

A Prospective Study on Assessment of Rationality in Prescribing Antimicrobial Agents at a Tertiary Care Hospital

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ABSTRACT

Introduction: Antimicrobial Agents (AMAs) rationality has become the most prevalent issue world wide as the irrational prescribing is leading to antimicrobial resistance. So, reporting interventions and identification of drug related problems, may help in avoidance or control or prevention the antimicrobial resistance.

Aim: To assess rationality in usage of AMAs in both infectious and non infectious conditions at a tertiary care hospital using ICMR guidelines, National Treatment Guidelines for Antimicrobial Use in Infectious Diseases, PCNE guidelines.

Materials and Methods: A prospective observational study was carried out at inpatient department in a tertiary care hospital. The data of 260 cases were collected and recorded during regular ward rounds and were thoroughly analysed to evaluate inappropriateness in drug usage by ICMR guidelines, WHO-INRUD drug core indicators, Pharmaceutical Care Network Europe (PCNE) guidelines and Essential Drug List (EDL). Data analysed also included the results on patient's demographics (age, gender, type of AMAs etc.). Errors obtained were reported to physician. Data analysis was performed using descriptive analysis.

Results: The findings of the study reveals that the average age of high incidence with AMAs was found to be 55.5 years, where male population were majority with 52% and female with 48% of AMAs prescriptions. Non infectious conditions (56.5%) were more than the infectious conditions (43.4%). Among 487 drugs prescribed in 260 prescriptions majority of them were antibiotic drugs (480), followed by antifungal drugs (6) and antiviral

drug (1). The most commonly prescribed category of antibiotic was cephalosporins with 100 drugs (22.5%), along with fixed dose combinations of 162 drugs (33.2%). More number of prescriptions were found with two antibiotics (104). Among all prescriptions 46 were found to be irrational and 214 prescriptions were rational, the irrationality was found mostly due to drug interactions. At the end of the study six types of drug related problems were identified in 46 prescriptions such as wrong drug (2), wrong dose (14), wrong frequency (5), drug interactions (28), therapeutic duplication (5), wrong indication (7). According to WHO INRUD guidelines average number of antibiotics per prescription was 1.87, percentage of antibiotics prescribed by generic name was 36.34%, percentage of encounters with an antibiotic prescribed was 100%, percentage of encounters with an injection prescribed was 73.26%, percentage antibiotics prescribed from EDL was 30.7%. Length of stay of 52% patients having AMAs in their prescription was more than five days, where as 19% of patients were admitted for less than five days. The average cost of antibiotics per prescription was found to be Rs 3800, whereas the equivalent antibiotics with different brands the cost was Rs.1282.04.

Conclusion: At the end of the study six types of drug related problems were identified in 46 prescriptions such as wrong drug, wrong dose, wrong frequency, therapeutic duplication, wrong indication, drug interactions, which lead to irrational prescriptions. Hence, there is a necessity of clinical pharmacist in hospital for minimising errors, thereby preventing the development of resistance towards antibiotics and reducing the prescription cost.

Keywords: Essential drug list, Indian council of medical research (ICMR) guidelines, Pharmaceutical care network europe classification, World health organisation-drug core indicators

INTRODUCTION

An Anti Microbial Agent (AMA) is an agent that kills or stops the growth of microorganisms. This category of drugs are most widely used. So, it is necessary to assess the rationality in antibiotic prescription based on standard guidelines to prevent antimicrobial resistance. Rational use of antibiotics is important, as antibiotic resistance is not only a problem for the individual patient but also reduces effectiveness of established treatment.

Inappropriate antibiotic use has become a serious public health concern all over the world and is a major determinant of the development of resistance. This limits the available treatment options. So, appropriate antibiotic use is a public health priority and fortunately some countries have also taken up the issue seriously [1].

The present study is novel in assessing the rationality of prescription based on the standard guidelines such as ICMR, National treatment guidelines for AMAs in infectious conditions and Essential Drug List (EDL). Guidelines will help physicians to prescribe rationally and to

choose the best effective, most appropriate empiric antibiotic for the patient. To check adherence towards guidelines, an audit of prescription or drug utilisation studies are needed to be done [2].

In view of this, it was proposed to study the utilisation patterns of AMAs and rationality of their use in the hospital that would help to: (a) determine the most commonly prescribed AMAs in the hospital; (b) identify various drug related problems; (c) calculate average costs of AMAs. Identified drug related problems were classified using PCNE classification of drug related problems, which were set very recently based on practicality for empirical use of antibiotics.

MATERIALS AND METHODS

The protocol for the proposed prospective study was submitted to the Institutional Ethics Committee (IEC) with Reference number: PD003/IRB/NRML/17-18. The protocol was approved by the IEC. The study was conducted from August 2017-January 2018 in medical wards of a tertiary care hospital, with 350 bed capacity. Patients of all age groups and of either sex were admitted to

the hospital during the study period were included in the study. Outpatients and pregnant women were excluded from the study.

Study material: All the necessary and relevant data were collected during clinical rounds in consultation with the treating physician.

STUDY PROCEDURE

Data Collection

Regular ward rounds were carried out in the various departments during the study period and all the necessary information from the case sheets of patients were collected using a data collection form, which included patient name, age, sex, inpatient/hospital number, height, weight, date of admission, date of discharge, chief complaints on admission, past medical and medication history, social and family history, laboratory reports, final diagnosis, daily progress notes, drugs prescribed with name of the medication, dose, route of administration, frequency, duration of the treatment and discharge summary. A total of 260 cases were collected during the study period.

Data Analysis

The data was evaluated by using ICMR guidelines which were given by Department of Health Research, New Delhi, India, 2017 with the instructions to use AMAs [3]. National treatment guidelines for AMAs in infectious conditions were given by National Centre for Disease Control, Directorate General and Health Services, Ministry of Health and Family Welfare, Government of India, in 2016 with the empirical therapy for all the infectious conditions EDL was given by WHO as a limit for use of drugs in different dosage forms [4].

The collected data was also evaluated using PCNE classification V.8.01 for Drug Related Problems (DRP's) for the use of the PCNE classification it is important to separate the real (or potential) problem (that affects or is going to affect the outcome) from its cause(s) [5].

The collected data from the prescriptions were thoroughly analysed and screened for possible drug-drug interactions using the Lexicomp (Uptodate software), Medscape and Drugs.com interaction checkers. The interactions were categorised based on their severity into three types like Major, Moderate and Minor drug interactions.

Pharmacist Interventions

The identified drug related problems were discussed with consultant and necessary pharmacist interventions were proposed after a peer review of text books and other academic sources and these identified problems were orally reported to the physician.

RESULTS

The average age of patients in the study was 55.5 years. Majority of the patients were male (134,52%) with AMAs in their prescriptions. Non infectious conditions (147,56.5%) were more than the infectious conditions (113,43.4%). Among 487 drugs prescribed in 260 prescriptions, majority of them were antibiotic drugs (480), followed by antifungal drugs (6) and antiviral drug (1). The most commonly prescribed category of antibiotic was cephalosporins with 100 drugs (22.5%), along with fixed dose combinations of 162 drugs (33.2%) [Table/Fig-1].

Name of AMAs	Number
Meropenam	9
Metronidazole	21
Teicoplanin	2
Ofloxacin	4
Rifamixin	15
Cefuroxime	24
Cefoperazone+Sulbactam	83

Levofloxacin	28
Cefotaxime	3
Ceftriaxone	32
Amikacin	35
Linezolid	11
Clindamycin	6
Ertapenem	18
Amoxicillin+Clavulanic acid	17
Doxycycline	22
Piperacillin+Tazobactam	47
Clarithromycin	11
Cefepime	17
Cefuroxime+Clavulanic acid	2
Streptomycin	1
Isoniazid+Rifampicin+Ethambutol+Pyrazinamide	4
Pyrazinamide	3
Cefpodoxime	3
Fluconazole	6
Sulfamethoxazole+Trimethoprim	3
Azithromycin	15
Ciprofloxacin	6
Ceftazidime	2
Ceftriaxone+Tazobactam	1
Ciprofloxacin+Tinidazole	2
Cefexime	17
Moxifloxacin	4
Vancomycin	1
Beclometasone+Clotrimazole+Neomycin	2
Tigecycline	3
Norfloxacin	2
Acyclovir	1
Ampicillin+Sulbactam	1
Ethambutol	1
Cefadroxil	1
Ceftizoxime	1

[Table/Fig-1]: Prescribing prevalence of various AMAs.

A total of 46 prescriptions were found to be irrational and 214 prescriptions were rational, the irrationality was found mostly due to drug interactions. At the end of the study 6 types of drug related problems were identified in 46 prescriptions such as wrong drug (2), wrong dose (14), wrong frequency (5), therapeutic duplication (5), wrong indication (7), drug interactions (28), according to PCNE Classification of drug related problems [Table/Fig-2-8].

According to WHO-INRUD guidelines, average number of antibiotics per prescription was 1.87, percentage of antibiotics prescribed by generic name was 36.34%, percentage of encounters with an antibiotic prescribed was 100%, percentage of encounters with an injection prescribed was 73.26%, percentage antibiotics prescribed from EDL was 30.7% [Table/Fig-9].

Among 260 prescriptions, 28 drug interactions within antibiotics were encountered, where majority of them were found to be moderate (19) followed by minor (7) and (2) major type of drug interactions.

A total of 135 patients (52%) having AMAs in their prescription were hospitalised for more than five days, where as 19% of patients were admitted for less than five days. The average cost of antibiotics per prescription was found to be Rs 3800, whereas the equivalent antibiotics with different available brands, the cost was found to be Rs.1282.04.

Code	Primary domains	Prescriptions
C1.1	1. Drug selection The cause of the (potential) DRP is related to the selection of the drug Inappropriate drug according to guidelines/formulary	2
C1.2	Inappropriate drug (within guidelines but otherwise contra-indicated)	7
C1.3	No indication for drug	---
C1.4	Inappropriate combination of drugs or drugs and herbal medication	---
C1.5	Inappropriate duplication of therapeutic group or active ingredient	5
C1.6	No drug treatment in spite of existing indication	---
C1.7	Too many drugs prescribed for indication	---
C2.1	2. Drug form The cause of the DRP is related to the selection of the drug form Inappropriate drug form (for this patient)	---
C3.1	3. Dose selection The cause of the DRP is related to the selection of the dose or dosage Drug dose too low	11
C3.2	Drug dose too high	3
C3.3	Dosage regimen not frequent enough	3
C3.4	Dosage regimen too frequent	2
C4.1	Duration of treatment too short	---
C4.2	Duration of treatment too long	---

[Table/Fig-2]: PCNE classification scheme for drug-related problems.

Disease	Dosage/frequency in prescription	Recommended dosage/frequency
Cellulitis	Inj.Invanz/1 gm/OD	Inj.Ceftriaxone/2 gm/OD (Or) Inj.Cefazolin/2 gm/QID
Cellulitis	Inj.Zosyn/4.5 gm/TID	Inj.Ceftriaxone/2 gm/OD (Or) Inj.Cefazolin/2 gm/QID

[Table/Fig-3]: C1.1 Inappropriate drug.

Condition	Drug	Dose given	Dose required	No. of prescriptions
Knee arthritis	Inj.Cegava	1.5 g BD	3 g BD	2
Necrotising pancreatitis	Inj.Invanz	1 g OD	3 g TID	1
Pneumonia	Inj.Magnex	1.5 g BD	3 g BD	2
Pyleonephritis	Inj.Zosyn	2.25 g TID	4.5 g QID	2
Osteoarthritis	Inj.Cegava	1.5 g BD	3 g BD	1
CLD	Inj.Piptaz	2 g TID	4.5 g TID	3
Dengue shock syndrome	Inj.Piptaz	3 g TID	4.5 g TID	1
CKD IV	T.Augementin	625 mg BD	250-500 mg OD	1
Acute pyleonephritis	Inj.Piptaz	4.5 g TID	2.25 g TID	1

[Table/Fig-4]: C3.1 and C3.2 Inappropriate dosage.

Condition	Name of drug	Dose/Frequency given	Dose/Frequency required
COPD	Azithromycin	500 mg/BD	500 mg/OD
Para thyroid disorder	inj.Azithral	500 mg/BD	500 mg/OD
CKD	inj.piptaz	2.25 g/BD	2.25 g/TID
Recurrent cholangitis	inj.piptaz	4.5 g/TID	4.5 g/QID
Gangrene	inj.piptaz	2.25 g/TID	2.25 g/QID

[Table/Fig-5]: C3.3 and C3.4 Inappropriate dosage regimen.

DISCUSSION

The rational use of AMAs is one of the main contributors to control worldwide emergence of antibacterial resistance, side effects and reduced cost of the treatment.

Diagnosis	Drug	Dose	Frequency
Acute pancreatitis	Inj.piptaz	4.5 g	TID
Acute pancreatitis	Inj.Monocef Inj.piptaz	1 g 4.5 g	BD TID
Acute pancreatitis	Inj.piptaz	4.5 g	TID
Acute pancreatitis	Inj.cefepime	1 g	BD
Acute pancreatitis	Inj.doxycycline	100 mg	TID
Acute pancreatitis	Inj.piptaz	4.5 g	TID
Acute pancreatitis	Inj.Cefepime	1 g	BD

[Table/Fig-6]: C1.2 Inappropriate drug (within guidelines but otherwise contra-indicated).

Diagnosis	Drug	Dose	Frequency	Duration
Right pneumothorax	Inj.Monocef	1 g	BD	D1-D2
	Inj.Zosyn	2.25 g	OID	D1-D2
Gangrene Rt. toe	T.Clarithromycin	500 mg	BD	D1-D3
	Inj.Ertapenem	1 g	OD	D1-D6
	Inj.Linezolid	600 mg	BD	D1
	T.fluconazole	200 mg	BD	D1-D10
	T.Augmentin	625 mg	BD	D6
Cervical Spondylitis, polyarthritis	T.Septran-DS	1 tab	BD	D6-D10
	Inj.Monocef	2 g	BD	D1-D5
Drug induced hepatitis	Inj.Magnex forte	1.5 g	BD	D1-D5
	Inj.Magnex forte	1.5 g	BD	D1-D3
	T.Linezolid	600 mg	BD	D1-D7
	T.Fluconazole	150 mg	OD	D1-D5
	Inj.Meropenem	1 g	TID	D2-D5
AKI	Inj.Magnex forte	2 g	BD	D1-D3
	Inj.ceftriaxone	1 g	BD	D1-D7

[Table/Fig-7]: C1.5 Inappropriate duplication of therapeutic group or active ingredient.

Description	Number
Drug	2
Dose	14
Interactions	28
Frequency	5
Therapeutic duplication	5
Indication	7

[Table/Fig-8]: Irrational use of AMAs.

Prescribing indicators	Number
Average number of antibiotics per prescription	1.87
Percentage of antibiotics prescribed by generic name	36.34
Percentage of encounters with an antibiotic prescribed	100
Percentage of encounters with an injection prescribed	73.26
Percentage antibiotics prescribed from EDL	30.7

[Table/Fig-9]: WHO-INRUD Core drug use indicators.

According to WHO, rational use of drugs requires that "patient receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community". It is necessary to assess the rationality in prescribing antibiotics to prevent development of resistance. Although antibiotics are essential for treating bacterial infections, extensive use promote resistance and transmission of nosocomial infections which effects their length of stay in hospital [6]. The present study is novel in assessing the rationality of prescription based on the standard guidelines such as ICMR, National treatment guidelines for AMAs in infectious conditions and EDL. Identified drug related problems were classified using PCNE classification of drug related problems, which were set very recently based on practicality for empirical use of antibiotics.

Upon evaluation of 260 prescriptions, 46 prescriptions were found to be irrational which were classified by PCNE guidelines into wrong drug (2), wrong dose (14), drug interactions (28), wrong frequency (5), therapeutic duplication (5), wrong indication (7) which leads to the development of resistance. Drug interactions within prescribed antibiotics were found to be major type of drug related problems which decreases the efficacy of administered antibiotics. Prescribing prevalence was found as cephalosporins >Quinolones >Amino glycosides >Carbapenems >Macrolides >Tetracyclines similar to a study conducted by Gopal VD et al., [7]. Based on ICMR, National treatment guidelines for antimicrobial use in infectious diseases and WHO-INRUD core drug use indicators the results were found to be deviating, such as percentage of antibiotics prescribed by generic name is 36.34 which is less than half whilst the aim is for 100% prescribing by generic as generic medicines are less expensive than branded medicines. Percentage of antibiotics from EDL is 30.7 whilst aim is for 100% prescribing from EDL [8].

The average cost of AMAs per prescription was found to be Rs 3800, whereas for alternate AMAs the cost was Rs.1282.04, which would help in minimising the patient's expenditure.

LIMITATION

This study was conducted on inpatients who were stable population whilst outpatients and pregnant women were excluded from the study. Rationality of prescription was assessed using standard guidelines while response towards administered drug was not recorded. However, further studies are required to evaluate rationality in prescriptions in different perspectives such as outcome assessment and in depth study on drug interactions.

CONCLUSION

From the results of current study, irrationality in prescribing antibiotics was present in 46 prescriptions based on standard

guidelines used in the study. At the end of the study six types of drug related problems were identified in 46 prescriptions such as wrong drug (2), wrong dose (14), wrong frequency (5), therapeutic duplication (5), wrong indication (7), drug interactions (28). Hence there is a necessity of clinical pharmacist in hospital for minimising errors, thereby preventing the development of resistance towards antibiotics and reducing the prescription cost.

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