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Assessment, Monitoring and Reporting of Adverse Drug Reactions Due to Polypharmacy

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ABSTRACT
Poly-pharmacy significantly increases the likelihood of adverse reactions to drugs, risk of hospitalization and medication errors related to drugs. It depends on the number of drugs, the disease and patient related factors. Poly-pharmacy is a major risk factor for severe adverse drug reactions (ADR'S) and is associated with increased risk of mortality. The main aim of this study was to assessment and monitoring of polypharmacy leading to adverse drug reaction. A Prospective observational study was carried out in Rajiv Gandhi institute of medical sciences (RIMS), a 750 bedded tertiary care teaching hospital, Kadapa, for the period of 7 months in the all deportments of hospital. A total of 448 cases of polypharmacy were identified, among that males were 246 and females were 202. Out of 448 cases, 252 patients were major polypharmacy and 196 were minor polypharmacy. Among 114 ADRs, 22.80% from MICU, 31.57% from MMW, 27.19% from FMW, 10.52% from PSY and 7.89 from DVL, The identified ADRs were reported to physician and the causality assessment was done for 114 ADRs by using Naranjo's scale. According to Naranjo's scale 24 (60.28%) ADRs were definitely, 52 (57.42%) were probable, 38 (81.37%) were possible. 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.
Keywords: *ADR's, Poly pharmacy, Assessment, Monitoring and Outcomes.*

INTRODUCTION

Poly-pharmacy significantly increases the likelihood of adverse reactions to drugs, risk of hospitalization and medication errors related to drugs. It depends on the number of drugs, the disease and patient related factors. Poly-pharmacy is a major risk factor for severe adverse drug reactions (ADR'S) and is associated with increased risk of mortality[1]. Poly-pharmacy carries negative connotations, including increased costs, poorer compliance and increased risk of side effects, drug interactions and adverse drug reactions[2]. 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 physiol-ogical function". Traditionally ADR'S are classif-ied into two categories- Type-A (Augmen-ted) and Type-B (Bizzare) reactions[3]. Poly-pharmacy 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 heal is defined as the concomitant use of two 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[4]. Adverse drug reactions are recognized hazards of drug therapy and it is an important cause of morbidity and mortality in both hospitalized and ambulatory patients[5]. ADR'S are the fourth leading cause of death ahead of pulmonary diseases, diabetes and acquired immune deficiency syndrome (AIDS)[6]. Multiple factors influence ADR susceptibility which includes multiple drug therapy, disease severity, age, drug interactions and number of drugs prescribed[7]. ADR'S rank among the top 10 leading causes of mortality. So there is a need to study ADR'S seriously to create awareness about ADR'S among patients to motivate health care professionals in the hospital to report ADR'S to minimize the risk[4].

MATERIALS AND METHODS

A Prospective observational study was carried out in Rajiv Gandhi institute of medical sciences (RIMS), a 750 bedded tertiary care teaching hospital. The main aim of this study was the assessment and monitoring of poly-pharmacy leading to adverse drug reaction. This study was including hospital in-patients who are treated for various diseases. Study was conducted between the periods of January 2016 to July 2106.

Inclusion criteria: Patients of age group between 20-70 years of both genders who admitted in hospital.

Exclusion criteria: Patients who are treated in out-patient departments, those who stayed in the hospital <20 hours were excluded.

The data was collected from the patient's case records, which included the medication history, for number of drugs prescribed and for number of possible drug interactions. Details of demograp-hics, clinical manifestations, patient history and treatment regimen were collected. Causality assessment of reported ADR'S was carried out by using Naranjo's algorithm scale. In Naranjo's algorithm, the ADR'S are classified as Definitely, Probable, Possible and Unlikely.

RESULTS

During the study period total of 850 patients got admitted in hospital (FMW, MMW, PSY, MICU, and DVL), 250 patients did not meet the criteria as 50 patients stayed for less than 20 hours and 52 were either critically ill or on mechanically venti-lated and few of them admitted for poisoning, then 448 cases of polypharmacy were identified.

Among 448 cases, males were 246 and females were 202. Out of 448 cases 252 patients were found to be with major polypharmacy and 196 were with minor polypharmacy. Out of 252 major polypharmacy patients, 34.12% of the patients were found in MICU followed by 55.55% in MMW, 14.28% in FMW, 10.31in PSY and 9.92% in DVL. There are 51.75% ADRs were identified in males and 48.24% ADRs were identified in females. Among 114 ADRs, 22.80% from MICU, 31.57% from MMW, 27.19% from FMW, 10.52% from PSY and 7.89 from DVL.

Categorization of polypharmacy was presented in table: 1, 2, and 3 based on age, gender and department. Our study showed that 252 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 medical diagnosis associated with polypharmacy was presented in table: 4.

Table: 1 Categorization of polypharmacy based on age

Age group	No. of patients	ADRs	%	Polypharmacy			
				Major	%	minor	%
20-40	176	36	31.57	96	38.09	52	26.53
41-60	109	59	51.75	156	61.90	96	48.97
61-70	163	19	16.66	100	39.68	48	24.48
Total	**448**	**114**	**100**	**252**	**100**	**196**	**100**

Table: 2 Categorization of polypharmacy based on gender

Gender	No. of patients	ADRs	%	Polypharmacy			
				Major	%	minor	%
Male	246	59	51.75	156	61.90	105	53.57
Female	202	55	48.24	96	38.09	91	46.42
Total	**448**	**114**	**100**	**252**	**100**	**196**	**100**

Table: 3 Categorization of polypharmacy based on department

Gender	No. of patients	ADRs	%	Polypharmacy			
				Major	%	minor	%
MICU	105	26	22.80	86	34.12	42	21.42
MMW	86	36	31.57	140	55.55	76	38.77
FMW	122	31	27.19	75	14.28	30	15.30
PSY	70	12	10.52	26	10.31	20	10.20
DVL	65	9	7.89	25	9.92	18	9.18
Total	**448**	**114**	**100**	**252**	**100**	**196**	**100**

Table: 4 Medical diagnoses associated with polypharmacy

Disorder	No. of patients	Percentage (%)
Respiratory	72	16.07
Cardiovascular	102	22.76
Renal	78	17.41
Endocrine	48	10.71
Hematological	39	8.70
Hepatic	48	10.71
Infection	61	13.61
Total	**448**	**100**

Most commonly prescribed drugs were enalapril, followed by ceftriaxone, hydrocortisone, phenytoin and metformin. Out of the 114 ADRs, 105 were accepted by physician and 9 were suspected. Among them34 ADRs were Type-A (augmented), 84 ADRs were Type-B (bizzare). Of these 14 ADRs were identified in patients had minor polypharmacy and 100 ADRs in patients had major polypharmacy.

ADRs ASSESSMENT

The causality assessment was done for 114 ADRs by using Naranjo's scale. The detailed information was presented in table: 5. According to Naranjo's scale 24 (60.28%) ADRs were definitely, 52 (57.42%) were probable, 38 (81.37%) were possible.

Table: 5 Severity of ADRs based on polypharmacy

Causality Assessment based on naranjos scale	Poly pharmacy			
	Major	%	Minor	%
Definite	19	18.62	5	41.66
Probable	51	49.09	1	8.33
Possible	32	31.37	6	50
Unlikely	00	00	00	00
Total	**102**	**100**	**12**	**100**

Around 15 ADRs were found in respiratory diseases like copd, pneumonia, emphysema and asthma. 11 in renal disease patients, 45 in cardio-vascular disease patients, 17 in infectious disease patients, 8 in endocrine disease patients , 10 in hematological disease patients and 8 in hepatic disease patients. Suspected ADRs were presented in table: 6 based on therapeutic category.

Table: 6 Suspected ADRs and causality assessment

Suspected drug	Suspected reaction	Number of ADRs	Naranjos scale
NSAIDs			
Diclofenac	Gastritis	5	Probable
Aspirin	GI-bleeding	1	Probable
Ibuprofen	Angioneuritic edema	1	Probable
Anti-cholinergic drugs			
Atropine	Dryness of mouth	5	Definite
Benzhexol	Dryness of mouth	3	Possible
Cyclopam	Stomach discomfort	1	Possible
Sympathomimmetic amine			
Dopamine	Tachycardia	3	Probable
Dobutamine	Tachycardia	2	Possible
Adrenalin	Tremors	1	Probable
Diuretics			
Frusemide	Hypokalemia	6	Definite
Spiranolactone	Hyperkalemia	4	Definite
Anti-histamines			
Cetrizine	Drowsiness	7	Probable
Avil	Drowsiness	5	Possible
Corticosteroids			
Prednisolone	Hyperglycemia	2	Possible
Hydrocortisone	Cushing syndrome	2	Possible
Dexamethasone	Hypertension	1	Possible
Oral-hypoglysemic			
Metformin	Metallic taste	3	Probable
Glimipride	Hypoglycemia	2	Probable
Anti- coagulants			
Heparin	Urticaria	2	Definite
Anti- platelets			
Ecospirin	Urticaria	5	Definite
Anti- epileptics			
Phenytoin	Gingival hyperplasia	2	Probable
Phenobarbitone	Anemia	1	Probable
Valproic acid	Hepatitis	1	Possible

Opioids			
Tramadol	Respiratory depression	1	Possible
Antipsychotic			
Clozapine	Weight gain	1	Possible
Olanzapine	Salivation	3	Probable
Anti-manic			Probable
Lithium	Tremors	4	
Anti-hyprtensive drugs			
Losartan	Hypotension	1	Probable
Nefedipine	Reflex tachycardia	1	Possible
Amlodipine	Pedal edema	1	Possible
Enalapril	Dry cough	5	Probable
Anti-anginal drugs			
Nitroglycerin	Head ach	8	Probable
Hypolipedemic drugs			
Atorvastatin	Muscle weekness	10	Possible
Anti retroviral drugs			
Zidovudine	Anemia	1	Definite
Anti- biotics			
Ceftriaxone	Allergic reactions	2	Possible
Cefixime	Skin rashes	1	Probable
Azithromycin	Epigastric pain	2	Probable
Amikacin	Nephro-toxicity	1	Definite
Augmentin	Diarrhea	3	Definite
Fluconazole	Skin rashes	2	Definite
Metronidazole	Metallic taste	2	Possible

DISCUSSION

Polypharmacy was a frequent condition in Indian population and mainly depends on the type of the diseases, co-morbid conditions, hereditary, economic status and malnutrition. Our present study showed that adults and young elder patients were more prone to polypharmacy due to different types of diseases with other co-morbid conditions. Among 448 cases, males were 246 and females were 202. Out of 448 cases 252 patients were found to be with major polypharmacy and 196 were with minor polypharmacy. Out of 252 major polypharmacy patients, 34.12% of the patients were found in MICU followed by 55.55% in MMW, 14.28% in FMW, 10.31in PSY and 9.92% in DVL. There are 51.75% ADRs were identified in males and 48.24% ADRs were identified in females. Among 114 ADRs, 22.80% from MICU, 31.57% from MMW, 27.19% from FMW, 10.52% from PSY and 7.89 from DVL, Most commonly prescribed drugs were enalapril, followed by ceftriaxone, hydrocortisone, phenytoin and metformin. Out of the 114 ADRs, 105 were accepted by physician and 9 were suspected. Among them34 ADRs were Type-A (augmented), 84 ADRs were Type-B (bizzare). Of these 14 ADRs were identified in patients had minor polypharmacy and 100 ADRs in patients had major polypharmacy. The causality assessment revealed that all suspected ADR'S 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.

CONCLUSION

Building awareness to healthcare professionals for spontaneous reporting of adverse drug reaction and following the evidence based medicine (EBM) would help in preventing polypharmacy 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.

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