Decoding polypharmacy: Traversing through the healthcare advancements

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Abstract

Senescence is a natural phenomenon of all living organisms in which the body functions of the man start declining over age. It has a huge impact on the Pharmacokinetics and Pharmacodynamics of the drug. Diet and exercise can alter the pace of ageing. A balanced diet is essential for performing the body's functions effectively. Antioxidants can slow down the process of ageing. The drug response gets altered as age advances, which in turn leads to a lack of efficacy of the drug as well as toxicity. The human being's liver, kidney and gastrointestinal tract are affected severely by the changes at the cellular level over age. This would urge healthcare professionals to adjust doses to certain drugs metabolized by the liver enzymes and eliminated by the kidneys. This review focuses on the types of polypharmacy and the ways by which we can detect polypharmacy. It also emphasizes the interrelationships of the human microbiome, genome and polypharmacy. Recent healthcare advancements have helped us develop strategies to combat polypharmacy.

Keywords: Polypharmacy, Tools, Deprescribing, Healthcare advancements

1. Introduction

Polypharmacy is a major public health concern which affects the quality of life of the elderly population. People above 65 years of age get prescribed more than or equal to five medications per prescription (1). Elderly people with co-morbidities are more prone to develop adverse events due to the use of multiple medications for multiple conditions at a time. Multiple prescriptions for the same health condition also cause polypharmacy. It increases the economic burden on the patient. According to Waren, older adults must be independent enough to overcome the disability (2). The elderly population has complex health conditions such as lack of sleep at night and loss of control during urination and defecation. As per the study on the influence of genetic factors in causing adverse events in Geriatrics, we could classify elderly people into favourable, intermediate and high-risk profiles for adverse drug events (3).

Cognitive dysfunction, depression, and malnutrition are commonly seen among older adults. The drug's absorption, distribution, metabolism, and excretion vary with age. The drug's response also varies based on the number of receptors and their affinity towards the drug at the site of action. Hence, detecting and implementing strategies to eradicate polypharmacy among older people is very important.

1.1. Variants of polypharmacy

- **Therapeutic polypharmacy**: Where there is the prescription of more than five medications, which is accepted due to unavoidable circumstances in which the benefits outweigh the risks (3).

- **Potentially appropriate polypharmacy**: The doctor prescribes drugs to optimize the patient's drug use based on the best practices available in medicine.
- **Problematic polypharmacy:** The physician prescribes numerous medications with no use to the patient, which is irrational (4).
- **Pseudopolypharmacy:** Record the increased number of medications in use rather than the actual number in use (5).

2. Screening tools to detect polypharmacy

Table 1: Tools to detect polypharmacy

Tools	Description	Ref
Beers criteria	Assessment of the appropriateness of the medications prescribed.	(6)
Screening Tool of Older People's Prescriptions (STOPP)	Identification of adverse drug events in older adults that result in hospitalizations	(7)
Screening Tool to Alert to Right Treatment(START)	Detection of the potential prescribing omissions.	(8)
Medication Appropriateness Index (MAI)	A ten-item scale is used to check the appropriateness of the medications prescribed.	(9)
Fit For The Aged (FORTA)	The medications used for treatment are categorized based on the safety, efficacy and appropriateness of age with the use of available evidence. **Category A (Absolutely):** Indispensable drug with definite outcomes. **Category B (Beneficial):** Efficacious but limited information regarding its safety. **Category C (Careful)**: Efficacy and safety profiles are compromised for older adults. It can be avoided if there are too many drugs. **Category D (Don't):** Strictly avoid these drugs in elderly people and find suitable alternatives for the same.	(10)
NO TEARS	This tool consists of seven parts to make sure that the most appropriate medication is prescribed for the patient. • Need an indication • Open end questions • Tests and monitoring • Evidence and guidelines • Adverse events • Risk reduction or prevention • Simplification and switches	(11)
Hyperpharmacotherapy Assessment Tool (HAT)	Efficient to use in patients with increased length of hospitalizations and assess medication adherence. It helps in optimizing the drug regimen, thereby promoting the use of the most appropriate therapeutic drug regimen after medication review.	(12)

3. Deprescribing in polypharmacy

Judicious use of medications such as Anticholinergic medications, Narcotics, Sedatives or Anxiolytics is recommended in the elderly population as it could exacerbate the existing medical conditions. “Deprescribing is the best method to prevent polypharmacy, a systematic process of identifying and discontinuing medications based on an assessment that the risks of a medication may outweigh the benefits” (3). Tapering the dose of medication is also a part of deprescribing. It helps reduce the length of hospitalization and the costs incurred during treatment. The steps involved in the process of deprescribing are detailed in Figure 01.

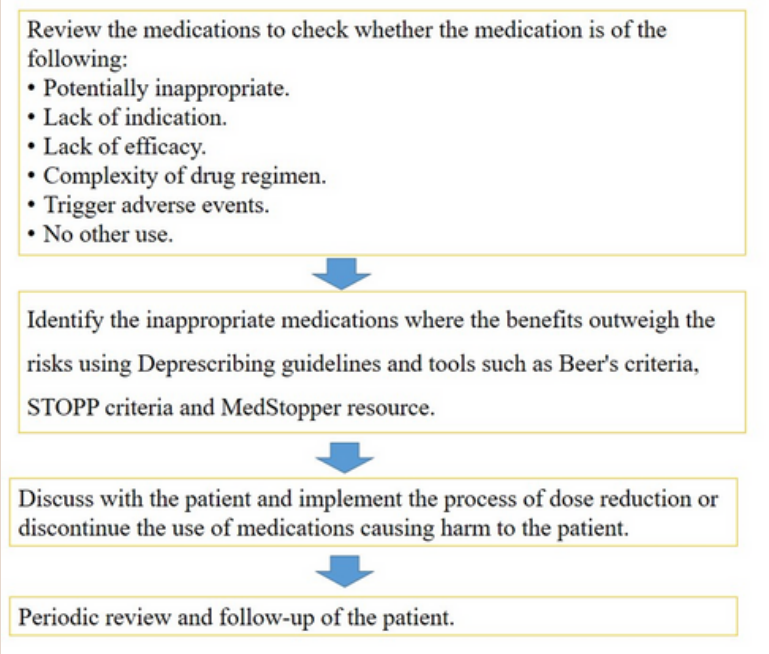

Figure 1. The Deprescribing process

4. Healthcare advancements and polypharmacy

4.1. Pharmacogenetics

The variations of the gene and the genome would lead to the development of altered drug responses. It was observed that the genetic polymorphism of Cytochrome P450 oxidase enzymes alter the drug response, leading to adverse events. Also, the variations of the drug transporters can cause adverse events. This, in turn, leads to multiple medication use. Most of the research studies identified Single Nucleotide Polymorphism (SNP) among the mutants of genes. Based on the genetic mutations, the diplotypes are categorized as follows:

- Poor metabolizers: Decreased enzymatic activity or complete activity loss was observed. Cautious selection of the dose is required as there is a chance of a sudden spike in the plasma concentration of the drug.
- Extensive metabolizers: They possess functional, active, and partially active mutant genes and promote drug metabolism.
- Intermediate metabolizers: Heterozygous carriers of the mutant genes and require a sub-therapeutic dose to achieve the drug's efficacy.
- Ultra-rapid metabolizers: The gene expression is high, and multiple functional alleles with plenty of duplications exist. A higher dose of the drug is required to achieve the therapeutic effect.

Pharmacogenetic testing helps identify the patient's metabolizer status and develop a tailored and more individualized drug regimen. It also helps prevent adverse events and thereby mitigate polypharmacy (13).

4.2. Pharmacomicrobiomics

It is the study of the effect of medications on the microbiome and its interindividual variations throughout the population. The gut microbiome, a second genome, has the potential to alter the drug's

absorption, distribution, metabolism, and excretion patterns. Similarly, drugs can cause changes in the composition and function of the microbiome (14). These changes can be attributed to factors such as variations within the individual and those that have been seen among the individuals.

One of the significant side effects of the chemotherapeutic regimen is diarrhea. It is due to the microbiome alteration caused by the chemotherapy for which probiotics are recommended. But, it threatens immune-compromised individuals due to the possibility of getting superinfections (15). Changes in the structure of the microbiome can affect the cardiovascular system, causing hypertension, atherosclerosis and cardiomyopathy. Stress plays a vital role in altering the microbiome and the drug response. It leads to multiple prescriptions for multiple health conditions. Lack of efficacy of the drugs can be attributed to the varied drug response of the patients.

4.3. Artificial intelligence and digital health

Use of machine learning and deep learning methods can be employed to develop effective tools to monitor the number of medications used for the treatment of patients. Electronic Health Record Systems can be adopted in the health care system to avoid duplication of drugs during treatment. It has been shown that the development of smart reminders and monitoring programmes helps enhance medication adherence in the patient (3).

4.4.Translational research

Age and infirmity are closely related. One of the research studies observed the effect of Frailty Inferred Geriatric Health Timeline (FRIGHT) and Analysis of Frailty and Death (AFRAID) clocks in the preclinical mouse models. The treatment groups of mice had monotherapy and polypharmacy. The effects were observed with deprescribing. Frailty index and mortality were interrelated, and there were no changes to the AFRAID clock. These clocks help predict the age and lifespan of the mice with the impact of polypharmacy and anticholinergic medications (16). It gives insight to conducting further studies on human beings so that real-time findings can be collected.

5. Conclusion

The advancement of science and technology can be applied to the healthcare system to strengthen the elderly population for good health and longevity with the utmost care and empathy. Patient or caregiver education is crucial in enhancing the quality of life. Moral support is the best therapy for aged people. Educational programmes can be conducted for the healthcare fraternity to highlight the importance of avoiding polypharmacy in older adults.

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