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ANALGESIC USE AND ASSOCIATED ADVERSE EVENTS IN PATIENTS WITH CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW

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Abstract

Background: *Chronic kidney disease and pain substantially impact the quality of life and hospital costs worldwide. Treating these conditions can be challenging due to characteristic pharmacokinetic and pharmacodynamic challenges.*

Aim: *This study aims to identify the correlation between analgesic consumption and adverse outcomes in individuals with chronic kidney disease.*

Methods: *The study complied with PRISMA 2020 guidelines and applied a timeframe of 2013-2023 to ensure similarity through comparison with existing literature. Specialists used online reference databases such as Pubmed and SagePub to identify review articles, preexisting publications, and incomplete works.*

Result: *219 and 112 articles have been extracted from PubMed and SagePub, respectively. In 2013, we collected 12 papers accomplishing specific research criteria, consisting of 8 from PubMed and 4 from SagePub.*

Conclusion: *Patients with CKD require a strategy to minimize adverse consequences and maximize beneficial effects.*

Keyword: *Adverse events; Analgesic; Chronic kidney disease*

INTRODUCTION

Analgesics are drugs used for pain management and treatment, such as acetaminophen, antidepressants, and opioids.[1] IASP states that pain is an unpleasant sensory and emotional experience associated with tissue damage.[2] CKD patients commonly suffer severe pain, which affects their quality of life and medical costs. The susceptible population's endemic pharmacokinetics and pharmacodynamics provide challenges for treatment.[3,4]

Doctors frequently depend on non-specific guidelines such as the WHO three-step ladder or clinical experience for prescribing in cancer pain management due to factors such as complex co-morbidities and limited evidence-based guidance.[5]

Previous Investigation indicates that it is beneficial to limit or avoid the use of NSAIDs in individuals with lower eGFR due to the heightened potential for toxicity, metabolite accumulation, and progression of CKD.[6,7] The association between elevated gabapentinoid usage, opioid prescriptions, drug-related fatality, and insufficient recognition in individuals with reduced eGFR warrants attention.[8]

Studies indicate a correlation between the utilization of analgesics and adverse effects in individuals with chronic kidney disease.

METHODS

The study followed the PRISMA 2020 guidelines to obtain current results regarding administering analgesics and adverse outcomes in individuals with chronic kidney disease. A literature review is essential for prompt intervention and emphasizing the topics' significance.

Researchers must submit documentation proving their eligibility for publication, including English manuscripts that concentrate on the use of analgesics and adverse events in patients with chronic kidney disease. The assessment will evaluate publications from 2014 to the present, which include editorials, non-DOI applications, previously published review articles, and submissions that resemble existing journal papers.

A systematic review investigated the association between analgesic use, chronic kidney disease, and adverse events. The study utilized the PubMed and SagePub databases: *("analgesic s"[All Fields] OR "analgesically"[All Fields] OR "analgesics"[Pharmacological Action] OR "analgesics"[MeSH Terms] OR "analgesics"[All Fields] OR "analgesic"[All Fields]) AND ("adverse"[All Fields] OR "adversely"[All Fields] OR "adverses"[All Fields]) AND ("event"[All Fields] OR "event s"[All Fields] OR "events"[All Fields]) AND ("renal insufficiency, chronic"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields] AND "chronic"[All Fields]) OR "chronic renal insufficiency"[All Fields] OR ("chronic"[All Fields] AND "kidney"[All Fields] AND "disease"[All Fields]) OR "chronic kidney disease"[All Fields])* used in searching the literature.

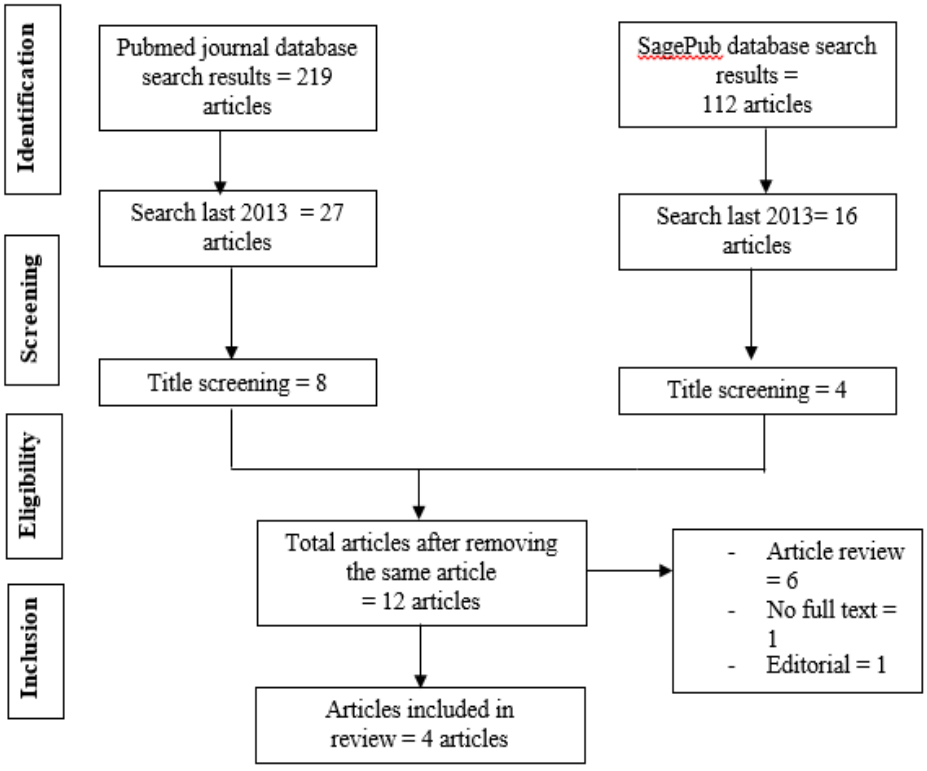

Figure 1. Article search flowchart

The study's validity was evaluated by examining the abstract and title, investigating historical records, and conducting experiments with comparable methodologies. The systematic review incorporated studies that met pre-established criteria. However, a limited number of outcomes were obtained. The research paper presented a list of subjects, authors, dates, places, topics, and parameters, eliminating duplicates. Two reviewers analyzed the titles and abstracts of the papers.

The study's validity was evaluated by examining the abstract and title, scrutinizing historical records, and conducting experiments with comparable methodologies. A systematic review was performed, with a focus on literature that met pre-established criteria. The research paper comprised distinct subjects, authors, dates, places, topics, and parameters, eliminating redundancies. Two reviewers assessed the feasibility of research and data collection by analyzing the titles and abstracts of papers. The judges decided, and the authors evaluated abstracts and labels to determine qualifying documents. After completing primary education, specific subjects were examined, and corresponding research and review articles were chosen.

RESULT

219 and 112 articles were retrieved from PubMed and SagePub, respectively. In 2013, we collated 12 papers, 8 from PubMed and 4 from SagePub, of which four met the research criteria.

Kimmel et al. (2017)[9] discovered that long-term opioid prescriptions were present in 20% of patients, leading to elevated mortality rates, discontinuation of dialysis, and hospitalization. The association between higher opioid doses and mortality indicates that opioid prescription could be an indication of the disease.

Advanced CKD patients are more likely to be prescribed opioids and gabapentinoids, which may be attributed to regional variation, as per Novick, et al (2018)[10] study. This underscores the necessity for enhanced awareness and safety investigations in clinical settings

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Kimmel, 2017[9]	United State of America (USA)	Retrospective cohort study	153,758 patients	Opioid prescriptions may elevate mortality risk and hospitalization rates among dialysis patients, potentially indicating morbidity. Reducing opioid prescriptions and addressing pain treatment is critical to optimizing patient outcomes.
Novick, 2018[10]	USA	Retrospective cohort study	333,049 patients	Further research is required to enhance awareness and safety measures concerning the utilization of opioids and gabapentinoids in patients with chronic kidney disease.
Lee, 2020[11]	Taiwan	Retrospective cohort study	26,029 patients with CKD	Opioid consumption is associated with higher mortality rates in individuals with chronic kidney disease but not those considered frail.
Zhan, 2020[12]	USA	Prospective cohort study	3,939 patients with CKD	Opioid usage correlates more strongly with adverse events of NSAIDs, while its association with the black race and renal disease outcomes is restricted.

According to the modified FRAIL scale, Lee (2020)[11] study, opioid use was associated with a significant increase in mortality risk, leading to a mortality rate of 18.4% of the population after 4.2 years. Opioid users had a higher risk of adverse effects than opioid-naive individuals, with a relationship accommodating to both dose and duration.

The subcohort study reported that time-updated NSAID usage was linked to an elevated risk of kidney disease composite and hospitalization. However, these associations did not reach statistical significance. Ethnicity was a significant factor in the association, with a higher risk observed among individuals of black ethnicity. The use of NSAIDs was linked to reduced risk of kidney failure requiring KRT in women and those with a glomerular filtration rate of 45mL/min/1.73m^2.[12]

DISCUSSION

CKD is a global public health concern that impacts kidney function at all levels, contributing to significant financial consequences.[13,14] Chronic Kidney Disease (CKD) is characterized by impaired kidney function, indicated by a decrease in Glomerular Filtration Rate (GFR) below 60 mL/min/1.73 m^2 for over three months. This condition is caused by reduced functional mass and loss of nephrons.[13,15]

Chronic kidney disease (CKD) patients experience high medication impact, pain management challenges, and the absence of established recommendations.[16,17] Patients with impaired renal function require specific measures for drug toxicity, adverse reactions, dose modifications, and drug interactions. Opiates and NSAIDs may prolong half-life, leading to central nervous system complications.[18]

Using NSAIDs in individuals with chronic kidney disease (CKD) increases the likelihood of experiencing gastrointestinal bleeding, acute renal impairment, and cardiovascular incidents. No significant difference was observed between the two groups. There was no observed association between NSAIDs and the development of CKD. Opioid use exhibited a stronger correlation with unfavorable occurrences compared to NSAIDs. However, the latter's association was restricted to individuals of black ethnicity.[12,19,20]

CKD patients typically experience neurological problems, which lead to increased lethargy and a higher prevalence of opioid use compared to NSAID consumption. The association between opioid abuse and morbidity and mortality has been established for a while. Confirmation promoting pain relief is inconclusive and demonstrates minimal advantages over a placebo.[11,19–21]

CKD patients frequently experience neurological impairment, leading to increased lethargy and a higher prevalence of opioid use compared to NSAID consumption, with a ratio of 1 per 2.5. The association between opioid use and morbidity and mortality is well-established. However, evidence supporting the efficacy of opioids in pain management is limited and often insignificant compared to placebo..[12,19]

The meta-analysis revealed that high doses of NSAIDs significantly elevate the risk of accelerated progression of CKD. In contrast, regular doses do not impact kidney function in patients with moderate to severe CKD. A recent meta-analysis revealed that the crude risk of acute kidney injury (AKI) was 1.63 times higher in patients with chronic kidney disease (CKD) who received NSAID treatment than those who did not. [22]

Additional research indicates a necessity for heightened consciousness concerning the utilization of opioids and gabapentinoids among individuals with chronic kidney disease. Furthermore, the results emphasize the need for further research to ascertain the safety of these medications in clinical settings.[10]

CONCLUSION

Patients with chronic kidney disease exhibit elevated rates of analgesic usage, necessitating meticulous evaluation for effective therapy and reduced adverse effects.

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