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Evaluation of NSAID-Drug Interactions in Elderly Patients: A Retrospective Study

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ABSTRACT

This study was carried out to evaluate the frequency, severity, and clinical significance of potential NSAID-related DDIs in elderly patients. Data from 131 elderly inpatients (60 years and older) taking NSAIDs were reviewed in a retrospective study at a medical center. Comorbidities, medication history, demographic data, and possible DDIs were all collected. Using online drug interaction checkers, drug interactions were categorized as minor, moderate, or severe based on their clinical significance. SPSS version 22 was used for the statistical analysis, and a significance level of $p < 0.05$ was used. On average, each patient had 1-4 encounters, and all 131 patients were exposed to ≥1 possible DDIs. The most common type of interaction was moderate (43.8%), followed by major (37.9%) and minor (18.4%). The most common major interaction was between aspirin and clopidogrel or anticoagulants, which increased the risk of gastrointestinal bleeding. The majority of patients (97.9%) were taking multiple medications, which was linked to a higher risk of DDIs ($p < 0.01$). DDIs were also more common in patients with more than one health problem ($p < 0.01$). This study concludes that older patients taking NSAIDs are very likely to have DDIs, especially those with other health problems and who take a lot of different medications. To reduce the chance of negative outcomes, doctors should watch out for DDIs and change treatment, if necessary, especially for high-risk patients.

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INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are utilised by a significant proportion of the elderly population for the management of inflammation and pain. Furthermore, NSAIDs are utilised in the treatment of numerous musculoskeletal conditions (1).

The mechanism by which NSAIDs exert their therapeutic effects involves the inhibition of cyclooxygenase (COX), an enzyme that plays a pivotal role in the synthesis of prostaglandins, which are vital for both pain perception and inflammatory responses (2). However, it is important to note that NSAIDs are associated with a number of adverse effects, particularly in older adults (3). The likelihood of adverse drug reactions is increased in older adults due to changes in their bodies that occur with aging, the use of multiple medications, and the presence of multiple health issues. Consequently, the utilisation of NSAIDs in this demographic poses significant challenges (4).

Polypharmacy, defined as the concurrent use of multiple medications, is a prevalent condition among older adults (5). Studies have shown that elderly individuals frequently take five or more medications, increasing the likelihood of drug-drug interactions (DDIs) (6). Non-steroidal anti-inflammatory drugs (NSAIDs) are known to interact with several commonly prescribed medications, including antihypertensives, anticoagulants, diuretics, and antidiabetic drugs (7). These interactions can lead to a reduction in the efficacy of concomitantly administered medications, or, more alarmingly, result in severe ADRs. For instance, NSAIDs have been shown to exacerbate the risk of gastrointestinal (GI) bleeding, especially when combined with anticoagulants, and can also induce or worsen renal impairment when used with diuretics or angiotensin-converting enzyme (ACE) inhibitors (3).

Furthermore, the cardiovascular risks associated with NSAIDs in older individuals have garnered significant attention. A number of NSAIDs, notably COX-2 inhibitors, have been associated with an elevated risk of myocardial infarction and cerebrovascular accidents (8). This is a particularly salient concern for older individuals, who frequently have pre-existing cardiovascular conditions and thus are more vulnerable to deleterious consequences. Moreover, older individuals are more prone to renal problems induced by NSAIDs due to the fact that their kidneys are typically less robust with advancing age (9). The mechanism by which NSAIDs exert their effect involves the inhibition of prostaglandin-mediated vasodilation, thereby reducing blood flow to the kidneys. This can result in kidney damage, particularly in patients with pre-existing renal conditions or those who are concomitantly taking other drugs that can be deleterious to the kidneys (10). Due to these risks, there is mounting concern regarding the safety of NSAID use in elderly individuals, emphasising the necessity for rigorous monitoring of potential interactions with other medications and adverse effects. Achieving an optimal balance between pain management and safety in this patient population necessitates the development of enhanced methodologies for NSAID utilisation. The primary objective of this study was to elucidate the impact of age, sex, and the number of medications on potential drug interactions in elderly patients undergoing NSAID

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therapy. The objective was to ascertain how these interactions can lead to toxicity in these patients at Sebha Medical Center.

METHODS

Study Design and Setting

The present study examined the medical files of patients over a period of 30 working days. The study was conducted at Sebha Medical Centre between 22 January and 29 February 2021. Approval for the study was granted by the research and ethics review committee of the University. The Medical Centre's head authorised data collection. The confidentiality of all patient information was strictly maintained, with its use being limited exclusively to the purposes of the research. It should be noted that the centre did not have clinical pharmacy services or computerised drug interaction screening programs available, and patient records were kept in handwritten format.

Study Population

This study examined a cohort of 131 elderly patients (aged 60 years and over) who were prescribed nonsteroidal anti-inflammatory drugs (NSAIDs). The inclusion criteria included inpatients of any gender, aged 60 and above, and currently receiving at least one NSAID. Patients under the age of 60, those not taking NSAIDs, outpatients, and those with incomplete medical records were excluded from the study. A comprehensive review of the subjects' medical records was conducted prior to their admission, encompassing demographic details, including age and gender, comorbidities, laboratory test results, concomitant medication, particularly those associated with gastrointestinal ulceration, and the dosage and frequency of administered medications. To ensure comprehensive data collection, online tools were employed to identify potential interactions between medications (DDIs). The aforementioned tools included Drugs.com, WebMD and Stockley's Drug Interactions book (11). The resulting interactions were then categorised into three distinct groups based on the severity of the reported consequences.

Statistical Analysis

The data collected were then subjected to analysis using SPSS version 25 (IBM Corp, New York, USA). Information that could be categorised was presented as the frequency with which it occurred and its percentage of the total. Information that could be quantified was presented as the mean ± standard deviation (SD). The frequency of DDIs was reported as n (%). The Pearson correlation coefficient was then utilised to ascertain the relationship between DDIs and the other variables of interest. A level of certainty greater than 95% was deemed to be significant.

RESULTS AND DISCUSSION

A total of 131 patient records were examined. The majority of patients were male (48.9%). The majority of patients were between 60 and 64 years of age (see Table 1 and Figure 1). The age range encompassed from 60 to ⩾90 years, with a mean age of 18.7 years (SD = 8.9).

A higher proportion of women were exposed to NSAIDs, which may be attributable to their increased propensity for certain health conditions, as has been observed in other studies (12, 13).

Table 1. Demographic data of patients (n = 131)

Gender	Frequency	%
Male	64	48.9
Female	67	51.1
Age	Mean 18.7±8.9	Range 60 to ≥ 90

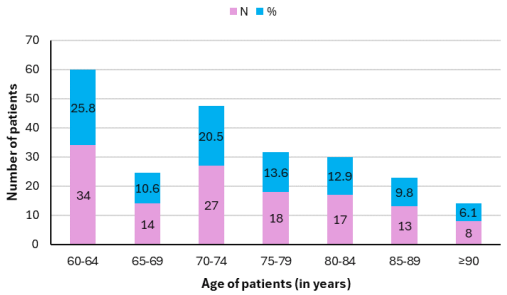

Figure 1. Distribution of the age of patients

Potential Drug Interactions with NSAIDs

The present study's findings are consistent with those of other reports that have identified a high prevalence of possible DDIs. Each patient in this study was exposed to one or more potential DDIs, with the number of DDIs per patient ranging from one to four. A separate study identified 400 possible DDIs in 100 prescriptions, with an average of 4 ± 5.42 DDIs per patient (14). This finding is consistent with those reports. This emphasises the necessity for meticulous medication review and the frequency of DDIs in clinical practice.

The most prevalent DDI identified was the concurrent use of aspirin and clopidogrel (see Figure 2).

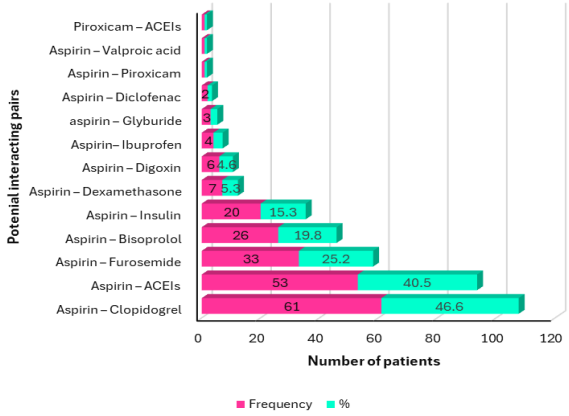

Figure 2. Distribution of NSAIDs-drug interactions

Subsequent analysis of the severity of these interactions revealed that moderate interactions were the most common (43.8%), followed by major (37.9%) and minor (18.4%) interactions (see Figure 3).

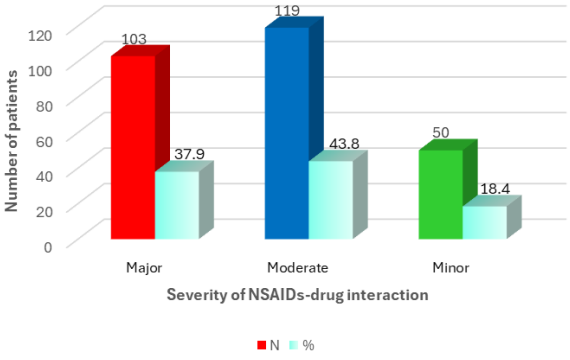

Figure 3. Severity of NSAIDs-drug interactions

NSAIDs-Drug Interactions and Adverse Drug Reactions

0.8% of adverse drug reactions (ADRs) were caused by NSAID-drug interactions. Since Sebha Medical Center did not use systematic methods to identify adverse drug interactions, the data probably underrepresents the actual incidence of ADRs.

NSAIDs Co-prescription and Potential Bleeding

A significant proportion of DDIs comprises the co-prescription of NSAIDs with medications that elevate the risk of gastrointestinal (GI) bleeding. This is a prevalent cause of DDIs. Of particular interest is the involvement of antiplatelets in 46.6% of interactions, corticosteroids, and other NSAIDs in 6.3% of interactions. The combination of aspirin with clopidogrel was identified as the most prevalent major DDI in 46.6% of cases. These findings are consistent with those reported by Lee and Cha (2024), who found that patients undergoing NSAID and anticoagulant therapy exhibited a 66% increased risk of gastrointestinal bleeding when compared to those on anticoagulant monotherapy (15). Furthermore, nonselective NSAIDs, such as ibuprofen, when used concomitantly with anticoagulants, have been implicated in 16.1% of interactions, as reported by Mehuys et al. (2022) (16). These findings underscore the imperative for medical professionals to exercise caution when prescribing NSAIDs in conjunction with anticoagulants and antiplatelets, emphasising the need to closely monitor for any gastrointestinal issues and consider alternative treatment options.

NSAID Co-prescription and Potential Hypertension

The utilisation of NSAIDs and antihypertensive medications was frequently observed to occur in conjunction with one another; 40.5% of patients were prescribed ACE inhibitors, 25.2% were administered diuretics (e.g. furosemide), and 19.8% were prescribed β-blockers. Aspirin was frequently prescribed in combination with diuretics, ACE inhibitors, and angiotensin receptor blockers (ARBs). It is important to note that NSAIDs have been demonstrated to increase peripheral vascular resistance and sodium retention, which can result in compromised blood pressure control (17).

NSAID Co-prescription and Potential Nephrotoxicity

The concomitant administration of NSAIDs and diuretics, ACE inhibitors, or ARBs (Angiotensin receptor blockers) in older patients has been shown to result in an increased propensity for kidney damage. This combination of drugs, known as the "triple whammy," has been demonstrated to engender a significant escalation in the risk of kidney injury (17).

Factors Associated with NSAID-Drug Interactions

Polypharmacy

A significant proportion of the study participants were prescribed multiple medications. A significant proportion of the patient population, specifically 97.9%, were found to be regularly ingesting a minimum of five medications. This finding was associated with an elevated probability of developing DDIs ($p < 0.01$), a conclusion that has been corroborated by subsequent studies (18-20).

Comorbidity

The present study has demonstrated a significant correlation between comorbidities and the likelihood of drug-drug interactions (DDIs), with a strong positive correlation observed between the number of comorbidities and potential DDIs (Pearson correlation = 0.802, $p < 0.01$). This finding aligns with the observations reported by Khan & Hussain (2024), who also identified a strong correlation between DDIs and concurrent diseases ($r = 0.782$, $P < 0.01$) (21). Moreover, the presence of multimorbidity has been shown to increase the likelihood of inappropriate prescribing, which can adversely impact health outcomes, as outlined in a systematic review and a retrospective study (20, 22). These results underscore the imperative for meticulous management of polypharmacy in patients with multiple comorbidities, to mitigate the risk of DDIs and ensure enhanced patient safety.

CONCLUSION

This study emphasises the prevalence of potential DDIs in older NSAID-using patients, particularly those with comorbidities and polypharmacy. The study identified drugs that elevate the risk of GI bleeding, hypertension, and nephrotoxicity as the primary subjects of moderate to major interactions, which were prevalent. The findings underscore the necessity for meticulous monitoring of elderly patients prescribed NSAIDs, particularly those afflicted with multiple comorbidities. The external validity of this study is tempered by several limitations, including its modest sample size, concise duration, and incomplete patient record data. Additionally, the analysis encompasses long-term prescriptions that may not accurately reflect current risks, and the exclusive focus on NSAIDs precludes the evaluation of other medications. In order to enhance the robustness of the findings, it is recommended that a more extensive range of medications be evaluated, that prospective studies be conducted with longer monitoring periods, that the clinical impact of drug-drug interactions (DDIs) in hospitalized patients be investigated, that access to trustworthy drug databases be expanded, and that clinical pharmacists be encouraged to document in a standardised manner to improve patient safety. These measures are proposed in order to overcome the limitations of the study and to provide a more comprehensive and reliable overview of the subject.

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