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POLYPHARMACY LEADING TO ADVERSE DRUG REACTIONS IN ELDERLY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Polypharmacy is a common occurrence in elderly patients due to reasons like multiple co-morbidities and multiple prescribing physicians. The present study was designed to identify the adverse drug reactions occurring in the elderly as a result of polypharmacy and also to assess the rationality of prescription based on World Health Organization (WHO) criteria and Beer's criteria. This study was conducted at Victoria hospital attached to Bangalore Medical College and Research Institute . Hundred patients aged ≥60 years and prescribed more than 5 drugs were included in the study. The analysis of data revealed, the number of drugs per prescription was 8.42±2.4. Of the total 842 drugs prescribed, number of drugs prescribed by generic name was 36 (4.27%) and number of drugs prescribed from WHO model list of essential medicine was 444 (52.7%). Adverse drug reactions were mainly seen in 15% of patients. 20 patients were prescribed potentially harmful drugs according to Beer's list. To conclude, polypharmacy was seen in majority of elderly patients but the use of injections and antibiotics were limited. Prescribing by generic name and from essential drug list needs to be improved. Many ADRs were noted for commonly prescribed drugs and also for inappropriate drugs as given in Beer's list.

KEYWORDS : Elderly, polypharmacy, adverse drug reactions, in-appropriate prescription, irrational drug combination.

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INTRODUCTION

Polypharmacy is defined as concurrent use of multiple medications, greater than five by a single patient. Polypharmacy is a common occurrence in elderly patients due to a variety of reasons like increasing number of chronic health conditions, patients being treated by multiple prescribing physicians, availability of nonprescription drugs, high cost of prescription medications, hoarding of old medications, inadequate patient knowledge of medications and medical conditions, patients using different sources of medication, often with little or no co-ordination between these sources, taking at least one medication for every diagnosis and tendency toward self-treatment/self-medication[1].

Adverse drug reactions are most frequently observed among the elderly. Responsiveness to drugs is modified among the elderly due to age-related changes such as decline in renal and liver function, hypoalbuminemia, reduced body weight, and multi-morbidity which may increase the risk of polypharmacy leading to high frequency of adverse drug reactions among the elderly. Polypharmacy increases the incidence of adverse drug reactions (ADRs), drug interactions, non- compliance which in turn leads to increase in hospital admissions and thus increases the health expenditure [2] . A study by Joshi et al showed an adverse drug reaction rate of 7% in patients taking 6-10drugs, increasing to 40% in those taking 16-20drugs [3].

In-appropriate prescription of medications in elderly due to wrong dosing, incorrect frequency of administration, prescribing ineffective medication, prescribing the wrong medication and duplicate therapy also leads to many ADRs. About one fourth of the ADRs are due to in-appropriate prescriptions in elderly[4]. Many studies have shown that in-appropriate medication use in elderly as per Beer's list[5] leads to increased morbidity and mortality [6,7].

Geriatrics is an upcoming field in India. The field of ageing and health has become a dominant area of concern in the 21st century. This is mainly due to an increase in the numbers of older people in both developed and developing countries. In the year 2000, there were an estimated 600 million people aged 60 years and above in the world. By 2025, this would double to about 1.2 billion people and by 2050 there will be 2 billion, with 80% of them living in developing countries[8]. Information about appropriateness of prescription medication use among elderly is limited in India.

Indian prospective studies focussing on polypharmacy resulting in adverse drug reactions in elderly is lacking. Therefore, the present study was designed to study the polypharmacy leading to adverse drug reactions in elderly in a south Indian tertiary care centre.

MATERIALS & METHODS

The is a prospective observational hospital based study which was conducted in the department of medicine of Victoria hospital attached to Bangalore Medical College and Research Institute from June 2010 to July 2010. Patients records, medication history and where appropriate, discussion with the patient, patients attendants and physicians formed the source of data. About 100 inpatients in the department of medicine were included in the study. Ethics Committee approval was obtained before initiating the study.

The entire study procedure was explained to the patients who volunteered and fulfilled the selection criteria. Informed consent was taken from the selected patients before starting the study. The patients were selected based on the following criteria.

Inclusion criteria

1. Patients ≥ 60 years.
2. Elderly patients who are on more than 5 drugs.
3. Patients who voluntarily gave informed consent.

Exclusion criteria

1. Patients less than 60years
2. Elderly patients who are on ≤ 5 drugs
3. Patients who did not gave voluntary informed consent.

The demographic data including in-patient number, name, age, sex, address, date of admission, date of discharge and complete medical history was recorded. The drug details which includes name of the drug, dosage, duration of therapy, route of drug administration, reasons for polypharmacy, previous medication history were recorded. Details of ADRs with causal drugs was also recorded.

Adverse drug reaction was defined as an effect that is noxious and unintended, and which occurs at doses used in man for prophylaxis, diagnosis and therapy as per WHO guidelines.

We followed the United Nations agreed cut-off ≥60 years to refer to the older population/elderly.[9]

The details of drugs collected were analysed according to WHO indicators for the following.

1. Number of drugs per prescription
2. Number of drugs prescribed by generic name
3. Number of drugs prescribed from WHO model list of essential medicine
4. Number of injections per prescription
5. Number of antibiotics per prescription

Statistics

The results were analysed using descriptive statistics. Mean ± SD and percentages were used to describe the results wherever applicable.

RESULTS

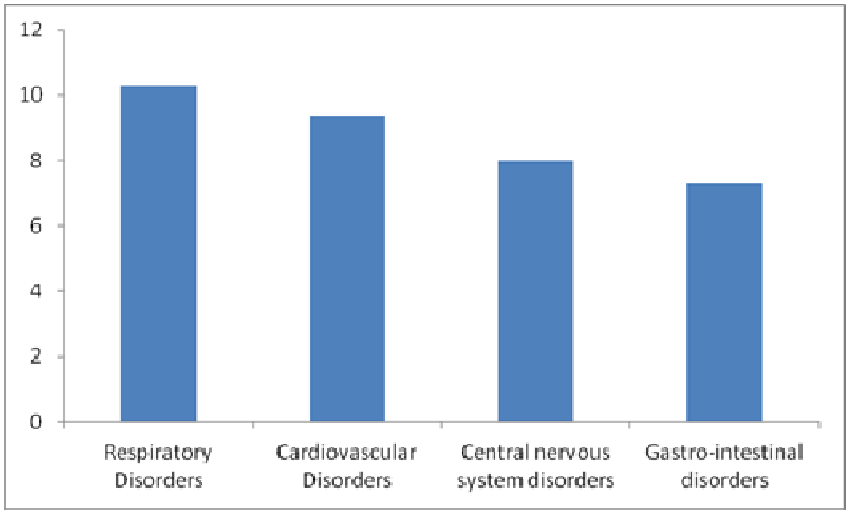
Hundred patients who satisfied the selection criteria were included in the study of which 62 were males and 38 were females.

About 66% patients were in the age group of 60-69years, 24% in the age group of 70-79 years, 10% in the age group of 80-89years.

Our study showed that 18% of the patients received six drugs, 24% of the patients received seven drugs, 20% of the patients received eight drugs and 38% of the patients received nine drugs or more than nine drugs.

The medical diagnosis associated with Polypharmacy is mentioned in Figure No. 1. Patients admitted with respiratory disorders received 10.3 drugs per patient, followed by patients admitted with cardiovascular disorders and central nervous system disorders receiving 9.4 and 8 drugs per patient respectively.

Figure 1
Medical diagnosis with number of drugs per prescription



The list of potentially harmful drugs prescribed for elderly as mentioned in Beer's list is given in Table No.1. 20 patients were prescribed potentially harmful drugs according to Beer's list. The drugs mainly prescribed in an in-appropriate manner according to Beer's list were ferrous sulphate, Chlorpheniramine Maleate, digoxin, amitryptyline, nifedipine and dicyclomine.

Table 1
Potentially harmful drugs prescribed as per Beer's list

Potentially Harmful drugs	No. of patients
Ferrous sulphate (>325mg/dl)	6
Chlorpheniramine Maleate	4
Digoxin	4
Amitryptyline	2
Nifedipine	2
Dicyclomine	2
TOTAL	**20**

Most commonly prescribed drugs in elderly is as shown in Table No. 2. Most commonly prescribed drug was ranitidine (78 patients), followed by cefotaxime (48 patients), salbutamol (40patients) and deriphylline (32patients).

Table No. 2
Most commonly prescribed drugs

Name of the drug	No. of Patients
Ranitidine	78
Cefotaxime	48
Salbutamol	40
Deriphylline	32
Diuretic (Hydrochlorothiazide)	26
Paracetamol	22
Amlodipine	18
Aspirin	18
Plain insulin	16

Irrational prescription of concurrent administration of the drugs noted in the study with theoretical reasons for irrationality are mentioned in Table No. 3. The drugs involved in majority of the drug interactions included ciprofloxacin, theophylline, ceftriaxone and azithromycin.

Table No. 3
Irrational prescription of drug combinations and the reasons for irrationality

Irrational drug combinations	Reasons for irrationality
Gentamycin+furosemide	Increases ototoxicity
Ceftriaxone+Acenocoumarol	Increases bleeding time
Azithromycin+Theophylline	Increases plasma concentration of theophylline
Aspirin+Diclofenac	Gastritis
Ramipril+Digoxin	Ramipril increases the concentration of digoxin
Ceftriaxone+Azithromycin	Bactericidal + Bacteriostatic antagonism
Enalapril+Aldactone	Hyperkalemia
Ciprofloxacin+Theophylline	Ciprofloxacin inhibits the metabolism of Theophylline

Adverse drug reactions noted in the study are mentioned in Table No. 4. Only certain and probable adverse drug reactions were taken for analysis. Adverse drug reactions were mainly seen for insulin (5 patients), followed by salbutamol (3 patients), amlodipine (2patients) and digoxin (2patients).

Table No 4
Drugs which caused adverse drug reactions.

Adverse drug Reaction	Drug responsible	No. of patients
Hypoglycemia	Insulin	5
Tremors	Salbutamol	3
Ankle oedema	Amlodipine	2
Palpitation	Digoxin	2
Dry mouth	Amitryptyline	1
Sedation	CPM	1
Cough	Enalapril	1
Epistaxis	Acenocoumarol	1
Tinnitus	Gentamycin	1

The rationality of prescriptions were assessed based on **WHO** criteria are as follows:
Percentages are calculated taking total number of the drugs prescribed (n=842)

1. Number of drugs per prescription: 8.42±2.4 drugs
2. Number of drugs prescribed by generic name: 36 (4.27%)
3. Number of drugs prescribed from WHO model list of essential medicine: 444 (52.7%)
4. Number of injections per prescription: 2.96±1.44 (35.2%)
5. Number of antibiotics per prescription: 1.72±0.36 (20.9%)

DISCUSSION

Our study results showed that out of 100 patients included in the study, 62% of them were males and 38% were females which is in contrary to a study shown in Indonesia where 66% of the patients were females[8].

This study showed that 38% of the patients received more than nine drugs followed by 24% of the patients received seven drugs which is in contrary to a study conducted in Hong Kong where 68% of the patients received less than four drugs[10]. As polypharmacy increases the risk of ADRs and inappropriate medication use in elderly, efforts should be made to improve the prescribing practices.

The study showed that respiratory disorders mainly exacerbation of COPD, pneumonia, upper respiratory tract infections were associated with polypharmacy followed by cardiovascular disorders mainly congestive heart failure, hypertension and coronary artery diseases. But cardiovascular disorders were found to be the main morbidity pattern observed by Zaveri et al in India[11]. This difference could be attributed to the seasonal variation, as the incidence of respiratory disorders is high in the month of June and July.

The average number of drugs per prescription is an important index of the standard of prescribing. The number of drugs per prescription in our study was 8.42±2.4 which is similar to a study by Jochen schuler et al[12] in Austria where the average number of drugs per prescription was 7.5±3.8. But a similar study in India showed average drugs per prescription was 4.27[11]. Hence there is a scope for improving prescribing practices by educational interventions in our hospital.

Prescribing by generic name can reduce the cost incurred on drugs and the risk of medication errors. Excess of prescribing by brand names may be considered as evidence of vigorous promotional activities by pharmaceutical companies. The number of drugs prescribed by generic name was only 4.27% in our study which is less compared to a similar study conducted by Mandavi et al in Punjab, India where 18% of the drugs were prescribed by generic name [13]. Hence, more emphasis needs to be given to improve prescribing by generic names in developing countries like India to make the treatment cost-effective.

The number of antibiotics prescribed should be as low as possible and should be prescribed for appropriate medical indication. Excessive use of injections consumes scarce

nursing resources and increases the risk of spread of infections. In our study, antibiotics were prescribed in 20.9% and injections in 35.2% of the total drugs prescribed. But in a study conducted in elderly from India showed that 88.2% of the patients were prescribed antibiotics and 86.4% of patients were prescribed injections[13]. Another study conducted in Nepal showed that an injection was prescribed in 5.21% of encounters while an antibiotic was prescribed in 31.4% of encounters[14]. Therefore, rational prescription of antibiotics should be encouraged to prevent polypharmacy and antibiotic mis-use.

About 52.7% of the prescribed drugs were from WHO model list of essential medicine[15] which is similar to another study conducted in Bangladesh[16]. Prescribing of Essential drugs should be encouraged at every hospital to make the treatment economical. Development of a hospital formulary would help in implementing the same.

Most commonly prescribed drugs include Ranitidine followed by cefotaxime, salbutamol and deriphylline. A study conducted in Austria[12] showed that diuretics, Proton pump inhibitors and ACE inhibitors were prescribed commonly.

In this study, based on Beer's list[5] , only 2.37% of total drugs were prescribed in an inappropriate manner which is lower than other two Indian studies which reported 7.42%[11] and 4.1%[17.] The Beer's list is a list of specific medications that are generally considered inappropriate when given to elderly people. For a wide variety of individual reasons, the medications listed tend to cause side effects in the elderly due to the physiologic changes of ageing. In-appropriately prescribed drugs like ferrous sulphate>325mg/day, chlorpheniramine maleate and digoxin were seen in other Indian studies also [11,18].

Many studies have shown that ADRs are commonly seen in elderly. In our study, 17% of the patients were reported with ADRs. Most common ADRs were due to insulin, followed by salbutamol and digoxin. A study by Rupawala et al [19] showed that antidiabetics, oral anticoagulants and antiplatelets lead to majority of ADRs in elderly. Another study by Harugeri et al[18] showed that insulin, frusemide and prednisolone were responsible for majority of the ADRs in elderly. Many potentially hazardous concurrent use of drugs were also noted in the study as shown in table 4. Many interactions involved ciprofloxacin, azithromycin and theophylline. Majority of the drugs producing ADRs were not listed in Beer's list. As these drugs are very commonly used in elderly, greater care should be taken in prescribing them to decrease the associated morbidity and mortality in elderly patients.

CONCLUSION

This study has shown that majority of the elderly patients received more than seven drugs. polypharmacy was associated mainly with respiratory disorders in elderly. Though the number of drugs per prescription was high, use of injections and antibiotics was limited. There is a scope for improvement in prescribing by generic name and opting drugs from WHO essential drug list. The use of inappropriate medications in elderly was minimal. But ADRs to many commonly used drugs and significant drug-drug interactions were noted which indicates the need for improving the awareness of physicians about prescribing in elderly. More prospective studies are required in Indian hospitals to assess the burden of ADRs in elderly. Educational programmes should be conducted to improve the habit of prescribing rationally by the prescribers. There is also a need for mass awareness among the physicians and patients about the concept of rational use of medications. Drug information services also should be set up in the hospitals to provide information about adverse effects and drug-drug interactions to the physicians. Awareness about reporting ADRs in India also needs to be improved.

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