

Polypharmacy in the Elderly: The Need for Concern and Strategies for its Control

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Abstract: In the last three decades, problems related to aging, multi-morbidity, and polypharmacy have become a prominent issue in global healthcare. In this study, Polypharmacy is defined as a concomitant use of five or more drugs simultaneously and/or the administration of more medications than are clinically indicated, representing unnecessary drug use. The purpose of this study was to describe and quantify the magnitude of polypharmacy, analyze the factors associated with this practice among elderly and suggest control measures for its reduction. Other objectives include creating awareness about the risks of multiple drug use in ageing population and propose practical recommendations/interventions regarding rational drug use for elderly age groups. Materials for this study were obtained from a search of the MEDLINE database and International Pharmaceutical Abstracts to identify articles in people aged 60 years and above. A combination of the search terms like polypharmacy, multiple medications, polymedicine, elderly, geriatric, and aged were used. This study found out that polypharmacy is a common problem and a known risk factor for important morbidity and mortality in the elderly. Many medications are associated with negative health outcomes, but more research is needed to delineate the consequences associated with unnecessary drug use in elderly patients. Health care professionals should be aware of the risks associated with polypharmacy and fully evaluate all medications at each patient visit in order to prevent polypharmacy from occurring.

Keywords: Polypharmacy, Elderly, Strategies, Concern, Control

INTRODUCTION

The definition of health as proposed by the World Health Organization as status of complete physical, mental and social wellbeing and not merely the absence of illness or infirmity may not be adequate for describing health for the elderly¹. An elderly individual is considered healthy when he/she is functionally capable, socially integrated and able to manage his/her own life in an independent fashion.. In Nigeria, the segment of the population aged 60 years or older totaled 6,987,047 in 2006 and is expected to reach 15 million by 2025². The increase in life expectancy leads to an increase in the number of individuals with non-communicable chronic diseases (NCCDs), which require continuous care. Medications play an important role in this scenario, as a large percentage of elderly individuals use medications on a regular basis^{3, 4, 5}. The treatment protocol for various NCCDs involves the combination of several medications and the combined prescriptions of an elderly individual with one or more NCCDs are likely to be classified as polypharmacy, which is the concomitant use of five or more medications^{6,7}. More than 40% of individuals aged 65 years or older take five or more medications per week and 12% take ten different agents⁷. Elderly individuals take a disproportional number of

prescription medicines; approximately one third purchase medications from more than one drugstore and half receive prescriptions from more than one prescriber⁸. Adverse drug events can compromise the functional capacity of elderly individuals exposed to polypharmacy and also constitute excess cost to the healthcare system⁹. Thus, medications can contribute to preserving functional capacity, but can also compromise it. Therefore, the risk-benefit of medications prescribed to elderly individuals must be evaluated adequately.

As elderly takes more medications, the risk for error increases. Also, as the body ages, it processes medications differently. Shepler and colleagues (2006)¹⁰ describe the four processes most affected by medication use in aging bodies: medications remain in the system longer than they should because absorption rates are slower; medications are highly concentrated in discrete parts of the body because of poor circulation; the liver shrinks and there is decreased cardiac output, which affects metabolism; and, finally, decreased renal function affects how the drug is excreted. Another concern for the elderly population is adverse drug reactions. The combination of age, multiple medications, and adverse drug reactions is cause for concern.

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Poly pharmacy is on the increase. There are several explanations for this rise. Asymptomatic people are increasingly treated with preventive interventions to reduce their future risk of mortality and disease. This is seen particularly with cardiovascular disease and medicines to reduce stroke and acute myocardial infarction events. Many elderly have several comorbidities. If each one of these morbidities is treated according to national guidelines, patients may end up taking a complicated cocktail of drugs. Proportionally, the elderly use more drugs compared to other age groups. For many patients polypharmacy might be entirely appropriate. There are many conditions in which the combined use of two, three or more drugs is beneficial and can improve outcomes especially in older people with multiple comorbidities (for example, type 2 diabetes complicated by coronary heart disease and hypertension). However, it is important to consider whether each drug has been prescribed appropriately or inappropriately, both individually and in the context of all the drugs being prescribed.

Under-prescribing in older people has also gained recognition as a concern. Paradoxically in some cases, drugs that are recommended for some conditions are actually not prescribed by doctors because of fears of causing polypharmacy-related problems in the patient. There can be a reluctance to prescribe additional drugs to patients with polypharmacy due to a perceived complexity of drug regimens, fear of adverse drug reactions, and concerns about drug–drug interactions or poor adherence. There are a multitude of definitions of polypharmacy in the literature. Many papers classify taking 5 or more drugs as polypharmacy¹¹. There aren't just the side effects from the single medications or the adverse reactions of taking multiple medications, but also the stress of simply having and needing multiple medications. Polypharmacy has been shown to be a strong predictor of “hospitalization, nursing home placement, death, hypoglycemia, fractures, impaired mobility, pneumonia and malnutrition”¹². Over-the-counter availability of formerly prescribed drugs can lead to polypharmacy as individuals' self-treat¹².

The general objective of this study is to provide information on the need for the concern and strategies for the control of polypharmacy in the elderly, while the specific objectives are: 1. To define and describe the various types of polypharmacy in the elderly. 2. To quantify the magnitude of polypharmacy in the elderly. 3. To describe the risk factors and effects of polypharmacy in the elderly. 4. To create awareness about the risks of multiple drug use in the elderly. 5. To suggest/propose practical recommendations/interventions regarding control of poly pharmacy and rational drug use among the

elderly.

LITERATURE REVIEW

Pharmacokinetic and Pharmacodynamics changes in the Elderly: Altered pharmacokinetics and pharmacodynamics in older clients are major factors to consider when discussing polypharmacy. Responses to medications differ with advancing age. The action system of drugs in an aged body is summarized as follows

1. Drugs remain in the system for a long time due to low absorption rates,
2. Drugs become highly concentrated in different parts of the body due to impairment in the circulation system,
3. The metabolism changes due to the changes in liver and cardiac outputs,
4. Decreased renal functions affect drug excretion.

Describing and Defining Polypharmacy:

Polypharmacy is defined as the concomitant intake of five or more medications by patient simultaneously¹³⁻¹⁵, or the use of clinically inappropriate medications¹⁶ by the same patient. Topical and herbal medications are generally excluded of this definition as they are often not included in the traditional methods of assessing prescription quality. Vitamins and minerals taken on as-needed basis are also generally excluded in these assessments because of the inconsistent inclusion of these medications in polypharmacy. Polypharmacy, however, is more complex than just the number of drugs that a patient takes. Clinically, the criteria utilized for identifying polypharmacy involve the following:

- Taking medications that have no apparent indication
- Using therapeutic equivalents to treat the same illness
- Concurrent usage of interacting medications
- Using an inappropriate dosage
- Utilizing other medications to treat adverse drug reactions

Types of Polypharmacy: Polypharmacy can be categorized into 2 major classes¹⁷.

Therapeutic Polypharmacy: This type occurs when multiple drug regimens are carefully monitored by clinicians and are necessary for the treatment of conditions and for achieving a therapeutic goal. An example of therapeutic polypharmacy is the combination therapy of isoniazid, rifampin, ethambutol, pyrazinamide, and pyridoxine in the initial treatment of tuberculosis.¹⁸ Another example of therapeutic polypharmacy is the multiple agents used in the management of congestive heart failure, such as digoxin, angiotensin-converting enzyme inhibitors,

and a diuretic.

Contra-therapeutic Polypharmacy: This type of polypharmacy occurs when an individual experiences unanticipated or unintentional adverse effects while he or she is on a drug regimen and is not monitored¹⁸. Therapeutic polypharmacy involves medications that are necessary for achieving an effective treatment and are prescribed by clinicians after a careful monitoring. Contra-therapeutic polypharmacy, on the other hand, involves use of long-term and often high-dose multiple agents, which cannot be monitored, which lead to undesired or unexpected side effects during drug intake, and depends on personal or professional preferences¹⁹.

Why elderly patients take so many medications:

Several factors contribute to polypharmacy among patients over age 65. Compared to the general population, a patient over 65 is more likely to have several chronic disorders, each requiring at least one medication.^{20,21} Elderly patients with more than one health condition are likely to receive care from several healthcare providers, each of whom may prescribe a different medication to treat the same symptoms.⁴⁵ Another factor in the equation is what's called the prescribing cascade: An elderly patient develops side effects from a medication he's taking; however, his healthcare provider interprets the symptoms not as side effects of the drug but as symptoms of a disease. The healthcare provider then prescribes yet another drug, creating the potential for even more side effects.^{22,23}

Prevalence of Polypharmacy: Previous studies reported prevalence of polypharmacy as between 4%⁴⁹ and 34%²⁴ among people aged 65 years and above. Passarelli et al²⁵ reported an average of between 9.9 and 13.6 drugs use in inpatients while the number of medications used in outpatient treatment was lower, ranging from 1.3 to 2.3 drug/patient²⁶. A Brazilian study of 45 elderly found polypharmacy in 33.3%. In one of the few prospective studies on polypharmacy, Veehof et al²⁷ followed up 1,544 elders for three years, and identified a 42% incidence rate of polypharmacy.

Aetiology (Predictors) & Risk factors: The etiology of polypharmacy is multi-factorial. Reported risk factors involved in polypharmacy are^{28,29}

1. Patients' going to different physicians and getting many prescriptions
2. Ease of getting non-prescription drugs
3. Physicians' inclination towards prescribing many medicines,
4. Patients' expectations for many different drugs,
5. Use of various medicines due to additional diseases,

6. Herbal preparations and over-the-counter medications,
7. Use of drugs without any knowledge of their side effects and interactions,
8. Consulting various physicians and receiving various prescriptions,
9. Inadequate communication and coordination,
10. Replacing medication due to drug side effects (prescription cascade),
11. Prescribing medication based on symptoms rather than diagnosis,
12. Tendency to quit the medication and start with a new one,
13. Automatic prescription of drugs that are known to the patient and the physician,
14. Presence of too many medications in the market,
15. Forgetfulness of the doctor to ask and of the patient to tell about the medication,
16. Tendency to use medications obtained from acquaintances.

Inappropriate drug prescription: In a medication appropriate index, indication, efficacy, dose, directions, drug-drug interaction, and drug-disease interaction must definitely be considered³⁰. Polypharmacy and higher age were the main risk factors for potentially inappropriate drug use in the elderly³¹. The most commonly used tools for prescriptions for advanced ages are: the Inappropriate Prescribing in the Elderly Tool (IPET), the Beers Criteria, the Medication Appropriateness Index (MAI), the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP), and the Screening Tool to alert Doctors to the Right Treatment (START)³². Among these, the most commonly used criteria in clinics seem to be the Beers Criteria. It aims to provide guidelines to the users about inappropriate drug names and their potential side effects. It makes distinctions such as "always inappropriate" and "potentially inappropriate". Medications are also rated according to high or low number of adverse events associated with them. The STOPP and START criteria that were developed to be used in Europe are viewed as being more comprehensive^{32,33}. The STOPP criteria attempt to classify 65 potentially inappropriate drugs according to the systems and define them in terms of drug-drug, drug-disease, falls, and therapeutic duplications. STOPP criteria identified a significantly higher proportion of patients requiring hospitalization due to potentially inappropriate medication related adverse events than Beers' criteria. Inappropriate medications in elderly adults can lead to confusion, falls, cognitive impairment, poor health status, and mortality³⁴⁻³⁸.

Adverse Drug Reactions: Adverse drug reactions (ADRs) may be defined as any response that is

noxious and unintended and that occurs at doses normally used in man for diagnosis, prophylaxis or therapy, and excluding a failure to accomplish the intended purpose³⁹. ADRs in older people are a common cause of admission to a Hospital and are an important cause of morbidity and death⁴⁰⁻⁴². The incidence of ADRs in Europe was around twice that in the USA, exceeding 20%⁴³. Whether advancing age is a cause of increased risk of ADRs is debatable, but the specific physiological changes associated with aging certainly play a critical role in ADRs. ADRs can be classified into 2 main types: type A or type B⁴⁴. Type A refers to the ADRs that are expected from the pharmacological properties of a drug, such as hypotension when taking enalapril, or heart block from beta-blocker therapy. These adverse effects often occur in patient who are unusually sensitive to the known pharmacological properties of the drug. They are largely dose-dependent and uncommon in normal doses. More than 80% of ADRs causing hospital admission or occurring in hospitals are type A in nature^{45, 46}. Antibiotics, anticoagulants, digoxin, diuretics, hypoglycemic agents, antineoplastic agents and non-steroidal anti-inflammatory drugs (NSAIDs) are responsible for 60% of ADRs leading to hospital admission, and 70% of ADRs occurring in hospital^{43, 47, 48}. Most of these medications have a low therapeutic index and are more likely to be used in the elderly. Type B reactions are the unexpected responses that are not related to the drug's pharmacological effect. They are often immunologically mediated, such as anaphylactic reactions to penicillin or malignant hyperpyrexia when inhaling halothane. This type of ADRs is much less common than type A reactions, and are generally more serious in nature⁴⁸. Apart from type A and B, type C and D reactions have also been described^{45, 46}. Type C refers to the adverse effects associated with long-term therapy, such as analgesic nephropathy; whereas type D is the delayed side effects, such as carcinogenicity or teratogenesis⁴⁵

Table 1. Strategies in preventing ADRs in the elderly.

Better application of pharmacokinetic principles

Better instructions to patients

Physician education

More accurate and visible recording of adverse effect history

Enhancement of clinical and laboratory monitoring

Timely referral of patients to other community agencies after hospital discharge.

Table 2: Good practice in drug prescription in the elderly

Accurate diagnosis of underlying disease and adequate clinical assessment of patients

Treat only the disorders that need to be treated

Keep drug regimens simple

Start with low dosage and increase slowly over time (often in weeks)

Keep the number of drugs to a minimum

Always consider drug-drug and food-drug interaction

Use newly marketed drugs with caution

Provide patients with clear instructions, both verbal and in writing

Regular medication reviews of patients and their medication their medications at clinics.

Regular medication review by qualified health professionals (e. g physicians, pharmacists or registered nurses) at patients' homes or aged care facilities

METHODOLOGY

A thorough literature search was conducted using PubMed and Google Scholar to select articles from 1999 till 2014 using key words like polypharmacy, geriatric patients, elderly care, Beer's criteria, inappropriate prescribing and adverse drug events. Key phrases like antihypertensive and "oral hypoglycaemic drugs as well as elderly" were also used to search articles for specific drugs. A literature search from Africa was also done through the Index Medicus. Thousands of citations were found during the initial literature search from which 125 most relevant articles were reviewed in detail. From African regional search, only a handful of articles were available. Some older articles which were historically relevant to polypharmacy and inappropriate prescribing were included in this review. Evidence-based non-drug interventions, and other interventions to minimise inappropriate prescribing were reviewed and included as well.

The MEDLINE database and International Pharmaceutical Abstracts (2007) were searched to identify articles on polypharmacy in the elderly. A

combination of the following search terms was used: polypharmacy, multiple medications, polymedicine, elderly, geriatric, and aged. A manual search of the reference lists from identified articles and the authors' article files, book chapters, and recent reviews to identify additional articles was also conducted. Articles were included only if they were: (1) in English; (2) involved those aged >65 years; (3) not a review; or (4) observational or randomized trials that either quantified the multiple use of medicines and their consequences or described interventions to reduce or control polypharmacy.

FINDINGS & DISCUSSION

From findings in this study, it is evident that more research in this area is needed. European countries appear to conduct more research regarding polypharmacy in the older population, while the focus in the United States appears to be inappropriate prescribing. For example, out of 12 studies that were conducted in the United States, 2 addressed polypharmacy and 10 addressed inappropriate prescribing. In European studies, information regarding prescription drug use and utilization of health care is recorded in a computerized research register.

Clients may have several diagnoses and comorbidities (e.g., diabetes, hypertension), necessitating the use of multiple medications; therefore, a definition of polypharmacy dependent upon the number of medications may be inappropriate. A definition focusing on whether the medication is clinically indicated may be more appropriate. Nonprescription medications were included in some of the studies reviewed. Potential medication interactions and duplications can occur between prescription and nonprescription medications. In future studies, detailing the use of nonprescription medication is necessary when examining polypharmacy. Another consideration is that non-prescription medications are more common in European countries. Medications that are available by prescription only in the United States are available without a prescription in European countries; therefore, including nonprescription medications in polypharmacy research is important. Several gaps in the literature are noted. There is a lack of research related to the methods used when assessing polypharmacy; this indicates additional research and education are necessary to provide care for the older population. Based upon the non-empirical articles reviewed, multiple methods exist to assess polypharmacy in older individuals (e.g., utilizing the SAIL, TIDE, brown bag approach, or Beers' criteria for reviewing medications). The research articles found addressed the brown bag approach, chart review, home visits, and the utilization of computerized medication databases to assess polypharmacy. Using Beers' criteria to determine

inappropriate medication prescribing is useful. The SAIL and TIDE criteria for reviewing medications may be useful, but limited research is available reporting the efficiency of each technique. Research related to the interventions utilized to decrease the incidence of medications that are not indicated was not addressed. There is serious dearth of literature concerning polypharmacy in the elderly in Africa. Study on polypharmacy in Nigeria is still at infancy.

Regardless of the definition, the high prevalence of polypharmacy with aging may lead to an increased risk of inappropriate drug use, under-use of effective treatments, medication errors, poor adherence, drug-drug and drug-disease interactions and, most importantly, adverse drug reactions^{49, 50}. The latter are usually related to the established fact that elderly people are often frail and highly sensitive to pharmacotherapy, because of changes in pharmacokinetic and pharmacodynamic parameters^{51, 52}. Polypharmacy is an important risk factor for inappropriate medication prescribing^{50, 53}, which is very frequent among elderly people⁵⁴. Certain drugs are considered inappropriate or potentially inappropriate in older patients not only because of the higher risk of intolerance related to adverse pharmacokinetics or pharmacodynamics or drug-disease interactions but also because they are prescribed at too high dosages or for too long⁵⁵. A European study involving 900 consecutive elderly patients admitted to university teaching hospitals in six countries found that potentially inappropriate prescribing ranged from 22 to 77%, depending on the criteria used⁵⁶. However, an understated aspect of inappropriate prescribing in elderly people is also the omission of medications known to be effective in patients with an adequate life expectancy and good quality of life, because of lack of knowledge and fear of adverse drug reactions, in addition to other irrational reasons^{57, 58}.

CONTROL STRATEGIES AND CLINICAL CORRELATES

1. Pharmacists should evaluate the aspects concerning the use of adequate medications; reduction of medication doses without affecting treatment efficiency; adjustment of doses beyond the drug safety margin; and correct use of the medication by elderly patients.
2. Avoid the use of inappropriate drugs.
3. The golden rules of prescribing must always be followed and these are:
 - Think carefully before prescribing
 - Prescribe with maximum knowledge about your patient and the drugs
 - Monitor patient for efficacy and side effects

- Help patient make better use of medicine
 - Review medication to discontinue, to reduce dose or to substitute with safer drug. One must consider “maximum benefit with least risk”, since there is no drug which does not carry some degree of risk.
4. Avoid conflicting information given by many different health professionals.
 5. Practice safe prescription which is defined as the process that recommends an adequate medication for a given patient in ideal conditions, providing a balance between therapeutical activity and adverse effect. In this context, the balanced prescription considers the physiological changes of the elderly and the adverse effects of the drugs aiming at an adequate dose which should be possible with the individualization of the therapy.
 6. Obtain a thorough medication history. This is very important before any new medication is prescribed. Both prescription and nonprescription medications need to be taken into account and should be brought with the patient to all health care provider visits. Once the prescriber has a complete medication history, he or she can then decide whether the addition of another medication is clinically indicated and if the benefits outweigh the risk of use.
 7. Encourage non-pharmacologic therapy, such as diet modification or exercise. This may be appropriate instead of medication in some cases. If a medication is determined to be clinically necessary, the drug's pharmacokinetic, pharmacodynamics, and adverse-event profile, along with the patient's renal and hepatic function, must be taken into account for proper dosing.
 8. Limit the prescribing of as-needed drugs
 9. Setting sensible therapeutic goals and assessing medication regimens periodically are also very important to ensure that polypharmacy is under control and does not lead to unnecessary medical problems.
 10. Simplify the patient's regimen as much as possible by, for example, prescribing a single agent rather than multiple drugs to treat a condition or choosing a drug that can be given once or twice, rather than three times a day. Always write the purpose of the drug on the order.
 11. Review the patient's medical record and eliminate duplicate medications—those prescribed by different healthcare providers for the same problem—and drugs with no therapeutic benefit or clinical indication. Substitute safer medications whenever possible.
 12. Avoid treating an adverse reaction caused by one drug with a second drug; if possible, discontinue the drug that's causing the problem or reduce the dosage. Starting doses are often lower in the elderly and may be administered differently than in younger patients to prevent toxicity from occurring. Other concomitant disease states and medications should be evaluated to prevent any drug-disease or drug-drug interactions from occurring.
 13. Educate both patients and their families verbally and in writing about their medications. This helps to improve adherence. Considering generic options, utilizing compliance aids (eg, pillboxes, medication calendars).
 14. Trainings should be provided for patients, their families and healthcare professionals on drug management for older adult
 15. Appropriate follow-ups should be carried out.

All these strategies allow the elderly to live a mentally and physically healthy and harmonic life, resulting in the reduction in medication use especially anti-depressive agents and sedatives.

CONCLUSION & RECOMMENDATIONS

Pharmacotherapy mishaps among elderly patients are a major healthcare issue and a problem for all healthcare practitioners treating elderly patients. Physicians, nurses, pharmacists, nurse practitioners, physicians' assistants, and patients' families and caregivers are responsible for improving the care provided to elderly patients. The health personnel need to receive training with regard to their responsibilities towards the older persons. More effort is needed to decrease the use of drugs without control/ prescription among older persons. Polypharmacy is common among the elderly. Many studies have found that various numbers of medications are associated with negative health outcomes, but more research is needed to further delineate the consequences associated with unnecessary drug use. Health care professionals should be aware of the risks and fully evaluate all medications at each patient visit to prevent polypharmacy from occurring.

Network systems specific to the elderly should be encouraged. This makes easier to trace medication lists. Provision of product information (e.g., drug interactions) in hard-copies by companies, on-line access to patient information, alerts through special

programs when inappropriate drugs are prescribed. Use of non-pharmacological treatment methods should be encouraged. A different dose and treatment calendar should be planned than those for younger age groups.

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