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Study on Clinical Pharmacist Initiated Interventions on COPD and Asthma Patients

[1]Irene Elizabeth Mathew, [1]Anisha Baby, [2]Siby Joseph, [3]Gireesh Kumar KP,[1]Anila K N

[1,2]Department of Pharmacy Practice, Amrita School of Pharmacy, Kochi, Amrita Vishwa Vidyapeetham, Amrita University, India

[3]Department of Emergency Medicine, Amrita Institute of Medical Sciences and Research Centre, Kochi, Amrita Vishwa Vidyapeetham, Amrita University, India

Abstract:

Drug induced morbidity has become a common problem; it is often preceded by a DRP (Drug related Problems). Only a few studies have been conducted on DRPs in hospitalized patients in India. A prospective interventional was conducted in general medicine and emergency medicine departments of AIMS, Kochi. to analyse the impact of clinical pharmacist interventions on DRPs in patients suffering from asthma and COPD. An aggregate of 43 and 69 DRPs were identified from retrospective & prospective groups respectively from a total of 215 patient cases. Of total DRPs , 81.16% (56) clinical pharmacist recommendations were accepted and solved in consultation with health care providers and 18.57% suggestions were rejected. Drug related problems are frequent in hospitalized patients with asthma and COPD in retrospective and prospective group. Clinical pharmacist could resolve most of DRPs in consultation with other health care providers by interventions and high acceptance rate of these interventions suggest that a joint cohort between clinical pharmacist and other health care professionals can ensure a safer system of patient care.

Key Words: drug related problems, drug interventions, asthma, COPD, clinical pharmacist

INTRODUCTION

Asthma and chronic obstructive disease are common obstructive airway disease characterized by decrease in airflow, inflammation and tissue remodeling. COPD is caused by tobacco, smoke or increasing age, mainly characterized by reversible airflow limitation that lead to decline in lung function leading to death [1], The most common conditions under this includes chronic bronchitis and emphysema. Emphysema is abnormal permanent enlargement of airspaces by destruction of their walls without fibrosis [2].

Spirometry is the instrument mainly used to estimate airflow limitation and for diagnosing and monitoring COPD. The forced vital capacity (FVC) may also be decreased in this condition[3].

Risk factors these airway diseases are environmental tobacco smoke, occupational dust and chemicals, indoor airflow population, genetic factors, infections, impaired lung factors.[2, 3]

Pathogenesis of COPD include oxidative stress and imbalance between aggressive and protective defence systems in lungs. Deficiency of alpha 1-antitrypsin (AAT) inhibits several protease enzymes, neutrophil elastase. Deficiency of AAT would lead to development of emphysema[3].

Asthma is a chronic inflammatory disorder of the airways in which many elements play a role such as mast cells, eosinophils, T- lymphocytes, macrophages, neutrophils, and epithelial cells. Patients may undergo wheezing, breathlessness, chest tightness and coughing.

Pathophysiology of asthma is characterized by airflow obstruction, bronchospasm, edema, and hypersecretion, BHR, and airway inflammation[4]. Inhaled allergens cause an early phase allergic reaction characterized by activation of cells such as IgE antibodies. Thereby rapid activation of airway mast cells and macrophages, which release pro inflammatory mediators such as histamine and eicosanoids, leading to vasodilation and exudation of plasma, 6-9 hrs after allergen provocation and activation of eosinophils, T-lymphocytes, basophils, neutrophils and cytokines[5]. T-lymphocytes activation leads to release of cytokines from T- helper cells that mediate allergic inflammation. T-helper cells produce IL-2 and interferon alpha which is necessary for defence mechanisms. Allergic asthmatic inflammation may result in imbalance between TH1 and TH2[4]. Mast cell degranulation in response to allergens result in release of mediators such as histamine, it is capable of inducing smooth muscle constriction leading mucosal edema and secretion. Neutrophils are the mediators that provide BHR and airway inflammation[2].

Patient safety is one of the most important aspects of health care systems. It can cure illness and at same time harm the patient if not appropriately used. Hence the medicines should receive right medication in the right amount and at right time[6]. Drugs are the most important tools in treating diseases like COPD and asthma. Adverse effects ranging from minor side effects to death. Any deviation from beneficial effects of medication results in a drug related problem (DRPs)[7]. Drug related problem is broad term as it includes problems related to the drug at any level of drug use; prescribing level, dispensing level, administration level, or patient level. It can include reduced quality increased hospital stay, overall increase health cost, morbidity and mortality[8]. Management of the DRPs is an essential component in the betterment of the diseases. Health care members has very crucial role in addressing and managing the drug related problems for improving patient care. Clinical pharmacists with vast and deep knowledge about medicines can play a pivotal role in finding drug related problems. Active participation clinical pharmacist can identify and prevent drug related problem and provide suggestions for interventions for such

issues[9]. Proper clinical review of patient's drug therapy by clinical pharmacist can benefit the patient in getting better therapy outcomes and quality of care[8].

The prevalence of asthma and COPD is increasing worldwide and becoming a relevant burden for healthcare systems. COPD patients death rate has also being rising for last decade, according to estimates of WHO. Patients are associated with complex spectrum of comorbidities including hypertension, diabetes, dyslipidemia, heart failure and coronary artery disease. Drug related problem in hospitalized patients which can interfere with desired therapeutic outcomes. ADR and drug interactions, especially theophylline present alarming problems in patients with COPD and asthma. In this context, they aimed to analyze clinical pharmacist interventions on drug related problems in patients suffering from asthma and COPD. In this case study they analyzed the prescriptions for drug related and intervene if there is any drug related problem.

METHODOLOGY

The study is a prospective interventional study. The study used retrospective data as the control and was carried out from 1st October 2014 to 31st May 2015. The study was done after getting the approval from institutional research and ethics committee. The medical record numbers of retrospective patients diagnosed with either asthma and or COPD and admitted under general medicine department were identified. A sample size of 215 patients were enrolled for the study. Out of the total 100 was from retrospective data and 115 were prospectively studied. Prospective patients was also enrolled from the same department. All the patients under general medicine during the study period were selected based on inclusion and exclusion criteria. Patient's demographic details, medical history, diagnosis, laboratory investigations were collected by reviewing patient's medical chart attending ward rounds, interviewing patients and their bystanders. Drug related problems and drug intervention on drug related were carried out by interaction with physicians during ward rounds or with nurses to collect administration errors. The drug related problems was identified while comparing with retrospective data of previous one year.

Drug related problems analyzed was classified according to PCNE (Pharmaceutical care network Europe) classification scheme for DRPs V6.2. The main classification had four primary domains for problems,8 primary domains for causes and 5 domains for problems, 8 primary domains for causes and 5 primary domains for interventions.

Causality assessment of ADR was carried out using Naranjo ADR probability scale.

Drug interactions were analyzed using LEXI- comp drug interactions checker. Category of C, D, X of drug interactions were considered. Adverse drug interactions or events occurred was classified based on WHO system. The outcomes of clinical pharmacist's recommendations by healthcare team was also assessed. The collected data was compiled using Microsoft excel and was presented using tables and graphs. Descriptive statistics was used to calculate the mean and standard deviation. Paired sample t-test was used to calculate associations within the group whereas student t-test and chi-square test were employed to find associations between groups. The relevant data were tabulated, analyzed and compared with relevant studies.

RESULT

A total of 215 patients were included in the study in which 100 patients were in the retrospective group and 115 in prospective group.

Our study 69.81% (43 no.s) asthma patients in retrospective and 76.74% (72 no.s) in prospective patients were in females whereas COPD patients in this study were males in both groups that is 74.64 % in retrospective and 81.94% in prospective.

Most of the patients were in the age group of 68-77 in retrospective and 58-67 in prospective group. The male to female ratio corresponds to 3:7 in retrospective and 2:8 in prospective group which represents that women are affected with asthma than men. The mean age in retrospective group was 70.93±11.93 whereas in retrospective group was 70.25±11.25.

Majority of COPD patients were in the age of 68-77 in both groups. Men had higher prevalence rate than women in retrospective of 74.46% and in prospective of 81.94% group. The mean age in retrospective group was 70.93±11.93 whereas in prospective group was 70.25±11.25. The statistical analysis for the age group of COPD patients verifies that there wasn't any significant difference (p=0.980).

Majority of retrospective patients were admitted during the month of July to September (33%) while 39% prospective patients were hospitalized during January to March.

Most of the patients had past medical history of asthma and COPD and with duration of 1-5 years of 34.88% and 11-15 years of 25% respectively.

Diabetes, hypertension dyslipidemia, renal failure, liver failure was the mostly observed comorbidities in both retrospective and prospective group.

A total of 57 and 92 drug related problems were identified from retrospective and prospective groups respectively. The most common drug related problems identified were 'inappropriate drug selection' in retrospective (62.80%) and prospective group (65.21%) followed by inappropriate dose selection which is given in table 1.

Drug related problems were classified according to Pharmaceutical care network Europe classification scheme V6.2 which is shown in table 2. Drug interactions was another problem, which accounted of 46.5% in retrospective and 39.135 in prospective group followed by inappropriate drug selection, therapeutic duplication, over dose, frequency inappropriate. Other causes of drug related problems like prescribing errors, dispensing errors, administration errors were also identified in table 2.

Recommendations on drug related problems by clinical pharmacist could have been done in retrospective group and those interventions were carried out in prospective patients are shown in table 3. Dose adjustments based on patients' creatinine clearance. Other interventions like monitoring of laboratory parameters, adverse drug effects were also proposed.

The outcomes of interventions were also assessed based on PCNE scheme . A total of 122 patients 81.43% of clinical pharmacist recommendations were accepted and solved the drug related problems and 18.57% suggestions were rejected by health care providers.

Adverse events were observed and classified based on WHO system Organ classification was shown in table 4 . Majority of adverse drug events occurred in retrospective group were gastro intestinal disorders of 35.29% whereas endocrine disorders of 33.33% account for highest in prospective group which include corticosteroid induced hyperglycemia and hypoglycemia caused by insulin.

Causality assessment of ADR was done using Naranjo probability scale. Out of 15 adverse drug reactions in prospective patients 13 were probable and 2 were possible which is shown in table 5.

Risk rating of drug interactions were also assessed using UPTODATE drug interaction checker. Category C interactions of 62.96% were observed in prospective patients. 9 interactions of category D were found and only one category X interaction was observed. In the retrospective group 20 drug interactions were observed, of which the number of category C and D interactions were equal which is shown in table 6.

Severity of the drug interactions was also assessed. Majority of the interactions were moderate significant of 65% in retrospective and 70% in prospective. Of total interactions 33.33% drug interactions was of major significance in prospective group which required therapeutic modification that is shown in table 1.

Table no. 1: Common drug related problems identified:

Types of DRP	Code V6.2	No(%)of DRP	
		RETROSPECTIVE N=43	PROSPECTIVE N=69
Drug selection	C1	27(62.80)	45(65.21)
Dose selection	C3	9(20.93)	13(18.84)
Treatment duration	C4	0	1(1.45)
Drug use	C5	4(9.30)	7(10.15)
Logistics	C6	3(6.97)	3(4.35)

Table no. 2: PCNE classification V6.2 mainly focusing on cause drug related problems (DRP)

Classification of DRPs	Code V6.2	Cause	No of DRP	
			retrospective	Prospective
Drug Selection	C1.1	Inappropriate drug(incl. contraindicated)	4	7
	C1.3	Inappropriate combination of drug of drugs and food	20	27
	C1.4	Inappropriate duplication of therapeutic group or active ingredient	3	6
	C1.5	Indication for drug treatment not noticed	0	1
	C1.9	New indication for drug treatment presented	0	4
Dose selection	C3.1	Drug dose too low	2	4
	C3.2	Drug dose too high	6	7
	C3.3	Dosage regimen not frequent enough	1	2
Treatment duration	C4.2	Duration of treatment too long	0	1
Drug use	C5.2	Drug not taken /administered at all	4	7
Logistics	C6.2	Prescribing error	3	3
		Total	43	69

Table 3: PCNE classification v6.2 (implying on intervention) of DRPs

Code V6.2	Interventions	No of interventions that could have been done in retrospective	No of interventions that were done in prospective
13.1	Drug changed to..	8	7
13.2	Dosage changed to..	10	13
13.5	Drug stopped	6	14
13.6	New drug started	0	6
14.1	Other interventions	19	29
	Total	43	69

Table 4. distribution of ADR based on WHO system organ classification (SOC) of adverse events

SOC ID	SOC CRITERIA	NO.OF ADRS	
		RETROSPECTIVE	PROSPECTIVE
05	Endocrine disorders	4	5
06	Metabolism and nutrition	5	2
11	Cardiac disorder	0	1
14	GI disorder	6	2
15	Hepatic-biliary disorder	1	2
17	Musculoskeletal, connective tissue and bone disorders	0	1
18	Renal and urinary disorder	0	1
23	investigation	1	1
	Total	17	15

Table 5: Causality assessement of ADR occurred in prospective patients based on naranjo ADR probablity scale

ADR probability	No of ADR in prospective group
definite	0
probable	13
possible	2
Doubtful	0

Table 6. Risk rating of drug interaction based on Lexi-comp drug interaction checker

RISK RATING	NO. OF DRUG INTERACTIONIN RETROSPECTIVE GROUP(n=20)	NO OF DRUG INTERACTION IN PROSPECTIVE GROUP (n=27)
C	10(50)	17(62.96)
D	10(50)	9(33.33)
X	0	1(3.70)

DISCUSSION

Chronic conditions accounts for more than 50% of the global disease burden. Asthma and COPD represent leading respiratory disease, with high prevalence and burden of symptoms. Most patients were aged individuals with several comorbidities and multiple drug treatments. For the optimal management of Asthma and COPD, a multidisciplinary team involving clinical pharmacist and other health care providers are essential. The current study revealed that men had higher prevalence rate of COPD than women. On the other hand, the number of female patients outnumbered the number of male patients were diagnosed with asthma. Statistical analysis was carried out and found significant association between gender and disease ($p<0.001$). A study conducted by *Jain et al*[10] in India shows that gender related difference do exist in COPD patients.

Young patients were more affected with asthma whereas elderly population was affected more by COPD. Most of the asthma and COPD patients were in age group of 68-77 years (27.08% and 42.01% respectively).

Chandra et al conducted a cohort study to identify seasonal difference in the frequency of hospital admissions due to acute exacerbation of chronic obstructive in the difference in the frequency of hospital admissions due to acute exacerbation of chronic obstructive pulmonary disease at tertiary care hospital in India. Study reported an average of 7.8 admissions per month and a sharp rise in admissions during the month of February (15 admissions)[11]. Our study shows admissions of retrospective patients of 33% were high in rainy season (July – September) and 33.13% of prospective patients were hospitalized during winter season (January- March).

Asthma and COPD is associated with relevant burden of comorbid diseases. Comorbidities may potentiate the morbidity of COPD, leading to increased hospitalization and health care costs[12]. In this study, the trend of comorbidities remained essential the same in both retrospective and prospective population. Hypertension ranked first and followed by diabetes and dyslipidemia .The comorbid conditions in COPD patients are at increased risk of developing complications.

The prime emphasis of this research was to portray the role of clinical pharmacist in the management of asthma ad COPD . the causes and intervention at drug level domain were exclusively studied. Degree of acceptance on these interventions by health care providers were also assessed.

The drug related problems (DRP) were evaluated and classified in accordance to Pharmaceutical Care Network Europe (PCNE) classification scheme V6.2. In appropriate drug selection (62.80% in retrospective and 65.21% in prospective) was the most common DRP observed in our study, which coincides with findings of another interventional study done by *Ganachari et al* from Belgaum, India where 35.13% inappropriate drug selection were reported. Inappropriate combination of drugs remained as major problem in our study (20 in retrospective and 27 in prospective)[13].

Drug interactions of category C, D, X were considered and severity of these interactions was also assessed per UPTODATE drug interaction checker[14]. Some of them were major (35% in retrospective and 33% in prospective) which required therapeutic modification. Majority of drug interactions observed were of moderate severity which had to be monitored closely. Interventions suggested for major drug interactions included substitution of one of the interacting drugs with non-interacting drug. High incidence of drug interactions may be due to inadequate knowledge of other health care providers about drug pharmacodynamics /pharmacokinetics properties.

Inappropriate dose selection exhibits a remarkable share in DRPs. Prescribing high dose was the major dosing issue (13.95% in retrospective and 10.14% in prospective study). During the study problems requiring drug dosing adjustments were mostly observed in situations were antibiotics like levofloxacin , piperacillin-tazobactum, clarithromycin etc. used in patients with reduced impaired renal functions for the adjustment of dose is required based on creatinine clearance.

A prospective study by *Alagiriswami et al* assessed the pharmacist initiated changes in drug therapy in tertiary care hospital in south India. A total of 261 DRP were identified from 189 patients. The most common DRP was found to be drug use without indication (18%) followed by improper drug selection (14%)[15]

In our study drug use without indication had minority of occurrence. Other DRPs like contraindicated drug prescribed, duplication of therapeutic duplication of therapeutic active ingredient, new indication for drug, prescribing error etc. were also a notable issue. The most common therapeutic duplication observed in this study was proton pump inhibitor (PPI) and H2 receptor antagonist prescribed together for gastro intestinal disturbances.

Adverse drug events or reactions were also assessed and categorized based on WHO System Organ Classification (SOC) of adverse events. Majority of adverse drug events occurred in retrospective were in gastro intestinal disorders (35.29%) whereas endocrine disorders (33.33%) account for highest in prospective group. High incidence of ADR may be due to older age, presence of comorbid disease, polypharmacy and renal impairment in these patients.

The acceptance and or response of health care providers

towards clinical pharmacist interventions were ascertained. Our results showed that other health care provider's response to clinical pharmacist interventions displayed a reasonable acceptance rate of 81.43%. The recommendations of clinical pharmacist on cessation of drug, dose adjustment, interventions on drug selections, new drug started.

To compare the frequency and incidence of DRP in retrospective group to prospective group, Pearson chi square test was done. The statistical analysis revealed that DRPs are not statistical significant different (p=0.39) which means that the DRP are occurring and recurring and clinical pharmacist can spot out the problems and enable other health care providers for a safe and effective therapy.

CONCLUSION

Clinical pharmacy services in hospital are not a novel concept. But in in context of India, it is a recently emerging discipline. Physician and nursing staff often treat multiple patients at once, with frequent interruptions. The combinations of interruptions, intense pressure, and fast paced environment can lead to medications and fewer error interceptions. Clinical pharmacy services helps in providing drug therapy and identifying and resolving drug related problems in consultation with other health care professionals.

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