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Therapeutic potential uses of drugs in older adults – A review

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Abstract
Major usage of medicine along with disease burden is much higher in older individuals, in general, compared with younger adults; yet premarketing drug clinical trials have often excluded them even for the drugs that have high utility in this age group. The older population is currently the fastest growing age group in the United States, and this trend is expected to continue for several decades. Herein, we discuss the information gap for older individuals and the need for a better understanding of the effect of aging on drug responses. We also present cases for future directions, urging the implementation of improved clinical trial designs using new and emerging pharmacokinetic and pharmacodynamic methods to allow the provision of evidence-based individualized treatment to this high drug use group.

Keywords: Therapeutic, Drugs.

Introduction
Medications need to be used with special caution because of age-related changes in pharmacokinetics (ie, absorption, distribution, metabolism, and excretion) and pharmacodynamics (the physiologic effects of the drug). The process of prescribing a medication to older adults is complex and includes: deciding that a drug is indicated, determining a dose and schedule appropriate for the patient's physiologic status, monitoring for effectiveness and toxicity, educating the patient about expected side effects [1].
An increased volume of distribution may result from the proportional increase in body fat relative to skeletal muscle with aging [2]. Decreased drug clearance may result from the natural decline in renal function with age, even in the absence of renal disease. The same dose of either medication would lead to higher plasma concentrations in an older, compared to younger, patient. As examples, the volume of distribution for diazepam is increased, and the clearance rate for lithium is reduced, in older adults. Also, from the pharmacodynamic perspective, increasing age may result in an increased sensitivity to the effects of certain drugs, including benzodiazepines [3-6] and opioids [7].

Medication Use by Older Adults
A survey in the United States of a representative sampling of 3005 community dwelling adults (aged 57 through 85 years) was conducted by in-home interviews and use of medication logs between 2005 and 2006 [8]. Medications are widely used by older adults.

Herbal and dietary supplements — Use of herbal or dietary supplements (eg, ginseng, ginkgo biloba extract, and glucosamine) by older adults has been increasing, from 14 percent in older women in 1998 [9] to 26 to 27 percent in 2002 [10, 11] and 59 percent in 2014. Often, clinicians do not question patients about use of herbal medicines and patients do not routinely volunteer this information [12, 13].
Herbal medicines may interact with prescribed drug therapies and lead to adverse events, Examples of herbal-drug therapy interactions include ginkgo biloba extract taken with warfarin, causing an increased risk of bleeding, and St. John's wort taken with serotonin-reuptake inhibitors, increasing the risk of serotonin syndrome in older adults [14]. A study of the use of 22 supplements in a survey of 369 patients aged 60 to 99 years found potential interactions between supplements and medications for 10 of the 22 supplements surveyed [15, 16].

Quality Measures of Drug

A 2013 systematic review of eight studies of different prescribing interventions in long-term care homes (medication review, case conferences, staff education, clinical decision support technology, and/or some combination of these) showed no effect of the interventions on hospital admissions, adverse drug events (ADEs), and mortality [17-19]

Polypharmacy

Polypharmacy is defined simply as the use of multiple medications by a patient. While polypharmacy most commonly refers to prescribed medications, it is important to also consider the number of over-the-counter and herbal/supplements used [20].

It is seen that 20 percent of Medicare beneficiaries have five or more chronic conditions and 50 percent receive five or more medications [21]. The issue of polypharmacy is of particular concern in older people who, compared to younger individuals, tend to have more disease conditions for which therapies are prescribed.

The use of greater numbers of drug therapies has been independently associated with an increased risk for an adverse drug event, irrespective of age [22].

There are multiple reasons why older adults are especially impacted by polypharmacy:

- Polypharmacy was an independent risk factor for hip fractures in older adults in one case-control study, although the number of drugs may have been an indicator of higher likelihood of exposure to specific types of drugs associated with falls (eg, CNS active drugs) [23, 24].
- Polypharmacy increases the possibility of "prescribing cascades". A prescribing cascade develops when an adverse drug event is misinterpreted as a new medical condition and additional drug therapy is then prescribed to treat this medical condition.
- Use of multiple medications can lead to problems with medication adherence, compounded by visual or cognitive compromise in many older adults [25, 27].

It is particularly important to reconsider medication appropriateness late in life. A model for appropriate prescribing for patients late in life has been proposed [28].

Anticholinergic activity

Anticholinergics can precipitate an acute glaucoma episode in patients with narrow angle glaucoma and acute urinary retention in patients with benign prostatic hypertrophy. In a population study of 6912 men and women 65 years and older, those taking anticholinergic drugs were at increased risk for cognitive decline and dementia and risk decreased with medication discontinuation. In addition, anticholinergic medication use was associated with increased mortality over a two year period after adjustment for multiple factors, including co morbid health conditions. Nonetheless, an analysis of US medication expenditures between 2005 and 2009 found that 23.3 percent of community-dwelling persons >65 years with dementia were prescribed medications with clinically-significant anticholinergic activity [29].

Summary and Recommendations

- The possibility of an adverse drug event (ADE) should always be borne in mind when evaluating an older adult; any new symptom should be considered drug-related until proven otherwise. Pharmacokinetic changes lead to increased plasma drug concentrations and pharmacodynamic changes lead to increased drug sensitivity in older adults.
- A step-wise approach to prescribing for older adults should include: periodic review of current drug therapy; discontinuing unnecessary medications; considering non-pharmacologic alternative strategies; considering safer alternative medications; using the lowest possible effective dose; including all necessary beneficial medications.

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