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Aprahamian, I.; Morley, John E.

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EDITORIAL

TO DRUG OR NOT TO DRUG: THE GERIATRICIAN DILEMMA OF POLYPHARMACY

I. APRAHAMIAN[1,2], J.E. MORLEY[3]

1. Group of Investigation on Multimorbidity and Mental Health in Aging (GIMMA), Geriatrics division, Jundiai Medical School, Jundiai, Brazil; 2. University of Groningen, University Medical Center Groningen, Department of Psychiatry, Groningen, The Netherlands; 3Division of Geriatric Medicine, Saint Louis University School of Medicine, St. Louis, Missouri, USA. Corresponding author: John E. Morley, MB, BCh, Division of Geriatric Medicine, Saint Louis University, SLUCare Academic Pavilion, Section 2500, 1008 S. Spring Ave., 2nd Floor, St. Louis, MO 63110, Email: john.morley@health.slu.edu, Twitter: @drjohnmorley

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"The first duties of the physician is to educate the masses not to take medicine." "imperative drugging – the ordering of medicine in any and every malady is no longer regarded as the chief function of the doctor."
~William Osler

Older adults often present with multimorbidity. More than half of those over the age of 65 have multiple chronic diseases, and this percentage goes up to 80% in persons aged 80 and more (1, 2). In Western medicine, most treatment strategies for chronic diseases rely on drugs. Reasons for treatment, beyond those related to specific consequences of single diseases, include several adverse outcomes of multimorbidity such as functional impairment, poor quality of life, and high health care utilization and its costs (2-4). Randomized controlled trials aimed to test the effectiveness of non-pharmacological approaches, multidimensional interventions or a patient-centered intervention are lacking, resulting in pharmacological treatment with multiple drugs being the most common strategy to treat older adults with multimorbidity (5-7). A recent nationally representative sample of 2206 community-dwelling older adults aged 62 through 85 years was conducted in the United States regarding the use of medication between 2005 and 2006, and again in 2010-2011 (8). Five or more prescribed drugs were used by 36% of participants. Moreover, in another report of Medicare beneficiaries admitted to a nursing facility after hospital discharge, an average of 14 medications were used by patients (9). At least 30% of these drugs showed side effects hazardous to 5 geriatric syndromes evaluated in this study. Polypharmacy refers to multiple medication use and is most commonly defined quantitatively as the chronic use of 5 or more prescribed drugs (10). Polypharmacy increases the adverse reactions burden associated with multimorbidity independently resulting in negative outcomes, such as frailty, falls, cognitive impairment, functional disability, weight loss, hospitalization and mortality (11-19).

The association between multimorbidity and polypharmacy among older adults appears to be unbalanced and often fails to take into account the physiological changes of aging that modulate the efficacy of medications (Figure 1). For example, 20% of Medicare patients in the USA present 5 or more chronic illnesses while 50% use 5 or more medications (20). The greater the use of prescribed and unprescribed (over-the-counter and herbal drugs), the greater the risk of an adverse drug event. This is particularly relevant for older individuals who intrinsically present pharmacokinetic and pharmacodynamic alterations of aging such as an increased body fat compartment relative to skeletal muscle composition, decreased drug clearance and hepatic metabolization, and increased plasma concentration. Notwithstanding, polypharmacy increases the risk of inappropriate prescribing, iatrogenic "prescribing cascades", drug-drug and drug-disease interactions, and exacerbation of adverse effects of individual medications such as antidepressants and antipsychotics (21). This later group of drugs deserves special attention due to their anticholinergic activity resulting in many adverse events such as blurred vision, newer or worsening cognitive impairment, confusion, hallucinations, pneumonia, dry mouth, constipation, urinary retention, tachycardia, and increased mortality (22). Most importantly, anticholinergic burden independently increases the risk of dementia and Alzheimer's disease (23). Three geriatric syndromes are also associated with polypharmacy, namely falls, frailty, and delirium. However, more longitudinal studies are needed. Polypharmacy was associated with increased risk for falls in adults aged 50 years and more with a 2-year follow-up (24). This risk was independent from the individual medication increased falling risks. A possible association between medication harm, polypharmacy and frailty has been suggested (25, 26). Polypharmacy presented high prevalence in most cross-sectional and longitudinal studies, and it was associated with incident frailty (27-31). The association between frailty and polypharmacy is not related to the number of medications involved (27) and presents more negative outcomes among those cognitively impaired or defined as cognitively frail (30, 32). Persons with polypharmacy are at a high risk of developing delirium and reducing drug burden, especially anticholinergic drugs, reduce delirium (33).

Overall, several adverse effects and consequent geriatric syndromes derived from polypharmacy may be related or interconnected. For example, a selective serotonin receptor

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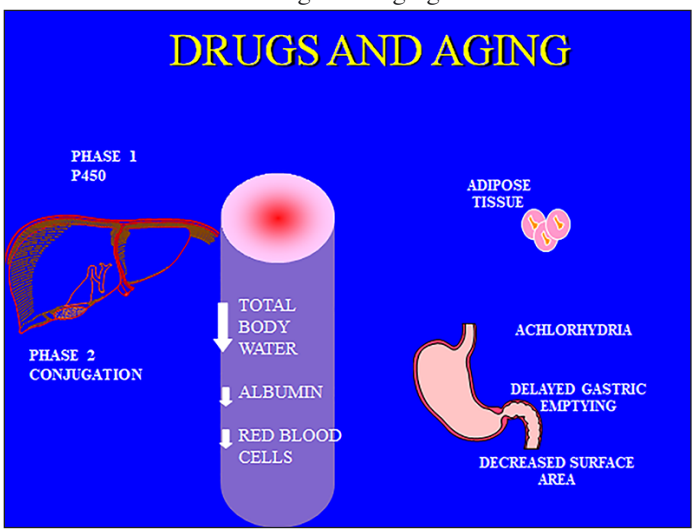
inhibitor could lead to a higher anticholinergic burden, hyponatremia, orthostatic hypotension and falls. Hospital admission, excessive prescribed rest and opioids could increase anticholinergic load, sarcopenia, cognitive impairment and delirium. The ultimate consequence would be frailty. It is common to identify an important iatrogenic component in the polypharmacy cycle of events in clinical practice (26). Several key steps might mitigate the negative effects of polypharmacy (34) (Table 1). First a regular medication review is mandatory to evaluate superfluous drugs, medication effectiveness, under-prescription, balancing risks and benefits of prescribed items, and establishing goals of individual drugs. It is mandatory to always reevaluate a patient's expectations regarding life expectancy, quality of life and disease course. The classical "start low and go slow" is a modern dogma when targeting polypharmacy. Most adverse events from medications are dose-related (35). Deprescribing medications is fundamental. In a large study with Medicare patients with a bone fracture, three quarter had been prescribed a high-risk medication for fracture a few months before falling, and only 7% of patients had that drug withdrawn (36). Most physicians are reluctant in withdrawing drugs. Several guidelines and instruments help in prescription decisions regarding over-prescription and inappropriate drug use in hospitalized, nursing home or outpatient setting. The most common criteria used are the 2019 updated Beers, the Screening Tool of Older Person's Prescriptions (STOPP), the STOPP/START (Screening Tool to Alert doctors to the Right Treatment), the FORTA (Fit FOR The Aged) list, and the Drug Burden Index (37-41). Any of these instruments are useful to help deprescribing decisions or drug substitutions especially in polypharmacy and when a high-risk of drug-interaction is suspected. It is recommended to stay alert and consider an adverse drug effect when a new symptom is referred to avoid an iatrogenic cycle. In modern times anytime a new drug is prescribed, the computer should check for drug-drug interactions and drugs that are not suitable for use by older persons. In more complex clinical scenarios, a pharmacist evaluation of prescribed items and non-pharmacologic treatments may present an important role. Finally, it is of utmost importance to reassure the patient's capacity to acquire and properly use a medication list, including their cognitive ability and social network (42). To deal with polypharmacy is the essence of being a geriatrician, and medication harm could be considered a geriatric syndrome that must be prevented (43). It is imperative to systematically address the dilemma of drug prescription among older adults.

To conclude, in a classical overstatement, Oliver Wendell Holmes said, "I firmly believe that if the whole material medica, as now used, could be sunk to the bottom of the sea, it would be all the better for mankind – and all the worse for the fishes." It must be recognized that most new drugs have not been tested in older persons and often produce a minimal improvement over older drugs at a large increase in price. The need to use these drugs needs to be carefully discerned by the physician and their use in a frail person with a limited lifespan be used only when there is a clear advantage.

Table 1
Proposed Strategies to Manage Polypharmacy

1.	Identify the target problem being treated by the drug
2.	Is the drug necessary?
3.	Does the drug interact with other drugs the patient is receiving causing side effects?
4.	Is the drug at the lowest necessary dose?
5.	Would discontinuing therapy with a medicine help reduce symptoms?
6.	Is the drug contraindicated in an older person?
7.	Does the drug have side effects that are more likely to occur in older persons?
8.	Is the drug the most cost-effective choice?
9.	Are nonpharmacologic therapies available?
10.	Is the patient noncompliant?

Figured 1
Drugs and Aging



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