Original Article

CLINICAL PHARMACIST'S INTERVENTIONS ON DRUG RELATED PROBLEMS IN A TERTIARY CARE HOSPITAL

RIJO MARY GEORGE, EMMANUEL JAMES, VIJAYALAKSHMI S*

Department of Pharmacy Practice, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham University, AIMS Health sciences Campus, Kochi 682041, Kerala, India
Email: vijayakunju92@gmail.com

ABSTRACT

Objective: To identify various drug related problems in patients admitted to the general ward of a tertiary care hospital and to make suitable drug therapy recommendations.

Methods: A prospective observational study was conducted in the Annex General ward in B Block of Amrita Institute of Medical Sciences, Kochi for a period of 6 months. All the patients admitted to the general ward on particular day of each week and who satisfied the selection criteria were included in this study.

Results: During the study period, a total of 598 drug related problems were identified of which 55.51% were due to prescribing of interacting drugs followed by drug choice problems (12.71%). Three hundred and thirty two drug interactions were observed in 224 patients. Thirty nine adverse drug reactions were observed in the study patients and cardiac drugs were the main class of drugs involved. Eighty seven drug interventions were done in 224 patients. It took an average of 25-35 minutes per intervention. Out of the total 87 interventions made, 41.4% (36) were at the prescriber level followed by 30% (27) at drug administration level. 23% of drug interventions were made at the patient level. 88.5% of the interventions were accepted and 11.5% were rejected.

Conclusion: This study shows the positive impact of clinical pharmacists in identification and resolution of drug related problems in a tertiary care hospital.

Keywords: Drug Related Problems, Clinical pharmacists, Drug interventions, Drug interactions, Adverse drug reactions.

INTRODUCTION

Patient safety is one of the most important aspects of health care system. Medicines can cure illness and at the same time harm the patient if not appropriately used. Hence every patient must receive the right medication, in the right amount and at the right time [1]. Drug induced morbidity has become a common problem [2]. Drug related problem (DRP) is a broad term as it includes problems related to the drug at any level of use i.e. at the prescribing level, dispensing level, administration level or at the patient or carer level. Adverse reactions to a drug (ADR), allergic reactions, drug not prescribed appropriately, drug prescribed not appropriate for indication, indication for which no drug is prescribed, contraindicated drug prescribed, duplication of drug therapy, administration and storage errors, inappropriate laboratory and non-laboratory monitoring, drug interactions, medical chart errors, patient noncompliance and unawareness about the usage of drugs etc. are some examples of DRPs [3].

Drug related problems can be classified as per different classification systems. These include American Society of Hospital Pharmacists (ASHP) System, Cipolle *et al.*, Granada consensus, Hepler/Strand, Pharmaceutical Care Network Europe (PCNE) classification, Problem-Intervention Documentation (PI-oc), and Westerlund classification [4]. World Health Organisation (WHO) defines ADRs as any response to a drug which is noxious, unintended and which occur at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases, or for the modification of physiological function [5]. Previous studies indicated that ADRs account for 5% of all hospital admissions and occur in 10-20% of hospitalized patients [6]. Prescription errors include prescription of a wrong drug for an indication, prescribing a contraindicated drug, prescribing interacting drugs together, prescribing a wrong dose or dosage form [7]. Clinical pharmacist can play a key role in promoting better medication use, ensuring that patients receive appropriate pharmacotherapy thus minimizing the risk of unfavourable outcomes of pharmacotherapy [8]. There are only few reported studies from India regarding drug related problems in a tertiary care hospital and the involvement of clinical pharmacists in overcoming these errors. [9-12]. The aim of the present study was to explore the various drug related problems that occur in patients admitted to the general ward of a tertiary care hospital and to make suitable drug therapy recommendations.

MATERIALS AND METHODS

A prospective observational study was conducted in the Annex General ward in B Block of Amrita Institute of Medical Sciences (AIMS), Kochi for a period of 6 months from September 2011 to February 2012. Ethical clearance for the study was obtained from the Institutional Review Board. Annex General ward has separate male and female sections with a total bed capacity of 120. Patients of various specialties like Nephrology, General Medicine, Gastroenterology, Neurology, Endocrinology, Oncology, Rheumatology, Pulmonary Medicine and Dermatology are admitted to this ward. On an average 15 new patients are admitted to the ward on a daily basis with an average daily bed occupancy rate of 92.5%.

All the patients admitted to general ward on the day of sampling were included in the study while patients admitted on days other than sampling day were excluded from the study. Similarly patients unwilling to provide informed signed consent were excluded from the study. Sampling was done on a weekly basis. i.e. In the first week of study all the patients admitted to the general ward on Sunday were selected and were followed up till they were discharged. In the second week all patients admitted to the ward on Monday were selected and followed up till they were discharged. Likewise sampling was done on subsequent days of the consecutive weeks for the duration of the study. Patient data were collected using standardized data collection form, drug related problem check list and pharmaceutical care intervention documentation form. DRPs were classified as per PCNE classification system [13]. Severity of the drug interactions were classified as per Uptodate® drug interaction [14] checker whereas modified Hartwig and Sagel scale [15] was used to assess the severity of the ADRs.

RESULTS AND DISCUSSION

A total of 224 patients were included in the study based on the inclusion and exclusion criteria out of which 133 patients were males (59.4%) with a mean age of 59.2±14.7 years and 91 patients were females (40.6%) with a mean age of 41.3±12.5 years. A similar prospective observational and interventional study conducted by Ganachari *et al.* [10] from Belgum, India also reported male (58.06%) predominance over females (41.93%).

Maximum number of patients were in the age group of 55-65 years (22.77%) followed by 45-55 (21.88%) years. Patients from the general medicine department (32.59%) were maximum followed by gastroenterology (25%). Out of the 2264 drugs prescribed, 1175 (78.4%) were branded drugs and 489 (21.6%) were generic drugs. Prescribing by generic name should be followed as it can reduce confusion among the pharmacists while dispensing. It also helps in cost minimization. For the comparison of brand vs. generic prescribing their proportions were compared using 'Z test'. Percentage of patients prescribed branded drugs was significantly higher than the percentage of patients prescribed generic drugs (p<0.001). An average of 10.1 drugs was prescribed per admitted patient. Mean duration of hospital stay of patients was 6.06±3.44 days. Majority of the patients received a total of 12 drugs during the hospital stay. 24.43% of total drugs prescribed were gastrointestinal and hepatobiliary drugs followed by cardiac drugs (15.37%), anti-infective drugs (14.97%), central nervous system drugs (10.56%) etc. Among the 224 patients in the study sample 70.54% (158) patients were prescribed antibiotics. 41.14% of the 158 patients were prescribed with only one antibiotic. Majority of patients were prescribed with more than one antibiotic (table 1).

Table 1: Percentage of patients prescribed antibiotics during the hospital stay (n=224)

No. of antibiotics prescribed per patient	No. (%) of patients
1	65 (41.14)
2	48 (30.38)
3	25(15.82)
4	18 (11.39)
5	1 (0.63)
6	1(0.63)

A total of 598 drug related problems were identified from 224 study patients (table 2). An average of 2.83±2.74 DRPs occurred per patient.

169 patients (75.5%) in the study sample had at least one DRP and 55 patients (24.5%) had no DRPs. 332 of these DRPs were due to prescribing of interacting drugs. Out of the 169 patients who had

DRPs 97 were males and 72 were females with a mean age of 59.4±15 years and 40.2±12.6 years respectively. Patient or provider related problems were the least identified DRPs. Patient or provider related problems include over use or under use of drug by the patient, non-adherence of the patient etc. As this study was conducted on inpatients this will not be significant because drugs were administered to the patients by the nurse or bystander at the prescribed time. So there was proper administration of patient's medications to a great extent.

Table 2: Drug related problems identified in the study patients as per PCNE V5 classification (n=598)

Types of DRPs	Frequency	Percentage
Adverse drug reactions	39	6.6
Drug choice problems	76	12.8
Dosing problems	17	2.9
Drug use problems	50	8.3
Drug interactions	332	55.5
Laboratory and non-laboratory monitoring problems	32	5.3
Patient or provider related problems	7	1.1
Medical chart errors	45	7.53

From table 3 it is evident that occurrence of DRPs was low in patients prescribed ≤ 4 drugs compared to patients prescribed ≥ 5 drugs. As the number of drugs prescribed to a patient increases, the chance of interactions and errors also increases. Polypharmacy refers to the effect of taking multiple medications, mostly more than five medications, to manage co-existing health problems [16]. To test the effect of poly pharmacy on DRPs, proportional cases with ≤4 drugs prescribed and ≥ 5 drugs prescribed we re compared using 'Z test'. Proportional DRPs for patients prescribed ≤4 drugs was significantly lower than for patients prescribed ≥ 5 drugs (p<0.001). Hence polypharmacy should be avoided at all costs unless absolutely necessary such as when the patient has comorbid disorders, or when the drug combination results in a favourable interaction.

Majority of patients with polypharmacy belonged to the age group of 50-75 years. Cardiac drugs (23.24%) were the main class of drugs involved in DRPs followed by CNS drugs (19.06%) and anti-infective drugs (18.89%). In a study conducted in 3 medical wards of a public teaching hospital in India antimicrobials (29.4%) were the main class of drugs involved in medication errors followed by cardiovascular drugs (15.4%), GI agents (8.6%) and CNS agents (8.2%) [17]. In our study, among the 2264 drugs prescribed, 330 drugs were involved in drug related problems. An average of 1.81 DRPs occurred per drug. About 192 (58.18%) drugs caused more than one drug related problem per patient.

Table 3: The effect of poly pharmacy on DRPs (n=224)

Number of DRPs	Number of patients with<4 drugs prescribed* (n=33)	Number of patients with 5-9 drugs prescribed* (n=70)	Number of patients with10-14 drugs prescribed* (n=84)	Number of patients with 15-19 drugs prescribed* (n=27)	Number of patients with 20-25 drugs prescribed* (n=10)
0 DRP	19	21	12	2	1
1DRP	8	13	14	3	-
2 DRPs	6	18	15	3	1
3 DRPs	-	12	17	2	1
4 DRPs	-	3	11	2	2
5 DRPs	-	-	9	4	-
6 DRPs	-	3	3	5	-
7 DRPs	-	-	1	2	-
8 DRPs	-	-	-	1	2
9 DRPs	-	-	1	-	2
10DRPs	-	-	1	1	-
>10 DRPs	-	-	-	2	1

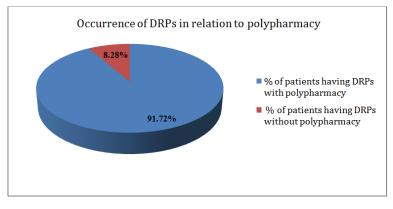*Total number of drugs prescribed during the hospital stay of the patients

Fig. 1: DRPs observed in relation to polypharmacy (n=224)

Drug interactions (55.51%) were the main type of DRPs identified. This may be because of the increased number of drug prescriptions to inpatients. An average of 10.11±4.74 drugs was prescribed per patient per admission. Some of these drug interactions were major (25.3%) which needed some intervention while some did not require any intervention, but had to be monitored for patient response. Interventions suggested for major drug interactions included reduction in dosage of one of the interacting drugs or substitution of the interacting drug with a non interacting drugs. A study conducted by Kumar *et al.* [17] in the medical wards of a public teaching hospital in India showed that drug interactions (68.2%) were the most frequently occurring type of DRPs.

A total of 332 drug interactions were observed in 224 patients. Majority of drug interactions observed were of moderate severity (44.7%) followed by interactions of major significance (25.3%) and then minor significance (30%). Amiodarone+Simvastatin: Amiodarone inhibits CYP3A4 enzyme which is responsible for simvastatin metabolism and thereby increases risk of rhabdomyolysis and Phenytoin+Nifedipine: Phenytoin may decrease the level of calcium channel blockers (CCBs) by inducing CYP3A4 enzyme responsible for the metabolism of CCBs, were the major significant interactions identified. Moderately significant interactions included Methotrexate+Proton Pump inhibitors (PPIs) (concurrent use of methotrexate and PPIs may result in elevated levels of Methotrexate causing Methotrexate related toxicities), Ciprofloxacin+Prednisolone (concurrent use may increase the risk of tendinitis and tendon rapture associated with flouroquinolone treatment), Ciprofloxacin+Theophylline (co-administration with Ciprofloxacin will increase serum concentration of Theophylline) etc. Huysmans *et al.*, in a report from Belgium [18] regarding drug related problems detected in community pharmacies, found that drug interactions were the main category of drug related problems.

A total of 39 ADRs were observed in 224 patients with a mean age group of 51.18±17.35. A higher percentage of ADRs were found in males (69.4%) than in females (30.6%). Cardiac drugs (30.78%) were the main class of drugs involved in causing ADRs followed by genitourinary drugs (17.95) and anti-infective drugs (17.95%).

Table 4: Classes of drugs involved in ADRs (n=39)

Classes of drugs	Frequency	% of total drugs involved
Cardiac drugs	12	30.78
Genitourinary	7	17.95
Anti-infective drugs	7	17.95
CNS* drugs	5	12.82
Musculoskeletal	5	12.82
Gastrointestinal and hepatobiliary	1	2.56
Antineoplastic drugs	1	2.56
Others	1	2.56

*CNS: Central Nervous System

Majority of drugs caused ADRs that affected gastrointestinal system; occular, cardiovascular and hematologic effects were the least occurred ones. Constipation caused by CCBs and diarrhoea by antibiotics were the main ADRs affecting gastrointestinal system. Banisadi *et al.* [19] regarding the role clinical pharmacy residents in increasing the ADR reporting, observed that the gastrointestinal system was the most frequently affected system involved in ADRs in an Iranian hospital.
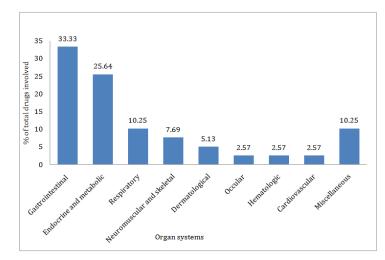

Fig. 2: Organ systems affected by ADRs (n=39)

Among the 39 ADRs observed 48.72% were of moderate severity and 46.16% were of major severity. Out of 224 study patients there were 8 drug related admissions. Steroids were the main group of drugs involved. One SLE (systemic lupus erythematosus) patient on oral Wysolone®(prednisolone) for 2 to 3 years developed adverse effects like facial puffiness, weight gain and hyperglycemia.

Table 5: Drug related hospital admissions (n=8)

Adverse drug effects	Frequency
Steroid induced hyperglycemia/myopathy	3
Furosemide induced hyponatremia	2
NSAIDs induced bronchospasm	2
Warfarin induced gum bleeding	1

A total of 87 interventions were done in 224 patients (table 6). It took an average of 25-35 minutes for per intervention. 88.5% of the interventions were accepted by the physicians.

Table 6: Types of pharmaceutical care interventions done (n=87)

Types of interventions	Frequency	Percentage
Drug choice	24	27.59%
a. Drug discontinuation	13	
b. Addition of a new drug	7	
c. Change of dosage form	4	
Dosing	17	19.54%
a. Decreased the dose	8	
b. Increased the dose	7	
c. Inappropriate duration	2	
Optimization of drug administration	37	42.53%
a. Change of administration route	7	
b. Administration modalities	30	
(Inappropriate timing, incompatibility with IV fluids)		
Others	9	10.34%

CONCLUSION

Clinical pharmacy services help in monitoring drug therapy and identifying drug related problems. This study shows that clinical pharmacist's interventions are successful in identifying and rectifying the different types of drug related problems occurring in patients admitted to a general ward. As there was a greater acceptance of the pharmaceutical care interventions a joint effort between clinical pharmacists and other health care professionals will provide a safer system of patient care and better utilization of resources. Hence there is a need for clinical pharmacists in the general wards to improve rational drug use and to give input to the physicians at the time of prescribing.

CONFLICT OF INTERESTS

Declared None

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