

POLYPHARMACY: TO ERR IS HUMAN, TO CORRECT DIVINE

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ABSTRACT

Objectives

Optimizing drug therapy for elderly is often challenging. Sometimes treatment causes more harm than the disease. The aim of this article is to review the body of literature addressing polypharmacy to determine its definition, explore how polypharmacy was assessed in primary care, and seek evidence based interventions that address polypharmacy.

Data Sources

An electronic search of the PUBMED database utilizing the search terms “polypharmacy,” “polypharmacy and elderly,” “adverse drug reactions,” “multiple medications”, “inappropriate prescribing”, and “Beers criteria” was performed and the search was supplemented with online site searches of relevant journals and review of reference lists of each article.

Results and discussion

Prescription of potentially inappropriate medications to older people is highly prevalent in the United States and Europe. Polypharmacy continues to be a significant issue. There is a gap in the literature regarding the interventions implemented by physicians to address polypharmacy. There are no robust prospective studies that test the clinical benefit to patients of using drug utilization review tools.

Conclusion

There is no specific definition for polypharmacy. It has been defined in many different ways depending upon patient population and study settings. Prospective randomized controlled trials are needed to identify useful interventions. Drug utilization review tools should be designed on the basis of a country's national drug formulary and should be evidence based as most existing drug utilization review tools have been designed on the basis of North American system.

INTRODUCTION:

Population demographics are changing worldwide, with life expectancy and the proportions of older persons increasing. Older people are the greatest consumers of medications and healthcare resources in developed countries. It is assumed that as more drugs become available and life expectancy continues to increase, the consumption of prescription drugs by older people will increase further and the incidence of potentially inappropriate prescribing will grow. A survey of non-institutionalized older adults in the United States showed an increased usage of all medications with advancing age, the highest prevalence of drug use being in women 65 years of age and older with 12% taking 10 or more medications and 23% taking at least five prescribed drug therapies¹. In most industrialized nations older people consume three times as many prescription medications as younger people and purchase 70% of non-prescription medications². In the United States, 12.5% of the population is over 65 years of age but consume 32% of all prescription medications and account for 25% of drug expenditure and 30% of total national healthcare expenditure³⁻⁵. In Ireland, 11-13% of population is over the age of 65 years but consume 47% of all prescription medications⁶. In Europe, people over 65 years of age consume

on average 2-3 times the amount of health care than do those <65 years of age⁷.

POLYPHARMACY:

Polypharmacy has been defined in many different ways and the appropriate definition may differ according to patient population and study setting⁹. Fulton and Allen¹⁰ define polypharmacy as: 'the use of medications that are not clinically indicated'. In practice, polypharmacy is defined as using more than a certain number of drugs, irrespective of the appropriateness of drug use^{8, 11, 12}. Inappropriate prescribing includes the use of medicines that introduce a significant risk of an adverse drug-related event where there is evidence for an equally or more effective but lower-risk alternative therapy available for treating the same condition. Inappropriate prescribing also includes the use of medicines at a higher frequency and for longer than clinically indicated, use of multiple medicines that have recognized drug-drug interactions and drug-disease interactions, and importantly, the under-use of beneficial medicines that are clinically indicated but not prescribed for some reasons. As older patients seek treatment for various ailments from a variety of physicians, they are at increasing risk of accumulating layers of drug therapy. Individuals aged 65 and older use a disproportionate number of

prescriptions and over-the-counter medications; 31% use more than one pharmacy and 50% receive prescriptions from more than one prescriber¹³. A higher number of primary care physicians and multiple dispensing pharmacies increase the risk of drug–drug interactions¹⁴. The number of medications prescribed to elderly patients, and the complexity of their drug regimens increase over time¹⁵.

The potential for an increased risk of drug–drug interactions and adverse drug reactions, and factors such as age-related changes in pharmacodynamics (PD) and pharmacokinetics (PK) must be considered. Diabetes and chronic lung disease predict a greater complexity and cost of drugs regimen in elderly patients with heart failure¹⁶. Besides the increase in diseases and worsening of diseases, the literature also mentions other factors as being responsible for the increase in polypharmacy, i.e. ageing, moving to a residential or nursing home and hospitalization^{17, 18}. The patient's expectations, the General Practitioner's attitude and consultations with several doctors have been associated with an increase in multiple drug use^{19, 20}.

EFFECTS OF AGING ON DRUG METABOLISM:

Drug absorption, distribution, metabolism and elimination change as a natural consequence of the ageing process. Changes in drug absorption in older patients may result from decreases in splanchnic blood flow and gastric motility, and increases in gastric pH, and other physiological changes that are associated with ageing. Blood flow and gastric motility may be further diminished by cardiovascular and gastrointestinal drugs used to treat co-morbid conditions. Ageing influences drug excretion. Age-related decreases in glomerular filtration rate are well known. These physiological declines coupled with co-morbid conditions and the use of multiple drugs means that medications eliminated by the renal route requires dose adjustment. Drugs that influence renal function and thus elimination/excretion have the potential to pose serious clinical problems if used concomitantly. With ageing, there is a decrease in lean body mass and total body water with a relative increase in total body fat²¹. These changes lead to a decreased volume of distribution for hydrophilic drugs such as lithium, and digoxin where unadjusted dosing can result in higher plasma concentrations, thus increasing the potential for adverse effects. Conversely, lipid soluble drugs such as long-acting benzodiazepines have an increased volume of distribution, thereby delaying their maximal effects and resulting in accumulation with continued use. There is a reduction in hepatic mass and blood flow with ageing²².

Drugs such as beta-blockers, nitrates and tricyclic anti-depressants that have a first pass effect in the liver may have a higher bioavailability in older people and thus be effective at lower doses. Cytochrome P450 oxidation declines with ageing²⁴ and drug–drug interactions involving these enzymes are important to recognize. Larger drug storage reservoirs and decreased clearance prolong drug half-lives and lead to increased plasma drug concentrations in older people. If serum albumin is decreased there will be an increase in the active unbound drug concentration for highly protein-bound drugs such as phenytoin, theophylline, warfarin and digoxin. Ageing is also

associated with changes in the end-organ responsiveness to drugs at receptor or post-receptor level²⁵. There is decreased sensitivity to beta-receptors along with a possible decreased clinical response to beta-blockers and beta-agonists²⁶. Increased sensitivity to drugs such as opiates and warfarin is common^{27, 28}.

ADVERSE DRUG REACTIONS (ADRs):

The number of elderly is increasing dramatically. In United States, in the next 25 years, as the baby boomer generation begins to turn 65 years old, the number of elderly is expected to double to approximately 70 million. Those older than 85, is now the fastest growing segment of our population. Thus, we can expect the number of adverse drug reactions to increase proportionately. Polypathology, the age-related increase of concurrent diseases, is likely to be the main determinant of drug consumption. However, both over-prescribing and improper prescribing has been reported and seems to contribute to the age-related increase in the prevalence of adverse drug reactions (ADRs)^{29, 30}. A hospital-based study from Norway showed that the risk of experiencing a drug-related problem increased linearly with the number of drugs on admission³¹. A study carried out in the USA found that nursing home patients receiving nine or more drugs were more than twice as likely as patients receiving a lower number of drugs, of experiencing an adverse effect³². On average, ADRs account for 3%–13% of all the admissions³³⁻³⁵ and complicate 5%–20% of the stays of patients over 65 years³⁶⁻³⁸. More than 40% of persons aged 65 and older use five or more different medications per week, and 12% use 10 or more different medications³⁹. If an elderly patient takes five or more drugs, he or she has a 35% chance of experiencing an adverse drug event⁴⁰.

Drug interactions are significant contributors to morbidity³⁵. Office visits for an adverse drug event increase from 9% of the population per year at age 25–44 years to as high as 56.8% between age 65 and 74 years⁴¹. Inappropriate drug use is one of the risk factors for adverse drug reactions in the elderly. The risk for an adverse drug event is 13% with the use of two medications, but the risk increases to 58% for five medications⁴². If seven or more medications are used, the incidence of adverse drug events increases to 82%⁴².

INTERVENTIONS:

Older people are a heterogenous group, often with multiple concomitant illnesses and multiple prescriptions. There is a thin line between a healthy old person and an ill old person. Prescribing for older people is challenging as any new medication must be considered in the context of altered pharmacokinetics, altered pharmacodynamics and age-related changes in body composition and physiology. Both over prescription and undue prescription seem to characterize the overall pharmacological therapy of the elderly.

Polypharmacy is the main risk factors for ADRs⁴³. Thus, attempts should be made to curtail inappropriate drug prescription by utilizing different available tools⁴⁴. An interdisciplinary medication review of older individuals in the community helps to reduce the cost and number of medications. Polypathology seems the most obvious

explanation of the high number of drugs taken by older people, but additional factors deserve consideration. Changes in patient's medical status over time can cause medications that have been used chronically to become unsafe or ineffective. Particular care must be taken in determining drug dosages and treatment options when prescribing for older adults. "Pill for an ill" approach should be discouraged as many a time pharmacological treatment may carry more adverse effects than the illness itself. Use of electronic medical records and other hand held devices to prescribe appropriate medication doses and check drug to drug interactions has been found useful in reducing the medication related errors and hence adopted by various medical groups and hospital practices.

Reviewing medications at every visit is a simple and very helpful tool too especially if patients are encouraged to bring with them a printed list of their current medications (including over the counter drugs). Printing an updated list of the medication changes in bold and large font after a visit with their physician helps patients to follow the recommendations especially in case of geriatric patients who may not remember all the new changes made at an office visit.

CONCLUSIONS:

Polypharmacy is an important issue in the elderly. The problem involves many issues, a number of which have been explored in this article. One of the most important issues involves adverse drug reactions. All pharmaceutical agents have the potential for side effects; therefore, it is obvious that the more drugs one takes the more side effects one will experience. The aging process results in altered metabolism and excretion of medications, and deficits in cognition and senses. Incidence of adverse drug reaction and interactions is increased with polypharmacy. Since adverse drug reactions are a significant cause of morbidity and mortality, as well as an important cause for hospital admissions, minimizing polypharmacy is an important consideration. The general principle of "Start Low and Go Slow" holds true in most scenarios but should be modified to "Start Low, Go Slow but Use Enough" to achieve desired therapeutic effect.

COMPETEING INTERESTS:

Serves as a speaker for Eisai Inc. and Pfizer Inc. for the 2008 ARICEPT LTC DELTA 2 (Dementia Education Leadership Training in Alzheimer's) Promotional Education Program

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