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Original article

Evaluation of Drug Interactions in Elderly Hypertensive Patients: A Retrospective Study

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Abstract
Elderly hypertensive patients often experience polypharmacy due to multiple comorbidities, increasing the risk of potential drug interactions (DDIs) and adverse drug effects (ADEs). This study examined the prevalence, patterns, and severity of potential drug interactions (PDIs) in elderly patients with hypertension, identifying the most common drug combinations and evaluating clinical risk factors. A retrospective cohort study conducted at Sebha Medical Centre, the medical records of patients aged ≥60 years who were prescribed antihypertensive agents were reviewed, excluding patients with incomplete medical records. Data on demographics, comorbidities, and treatment regimens were collected, and potential DDIs were classified based on severity. Among the 70 patients assessed (mean age 72.2±7.9 years; 52.9% female), the mean number of medications prescribed was 8.2. Potential drug interactions were identified in 81% of patients, resulting in 210 unique interactions, most of which were moderate to severe. The most affected drug classes were ACE inhibitors, aspirin, and furosemide. A significant correlation was observed between polypharmacy and an increased risk of potential DDI (p=0.026), while comorbidities showed no significant correlation. These findings highlight the high prevalence of polypharmacy and its effect on pDDIs risk in elderly hypertensive patients, underscoring the need for regular medication reassessment and clinical pharmacist engagement to reduce adverse effects in this population.
Keywords. Hypertension, Elderly, Drug-Drug Interactions, Polypharmacy, Retrospective Study, Adverse Drug Events.

Introduction

Hypertension continues to comprise a relevant morbidity and mortality on a global scale, with approximately 1.3 billion patients with hypertension accounting for nearly 17.9 million deaths annually [1]. The global burden of hypertension should be of particular concern in the elderly population because older adults are at greater risk of having more comorbidities, which complicate their pharmacotherapy [2]. While polypharmacy may be unavoidable at times, it significantly increases the chances of potential drug-drug interactions (pDDIs) leading indicative adverse drug events (ADEs), greater healthcare resource utilization, and poorer outcomes [3-5].

Physiological changes, which are part of the natural aging process among adults, can cause drug-drug interactions. Drug-drug interactions can lead to adverse drug events, which have often been connected to the consequences of age-related reductions in hepatic and renal function, which increases the risk of clinically meaningful DDIs in patients with co-existing conditions or multiple comorbidities [6]. The antihypertensive agents, antiplatelets, diuretics, and other common medications used in this population all have a present risk of drug interaction. For example, the concurrent use of an angiotensin-converting enzyme (ACE) inhibitor (which will continue to be the gold standard for treatment) with potassium-sparing diuretics would potentially present a risk of rapid life-threatening hyperkalemia [7]. Additionally, concomitant use of clopidogrel and some PPIs, such as omeprazole, has been shown to reduce the clopidogrel antiplatelet effect with increased risk of thrombosis [8]. Despite a general awareness of these dangers, there is still limited and inadequate knowledge of the prevalence and clinical correlates of pDDIs in elderly hypertensive patients in the real world, particularly in lower and middle-income countries [9, 10]. It is crucial to understand these patterns to help reduce these risks and implement specific changes to prescribing practices. So, this study aims to, firstly, identify how common and severe pDDIs are among elderly hypertensive patients; secondly, to characterize the most frequent interacting drug pairs; and, finally, to assess how pDDIs relate to polypharmacy and comorbidities.

Methods

Study Design and Setting

The present retrospective cohort study was conducted at Sebha Medical Centre, Sebha, Libya, after ethical clearance was obtained from the research and ethics review committee of the faculty of pharmacy, Sebha University. The permission to collect data was obtained after official letters were approved by the head of Sebha Medical Centre.

Patient Selection

We have included patients with an age ≥60 years, and documented diagnosis of hypertension, with a prescribed antihypertensive medication during the study period. Incomplete or illegible medical records we excluded.

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Data Collection

The data were collected over 30 working days, from January 22 to February 29, 2021. The extraction of information from manual medical records was conducted by trained study personnel, employing a standardized data collection form. The following variables were extracted: The following data were collated for each patient: 1) Their age and gender; 2) Their clinical characteristics, including any comorbidities; 3) The complete medication lists, including doses and routes of administration; 4) The laboratory values, where available; and 5) The identification and classification of pDDIs.

All prescribed medications were screened for potential drug-drug interactions using Stockley's Drug Interactions book [11]. pDDIs were classified by severity: Major: May be life-threatening or require medical intervention. Moderate: It is possible that a dose adjustment, monitoring, or therapy modification will be required. Minor: It is improbable that the condition will result in substantial harm or necessitate modification of the therapeutic regimen.

Statistical Analysis

Descriptive statistics summarized the demographic and clinical data, and the pDDI prevalence and severity were calculated as proportions. Relationships between pDDI count, medications (polypharmacy), and comorbidities were determined, using Pearson's correlation coefficients. Statistical significance was set at $p<0.05$. All analyses were performed using SPSS (version 25).

Results

Patient Characteristics

A total of 70 patients fulfilled the criteria for selection, with an average age of 72. 2 years, plus or minus 7. 9 years, ranging from 60 to 94 years. Among the patients, 52. 9% were female, totaling 37 individuals. On average, each patient was taking 8. 2 medications, with a median of 8, and a range from 5 to 12. A significant majority of the patients, 95. 7%, had one or more additional health issues, with the most frequently noted being cardiovascular disease at 48. 6%, diabetes mellitus at 30%, and hyperlipidemia at 14. 3%, as detailed in Table 1.

Table 1. Demographic and Clinical Characteristics of Study Population

Characteristic	Value
N	70
Female, n (%)	37 (52.9)
Age, mean ± SD (years)	72.2 ± 7.9
Number of medications, mean ± SD	8.2 ± 1.7
≥1 comorbidity, n (%)	67 (95.7)
Common comorbidities	
Cardiovascular	34 (48.6)
Diabetes mellitus	21 (30.0)
Hyperlipidemia	10 (14.3)
Chronic kidney disease	4 (5.7)

Prevalence and Severity of pDDIs

This study found that 81% (n=57) of patients had at least one pDDI, and the total pDDIs identified were 210, with an average of 3.0 pDDIs/patient. Moreover, the review of patient medications identified several drug-drug interactions of varying severity. Major interactions were most frequently associated with combinations involving antiplatelet agents, anticoagulants, and certain cardiovascular drugs. Moderate interactions were common among antihypertensives, diuretics, and antidiabetic medications, while minor interactions were less prevalent (Table 2).

Table 2. Classification and Frequency of pDDIs Identified

Severity	Number of pDDIs	Percentage (%)
Major	70	33.3
Moderate	133	63.3
Minor	7	3.3
Total	210	100

Frequently Implicated Drug Combinations

The most common interacting pairs were presented in Figure 1. Other significant combinations featured ACE inhibitors paired with digoxin, furosemide alongside ceftriaxone, and aspirin together with heparin.

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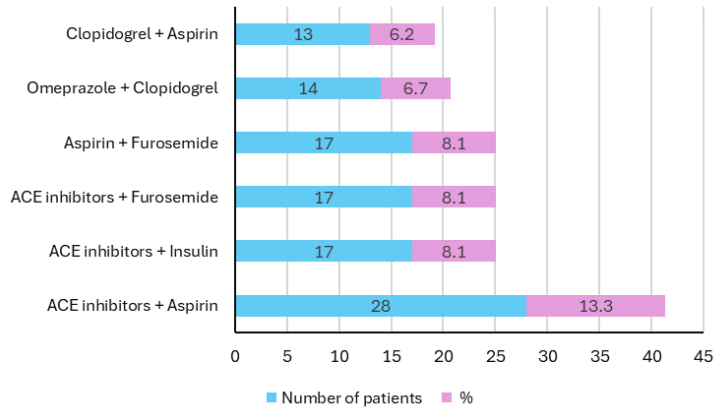

Figure 1. Most Frequent Drug Combinations Implicated in pDDIs

Factors Associated with pDDIs

There was a moderate positive correlation between the total number of medications prescribed and the total number of pDDIs (Pearson's r = 0.266, p = 0.026). There was no significant correlation found between the total number of comorbidities and pDDIs (Pearson's r = 0.034, p = 0.781).

Discussion

The current study showed a high prevalence of potential drug-drug interactions (pDDIs) in older people with hypertension. A total of 81% of patients had at least one pDDI, and most of the pDDIs were moderate or major, which indicates that polypharmacy is an issue that needs to be given attention in the clinical setting with elderly hypertensive patients. This is consistent with prior research studies that also demonstrated that pDDIs were a concern for older adults with hypertension. Alhumaidi et al. (2023) reported that 85.3% of elderly patients had at least one pDDI in Saudi Arabia, and Gotardelo et al. (2014) reported that 55.6% of elderly patients had a pDDI in Brazil, with most of the pDDIs involving a cardiovascular medication [3, 12]. Similarly, Hughes et al. (2021) reported that over 22.65% of older adults experienced a severe drug interaction that was involving cardiovascular medications i.e., Aspirin or Warfarin, in their study population [13]. This data highlights the need for effective medication management and ongoing medication reviews of the drug therapy regimens for elderly patients with hypertension to assist in controlling and managing the potential complications associated with polypharmacy and pDDIs in the management of their medical condition [3,12,13].

Of note, the pair interactions of ACE inhibitors and aspirin, as well as omeprazole and clopidogrel, made up a number of the significant pDDIs. Moreover, these combinations are well described in the literature as combinations that reduce therapeutic efficacy or increase toxicity [8, 14]. For example, omeprazole inhibits the activation of clopidogrel and reduces the antiplatelet effect of clopidogrel, increasing the risk of thrombosis [8]. Another example of a combination that is dangerous can occur with the combination of the ACE inhibitors and potassium-sparing agents, which can lead to dangerous hyperkalemia, mostly in older populations [7].

Interestingly, in our sample, the number of comorbidities had no significant association with pDDIs despite many studies identifying multi-morbidity as a risk factor for DDIs [15-18]. It may be due to effective approaches to disease management or treatment patterns at our site being unique. In contrast, the quantity of medications prescribed (polypharmacy) was significantly associated with pDDIs, highlighting the importance of careful management of medications in this population.

An important finding is a significant association between polypharmacy and pDDI risk, controlling for comorbidity burden. This supports that polypharmacy overall (number of medications), rather than the added complexity of disease per se, is the important factor driving interaction risk in elderly hypertensive patients. This finding is consistent with the literature and underscores a timely need for continuing medication reviews and pharmacy involvement in care [19-21].

Considering the extremely high burden of pDDIs and their likelihood to cause harm, namely through adverse drug events, employing validated interaction checkers routinely and pharmacist-led medication reviews should become routine practice, especially in the elderly who are often taking multiple medications. Clinicians should be especially cautious of high-risk combinations and should actively seek safer options when possible (e.g., pantoprazole over omeprazole in patients taking clopidogrel).

Limitations

Longitudinal design and dependent on the accuracy of medical records. Evaluation was restricted to assessing possible interactions. True clinical measures (ADEs, hospitalization) were not evaluated. Single-center and a fairly small sample size may limit generalizability.

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Conclusion

The use of multiple medications is quite frequent, particularly among elderly individuals with high blood pressure, and it is significantly linked to an increased chance of harmful interactions between medications. Evaluating medications and working together with a pharmacist, in addition to careful prescribing methods, are strategies that can assist in reducing avoidable risks for older patients dealing with hypertension. Future research involving bigger groups of people is needed to evaluate the health effects of potentially dangerous drug interactions, along with methods to lessen the use of multiple medications.

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Conflicts of Interest

There are no conflicts of interest to declare.

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