

Management of Drug Related Problems in the Elderly - A Review

Satish S¹, Febin Benny², AR Shabaraya³

¹Professor, Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, Karnataka, India

²Intern Pharm D, Department of Pharmacy Practice, Srinivas College of Pharmacy, Mangalore, Karnataka, India

³Principal, Srinivas College of Pharmacy, Mangalore, Karnataka, India

Corresponding Author: Febin Benny

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ABSTRACT

Drug Related Problems (DRPs) also known as Medication Related Problems (MRPs) are the problems that occur because of the drugs when a person is undergoing a treatment. Older patients are particularly vulnerable to ADRs because of age-related changes in pharmacokinetics and pharmacodynamics, such as reduced hepatic and renal function, prolonged elimination half-life, and increased sensitivity to drugs, which have been shown to be associated with an increased risk of ADRs.

This may (in most cases) interfere with the desired outcome of the therapy. This in turn, reduces the quality of life of a person. DRPs may be life-threatening in some and this poses the importance of identification of DRPs. The DRPs can be identified and can be categorized as whether it is preventable or not. It can also be classified into different classes- Adverse Drug Reaction (ADR) and Drug Interaction being the most common causes for the incidence of DRP. The pharmacist can play a key role in identification, categorization and prevention of DRPs.

The aim of this review is for the better understanding of DRPs and to shine light on the causes of DRPs that is often left unseen or under-estimated. This review also aims to show the big role that can be played by pharmacist in identifying, preventing DRPs and thereby improving the quality of life of patients.

Keywords: Drug related problems, Quality of life, Pharmacist's role

INTRODUCTION

Geriatrics is concerned with the clinical, preventive, remedial, and social aspects of illness within the elderly and is a branch of sub-speciality of internal medicine/general medicine. The term 'elderly' generally refers to patients aged 60 years or over. They represent 21% of the world population and consume over one-third of the prescription drugs. [1, 2]

Older age, overburdened healthcare system, number of prescribed drugs, comorbidities, Charlson comorbidity index, and multiple prescribers to one patient are significant risk factors for the occurrence of medication errors. The elderly is at high risk of experiencing drug-related problems due to their complex medical problems and long-term usage of multiple medications. [2]

The elderly was found to be using three times more drugs than the younger patients for the treatment of chronic diseases. DRPs are associated with increased risk of hospital readmissions, morbidity and mortality due to the increased comorbidities and usage of multiple diseases. The patients having more than five drugs (polypharmacy) are at higher risk of experiencing DRPs. [3]

The Pharmaceutical Care Network of Europe (PCNE) defines DRPs as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. They can cause disability, gait, disturbances, depression and

falls. It is also the third or fourth leading cause of death in the elderly. [4, 5]

Different classifications were published DRPs in different literatures. But none of them are standardized. These include-American Society of Hospital Pharmacists (AHSP) classification, Cipolle/Morley/Strand classification, Granada consensus, Hanlon approach, Hepler-Strand classification, Krska system, Problem-Intervention documentation (PI-Doc), Westerlund system, etc. [6, 7]

According to the Hepler-Strand classification, Drug Related Problems (DRPs) can be classified into eight categories. [8] They are-

1. **Untreated indication:** The patient is not receiving a drug for a condition/indication and is left untreated.
2. **Improper drug selection:** The patient is being treated with an inappropriate drug or wrong drug.
3. **Subtherapeutic dosage:** The patient is being treated with correct drug but with low dose of it.
4. **Failure to receive drugs:** The patient is not receiving a medication due to economic, psychological, sociological, or pharmaceutical reasons and is the cause of the medical condition.
5. **Over dosage:** The patient is being treated with correct drug but with high dose of it and may lead to toxicity.
6. **Adverse reactions:** The patient's medical problem is caused due to an Adverse Drug Reaction or Adverse Effect.
7. **Drug interactions:** The patient's medical problem is caused due to drug-drug, drug-food or drug-laboratory interaction.
8. **Drug use without indication:** The patient is taking a drug without any condition/indication.

Starting from prescribing to dispensing DRPs can occur in all the stages. DRPs can affect the patient's clinical outcomes and can result in morbidity and mortality. And hence, a clinical pharmacist can assure safe

and effective medication use through evidence-based medicine and can also give the necessary pharmaceutical care to the patient. [9, 10]

DRUG RELATED PROBLEMS

Following hospital discharge, DRP occur frequently among elderly patients using five or more drugs for the treatment of chronic disease. The number of DRP increased with the number of drugs used. An important task for community pharmacists is to identify, resolve, and prevent the occurrence of DRP among this patient group. Since DRP are associated with an increased risk of hospital readmissions, morbidity, and mortality, it is very important to develop intervention strategies to resolve and prevent DRP.

Drug related problems are substantially high among geriatric inpatients. Patients with polypharmacy and comorbidities have a much higher chance of developing DRPs. Hence, special attention is needed to prevent the occurrence of DRPs in these patients. A recent study by Abhishek Pradhan, Febin Benny and AR Shabaraya is also supportive of this. They had found that more than 51% of the DRPs assessed were in the geriatric population. They also found that the occurrence of DRPs were more in females (75%) when compared to males. [11]

Medications are one of the key tools in the therapeutic management of disease. However, they are not always used in an ideal, or appropriate, manner. When medications are not used appropriately, patients may experience adverse events or fail to achieve their therapeutic goals. In turn, this results in suboptimal quality of life and wasted resources for our society.

DRPs may arise due to inappropriate prescribing, inappropriate dispensing/administration of the drug, inappropriate behaviour by the patient, inappropriate monitoring of the patient, or patient idiosyncrasy. Although idiosyncrasy is inherently unpreventable, most of the other causes of DRPs can be prevented. The following section of this review will provide

a framework for management of medication related problems.

A) Untreated Indication or Condition left Untreated

The patient having a medical problem that requires drug therapy, but is not receiving a drug for that indication. Medical conditions might go untreated for several reasons. Patients may not disclose physicians about symptoms, eg. Constipation, pain, or feelings of depression, and physicians fails to enquire. Patients go for self-medication, when actually treatment requires medical attention or sometimes physicians incorrectly might attribute symptoms simply to the aging process without further evaluation. Omission of therapy also is an example of an untreated indication. Examples include absence of a beta blocker following a heart attack.

In many cases, the patients are not treated/prescribed with needed medication, despite having a clear indication for a drug. According to the International guidelines, a lipid-lowering drug should be added to the treatment regimen of a patient with Type Diabetes Mellitus. [12] The absence of lipid-lowering drugs contributed to the presence of DRP of untreated indication. [3]

A study done by Yvonne Koh et al. in hospitalized patients had found 118 cases of untreated indication (26.22%) out of the 450 cases of DRPs that had been assessed. [13] Another study done by Hasniza Zaman Huri and Hoo Fun Wee had found that almost 4% of DRPs were due to a condition being left untreated. [14]

B) Improper Drug Selection or Drug Ineffectiveness

The Patient has a reason for taking the drug; however, a different drug is warranted because of safety or effectiveness issues. Explicit criteria are available regarding potentially inappropriate medication use in older adults. Use of medications on these lists generally is discouraged because harmful effects outweigh potential benefit in older adults. In most cases, safer alternatives

are available that are preferred for this population.

Drugs must be given to a patient according to a patient's need and treating a patient otherwise can result in DRP. [15] Studies done by Berhane Yohannes Hailu et al. found the DRP due to inappropriate drug selection was at a whopping 54.1% [7] and another study by Kirsten K Vitkil et al. which was done in 2 groups of patients had showed that 3.4% and 2.7% of the DRPs identified were due to non-optimal drug selection. [16]

C) Sub-therapeutic Dosage or Under-dosage

The Patient has a medical condition that is being treated with too little of the correct drug, geriatrics are more sensitive to the effects of drugs and require lower initial doses so, doses need to be titrated to reach effective or therapeutic doses. Examples include a Patient receiving pharmacotherapy for hypertension or cholesterol, but the Patient's blood pressure or lipid levels, respectively, remain elevated

This involves prescription of a dose that is inferior or lower than the recommended dose for the treatment. This causes the drug to produce an action that is much lower than what is intended. A recent study by A H Al-Hajje et al. found that 10% of the DRPs were caused due to the use of an inferior dose of a drug. [17] Similarly in another study by Hasniza Zaman Huri and Hoo Fun Wee 1.3% of DRPs identified were due to sub-therapeutic dosage of drug. [14]

D) Failure to Receive Drugs

The Patient has a medical problem that is the result of his or her not receiving the drug. In other words, medications cannot be effective if Patients do not take them. There are a multitude of reasons why Patients might not receive a medication: pharmaceutical reasons (e.g., drug was not absorbed in the bloodstream because of a drug interaction), psychological or sociologic reasons (Patient is afraid of side effects; poor health literacy; does not

believe he needs the medication; caregiver withholds medication from Patient), economic reasons (Patient cannot afford to get a medication filled or refilled), system issues (drug not available at the pharmacy).

This class of DRPs particularly occurs when the patient fails to receive the drug. This may be due to psychological, sociological, economic or pharmaceutical reasons resulting in non-compliance. [15]

Study by Yvonne Koh et al. found that non-compliance caused DRPs in 28.1% of the patients who were found to have DRPs upon admission. [13]

In a study by Hasniza Zaman Huri and Hoo Fun Wee done on Type 2 Diabetes Mellitus patients, they had found that approximately 13% of the DRPs were caused due to non-compliance to the treatment. They also found that this non-compliance was a frequent scenario in patients who have been prescribed with anti-hypertensive and hypoglycemic agents. [14]

E) Overdosage

The Patient has a medical problem that is being treated with too much of the correct drug. Excessive dosing is one of the more common MRPs in older adults. Age-related pharmacokinetic and pharmacodynamic changes often necessitate a lower dosage. Indeed, for many drugs, the initial gerontological dose is smaller than the usual adult dose, such as with warfarin or drugs used to treat insomnia, depression, or blood pressure. Drugs that undergo renal elimination need to be dose adjusted. Failure to do so is a major source of preventable adverse drug events.

Overdosage of a drug occurs when a much higher dose of a drug (than what is required) is given to a patient. [15] Many times it can also be because of not considering hepatic/renal function of the person receiving the drug. [13]

Prevalence of DRP due to overdosage was almost 2% in a study conducted by Ema I Paulino et al. in patients discharged from a hospital. [18] Similarly, a study by Sek Hung Chau et al. done on elderly population of

Netherlands found an incidence rate of 5% in DRPs associated with overdosage of drugs. [19]

F) Adverse Reaction

The Patient has a medical problem that results from an ADR. ADR refers to any harmful or unintended response to a drug that occurs with normally used dosages. ADRs can be dose-related or non-dose related. Dose-related reactions tend to be predictable, common, and an extension of a drug's known pharmacologic effects. Examples include sedation from benzodiazepine use. Note that drug interactions or reduced kidney function in older adults can cause higher than expected drug levels, even though the dose is considered in the usual range. In contrast, non-dose related reactions are unpredictable, uncommon, and unrelated to the pharmacologic effect of the drug. They are often more serious than dose-related reactions. Examples of these more serious reactions include hypersensitivity reactions, agranulocytosis, and platelet dysfunction. Careful drug selection, monitoring drug therapy, and patient education can help reduce ADR occurrence. Unfortunately, ADRs in older adults might erroneously be attributed to aging or an existing medical condition. Examples of such nonspecific symptoms include weakness, loss of appetite, depression, and decreased memory or confusion. Unidentified ADRs can lead to a prescribing cascade, in which additional medications are prescribed to treat an ADR. Adverse reactions are the unintended effect of a drug that occurs at dose normally used in human. [20] These may also be classified as preventable and non-preventable. [21] They cause morbidity and mortality in a patient. [20] 5.7% of the patients participated in the study done by Srecko Marusic et al. had ADR. [20] In a study conducted by F A da Costa et al. had found incidence of ADR in 35.1% of the patients making it one of the most common causes of DRPs. [22] ADR was also categorized as the most frequently found DRP in a study done on elderly

patients by Cristina Silva et al. They had found a prevalence of incidence of ADR in 49.51% of the cases of DRPs assessed. [23]

G) Drug Interaction

Drugs can interact not only with other drugs, but also with disease states (e.g., pioglitazone and NSAIDs can worsen heart failure) and foods and nutrients (e.g., grapefruit juice increases blood levels of diltiazem). Many drug-drug interactions result from inhibiting or inducing metabolism of other drugs in the liver. Amiodarone, calcium channel blockers, are just a few drugs that are metabolized by the liver and can affect metabolism of other medications metabolized by similar pathways. Another type of pharmacokinetic drug interaction is decreased effectiveness due to reduced absorption from the stomach; for example, antacids prevent absorption of antibiotic ciprofloxacin in the stomach. Pharmacodynamic drug interactions include orthostatic hypotension from taking multiple antihypertensive agents and bleeding that results from the combined use of aspirin and clopidogrel or an NSAID and warfarin. Although clinicians often are able to identify the possibility of a drug interaction based on pharmacologic characteristics, interactions are not always preventable. Namely, interactions that involve newer medications may not yet be known or fully understood. Some drug interactions are rarely clinically significant, but can be due to variable Patient response to medications. Thus, a Patient might unexpectedly be more susceptible to an interaction that would be detected only once it occurs and not preventable a priori based on population data.

A recent study by A H Al-Hajje et al. showed that the highest prevalence of DRPs were due to drug interactions (37%). [17] A similar research conducted by Hasniza Zaman Huri and Hoo Fun Wee found that drug interaction was the cause of DRPs in 16.3% of the cases and the drugs that were mostly involved in drug interactions were

Aspirin, Clopidogrel, Simvastatin and Amlodipine. [14]

H) Drug use without indication

It occurs when the Patient is taking a drug for no medically valid indication which increases a Patient's risk of drug interactions, ADRs, and other MRPs. Unfortunately, medications are more easily added to a Patient's regimen than discontinued. Medication use without an indication can occur in a variety of scenarios. Medications that were started during a hospitalization may no longer be appropriate upon discharge. For example, a PPI might be started for ulcer prophylaxis in a critical care unit, continued throughout the hospitalization, and inadvertently written as a discharge medicine. Iron or vitamin B12 replacement therapy might be continued once normal levels are restored or underlying cause is addressed. Medications intended for short-term use, such as treatment for reflux symptoms or insomnia, might be continued despite resolution of symptoms. Finally, a medication might have been appropriately started concomitant with another medication (e.g., a PPI with an NSAID for ulcer prophylaxis or folic acid with methotrexate to prevent toxicity), but continued once the other medication was stopped. These varied examples illustrate why older adults often take unnecessary medications and underscore the value of periodic medication reviews to detect this category of MRPs.

A drug is inappropriate if its potential for harm is greater than its potential for benefit. Inappropriate use of a drug may involve Choice of an unsuitable drug, dose, frequency of dosing, or duration of therapy Duplication of therapy Failure to consider drug interactions and appropriate indications for a drug, appropriate drugs that are mistakenly continued once an acute condition resolves (as may happen when patients move from one health care setting to another and the indication is not reevaluated). [24]

PREVENTABILITY OF DRPS

The DRPs can be assessed and can be categorized as-

1. **Definitely preventable-** The DRP may have been due to a specific drug treatment or may have been due to an erroneous prescription. Removal of the drug resolves the DRP.
2. **Possibly preventable-** The DRP was not due to an erroneous prescription, but it could have been avoided by taking appropriate measures.
3. **Not preventable-** The DRP was not preventable or may also have been an unprecedented event during the course of the treatment (like a rare side-effect).^[25]

DEPRESCRIBING AND PREVENTABILITY OF DRP

A recent comprehensive review of the evidence for de-prescribing was performed by Scott and colleagues. They summarized drug withdrawal trials, as well as studies of interventions for reducing inappropriate medications. They concluded that rational de-prescribing is a good step in for reducing the risk of development of adverse reactions due to polypharmacy.^[26] While a number of trials demonstrated safety and feasibility of drug discontinuation, there is a paucity of high-quality evidence reporting on patient-centred clinical outcomes.

PREVENTING DRUG INTERACTIONS IN OLDER ADULTS

Drug interactions are a serious potential problem faced by older adults when taking multiple medications. They consume a large share of the nation's medications, with adults over age 60 buying 30 % of all prescription drugs and 40 % of all OTC drugs. Prevention of drug interactions can be achieved by keeping track of side effects as new symptoms may not be from old age but may be also from the medication. Having complete information about drugs by asking questions and reading the package inserts both doctor and pharmacist can be alert about possible interactions between

drugs, how to take any drug properly, and whether there's a less expensive generic drug available. Pharmacist should educate about foods to take with each drug as some drugs are better absorbed with certain foods, and some drugs shouldn't be taken with certain foods. Following directions and by reading the label every time before taking the medication to prevent mistakes and confirm about the timing and dosage prescribed.

ROLE OF PHARMACIST IN REDUCING DRP

The, pharmacists have an important role in the safe and effective use of pharmaceuticals by providing sufficient and accurate information to the patient, and monitoring the drug therapy. Pharmacists can prevent DRPs through providing drug information to doctors or other health professionals so that increased communication between health professionals is required.

Pharmaceutical care is a form of service and direct responsibility of the pharmacist profession in pharmaceutical work to improve the patient life quality. In an effort to prevent drug-related problems, a pharmacist can play an important role based on pharmaceutical service standards in hospitals.

The real role of clinical pharmacist in preventing potential DRPs and this can be achieved by screening prescription in administrative, pharmaceutical, and clinical aspects. The role of this clinical pharmacy should be listed in hospital accreditation standards and for conducting screening quickly and precisely, it is necessary to map problems by identifying drug-related problems (DRPs) especially in outpatient prescriptions.

An important role in identification, assessment and prevention of DRPs in patients can be played by the community and clinical pharmacists.^[27] According to a scientific journal published by Westerlund T et al. in 1999.

The pharmacist interventions can be categorized as- [18, 28]

- a. No interventions
- b. Medication counselling given to the patient
- c. Practical instructions given to the patient
- d. Patient has been referred to the prescriber or to other physician
- e. Prescriber informed
- f. Information or intervention were asked by the physician
- g. Intervention was put forward by the pharmacist and it was approved by the prescriber or the other physician
- h. Intervention was put forward by the pharmacist, but was disapproved by the prescriber or the other physician
- i. The drug was changed to another dose, dosage form or was replaced with another drug
- j. Referred to a colleague
- k. Other interventions like cancellation of therapy.

The pharmacist can also provide written educational intervention for the practitioners regarding the DRP and the recent studies. Distribution of patient information leaflets and giving proper education to the patient addressing the patient's fear of side-effects is also needed. These all can greatly improve the patient compliance. [29]

In a study conducted by Ema I Paulino et al. the pharmacist had intervened in majority of the DRPs. And in most of the cases (87.1%) the interventions put forward by the pharmacist were approved by the prescriber or other physician. [18] Similarly, a randomized controlled trial done by Thijs H A M Vinks et al. had also found a significant reduction in the mean number of DRPs following the interventions made by the pharmacists. [27]

Thus, involving clinical pharmacists in continuous identification and resolution of DRPs can help improve the quality of life and health status of the patient and this also can play a major role in advancement of optimal clinical outcomes. [30-32]

CONCLUSION

Due to the increasing cost of healthcare services, there is an urgent need to consider medication errors in routine clinical practice to reduce the burden on the healthcare system. Reduction of complexity in the act of prescribing and improving a prescriber's knowledge by education, use of feedback control systems, and monitoring of the effects of interventions that can help in the reduction of medication errors. Most of the medication errors are preventable; medication review of the prescriptions by an experienced clinical pharmacist can detect these errors, and reconciliation can help remove such errors before these reach the patient. Thus a pharmacist can play many roles in both community and clinical health sector for the better care and wellbeing of the patient and can help in maintaining health standards.

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