug, used for its main indication in adults. DDD is assigned only to drugs that have an ATC code. It should be emphasized that the DDD is a unit of measurement and does not necessarily reflect PDD. DDD's/1000 inhabitants/day provide an estimate of the proportion of population within defined area, treated daily with certain drugs. PDD gives average daily amount of a drug that is actually prescribed. Formula for calculation of DDD's/1000 inhabitants/day is as under:[10]

DDD's/1000 inhabitants/day =

$$\frac{\text{Total use of drug (mg) during study} \times 1000}{\text{DDD (mg)} \times \text{duration of study (in days)} \times \text{sample size}}$$

Results

Out of total 400 records analyzed 177 were males (44.2%) and 223 were females (55.7%). URTI accounted for 240 cases (60%), while LRTI was found in 160 cases (40%). Incidence of both was maximum in age group >45 years.

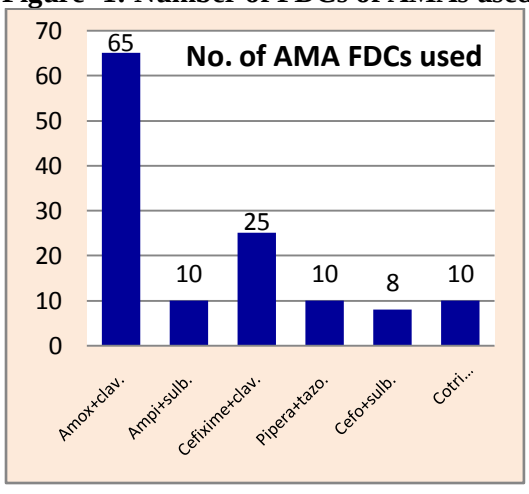
Among URTI, most common etiology was non-specific URTI (25%) and non-specific LRTI was the main culprit in LRTI (44.3%) table- 1. Fever+ cough+ throat pain predominated the symptom list (30%), and it was found that all these patients were prescribed with AMAs. Other symptoms were throat pain, cold and nonspecific flu.

Only 15 patients did not receive AMAs. Average number of AMA per patient was 1.14%. Single AMA therapy was given in 340 patients (88.3%), 2 AMAs in 41 patients (10.6%), 3 AMAs in 4 patients (1%). AMAs were administered orally in 267(61.6%) and parenterally in 167 patients (38.4%). Oral route was used predominantly in URTI and parenteral route was used maximum in LRTI. Average cost of hospital stay was 441.56 Indian Rupees. Maximum cost of individual AMA shared by Penicillin, Cephalosporin and Azithromycin. Favorable outcome was seen in 96.2 % cases. Percentage of total AMA prescribed from WHO essential drug list were single drug- 7 out of 9 (66.7%), FDC -2 out of 6 (33.3%) and overall-9 out of 15 (60%). Most common AMA prescribed was azithromycin (23.9%). Among the Fixed Dose Combination (FDC), amoxicillin + clavulanic acid (14.9%) was most commonly prescribed (Figure- 1).

Table- 1: RTI distribution

Illness	Number (%)	Male (%)	Female (%)	Most affected Age Group
URTI				
Non-sp. URTI	60(25)	25(14.1)	35(15.7)	>45 years
Sinusitis	56(23.3)	30(17)	26(11.6)	30-45 years
Pharyngitis	48(20)	17(9.6)	31(14)	>45 years
ASOM	34(14.1)	20(11.2)	14(6.2)	>45 years
Tonsillitis	42(17.5)	12(6.8)	30(13.4)	15-30 years
LRTI				
Non-sp. LRTI	71(44.3)	32(18)	39(17.4)	>45 years
Pneumonia	65(40.6)	27(15.2)	38(17)	>45 years
Bronchitis	24(15)	14(7.9)	10(4.4)	30-45 years
Total	**400**	**177(44.2)**	**223(55.7)**	

Figure- 1: Number of FDCs of AMAs used



Amox- Amoxicillin, Clav- Clavulanic acid
Ampi- Ampicillin, Sulb- Sulbactam
Pipera- Piperacillin, Cefo- Cefoperazone
Cotri- Cotrimoxazole, TMP- Trimethoprim
SMX- Sulfamethoxazole

Culture/sensitivity (C/S) was done in 20 patients (5%) and most common organism isolated was Staphylococcus aureus, followed by alpha hemolytic Streptococcus pneumoniae in URTI and Kleibsiella pneumoniae, followed by Pseudomonas in LRTI, which was found sensitive to amoxicillin+clavulanic acid, 3rd and 4th generation cephalosporins. AMA was changed in 10 patients after C/S report. Maximum cost was shared by macrolide (azithromycin), penicillins, cephalosporin. PDD was calculated for each drug and compared with DDD. DDDs/1000 inhabitants/day was also calculated for each drug and maximum value was found in azithromycin (2.8472) and least in ofloxacin (0.0138). PDD> DDD was found in amoxicillin (O & P), cefuroxime, azithromycin, doxycycline, cefixime + clavulanic acid, piperacillin + tazobactam, cotrimoxazole, levofloxacin(O), cefixime. PDD=DDD was

found in ceftriaxone, ofloxacin (O), amoxicillin + clavulanic acid (O). PDD<DDD was found in cefotaxime, ofloxacin (P), amoxicillin + clavulanic acid (P), ampicillin + sulbactam, cefoperazone+sulbactam, levofloxacin (P). 379 patients (96.2%) showed improvement. Average cost/stay was 441.56 Rs. No generic drug was used. No pattern of frequency of AMA prescription was found in correlation with socio-economic status of the patient (Table- 2 & 3).

Table- 2: ATC/DDD classification of AMAs prescribed

AMA used	ATC code	DDD in mg	PDD in mg	DDDs/1000 inhabitants/day
Amox (O)	J01CA04	1000	1161.1	0.625
Amox(P)	J01CA04	1000	1833.3	0.1388
Ceftriaxone	J01DD04	2000	2000	0.0583
Cefotaxime	J01DD01	4000	3000	0.3518
Cefixime	J01DD08	400	519.4	1.0281
Cefuroxime	J01DC02	500	625	0.1111
Azithromycin	J01FA10	300	519.23	2.8472
Levofloxacin(O)	J01MA12	500	600	0.0333
Levofloxacin(P)	J01MA12	500	400	0.0416
Ofloxacin(O)	J01MA01	400	400	0.0138
Ofloxacin(P)	J01MA01	400	318.4	0.1247
Doxycycline	J01AA02	100	175	0.3333
Amoxicillin+Clavulanate(O)	J01CR02	1000	1000	0.0687
Amoxicillin+Clavulanate(P)	J01CR02	3000	2800	0.301
Ampicillin+sulbactam	J01CR01	2000	1654.13	0.1814
Cefixime+clavulanate	J01DD08	400	500	0.6518
Piperacillin+tazobactam	J01CR05	14000	15679.47	0.4273
Cefoperazone+sulbactam	J01DD62	4000	3012.43	0.1624
Cotrimoxazole(TMP+SMX)	J01EE01	1920	2000	0.2123

Table- 3: Comparison of PDD and DDD

PDD=DDD	PDD>DDD	PDD<DDD
Ceftriaxone	Amoxicillin(O)	Cefotaxime
Ofloxacin(O)	Amoxicillin(P)	Ofloxacin(P)
Amoxicillin+clavulanic acid(O)	Cefuroxime	Amoxicillin+clavulanic acid(P)
	Azithromycin	Ampicillin+sulbactam
	Doxycycline	Cefoperazone+sulbactam
	Cefixime+clavulanic acid	Levofloxacin(P)
	Piperacillin+tazobactam	
	Cotrimoxazole(TMP+SMX)	
	Levofloxacin(O)	
	Cefixime	

Discussion

RTI is one of the most common cause for absenteeism from work and studies.[2] Prescribing drugs, is a multifactorial, complicated process which is influenced by socio- cultural factors like national drug policy, illiteracy, poverty, use of multiple health care

systems, drug advice and promotion, sale of prescription drugs without prescription, competition in the medical and pharmacological market place and limited availability of independent, unbiased information. Improper use of drug echoes in the form of rise in cost of medical care, antimicrobial resistance, adverse effects, patient morbidity and mortality.[14] In the present study, incidence of URTI was more as compared to LRTI. Most common perpetrator in URTI was non-specific URTI and non-specific LRTI in LRTI. Incidence of both was found more in age group >45 years, other studies showing maximum incidence in younger age groups[15,16] AMAs were prescribed in all, except in 15 patients. Most probable reason of such high rate of AMA use may be higher expectation of patient, and hence overprescribing by the physician to meet the same.[4] Average number of AMA/patient was one, which is a welcome sign, since least use of AMA in uncomplicated RTI is always expected. This findings were in contrast to other studies, which showed AMAs per patient to be 2,2.5,3,4.[17,18,19,20] Most common AMA prescribed was azithromycin. Generic drugs were not prescribed at all. Of 15 AMAs prescribed, 9 were included in WHO essential drug list (60%), while other studies showed lower percentages.[6,20] Most common route of drug administration was oral in URTI and parenteral in LRTI. C/S was done in 20 patients and most common organism isolate in URTI and LRTI was Staphylococcus aureus and Kleibsiella pneumoniae respectively, while other studies showed alfa hemolytic streptococci followed by Neisseria species.[16] Findings of comparison between DDD and PDD were in contrast with other studies.[1,2] PDD can vary according to both, illness treated and national therapy traditions. For the anti-infectives, for instance, PDDs vary according to the severity of the infection. It should be noted that the PDD does not necessarily reflect actual dose consumed. It should also be emphasized that the DDD is a unit of measurement and does not necessarily reflect PDD. Doses for individual patient and patient groups will often differ from the DDD and will have to be based on individual characteristics of the patient- age, weight, and pharmacokinetic considerations. PDD/1000 inhabitants/day was maximum in azithromycin, which was similar in other study[1], indicating that it is most favored AMA of choice amongst the physicians. The present study carries weightage since it combined latest WHO-DU indicators and conventional approach of DU study i.e. to tally actually prescribed AMAs with essential drug list, thus making it more comprehensive, covering maximum aspects of DU study. Our study had plethora of significant findings, which will probably help in designing prescribing strategies, such that they decrease unnecessary use of AMAs, thus decreasing cost of treatment and most importantly curb the spread of AMA resistance.

Conclusion

Patients with fever+cough+throat pain were prescribed with maximum AMAs, although it is well known that this symptoms are found mostly in viral fever, which do not benefit by use of AMAs, thus indicating their unnecessary use. This results in emergence of resistance, which prompts the physician to use newer AMAs, which are costly. Use of generic drugs should be encouraged or if possible, made compulsory. Physicians should be educated about rational drug prescribing, cost-effectiveness and adhering to established treatment guidelines, through CMEs, workshops, clinical meetings. Guidelines should be prepared by the concerned departments of the institute concerning judicious and effective use of AMA/s.

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