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Research Article

A PROSPECTIVE OBSERVATIONAL STUDY ON POLYPHARMACY LEADING TO ADVERSE DRUG REACTIONS IN A DEPARTMENT OF MEDICINE

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ABSTRACT

Poly pharmacy significantly raises the likelihood of adverse reactions to drugs, risk of hospitalization and medical errors related to drugs. It depends on the number of drugs, the diseases, and patient related factors. Poly pharmacy is a risk factor for severe adverse drug reactions (ADRs) and is associated with an increased risk of mortality. The main aim of the study was to assess the poly pharmacy leading to adverse drug reaction. This is a prospective observational study conducted at Basaveshwara Medical College Hospital and Research Center (BMCH and RC), Chitradurga, India for the period of 4 months in the department of Medicine. In this study 601 patients of both genders were included. The identified ADRs are reported to the physician and causality assessment of adverse drug reactions (ADR's) was done by using the Naranjo's scale and Modified Hartwig Seigle scale. About 601 patients screened among them 315 patients were males and 286 were females and average drugs per prescription were 6.17. There are 356 (59.23 %) patients with major poly pharmacy (≥ 6 drugs) and 245 (40.76 %) with minor poly pharmacy (3-5 drugs). During the study 32 ADRs were identified and reported to the Physicians; in this 28 ADRs were accepted. The prevalence of ADRs seen during the study was 5.32 % and in this 3.49 % (n = 21) were seen patients who had major poly pharmacy. Our study showed that females were more prone to develop ADRs compared to the males i.e., 53.12 % (n = 17) of ADRs were identified in female gender and 46.87 % (n = 15) in male gender. Out of 32 ADRs 21 (65.62 %) were identified in patients with major poly pharmacy and 11 (34.37 %) with minor poly pharmacy. There were more ADRs associated with major poly pharmacy and female gender. It is necessary to create the awareness to curb irrational prescription of poly pharmacy which helps in prevention of drug related problems like ADRs.

Keywords: Poly pharmacy, adverse drug reaction, Gender.

INTRODUCTION

Medications are the most commonly used in clinical intervention and complications associated with their use constitute one of the most common causes of adverse drug reactions in health care[1]. Poly pharmacy Medications are the most commonly used in clinical intervention and complications associated with their use continue one of the most common causes of adverse drug reactions in heal is defined as the concomitant use of 2 or more drugs and or the administration of more medications than are clinically indicated, representing unnecessary drug use and it could enhance drug interactions and adverse drug reactions. It depends on the type of drugs, the diseases, and complaints of the patient[2]. The use of multiple medications increases the possibility of adverse reactions to drugs, risk of hospitalization and medical errors caused by drugs[3]. Poly pharmacy is a risk factor for severe adverse drug reactions (ADR's) and is associated with an increased risk of mortality[4]. Poly pharmacy carries negative connotations, including increased costs, poorer compliance, and increased risk of side effects, drug interactions and adverse drug reactions[5]. The study was aimed to assess the poly pharmacy leading to adverse drug reactions. The World Health Organization (WHO) defines an adverse drug reaction (ADR) as 'any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological function'. Traditionally ADRs are classified into two categories- Type-A (Augmented) and Type-B (Bizarre) reactions[6]. Adverse reactions are recognized hazards of drug therapy and it is an important cause of morbidity and mortality in both hospitalized and ambulatory patients[7]. ADRs are a major cause of morbidity, which accounts for nearly 5 % of all hospitalizations all over the world and it is estimated that adverse reactions cause 2-3 % of consultations in general practice, up to 3 % of admissions to intensive care units and 0.3 % of general hospital admissions are due to adverse drug reactions[8-10]. ADRs are the fourth leading cause of death ahead of pulmonary diseases, diabetes and acquired immune deficiency syndrome (AIDS)[11]. Multiple factors influence ADR susceptibility which includes multiple drug therapy, disease severity, age, drug interactions and number of drugs prescribed[9]. In many countries ADRs rank among the top 10 leading causes of mortality. So there is a need to study ADRs seriously to create awareness about ADRs among patients to motivate health care professionals in the hospital to report ADRs to minimize the risk[7].

MATERIALS AND METHODS

This is a prospective observational study which was conducted in the department of Medicine of Basaveshwara Medical College Hospital and Research Centre (BMCH and RC) from Feb to May 2014 at Chitradurga, India. This study included patients admitted in Medical Intensive Care Unit (MICU), Male Medical Ward (MMW) and Female Medical Ward (FMW) for various diseases. The patients of both sexes, who were aged between 21-80 years, were included in the study. Patients who do not require hospital stay and those who stayed less than 24 hours in the hospital were excluded from the study. IV fluid was not counted in the total number of drugs received. The data was collected from the patient's case records and interviewing with the patient. The data collection includes demographic details of the patient, clinical manifestations and drug details like drug name, dosage, and route of administration, frequency and duration of therapy. Causality assessment of reported ADRs was carried out by using Naranjo's algorithm scale[12] and Modified Hartwig Seigle Scale followed after confirming the

reactions. In Naranjo's algorithm, the ADRs are classified as Definitely, Probable, Possible and Unlikely. The modified Hartwig Seigle scale[13] classified them as Severe, Moderate and mild with various levels according to various factors.

RESULTS

During the study period total of 1823 patients got admitted in department of medicine, 977 patients did not meet the criteria as 630 patients stayed for less than 24 hours and 347 were excluded because they were either critically ill or on mechanically ventilated and few of them were admitted for poisoning. Among the 846 patients who qualified for the study, 601 cases of poly pharmacy were identified. About 3712 drugs were prescribed with an average of 6.17 drugs per prescription. Among 601 cases male to female ratio was 1:0.91 (315 and 286). Out of 601 patients, it was observed that 356 (59.23 %) patients had major poly pharmacy and 245 (40.76 %) patients had minor poly pharmacy. Out of 356 major poly pharmacy patients, 55.05 % of patients were found in MICU followed by 24.15 % in FMW and 20.78 % in MMW. There were 53.12 % of ADRs identified in females and 46.87 % in males. Among the 32 ADRs, 12 from FMW, 11 from MICU and 9 from MMW were reported. The prevalence of ADR's seen more in the age group of 41-60 years followed by 21-40 years. The prevalence of ADRs in hospitalization during the study was 5.24 %. Categorizations of Poly pharmacy were presented in (Table 1) based on age, gender and department. Our study showed that 356 patients receiving ≥ 6 drugs, of these 11.79 % of the patients received more than 10 drugs, 28.08 % of the patients received 8-9 drugs and 60.11 % of the patients received 6-7 drugs. The prevalence rates were calculated based on number of patients admitted to hospital during the study period. The medical diagnosis associated with poly pharmacy is as follows; 16.63 % (n = 100) patients with Respiratory disorders, 15.97 % (n = 96) patients with Cardiovascular disorders, 12.97 % (n = 78) patients with Gastro-intestinal disorders, 11.64 % (n = 70) patients with Endocrine disorders, 10.64 % (n = 64) with Hematological disorders, 6.65 % (n = 40) with Hepatic disorders, 8.65 % (n = 52) with infectious diseases 16.80 % (n = 101) with Co-morbid disorders patients were admitted. Division of poly pharmacy based on therapeutic category as shown in (Figure 1). Most commonly prescribed drugs were ceftriaxone followed by pantoprazole, salbutamol, paracetamol and ondansetron. Out of the 32 ADRs, 28 were accepted by the physician and 4 were suspected. Among them 1 (3.12 %) ADRs were Type A (Augmented) and 31 (96.87 %) ADRs were Type B Bizarre). Of these 21 ADRs were identified in patients had major poly pharmacy and 11 ADRs in patients had minor poly pharmacy. Division of ADRs as shown in (Figure 2) based on Poly pharmacy.

Causality Assessment

The causality assessment was done for 32 ADRs by using Naranjo's and Modified Hartwig Seigles Scale and detailed information is given in (Table 5.3). Of these according to Naranjo's Scale; 4 (12.5 %) were definitely, 13 (40.62 %) were Probable and 15 (46.87 %) were Possible. According to the Modified Hartwig Seigle scale 4 (12.5 %) were severe, 16 (50.0 %) were moderate and 12 (37.5 %) were Mild. According to therapeutic classification, NSAIDs were identified to have more ADRs followed by antibiotics. Around 12 ADRs were found in patients with co-morbid diseases like COPD with MI, DM-2 with Asthma, DM-2 with Hypertension and Acute gastroenteritis etc., 7 with chronic diseases like Tuberculosis, DM and Renal failure, 9 in infectious diseases and 4 in hepatic diseases. Identified ADRs were shown in (Table 2) based on therapeutic category and severity of ADRs based on the poly pharmacy as shown in (Table 3).

DISCUSSION

Poly pharmacy was a frequent condition in Indian population and mainly depends on the type of the diseases, co-morbid conditions, hereditary, economic status and mal-nutrition. Our present study showed that adults and young elder patients were more prone to poly pharmacy due to different types of diseases with other co-morbid conditions and also might be changes in normal physiology of aging, pharmacokinetic and pharmacodynamics, that gives the stepping stone to cause the ADRs. In our study 52.41 % of patients were males and 47.58 % were females, there is similar study conducted in victoria hospital in Bangalore, India where 62 % of the study populations were males[16]. The study conducted by Jochen Schuler *et al*[18] in Australia reported that the average number of drugs per prescription were 7.5 ± 3.8 and similar study in India showed that average drugs per prescription was 4.27[17]. In our study the average number of drugs per prescription was found to be 6.17. There are several explanations for giving poly pharmacy to the patients in the medicine department is that the asymptomatic people are increasingly treated with preventive interventions to reduce their future risk of morbidity and mortality. This is seen particularly with the cardiovascular and endocrine disorders to reduce the further complications and several patients received drugs empirically until lab reports were made available. This study results showed that respiratory disorders were associated with major poly pharmacy followed by cardiovascular disorders. But cardiovascular disorders were found to be associated with worsen as morbidity pattern as observed by Zaveri *et al* in India[17]. During the study most commonly prescribed drugs include ceftriaxone followed by pantoprazole, salbutamol, paracetamol and ondansetron. A study conducted in Bangalore, India[16], in which commonly prescribed drugs were ranitidine, cefotaxime, salbutamol and deriphylline. The Italian REPOSI study Nobili *et al*[21] has shown that age, cardiovascular conditions and COPD are all independently associated with poly pharmacy. Work in Switzerland has also shown widespread use of multiple medicines among the hospitalized patients with the adverse drug reactions is a common problem[22]. In our study the most of the ADRs are associated with the major poly pharmacy. Most of the adverse reactions belonged to Possible, based on a causality assessment, which is similar to results in another study by T.M Vijay Kumar[10], but different results observed in the study by Murthy and Frigo[19] in which more of reactions noticed were possible. Drug withdrawal is the important for the management of an ADR. In our study, 78.12 % (n = 25) of suspected drug was withdrawn after ADRs confirmed which is comparable to study by Gallelli *et al*[20]. Our study suggests that current practice in our hospital is associated with poly pharmacy exists in department of medicine. In the present study around 5.32 % of hospital admissions were associated with ADRs and higher rates were found in major poly pharmacy (3.49 %) patients. The causality assessment revealed that all suspected ADRs fell under the definitely, probable and possible. The goal should be to prescribe the least complex drug regimen for the patient as possible while considering the medication problem and symptoms and of course the cost of therapy. Building awareness to healthcare professionals for spontaneous reporting of adverse drug reaction and following the evidence-based medicine (EBM) would help in preventing poly pharmacy and medication related problems like ADR. The role of pharmacists is important to continually educate but also to have access to complete patient records, so they could look at all of the medications that may be given to the patient for better patient care.

Table 1: Categorization of Poly pharmacy based on Gender, Age Group and Department

		No. of Patients	ADRs	Percentage (%)	Poly pharmacy			
					Major	Percentage (%)	Minor	Percentage (%)
Gender	Male	315	15	46.87	162	45.50	153	62.44
	Female	286	**17**	**53.12**	**194**	**54.49**	92	37.55
Total		601	32	100	356	100	245	100
Department	MICU	262	11	34.37	**196**	**55.05**	66	26.93
	MMW	159	9	28.12	74	20.78	85	34.69
	FMW	180	**12**	**37.5**	86	24.15	94	38.36
Total		601	32	100	356	100	245	100
Age group	21-40 yrs	198	10	31.25	100	28.08	98	40.0
	41-60 yrs	209	**14**	**43.75**	**138**	**38.76**	71	28.97
	61-80 yrs	193	8	25.0	118	33.14	75	30.61
Total		601	32	100	356	100	245	100

Table 2: Identified ADRs Categorized based on the Therapeutic Class

Drug name	Description of reaction	No. of ADRs	Naranjo's Scale	Hartwig Seigles
1.Corticosteroids				
A. T. Betamethasone	Cushing syndrome	1	Probable	Moderate
B. T. Prednisolone	Cushing syndrome	1	Probable	Moderate
	Diabetes Mellitus	2	Definitely	Severe
C. T. Hydrocortisone	Cushing syndrome	1	Probable	Moderate
2. NSAIDS				
A. T. Diclofenac	Hepatomegaly	2	Probable	Moderate
B. T. Aspirin	Acute Gastritis	2	Possible	Moderate
C. Inj. Diclofenac	Gastrointestinal hemorrhage	2	Definitely	Severe
	Vomiting	2	Possible	Mild
D. T. Acetaminophen + Tramadol	Constipation	1	Possible	Mild
3. Antibiotics				
A. T. Clindamycin	Diarrhea	2	Probable	Moderate
B. Inj. Ceftriaxone	Burning sensation and itching over the body	3	Possible	Mild
C. Inj. Ofloxacin	Skin rashes	1	Possible	Mild
D. Amoxicillin + Clavulanate	Skin rashes	1	Possible	Mild
4. Anti-TB drugs				
A. T. Isoniazid	Rashes all over the body	2	Possible	Moderate
	Joint Pains	1	Probable	Mild
B. Tab. H+R+E+Z*	Hyperuricemia	1	Probable	Mild
	Hepatitis	1	Probable	Moderate
5. Proton pump inhibitors				
A. Inj. Rabeprazole	Vomiting	2	Probable	Moderate
6. Vitamins	Decreased urine output	1	Possible	Moderate
A. T. Thyroxine	Swelling of foot	1	Probable	Moderate
7. Anti-emetics				
Inj. Ondansetron	Dry mouth	2	Possible	Mild

*(Isoniazid + Rifampicin + Ethambutiol + Pyrazinamide)

Table 3: Severity of ADRS based on Poly pharmacy

Severity of ADRs based on Causality scale		Poly pharmacy			
		Major	Percentage (%)	Minor	Percentage (%)
Naranjo's Scale	Definitely	3	9.37	1	3.12
	Probable	10	31.25	3	9.37
	Possible	8	38.09	7	21.87
	Unlikely	0	00	0	00
Modified Hartwig Seigle Scale	Severe	4	19.04	0	00
	Moderate	11	34.37	5	15.62
	Mild	6	18.75	6	18.75

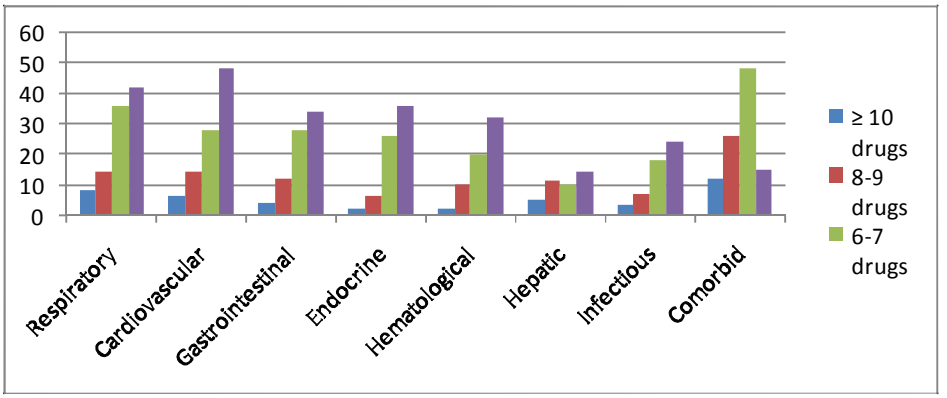

Figure 1: Division of Poly pharmacy Vs Therapeutic Category

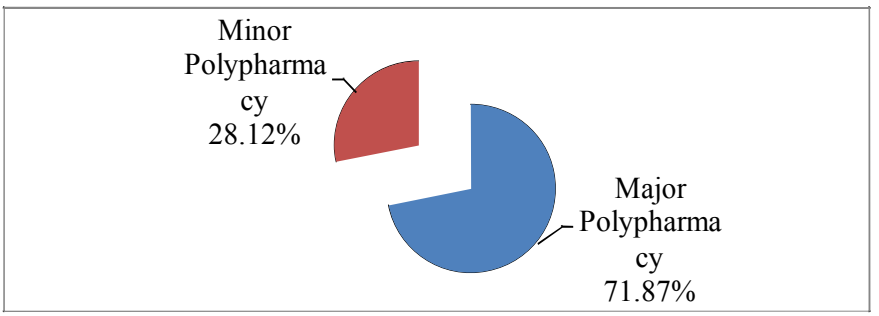

Figure 2: Division of ADR's based on Poly pharmacy

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