



## Clinical Pharmacist Interventions on rational use of higher antibiotics in a tertiary care hospital

Anjali Krishnan K.<sup>1</sup>, Christa Dominic<sup>2</sup>, Sameera K.V.<sup>3</sup>, Siby Joseph<sup>4</sup>, Binu Upendran<sup>5</sup>

1,2,3,4 Department of pharmacy practice, St.Joseph's college of pharmacy, Cherthala, Kerala, India.

5 Department of nephrology Lourde's hospital Ernakulam, Kochi, Kerala, India.

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### \*Corresponding author:

Email : sibymadappallil@gmail.com

Phone : +91 -

### ABSTRACT

The aim of this study was to analyze the impact of clinical pharmacist interventions on rational use of higher antibiotics in a selected tertiary care hospital. It was a prospective interventional study using retrospective data as control and the patients admitted under medical departments prescribed with higher antibiotics with age  $\geq 18$  yrs were selected. A total of 200 patients were included in the study based on convenient sampling. Many drug related problems were identified in both retrospective as well as prospective arms with no statistically significant difference between the arms based on chi square test at 5 % level of significance. The DRPs were evaluated and classified in accordance to Pharmaceutical care network Europe (PCNE) system. In prospective group, out of 100 cases around 43 cases were identified and intervened with DRPs. And in retrospective group 42 out of 100 cases were identified with DRPs that could have been intervened. The degree of agreement with empirical therapy and culture report reduced from 42.4 % (retrospective arm) to 41.1% (Prospective arm). Clinical pharmacist can play an important role in minimizing drug related problems, a contributing factor of antibiotic resistance; hence prevent the emergence of antibiotic resistance to some extent.

### INTRODUCTION

Antibiotics play a crucial role in the treatment of infectious diseases. A safe and effective strategy for antibiotic use involves prescribing an antibiotic only when it is needed and selecting an appropriate and effective antibiotic at the recommended dose, with the narrowest spectrum of antimicrobial activity, fewest adverse effects and lowest cost. The emergence of resistance in pathogens has become a matter of great public health concern. Infections caused by antimicrobial-resistant microorganisms in hospitals are associated with increased morbidity, mortality and healthcare costs. Evidence is accumulating from developed countries that clinical pharmacy activities lead to improved patient care, with better use of medicines that in many cases is more cost-effective as well [1-6].

A drug related problem is an event or circumstances involving drug therapy that actually or potentially interferes with desired health outcome. It can be considered as a broad issue as it comprises of problems related to the drug at any level of drug use from prescriber level to patient level. Drug related problems may lead to reduced quality of life, increase hospital stay, overall increase in health cost, and even increased risk of morbidity and mortality. A medication error does not necessarily have led to a

drug related problem, there can be no problem or the problem is potential [7].

The drug related problems which directly or indirectly contribute to the development of antibiotic resistance include the over dose, under dose, duration of administration of the antibiotic, the compatibility of antibiotics with intravenous fluids, stability of antibiotics after reconstitution etc. Clinical pharmacists can identify the drug related problems and can intervene all these drug related problems in consultation with other health care providers including the clinicians and the nurses [8-10].

### METHODS

#### *Study Design:*

A Prospective interventional study was conducted in medical departments of a tertiary care hospital using Retrospective control group. The study site was a 500 bedded multispecialty tertiary care referral teaching hospital with wide range of amenities. A six months retrospective data was collected as control group and six months data was collected prospectively as intervention group. A total of 200 patients (100 in retrospective and 100 in prospective group) were included in the study based on convenient sampling method. Patients were randomized using graph pad software and

selected on the basis of inclusion and exclusion criteria. The medical record numbers (patient identification numbers) of retrospective populace who were prescribed with meropenem, linezolid, piperacillin tazobactam, colistin, vancomycin, cefepime in medical departments were identified. Prospective cases were enrolled from the same medical departments. The data were collected using specially designed data collection form, Clinical Pharmacist's intervention form and PCNE V8.01 Classification system for DRPs. Retrospective patient demographic details, pertinent laboratory as well as treatment details including medical and medication history, provisional diagnosis with empirical antibiotic regime were extracted from medical records. In addition to this direct interaction with the patient and / or caregivers and health care providers (HCPs) were carried out during prospective data collection.

DRPs identified were classified according to the PCNE (Pharmaceutical Care Network Europe) Classification scheme for DRPs V8.01. The basic classification has 3 primary domains for problems, 8 primary domains for causes and 4 primary domains for interventions. On a more detailed level there are 7 grouped sub domains for problems, 36 grouped sub domains for causes and 16 grouped sub domains for intervention. Those sub-domains are explanatory for the principal domains.

The causes and interventions of drug related problems at drug level domain were exclusively studied. The outcome and impact of these interventions and level of acceptance by HCPs were also assessed. The impact of CPs intervention in higher antibiotics prescription with respect to microbiological culture sensitivity results, managing adverse drug events with associated drug related problems were reviewed.

### Study Population

All the patients who were prescribed with higher antibiotics and met the inclusion and exclusion criteria were selected.

### Inclusion criteria

1) Patients admitted under medical departments; and 2) Patients who were prescribed with higher antibiotics with age  $\geq$  18 yrs

### Exclusion criteria

1) Patient and/or their caregivers who were not willing to participate in the study; 2) Patients who got discharged against medical advice

### Statistical analysis

The collected data were compiled using Microsoft Excel and were presented using tables and graphs. To identify the association of data chi-square test were employed. The data were tabulated, analysed and compared with relevant studies. Analyses were carried out at 5% level of statistical significance.

## RESULTS

Among the study population more number of study subjects was in the age group of 58-67 in both the population but there was a male preponderance among study subjects in both arms. The DRPs identified were evaluated and classified in accordance to the PCNE system (Table N0.1). Deterioration / improvement of disease state requiring dosage adjustment remained as a prominent problem. Majority of them were being failure to give loading dose of antibiotics, inaccurate dosage adjustment in the renal impairment. Inappropriate frequencies, treatment duration, dose selection in targeting pharmacotherapy of severe infections were also identified.

The drug related problems identified in both the arms were compared for statistical significance using chi-square test. The DRPs found in both arms were compared but the differences were not statistically significant at 5% level of significance. (Table No.2)

**Table 1 :** Drug related problems identified and classified implying on cause according to PCNE classification V8.01.

Classification of DRPs	Retrospective	Prospective
<b>Drug selection</b>		
C1	5	1
<b>Drug form</b>		
C2	0	0
<b>Dose selection</b>		
C3	21	23
<b>Treatment duration</b>		
C4	6	1
<b>Dispensing</b>		
C5	0	0
<b>Drug use/process</b>		
C6	9	14
<b>Patient related</b>		
C7	0	0
<b>Other</b>		
C8	3	4

**Table 2 :** Comparison of drug related problems identified in control and test group

Problem identified related to	Case sheets		Total	$\chi^2$	Df	p- value
	Retrospective	Prospective				
Drug selection	5	1	6	2.72	1	$p > 0.05$
Dose selection	21	23	44	0.1165	1	$p > 0.05$
Treatment duration	6	1	7	3.7	1	$p > 0.05$
Drug Use / Administration process	7	14	21	2.61	1	$p > 0.05$

**Table 3 :** Drug related problems identified and level of acceptance on Interventions

Category	Subcategory	Interventions carried out in prospective Arm	Acceptance	Interventions required in Retrospective Arm
Drug selection	Too many drug for an indication	1	1	5
	Inappropriate dosage form	0	0	0
Over dose/Under dose	Inadequate dosage adjustment	23	15	16
	Prescribed dose too low	0	0	5
	Prescribed dose too high	0	0	0
Drug administration related	Inappropriate frequency	14	7	7
	Inappropriate reconstitution	0	0	0
Treatment duration	Treatment duration too short	1	0	6
Others	Loading dose not prescribed	4	1	3
Total		43	25	42

There were 43 drug related problems which could be intervened by the researchers. Among these 43 cases intervened, 25 interventions were accepted by other health care providers. Out of that all the 23 cases in prospective under the subcategory of inadequate dosage adjustment, 15 cases got accepted. Among retrospective group, 16 cases fall under the subcategory of inadequate dosage adjustment and 5 cases under prescribed dose too low. That means around 21 cases with dose selection related drug problem in retrospective data that could have been corrected.

The researchers could correct 50% of drug related problems with respect to administration of drug out of 14 cases identified in the prospective arm. The researchers identified 4 cases without administering the loading dose among which only 1 case got accepted by the clinicians. (Table No.3)

The drug related problems intervened were classified into prescriber level and nursing care domains. Among the 41 cases intervened at prescriber level, 25 cases were approved by the

**Table 4 :** Acceptance level of clinical pharmacist interventions by other healthcare providers.

Primary domain	Intervention	No. of cases	Acceptance (%)	
At prescriber level(n=41)	Intervention proposed, Approved by prescriber	25	60.97	58.1
	Intervention proposed, NOT approved by the prescriber	16		
A nursing care level (n=2)	Intervention proposed, approved by nurse	Nil	0	
	Intervention proposed, NOT approved by nurse	2		

prescriber( 60.97 %) and at nursing care level out of 2 cases intervened no cases were approved.(Table No.4)

The reasons for rejection of clinical pharmacist intervention were analysed and it was found that 9 cases were rejected because of critical clinical status of the patient. About 5 cases were rejected due to personal clinical experience of the physician says otherwise and 1 case got rejected due to lack of solid evidence. The reason for the rejection of 2 cases were lack of time to prolong administration duration.

The agreement between empirical therapy and definitive therapy based on culture sensitivity report were analyzed in both retrospective and prospective arm and it was found that, 42.4 % shown agreement between empirical therapy and culture report in retrospective arm but in the prospective arm it was reduced to 41.1%.

## DISCUSSION

In this study we evaluated the impact of clinical pharmacist interventions on rational use of higher antibiotics in a tertiary care hospital. Among the study population more number of patients was in the age group of 58-67 in both the population which represents that aged populations are more prone to infectious diseases who required higher antibiotics. A significant number of drug related problems including drug selection, dose, and duration of treatment in targeting pharmacotherapy of infectious diseases were found in our study. As our study focussed on higher end antibiotics, inappropriate usage of the same even against susceptible microbes might lead to the phenomena of antimicrobial resistance which is already a global issue. Ramya movva, Anusha jampani et al conducted an observational study to identify and resolve drug related problems in consultation with other healthcare providers and found average 2.2 DRPs per patient [11]. Our study results support this study as significant number of drug related problems were identified in both the arms. The reduction in the number of drug related problems in our study would be due to the fact that our study was confined to higher end antibiotics which are prescribed after close monitoring of severely ill patients.

As there is no statistically significant difference in the incidence of drug related problems between the retrospective and prospective arm, it is clear that these type of drug related problems are there all the time and not occurred by chance in certain period

of time and proper corrective measures should be implemented to prevent the same.

In our study all the drug related problems identified in the prospective arm were intervened by the researchers. The high acceptance of our interventions by other health care providers highlights the importance of clinical pharmacists working in tandem with other health care providers for better patient outcome. An interventional study conducted in India by Lucca JM et al to assess the impact of clinical pharmacist interventions on DRPs received a good rate of acceptance (85%) [12]. Likewise in our study HCPs acceptance rate of clinical pharmacist intervention was 58.1%, and the main reason for rejection of our interventions would be due to the fact that our study was the first interventional study by clinical pharmacist in our study setting and interventions were mainly on critically ill patients on higher antibiotics.

The agreement between the empirical therapy and definitive therapy shown a reduction in agreement from retrospective arm to prospective arm which implies that antibiotic resistance is increasing and an antibiotic policy should be implemented for empirical therapy in order to maintain the sharpness of the miracle drugs to fight against infections of bacterial origin.

### Limitations

The study setting was limited to a single centre and the duration of study was limited so the results cannot be generalised. The study was focused on limited number of antibiotics only.

### Recommendations

Clinical pharmacist is an integral part of clinical team for identifying and resolving drug related problems and promoting rational use of antimicrobials.

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### CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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