

To what extent does polypharmacy affect renal and cardiovascular homeostasis in elderly individuals

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Abstract

Polypharmacy refers to the concurrent use of five or more medications, a practice that is becoming common among elderly individuals due to multiple chronic conditions. While polypharmacy may improve clinical outcomes in some cases, it is also associated with increased hospitalisation, healthcare costs, and physiological and probably even psychological complications. This paper examines how polypharmacy affects homeostasis, with a specific focus on renal and cardiovascular systems in elderly patients. Age-related decline in organ function reduces the body's ability to maintain internal stability when exposed to multiple medications. Both acute and chronic homeostatic responses may be impaired, leading to disturbances in fluid balance, blood pressure regulation, and even waste excretion. Understanding the impact of polypharmacy on renal and cardiovascular homeostasis is essential for improving patient safety and optimising treatment strategies. This review highlights the importance of careful medication management to minimise adverse effects while maintaining therapeutic benefit.

1. Introduction

1.1 Polypharmacy

Medicines used to treat patients and extend their lives are referred to as polypharmacy. Polypharmacy, according to the common people, is termed as an “overdose” of medications. Still, clinically, it’s just 5 or more therapeutic medicines put together to revive, treat or extend an elderly patient's life. However, the effect of polypharmacy is a huge, debatable argument; some say that polypharmacy can lead to better outcomes in elderly patients¹, whilst some say that it is associated with increased hospitalisations and higher cost of care for individuals². Increased hospitalisations mean a greater illness.

1.2 Homeostasis

Due to polypharmacy, the body’s natural process of maintaining a stable, balanced internal environment, that is homeostasis, is affected. The greater the number of medicines, the more the body gets confused, thereby influencing the process of homeostasis.

¹ <https://pmc.ncbi.nlm.nih.gov/articles/PMC4295469/>

² <https://www.sciencedirect.com/science/article/abs/pii/S0025619620306169>

1.3 Acute and Chronic Homeostatic Responses

There are two different types of responses linked to homeostasis. One is an acute homeostatic response, and the other is a chronic homeostatic response. In the context of an acute homeostatic response, a rapid and temporary physiological adjustment is made by the body to counteract sudden stressors caused by the external environment. For instance, a response to body heat during exercise would cause sweat glands to activate and skin blood vessels to dilate (vasodilate) to facilitate heat loss through evaporation and radiation. Whereas a chronic homeostatic response is a long-term, sustained adjustment in the body's internal systems to manage the persistent, ongoing stress or environmental changes. For example, acclimatisation to high altitudes; when a person moves to a high-altitude region, they are exposed to lower levels of oxygen within the atmosphere as well as lower temperature levels. The body responds to this by increasing the production of red blood cells (erythrocytes) to enhance the oxygen-carrying capacity. This increase in erythrocyte count is maintained for as long as the person stays in high altitude regions³.

³ <https://academic.oup.com/icb/article-abstract/46/1/25/661337?redirectedFrom=fulltext>

This paper, therefore, aims to examine how polypharmacy affects renal and cardiovascular homeostasis in elderly individuals.

2. Polypharmacy in Elderly Individuals

Polypharmacy in elderly individuals is the key point of this research paper, solely because elderly individuals are far more susceptible to chronic diseases such as hypertension, diabetes, cardiovascular disease, arthritis, etc. Sometimes, an elderly individual can have more than three chronic diseases at the same time, which would lead the prescriber to prescribe more than five medications. The reason why elderly patients are far more susceptible to chronic diseases like these could be because of weakened immunity, reduced organ function, and even increased cellular damage⁴. More often than not, doctors prescribe more drugs to prevent future complications, which contributes to polypharmacy.

Moreover, elderly people have a greater relevance to renal and cardiovascular homeostatic responses because, as time passes by, functions of systems like the renal and cardiovascular slowly deteriorate. For instance, within the renal system, the kidney size could decrease, and the glomerular filtration rate (GFR) would be slower than that of middle-aged people. Also, the drug

⁴ <https://www.ncoa.org/article/the-top-10-most-common-chronic-conditions-in-older-adults/>

excretion would be slower as it's linked to the glomerular filtration rate.

There are multiple cardiovascular changes as well. There would be a reduced cardiac output, a decrease in baroreceptor sensitivity, meaning that the sensory nerves in the heart and blood vessels become less responsive to changes in blood pressure. There could also be an increase in arterial stiffness, which would cause a higher systolic blood pressure and even a higher pulse pressure.

Due to these age-related changes, the homeostatic responses in the body due to an increase in medication would also change.

3. Polypharmacy and Renal Homeostasis

3.1 Normal Renal Homeostasis

Renal homeostasis is an ongoing process that occurs 24/7. It is a process where the kidneys regulate the body fluid volume and the concentration of ions such as Na^+ , K^+ and Ca^{2+} to balance out the acid:base ratio (pH) within the body. Moreover, the kidneys also manage the fluid & electrolyte balance which occurs constantly by adjusting water and solute excretion to match intake, such as during hydration shifts. The process of homeostasis occurs when the also to remove metabolic waste such as urea (NH_2CONH_2).

3.2 Effects of Polypharmacy on Renal Homeostasis

Polypharmacy can significantly disrupt renal homeostasis in elderly individuals due to age-related decline in kidney function. As many medications pass through the kidneys, the simultaneous use of multiple drugs increases the risk of drug accumulation, particularly when renal clearance is reduced. This accumulation would result in elevated plasma drug concentrations, thereby increasing the likelihood of adverse effects and toxicity.

The reduced kidney function, including a decreased glomerular filtration rate, further limits the body's ability to effectively excrete medications and metabolites. As a result, normal

regulation of fluid and electrolyte balance may be impaired, contributing to homeostatic instability.

In some cases, polypharmacy can lead to acute kidney injury, especially when certain medications place additional stress on renal tissues or interfere with renal blood flow. An acute kidney injury (AKI) is a sudden irreversible loss of kidney function where the kidneys rapidly lose their capability to filter waste, control fluid balance, and regulate electrolytes⁵.

⁵ <https://www.mayoclinic.org/diseases-conditions/kidney-failure/symptoms-causes/syc-20369048>

4. Polypharmacy and Cardiovascular homeostasis

4.1 Normal Cardiovascular Homeostasis

Normal cardiovascular homeostasis is the regulation of blood circulation, heart function and resistance to maintain a stable, optimal pressure and tissue perfusion, regardless of whether the body is active or not.

Blood pressure adjustment is a constant cycle and it adjusts instantly due to body changes such as stress, exercise and the position of the body. Moreover, neural, hormonal and renal mechanisms.

According to the National Library of Medicine the Baroreceptor reflex responds to acute changes in blood pressure, the body responds through the baroreceptors located within blood vessels. Baroreceptors are a form of mechanoreceptor that become activated by the stretching of the vessel. This sensory information is conveyed to the central nervous system and used to influence peripheral vascular resistance and cardiac output⁶.

4.2 Effects of Polypharmacy on Cardiovascular Homeostasis

Polypharmacy can significantly disrupt the cardiovascular homeostasis in elderly individuals due to the consumption of a plethora of medications by the individual. These medication would affect the function of the heart as well as blood pressure regulation. Commonly prescribed drugs influence multiple things, such as vascular tone (vasodilation, vasoconstriction), heart rate, and even cardiac output (volume of blood pumped by the heart within a particular time period). When multiple medications are ingested within the body of the individual, there may not only be physiological issues but even psychological issues that may occur to the individual⁷.

One major consequence of polypharmacy is hypotension, which is low blood pressure. (hypertension $\neq$ hypotension). Hypotension, particularly orthostatic hypotension. The combined action of multiple antihypertensive (medications that are used to treat hypertension; basically they lower the blood pressure). Due to excessive reductions in the blood pressure, the cognitive and cerebral ability to comprehend anything⁸.

Another major consequence of polypharmacy is arrhythmias. Arrhythmias is the irregular beating of the heart. This occurs mainly due to durg-durg interactions that alter the cardiac

⁷ <https://www.who.int/publications/i/item/WHO-UHC-SDS-2019.11>

⁸ <https://pmc.ncbi.nlm.nih.gov/articles/PMC3532005/>

electrical activity. Age related changes in cardiac conduction further increase the susceptibility of irregular heart rhythms in elderly individuals⁹.

As a result of hypotension and arrhythmias, elderly patients experiencing polypharmacy face a higher risk of falls. Reduced blood flow to the brain causes dizziness to compromise balance, making falls a significant clinical outcome of disrupted cardiovascular homeostasis¹⁰.

⁹ <https://pmc.ncbi.nlm.nih.gov/articles/PMC4378642/>

¹⁰ <https://pmc.ncbi.nlm.nih.gov/articles/PMC5806601/>

5. Acute and Chronic Homeostatic Stress Due to Polypharmacy

Polypharmacy occurs in both acute and chronic homeostatic behaviour in the form of stress. This affects the body's homeostatic mechanisms in elderly individuals. Acute homeostatic stress occurs when the body is exposed to sudden physiological changes caused by the combined effects of multiple medications/drugs. In the short term, the blood pressure may rapidly drop, imbalancing the electrolyte concentration within the body and eventually leading to acute kidney injury (AKI). These rapid/sudden disturbances require immediate responses; however, age-related decline in the physiological reserve limits the ability of elderly individuals to effectively restore the function of that organ^{11 12}.

In contrast, chronic homeostatic stress arises from prolonged exposure to multiple medications over a period of time. Continuous pharmacological pressure can gradually impair the body's systems, leading to long-term instability in renal and cardiovascular function. Persistent stress on the kidneys may contribute to progressive decline in renal function, while long-term cardiovascular effects may include sustained blood pressure dysregulation and reduced adaptive capacity¹³.

¹¹<https://academic.oup.com/ageing/article-abstract/43/4/567/2812232?redirectedFrom=fulltext&login=false>

¹² <https://bpspubs.onlinelibrary.wiley.com/doi/10.1046/j.1365-2125.2003.02007.x>

¹³https://karger.com/nef/article-abstract/132/4/327/211754/The-Value-of-Monitoring-the-Serum-Concentration-of?redirectedFrom=fulltext&__cf_chl_tk=5Y7KliLAHVsqgX7ah7COY74kuKcNKrH3po_k7mldo-1781595682-1.0.1.1-yJx8p5sAnfoRdk8ovM5EQWuyjokUq8nNzvwLe7zJaCQ

While acute homeostatic responses are designed to provide immediate and rapid response, it temporarily corrects the issue. Chronic exposure to polypharmacy can “saturate” the body's mechanisms. As a result, the body’s ability to maintain internal conditions becomes compromised, thereby increasing the vulnerability to health issues in elderly individuals.

6. Clinical Consequences of Polypharmacy

There are multiple consequences of polypharmacy, including hospitalisation, an increased cost of care, and a reduced quality of life. Polypharmacy in elderly individuals is associated with several negative clinical outcomes, largely due to its effects on normal physiological regulation. One of the most common consequences is an increase in hospitalisations, often caused by adverse drug reactions, drug–drug interactions, or sudden deterioration in renal or cardiovascular function. Frequent hospital admissions indicate a higher disease burden and contribute to increased healthcare costs¹⁴.

Another significant clinical consequence of polypharmacy is the increased risk of falls and related injuries. The combined effects of multiple medications on blood pressure and heart rhythm can cause dizziness, fainting, and impaired balance. Falls are a major concern in elderly populations, as they often lead to fractures, reduced mobility, and loss of independence.

Polypharmacy may also result in a decline in functional ability and quality of life. Side effects such as fatigue, confusion, and reduced physical strength can limit an individual's ability to perform daily activities. In addition, long-term stress on the kidneys due to multiple medications may accelerate the

¹⁴ <https://www.tandfonline.com/doi/full/10.1517/14740338.2013.827660>

progression of chronic kidney disease, further increasing morbidity.

Overall, there are multiple clinical consequences of polypharmacy which extend beyond just one specific organ system. This highlights one of the key consequences of polypharmacy¹⁵.

¹⁵ <https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/jgs.12853>

7. Ethical and Medical Considerations

Multiple ethical and medical considerations need to be understood while prescribing and consuming medicines. Firstly, regular evaluation of all prescribed medications needs to be properly documented and also ethically lab tested. The drug would need to be tested to determine whether it's safe, necessary and effective.

Another important ethical issue is patient understanding and consent. Elderly patients should be clearly informed about why they are taking each medication, how it works, and what they should watch out for in terms of side effects. This allows patients to take part in decisions about their own treatment. When patients are not properly informed, they may take medications incorrectly or feel confused, which can worsen health outcomes

Overall, ethical medication use requires careful decision-making, clear communication, and regular review of treatment plans. By following ethical principles, healthcare professionals can reduce the risks of polypharmacy while ensuring elderly patients receive safe and effective care¹⁶.

¹⁶ <https://www.bmj.com/content/350/bmj.h949>

8. Limitations of the Study

As there was no ethically approved patient data available online regarding the direct physiological changes caused by polypharmacy, this paper focuses mainly on the general effects and overall problems associated with polypharmacy. It does not provide a detailed or patient-specific understanding of how polypharmacy affects individual physiological systems in real-life clinical settings.

Furthermore, this paper relies entirely on secondary data. The information used was collected only from ethical websites, textbooks, and previously published research papers. As no primary research or experimental data was included, the findings of this paper are limited to existing knowledge and may not reflect all variations seen in elderly patients.

9. Common Multivitamins taken for patients with such diseases

Nutritional supplementation plays a significant role in the management of chronic diseases, particularly chronic kidney disease (CKD) and cardiovascular disease (CVD). Patients affected by these conditions frequently experience nutritional deficiencies due to altered metabolism, dietary restrictions, impaired nutrient absorption, or the effects of long-term medication use. Consequently, healthcare professionals may recommend targeted vitamin and mineral supplementation to support physiological function and improve overall health outcomes.

In individuals with chronic kidney disease, renal-specific multivitamins such as Nephro-Vite, Renal-Vite, and Diallyvite are commonly prescribed. These supplements are formulated to provide water-soluble vitamins, including B-complex vitamins and vitamin C, which may be lost during dialysis treatments. Unlike standard multivitamins, renal formulations typically avoid excessive amounts of vitamins A, E, and K, as these fat-soluble vitamins can accumulate in the body when kidney function is impaired. Vitamin D supplementation is also frequently utilized in CKD management because damaged kidneys are less capable of converting vitamin D into its active form. Adequate vitamin D levels are essential for maintaining calcium homeostasis, bone mineralization, and overall skeletal health.

Patients with cardiovascular disease may similarly benefit from targeted nutritional supplementation. Omega-3 fatty acids, commonly obtained through fish oil supplements, are among the most widely used cardiovascular supplements. These compounds have been associated with reduced triglyceride levels and may contribute to improved cardiovascular health. Coenzyme Q10 (CoQ10) is another supplement frequently used in patients with heart failure or those undergoing statin therapy, as it may support cellular energy production and help alleviate certain treatment-related symptoms. Additionally, B-complex vitamins, particularly vitamins B6, B12, and folic acid, are often recommended to support homocysteine metabolism, as elevated homocysteine levels have been linked to an increased risk of cardiovascular complications.

Despite their potential benefits, nutritional supplements should not be regarded as substitutes for evidence-based medical treatment. Their use must be carefully monitored by healthcare professionals to minimize adverse effects, prevent nutrient imbalances, and avoid interactions with prescribed medications. Furthermore, supplementation strategies should be individualized according to the patient's age, medical history, disease severity, and nutritional status. Through appropriate clinical supervision, targeted supplementation can serve as a valuable component of comprehensive disease management in both renal and cardiovascular patients.

10. Conclusion

Polypharmacy has become an increasingly prevalent issue in elderly populations due to the rising burden of chronic diseases and the need for long-term pharmacological management. While the concurrent use of multiple medications may be clinically justified in certain circumstances, this paper demonstrates that polypharmacy poses significant challenges to the maintenance of homeostasis, particularly within the renal and cardiovascular systems. Age-related physiological decline reduces the body's capacity to adapt to both acute and chronic pharmacological stress, increasing susceptibility to drug accumulation, adverse drug reactions, and organ dysfunction.

The findings discussed highlight how impaired renal clearance and altered cardiovascular regulation can disrupt fluid balance, electrolyte stability, blood pressure control, and cardiac rhythm. These disturbances not only compromise homeostatic stability but also contribute to serious clinical consequences, including acute kidney injury, hypotension, arrhythmias, falls, increased hospitalisations, and reduced quality of life. Furthermore, prolonged exposure to multiple medications places chronic stress on regulatory systems, gradually diminishing the body's adaptive capacity.

Overall, this review underscores the importance of cautious and individualised medication management in elderly patients. Regular medication reviews, consideration of age-related physiological changes, and ethical prescribing practices are essential to minimise harm while preserving therapeutic benefit. By improving awareness of the homeostatic implications of polypharmacy, healthcare professionals can make more informed decisions that enhance patient safety, optimise clinical outcomes, and support healthier ageing.

11. References

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