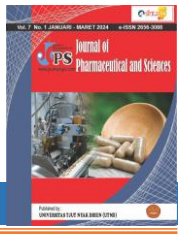
Journal of Pharmaceutical and Sciences
Electronic ISSN: 2656-3088 DOI: https://doi.org/10.36490/journal-jps.com
Homepage: https://journal-jps.com
REVIEW ARTICLE JPS. 2026, 9(1), 360-369



Drug Interactions in Geriatric Patients: An Evidence-Based Review of the Combination of Antihypertensives and Non-Steroidal Anti-Inflammatory Drugs

Interaksi Obat Pada Pasien Geriatri: Kajian Berbasis Evidence Tentang Kombinasi Antihipertensi dan Obat Non Steroidal Anti-Inflammatory

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Abstract

The number of elderly individuals continues to increase globally, accompanied by a high prevalence of chronic diseases, particularly hypertension and musculoskeletal disorders. This condition makes geriatric patients vulnerable to polypharmacy, which increases the risk of drug interactions, one of which is between antihypertensives and non-steroidal anti-inflammatory drugs (NSAIDs). Such interactions can potentially reduce therapy effectiveness, cause electrolyte disturbances, and lead to acute kidney injury (AKI). This study aims to comprehensively examine the interaction between antihypertensives and NSAIDs in geriatric patients and its impact on therapy safety. The method used is a literature review by selecting national and international articles published between 2015 and 2025, written in either Indonesian or English, specifically investigating interactions between antihypertensives (β-blockers, ACE inhibitors, ARBs, diuretics, and CCBs) and NSAIDs. The review results indicate that most interactions are pharmacodynamic, involving either antagonism or negative synergism. NSAIDs can reduce the effectiveness of antihypertensive therapy through mechanisms such as sodium retention, afferent arteriolar vasoconstriction, and decreased renal perfusion. In certain combinations, such as the triple whammy phenomenon (NSAIDs, diuretics, and RAAS inhibitors), the risk of AKI and hyperkalemia increases significantly. This risk is higher in geriatric patients with decreased kidney function, comorbidities, and concurrent use of multiple drugs. In conclusion, the interaction between antihypertensives and NSAIDs in the elderly population is an important clinical issue. Therefore, close monitoring of kidney function and electrolytes, using the lowest effective dose for the shortest possible duration, and patient education to avoid self-medication are necessary to ensure therapy safety.

***Keywords*: Geriatrics, Antihypertensives, NSAIDs, Drug Interactions.**

Abstrak

Jumlah penduduk lanjut usia terus meningkat secara global dan diikuti dengan tingginya prevalensi penyakit kronis, terutama hipertensi dan penyakit muskuloskeletal. Kondisi ini menyebabkan pasien geriatri rentan mengalami polifarmasi yang meningkatkan risiko interaksi obat, salah satunya antara antihipertensi dan non-steroidal anti-inflammatory drugs (NSAID). Interaksi tersebut berpotensi menurunkan efektivitas terapi, menimbulkan gangguan elektrolit, hingga menyebabkan acute kidney injury (AKI). Penelitian ini bertujuan untuk mengkaji secara komprehensif interaksi antara antihipertensi dan NSAID pada pasien geriatri serta dampaknya terhadap keselamatan terapi. Metode yang digunakan adalah literature review dengan menyeleksi artikel nasional dan internasional yang diterbitkan dalam kurun waktu 2015–2025, menggunakan bahasa Indonesia maupun Inggris, dan secara khusus meneliti interaksi antihipertensi (β-blocker, ACE inhibitor, ARB, diuretik, dan CCB) dengan NSAID. Hasil kajian menunjukkan bahwa sebagian besar interaksi bersifat farmakodinamik, baik antagonisme maupun sinergisme negatif. NSAID dapat menurunkan efektivitas terapi antihipertensi melalui mekanisme retensi natrium, vasokonstriksi arteriol aferen, serta

penurunan perfusi ginjal. Pada kombinasi tertentu, seperti fenomena triple whammy (NSAID, diuretik, dan RAAS inhibitor), risiko AKI dan hiperkalemia meningkat secara signifikan. Risiko ini lebih tinggi pada pasien geriatri dengan fungsi ginjal yang menurun, komorbiditas, serta penggunaan banyak obat secara bersamaan. Kesimpulannya, interaksi antara antihipertensi dan NSAID pada populasi lanjut usia merupakan masalah klinis yang penting, sehingga diperlukan pemantauan ketat fungsi ginjal dan elektrolit, penggunaan dosis efektif terendah dengan durasi sesingkat mungkin, serta edukasi pasien untuk menghindari swamedikasi guna menjaga keselamatan terapi.

Kata Kunci: Geriatri, Antihipertensi, NSAID, Interaksi Obat.

Article History:
Received: 30/08/2025,
Revised: 17/11/2025
Accepted: 17/11/2025,
Available Online: 10/02/2026 .
QR access this Article

https://doi.org/10.36490/journal-jps.com.v9i1.1182

Introduction

Globally, the number of elderly individuals continues to increase rapidly, posing a significant challenge to the healthcare system. The WHO estimates that by 2030, one in six people in the world will be aged ≥60 years, totaling more than 1.4 billion [1]. This increase in life expectancy is accompanied by a rise in the prevalence of chronic diseases such as hypertension, cardiovascular diseases, osteoarthritis, and other musculoskeletal disorders [1]. These conditions make the geriatric population increasingly vulnerable to various complex health problems, particularly related to the management of long-term drug therapy. Polypharmacy, generally defined as the concurrent use of five or more medications, is a common phenomenon among the elderly population [2]. The simultaneous use of multiple drugs can increase the risk of drug interactions, side effects, decreased adherence, and ultimately lead to higher morbidity and mortality [2,3]. In geriatric patients, this risk is even greater due to physiological changes, reduced organ function, and alterations in pharmacokinetics and pharmacodynamics that affect the body's response to medications.

Hypertension is one of the most common chronic diseases encountered in the geriatric population, with a global prevalence of over 60% in individuals aged ≥60 years [4]. Managing hypertension in this group often requires combination therapy using several classes of antihypertensives, such as ACE inhibitors, Angiotensin Receptor Blockers (ARB), β-blockers, Calcium Channel Blockers (CCB), and Diuretics [5]. The combination of these various antihypertensives increases the likelihood of interactions, especially if patients are also taking other medications for comorbid conditions. One of the most common comorbidities experienced by elderly patients is musculoskeletal pain, such as osteoarthritis. This condition is a leading cause of disability among the elderly worldwide [6]. To manage pain and inflammation, non-steroidal anti-inflammatory drugs (NSAIDs) remain the primary therapy of choice, both for short-term and long-term management [7].

However, the concurrent use of NSAIDs with antihypertensives has the potential for serious interactions. NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) are known to reduce the effectiveness of antihypertensive therapy through various interrelated physiological mechanisms. One of the main mechanisms is sodium and water retention due to the inhibition of prostaglandin synthesis in the kidneys, which plays a crucial role in maintaining fluid balance and blood pressure. In addition, NSAIDs can also cause constriction of the afferent arterioles, thereby reducing blood flow to the glomerulus and disrupting kidney filtration function. As a result, blood pressure becomes difficult to control even though the patient has been taking antihypertensive medication as prescribed. This condition has the potential to increase the risk of serious complications such as kidney disorders, electrolyte imbalances, and cardiovascular events such as

heart failure or stroke [8,9]. These effects can occur with various types of NSAIDs, whether selective for COX-2 (such as celecoxib) or non-selective (such as ibuprofen and diclofenac), with varying risk levels depending on the duration and dosage of use.

Geriatric patients are the most vulnerable group to the effects of drug interactions due to various physiological changes that occur with aging, such as decreased kidney and liver function, which play an important role in drug metabolism and elimination. In addition, the high prevalence of polypharmacy, or the use of multiple medications simultaneously to treat various chronic diseases, also increases the risk of both pharmacodynamic and pharmacokinetic interactions [9]. A study conducted in Semarang showed that more than 90% of hospitalized geriatric patients experienced drug interactions, with 61.5% of them being pharmacodynamic interactions [10]. These figures illustrate how frequently drug interactions occur in the elderly population and highlight the potential risk to patient safety. Based on this, close monitoring of medication use in geriatric patients is essential, especially for drug combinations that have the potential to cause serious interactions, such as between antihypertensives and nonsteroidal anti-inflammatory drugs (NSAIDs).

Although various studies have discussed this drug interaction, comprehensive reviews specifically highlighting the mechanisms, risks, and clinical impact of combining antihypertensives and NSAIDs in geriatric patients remain limited. The lack of comprehensive reviews creates a knowledge gap regarding the extent to which this combination can affect blood pressure control effectiveness and increase the risk of side effects. Therefore, this study aims to systematically examine the scientific evidence on the interaction between antihypertensives and NSAIDs in geriatric patients, focusing on effects on therapy effectiveness and patient safety. The results of this study are expected to provide significant scientific contributions in supporting more rational and evidence-based clinical practices for geriatric patients.

Method

The review used is a literature review on several national and international articles with a systematic approach to identify, select, evaluate, and synthesize research results related to drug interactions between antihypertensive and anti-inflammatory drugs. Journal searches were conducted using journal databases such as Google Scholar, PubMed, Science Direct, and Publish or Perish. The articles used were required to be published within the last 10 years, from 2015 to 2025. Articles must meet the inclusion and exclusion criteria in **Table 1** below.

Table 1. Inclusion and Exclusion criteria applied in the selection of articles for this literature review.

Inclusion	Exclusion
Articles published between 2015-2025	Articles published before 2015 or after 2025
Articles available in Indonesian and English	Articles written in languages other than English and Indonesian
Studies evaluating drug interactions between antihypertensive agents (ACE inhibitors, ARBs, diuretics, β-blockers, and calcium channel blockers) and non-steroidal anti-inflammatory drugs (NSAIDs).	Studies that evaluated only one drug class (antihypertensive drugs or NSAIDs) without assessing drug interactions.
Studies involving geriatric or older adult populations, or studies in which elderly patients constituted a significant proportion of the study population.	Articles in the form of editorials, commentaries, letters to the editor, single case reports, conference abstracts, book chapters, or study protocols without outcome data
Original research articles (cohort, cross-sectional, case–control, or retrospective studies) as well as relevant review articles that provide mechanistic or clinical outcome data.	
Open-access or publicly accessible full-text articles.	

Strategy for Data Extraction

Data extraction was conducted independently by reviewing the full text of each selected article. Key information extracted from each study included: author and year of publication, study design (cohort, cross-sectional, case–control, or retrospective study), study population (with emphasis on geriatric patients), type of antihypertensive and NSAID involved, type of drug interaction (pharmacodynamic or pharmacokinetic), proposed interaction mechanisms, and reported clinical outcomes such as changes in blood pressure, acute

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kidney injury (AKI), hyperkalemia, or hospitalization risk. When quantitative measures such as odds ratios (OR), relative risks (RR), or hazard ratios (HR) were reported, these data were recorded to support qualitative comparison across studies. Any discrepancies or unclear data were resolved through re-evaluation of the original articles.

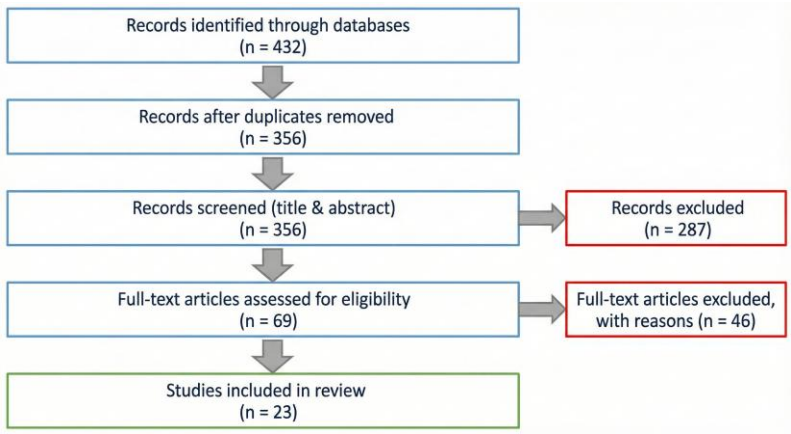

Figure 1. A PRISMA-based flow diagram was used to illustrate the article selection process. Articles were identified from several electronic databases, screened for relevance, assessed for eligibility, and selected based on predefined inclusion and exclusion criteria.

Data Synthesis

Data synthesis was performed using a qualitative descriptive approach due to the heterogeneity of study designs, populations, and outcome measures across the included studies. The extracted data were grouped according to classes of antihypertensive drugs (β-blockers, ACE inhibitors, ARBs, diuretics, and calcium channel blockers) and analyzed in relation to their interactions with NSAIDs. The findings were then compared and interpreted based on similarities and differences in interaction mechanisms, clinical outcomes, and risk factors reported in each study. Special attention was given to identifying recurring patterns such as antagonistic effects on blood pressure control and synergistic mechanisms leading to acute kidney injury, particularly in the context of the "triple whammy" phenomenon. The synthesis focused on integrating pharmacological mechanisms with clinical implications to provide an evidence-based overview of therapy safety in geriatric patients.

Result

Table 2. The results

Source	Study Population / Design	Drug Combination	Type of Interaction	Main Outcomes / Reported Risk	Key Mechanism	Study Limitations
[11]	Hypertensive adults; population-based cohort study	β-blockers + NSAIDs	Pharmacodynamics (antagonism)	Reduced antihypertensive response; no significant increase in major CV events	Prostaglandin inhibition causing sodium and fluid retention	Observational study; short-term NSAID exposure
[12]	Narrative review of clinical and physiological studies	β-blockers + NSAIDs	Pharmacodynamics (antagonism)	Increased blood pressure and edema reported	Reduced renal prostaglandin synthesis and increased vascular tone	Narrative review; no quantitative risk
[13]	Elderly patients; cross-sectional study	β-blockers + NSAIDs	Pharmacodynamics (antagonism)	Increased BP and reduced BP control; AOR for NSAID use = 9.06	Suppression of vasodilatory prostaglandins	Cross-sectional; causality cannot be inferred

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[14]	Hospitalized patients; post hoc analysis	ACEI/ARB + diuretics + NSAIDs	Pharmacodynamics (synergism)	Increased hospitalization due to AKI	Afferent vasoconstriction and efferent vasodilation reducing GFR	Retrospective design
[9]	Older adults (≥65 years); retrospective cohort	ACEI/ARB + NSAIDs	Pharmacodynamics (Synergism)	AKI and hyperkalemia incidence 16.7% within 30 days	Reduced renal perfusion and potassium retention	Confounding by comorbidities
[15]	Primary care patients; retrospective cohort	ACEI + NSAIDs	Pharmacodynamics (Synergism)	Increased AKI alerts in NSAID users	Impaired glomerular hemodynamics	Reliance on electronic alerts
[16]	Systematic review protocol	ARB + NSAIDs + diuretics	Pharmacodynamics (Synergism)	Increased AKI risk reported	Combined effects on renal perfusion	Protocol paper; no outcome data
[17]	Narrative review	ARB + NSAIDs	Pharmacodynamics (Synergism)	Increased risk of renal impairment	Afferent vasoconstriction and efferent vasodilation	Narrative review
[8]	Older adults; population-based cohort	ARB + NSAIDs	Pharmacodynamics (Synergism)	Increased AKI and hyperkalemia risk (first 30 days)	Decreased GFR due to altered renal blood flow	Observational design
[18]	Hospitalized geriatric patients; retrospective cohort	NSAIDs + diuretics + RAAS inhibitors	Pharmacodynamic (Negative synergy)	AKI risk increased 2–3 fold	Hypovolemia and reduced renal perfusion	Single-center study
[19]	Hospitalized patients; case–control study	NSAIDs + diuretics	Pharmacodynamic (Negative synergy)	NSAIDs (OR 2.39) and diuretics (OR 2.64) for D-AKI.	Reduced intravascular volume and renal blood flow	Hospital-based population
[20]	Older adults; nationwide cohort study	NSAIDs + RAAS inhibitors + diuretics	Pharmacodynamic (Negative synergy)	Nearly doubled AKI incidence	Combined nephrotoxic hemodynamic effects	Administrative data
[21]	Hypertensive patients with osteoarthritis; prospective study	Amlodipine / Ramipril + Aceclofenac	Pharmacodynamic (Antagonism)	Greater BP increase with ACEI than CCB	Reduced vasodilatory prostaglandins	Small sample size
[22]	Hypertensive patients; experimental study	Meloxicam + antihypertensives	Pharmacodynamics (Antagonism)	Increased BP parameters	Sodium retention and vasoconstriction	Short duration
[23]	Primary care patients; observational study	Amlodipine + Piroxicam	Pharmacodynamics (Antagonism)	Reduced BP-lowering effect	Renal prostaglandin inhibition	Single-center study

Table 2. Summarizes the characteristics of the included studies by presenting study population, design, type of drug interaction, reported clinical outcomes, and key limitations. Quantitative risk estimates such as odds ratios or incidence rates are reported when available to emphasize clinical relevance. For studies without numerical risk data, outcomes are described qualitatively. This structured presentation facilitates comparison of evidence strength across heterogeneous study designs.

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Discussion

Interaction of β-blocker Drugs with NSAID Drugs

Overall, the interaction between β-blockers and NSAIDs is predominantly pharmacodynamic and is mainly associated with attenuation of antihypertensive efficacy rather than a consistent increase in major cardiovascular events. Several studies indicate that NSAID use can interfere with blood pressure control in patients receiving β-blockers by inhibiting prostaglandin synthesis, leading to sodium and fluid retention and increased peripheral vascular resistance. These effects are particularly relevant in elderly patients, who often have reduced renal reserve and are more susceptible to volume-related blood pressure changes.

However, the clinical significance of this interaction varies across studies. While multiple observational studies report worsened blood pressure control with chronic NSAID use, Dong et al. [11] did not observe a significant increase in major cardiovascular outcomes among hypertensive patients using NSAIDs concomitantly with β-blockers. This discrepancy may be explained by differences in study endpoints and exposure duration. Dong et al. focused on short-term cardiovascular outcomes and moderate NSAID exposure, whereas other studies primarily assessed longitudinal blood pressure changes, which may be more sensitive to prostaglandin-mediated renal and vascular effects.

In addition, heterogeneity in NSAID type (selective versus non-selective COX inhibitors), baseline renal function, and concomitant antihypertensive regimens may further contribute to inconsistent findings. Taken together, the current body of evidence suggests that although β-blocker–NSAID interactions may not substantially increase short-term cardiovascular risk, they can compromise long-term blood pressure control, particularly in geriatric patients with prolonged NSAID use. The overall strength of evidence is moderate, as most studies are observational and subject to residual confounding.

Interaction of ACE Inhibitor Drugs with NSAID Drugs

The interaction between ACE inhibitors and NSAIDs has been more consistently associated with adverse renal outcomes, particularly acute kidney injury (AKI). Mechanistically, ACE inhibitors induce efferent arteriolar vasodilation, reducing intraglomerular pressure, while NSAIDs inhibit prostaglandin-mediated afferent arteriolar vasodilation. The combined effect results in reduced glomerular filtration, especially in patients with compromised renal perfusion.

Evidence from cohort and retrospective studies suggests that the concurrent use of ACE inhibitors and NSAIDs significantly increases the risk of AKI and electrolyte disturbances in elderly patients. For instance, Lim et al. [9] reported a 16.7% incidence of AKI and hyperkalemia within 30 days of NSAID initiation among older adults receiving ACE inhibitors or ARBs, underscoring the clinical relevance of this interaction. Studies reporting higher renal risk often involved prolonged NSAID exposure or concomitant diuretic use, indicating a cumulative pharmacodynamic effect.

Variability in reported risk magnitude may be attributed to differences in baseline renal function, NSAID dosing, and duration of exposure. Despite these variations, the direction of effect across studies remains consistent. Overall, the strength of evidence supporting ACE inhibitor–NSAID interactions is moderate to high, supported by biological plausibility and reproducible findings across large observational cohorts.

Interaction of ARB Class Drugs with NSAID Class Drugs

Similar to ACE inhibitors, ARBs interact with NSAIDs primarily through pharmacodynamic mechanisms affecting renal hemodynamics. ARBs reduce intraglomerular pressure by dilating efferent arterioles, while NSAIDs cause afferent arteriolar vasoconstriction through prostaglandin inhibition. Even in the absence of diuretics, this combination can lead to a clinically meaningful reduction in glomerular filtration rate.

Population-based studies consistently demonstrate an elevated risk of AKI and hyperkalemia following NSAID initiation in patients receiving ARBs. For example, Nash et al. [8] showed a significantly increased risk of renal adverse events in older adults during the first 30 days of concomitant ARB and NSAID therapy, suggesting that the early phase of combined exposure represents a critical window of vulnerability. Differences in reported outcomes likely reflect variations in NSAID potency, dosing, and patient comorbidity profiles.

Although most evidence is derived from observational studies, the consistency of findings across populations strengthens the overall conclusion. The ARB–NSAID interaction poses a clinically relevant renal risk in geriatric patients, and the overall strength of evidence is considered moderate.

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Interaction of Diuretic Drugs with NSAID Drugs

The interaction between diuretics and NSAIDs is a central component of the well-recognized "triple whammy" effect when combined with RAAS inhibitors. Diuretics reduce intravascular volume, NSAIDs impair compensatory afferent arteriolar vasodilation, and RAAS inhibitors reduce efferent arteriolar tone, collectively leading to a marked reduction in renal perfusion.

Several retrospective cohort and case–control studies demonstrate that the combined use of NSAIDs and diuretics substantially increases the risk of AKI in elderly patients. Bories et al. [18], for instance, reported a two to three-fold increase in AKI incidence among hospitalized older adults receiving NSAIDs in combination with diuretics and RAAS inhibitors. These risks are further exacerbated by dehydration, acute illness, and pre-existing renal impairment.

Despite the observational nature of the data, the consistency of findings across different clinical settings strengthens the evidence base. Among antihypertensive drug classes, the diuretic–NSAID interaction represents one of the most clinically significant risks in geriatric pharmacotherapy. The overall strength of evidence is moderate to high.

Drug Interactions Between Calcium Channel Blockers and NSAID Drugs

Compared with other antihypertensive classes, calcium channel blockers appear to be less affected by NSAID-induced prostaglandin inhibition. CCBs lower blood pressure primarily through direct vascular smooth muscle relaxation, a mechanism less dependent on renal prostaglandins. Consequently, several studies report only modest attenuation of antihypertensive efficacy when CCBs are used concomitantly with NSAIDs.

This relative resistance is supported by comparative clinical studies. Raman et al. [21] demonstrated that aceclofenac caused a smaller increase in blood pressure among patients treated with amlodipine compared with those receiving ACE inhibitors, highlighting class-specific differences in NSAID sensitivity. These findings suggest that CCBs may be preferable in patients requiring concomitant NSAID therapy.

Nevertheless, elderly patients receiving CCBs and NSAIDs remain at risk of renal adverse effects related to sodium retention and reduced renal perfusion. Most evidence in this area is derived from small prospective studies and observational data, limiting generalizability. Overall, the strength of evidence for clinically significant CCB–NSAID interactions is low to moderate.

Differences Between Non-Selective and COX-2 Selective NSAIDs

Although NSAIDs are often discussed as a single class, clinically relevant differences exist between non-selective NSAIDs and COX-2 selective inhibitors. Non-selective NSAIDs inhibit both COX-1 and COX-2, leading to greater prostaglandin suppression, sodium retention, and attenuation of antihypertensive effects. In contrast, COX-2 selective inhibitors may exert a relatively smaller impact on blood pressure control but remain associated with renal effects and increased cardiovascular risk in susceptible patients.

Evidence from included studies, including Dong et al. [11] suggests a graded risk rather than a uniform effect across NSAID classes when used concomitantly with antihypertensive therapy. These findings indicate that recommendations for avoidance or intensive monitoring should not be uniformly applied to all NSAIDs. Instead, NSAID selection and monitoring in geriatric patients should be individualized based on NSAID class, duration of use, dose, and patient-specific renal and cardiovascular risk factors.

Overall Strength and Limitations of the Evidence

Across antihypertensive classes, interactions with NSAIDs in geriatric patients are predominantly pharmacodynamic and clinically relevant, particularly with prolonged NSAID exposure. However, the majority of available evidence is observational, with inherent limitations including confounding by indication, heterogeneous study designs, and variability in NSAID type, dosage, and treatment duration. Randomized controlled trials focusing specifically on elderly populations remain limited.

Despite these limitations, the consistency of mechanistic pathways and recurring findings of impaired blood pressure control and increased renal risk support the clinical importance of these interactions. From a clinical perspective, careful patient selection, routine monitoring of renal function and electrolytes, and the use of the lowest effective NSAID dose for the shortest possible duration are essential strategies when managing geriatric patients receiving antihypertensive therapy.

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Potential Pharmacokinetic Interactions and Scope of the Review

Although the interactions between antihypertensive drugs and NSAIDs are predominantly pharmacodynamic, potential pharmacokinetic interactions may also occur, particularly in geriatric patients. Age-related changes in body composition, plasma protein levels, and hepatic metabolic capacity may influence drug distribution and metabolism. For example, competition for plasma protein binding sites could theoretically alter the free fraction of highly protein-bound drugs, while alterations in cytochrome P450 enzyme activity may affect the metabolism of certain antihypertensive agents and NSAIDs.

However, current evidence suggests that these pharmacokinetic interactions are less consistently documented and are generally of limited clinical significance compared with pharmacodynamic mechanisms. Most reported adverse outcomes, including impaired blood pressure control and renal dysfunction, are more directly attributable to pharmacodynamic effects on renal hemodynamics and vascular regulation. Therefore, this review primarily focuses on pharmacodynamic interactions that are supported by stronger and more clinically relevant evidence, while acknowledging the potential contribution of pharmacokinetic mechanisms in specific clinical contexts.

Clinical Implications, Pain Management Strategies, and Therapeutic Alternatives

In geriatric patients with hypertension, pain management should prioritize therapeutic options with minimal impact on blood pressure and renal function. Paracetamol remains the first-line analgesic for mild to moderate pain due to its favorable cardiovascular and renal safety profile. When inflammatory pain requires additional treatment, topical NSAIDs may be considered to limit systemic exposure, while systemic NSAIDs should be reserved for short-term use at the lowest effective dose.

For chronic musculoskeletal or neuropathic pain, adjuvant analgesics such as antidepressants (e.g., duloxetine) and anticonvulsants (e.g., pregabalin) may represent effective alternatives, potentially reducing the need for NSAID therapy. Non-pharmacological interventions, including physiotherapy, weight reduction, and transcutaneous electrical nerve stimulation (TENS), play a crucial role in pain management and are particularly suitable for elderly populations.

When systemic NSAIDs are unavoidable, careful agent selection, limited duration of therapy, and structured monitoring of renal function and electrolytes are essential. Gastroprotective strategies, such as proton pump inhibitors, should be considered in patients at increased gastrointestinal risk, while remaining mindful of overall medication burden and potential drug–drug interactions.

Limitations of the Review

This review has several limitations. Most included studies were observational, limiting causal inference. Heterogeneity in study design, outcome definitions, and populations precluded quantitative meta-analysis, resulting in a qualitative synthesis. Publication bias cannot be excluded, as studies with negative findings may be underrepresented. Although the search period was defined as 2015–2025, only articles available at the time of manuscript preparation were included.

Conclusions

This review highlights clinically relevant interactions between antihypertensive drugs and NSAIDs in geriatric patients, predominantly mediated through pharmacodynamic mechanisms affecting blood pressure control and renal function. Given the heterogeneity of risk across antihypertensive classes and NSAID types, a risk-stratified and individualized approach is essential. Optimizing pain management through safer pharmacological alternatives, non-pharmacological interventions, and appropriate monitoring may substantially reduce preventable drug-related harm while maintaining effective hypertension control in elderly populations.

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