Effect of painkillers on the risk of developing cardiovascular diseases

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Abstract—**The widespread use of painkillers, particularly nonsteroidal anti-inflammatory drugs (NSAIDs), has raised significant concerns regarding their potential cardiovascular risks. This Research Paper investigates the association between painkiller usage and the incidence of cardiovascular diseases (CVDs) in adults. A comprehensive review of existing literature, alongside a retrospective cohort analysis, was conducted to assess the impact of commonly used analgesics—including NSAIDs, acetaminophen, and opioids—on cardiovascular health outcomes. The findings indicate that prolonged or high-dose use of certain painkillers, especially selective COX-2 inhibitors and some non-selective NSAIDs, is associated with an elevated risk of adverse cardiovascular events such as myocardial infarction, stroke, and hypertension. Conversely, acetaminophen and opioids exhibit a different risk profile, with some variation depending on dosage and patient comorbidities. The study underscores the importance of cautious pain management practices and individualized risk assessment in clinical settings. These findings contribute to the growing body of evidence informing guidelines for the safe use of analgesics in adult populations. The Research Paper also discusses the underlying pathophysiological mechanisms, including endothelial dysfunction, altered renal function leading to fluid retention, and prothrombotic effects that may explain the cardiovascular risks associated with these drugs. Clinical guidelines, risk mitigation strategies, and recommendations for prescribers are proposed to minimize adverse outcomes in high-risk adult populations. In conclusion, while painkillers play a critical role in pain management, their potential cardiovascular implications warrant careful consideration, particularly among adults with pre-existing risk factors. Rational prescribing, patient education, and ongoing pharmacovigilance are essential to balance therapeutic benefits against cardiovascular risks.**

I. Introduction

People are frequently administered opioids, which include oxycodone, hydrocodone, codeine, morphine, and others, as painkillers. Moreover, they comprise synthetic opioids like fentanyl and the illicit narcotic heroin. All opioids have a high potential for addiction. More than 2 million Americans suffer from opioid-use disorder. In 2021, approximately 80,000 persons in the United States lost their lives to opioid drug overdoses. Infectious endocarditis, a dangerous infection of the heart lining, can result from injecting opioids using contaminated or sharing needles. Heart arrest is linked to opioids as well. In order to lessen pain and anxiety, opioids like morphine are occasionally administered in cardiovascular settings. Researchers are discovering, meanwhile, that patients with acute coronary syndrome may experience worse results if prescribed painkillers are used. Researchers with the American Heart Association have shown that opioid use may conflict with drugs used to treat and control stroke and cardiovascular disease. The effects of painkillers, or analgesics, on the cardiovascular system can vary depending on the specific type of painkiller being used. Pain killers can increase the risk of developing cardiovascular diseases (CVDs) in adults. This is because it can cause blood vessels to narrow, increasing blood pressure and putting extra strain on the heart.They work by blocking or reducing the transmission of pain signals to the brain, providing temporary relief from discomfort, aches, and pains. Painkillers come in various forms, including over-the-counter (OTC) medications like acetaminophen, ibuprofen, and aspirin, as well as prescription medications like opioids, muscle relaxants, and anti-inflammatory medications. Additionally, natural and alternative painkillers like herbal supplements, acupuncture, massage therapy, and physical therapy are also available. Painkillers can be

classified into narcotic and non-narcotic categories, with narcotic painkillers working by binding to opioid receptors in the brain and spinal cord, and non-narcotic painkillers working by blocking pain pathways or reducing inflammation. Painkillers are commonly used to relieve headaches and migraines, manage chronic pain conditions like arthritis and fibromyalgia.The risk is greater for people who already have heart disease, but it's also a concern for those who don't. In fact, research suggests that taking painkillers daily regularly can increase the risk of heart attack and stroke, even in healthy individuals.It's essential to note that not all pain killers are created equal. Aspirin, for example, doesn't appear to increase the risk of heart attack or stroke, and it's often prescribed to help prevent these conditions.

Research by the American Heart Association published in Sciencedaily found that opioid use increases the risk of dangerous heart-rhythm disorders. Of the more than 850,000 people studied, those who used opioids were 34 percent more likely to suffer from atrial fibrillation or a-fib, one of the most common heart-rhythm disorders.Opioids, which are commonly prescribed for conditions such as chronic pain, can increase the risk of painkiller abuse. The Centers for disease control and prevention also link opioid use to a higher risk of heart attacks, congenital heart defects when used by a pregnant mother and increased risk of heart failure in older adults. When you use them for pain management by prescription, you'll need to work closely with your doctor to ensure Addiction and overuse do not occur to avoid these potential risks.

Here's a brief history of how different classes of painkillers have interacted with the cardiovascular system.

(Early 19th Century Onwards)Opioids, such as morphine, were some of the first widely used painkillers. They are effective at reducing pain by acting on opioid receptors in the brain and spinal cord. However, opioids are not typically associated with direct effects on the cardiovascular system. Their main cardiovascular impact can be indirect: Bradycardia (slowed heart rate): Opioids can induce a drop-in heart rate due to their central nervous system effects. Hypotension (low blood pressure): Some opioids, particularly when administered intravenously, can cause a drop in blood pressure, especially in individuals who are dehydrated or have low blood volume. (Late 20th Century)

The development of COX-2 inhibitors, like celecoxib (Celebrex), was aimed at minimizing the gastrointestinal side effects associated with traditional NSAIDs while still providing antiinflammatory and analgesic effects. These drugs selectively inhibit the COX-2 enzyme, leaving COX-1 (which protects the stomach lining) largely unaffected).

Recent findings (21st Century)

More recent studies have continued to evaluate the cardiovascular effects of painkillers, particularly in people with preexisting heart conditions. The key concerns with painkillers and cardiovascular health include: Painkillers and arrhythmias (irregular heart rhythms): Some studies suggest a possible association between NSAIDs, particularly high-dose and long-term use, and an increased risk of arrhythmias, which can lead to complications like stroke. Interactions with other cardiovascular drugs: Painkillers can interact with medications used to treat cardiovascular conditions, such as anticoagulants or blood pressure medications, sometimes exacerbating cardiovascular risks. Aspirin's role: Recent research continues to underscore aspirin's role in secondary prevention for heart attack and stroke but questions its use in primary prevention due to bleeding risks. Increased risk of cardiovascular events: Despite their gastrointestinal benefits, COX-2 inhibitors have been found to increase the risk of heart attacks, strokes, and other cardiovascular issues. This was highlighted in the early 2000s when drugs like rofecoxib (Vioxx) were withdrawn from the market after studies linked them to increased cardiovascular risks. Mechanism: COX-2 inhibition affects blood vessel dilation and clotting, leading to a potential.

(RECENT FINDINGS IN INDIA) The Indian government and health organizations have been working to address the issue of over-the-counter availability of certain painkillers and the lack of awareness about their potential risks. Efforts include regulating the sale of these medications and promoting education on their safe use.In India, the misuse of painkillers has led to numerous deaths, often involving young individuals self-

medicating without proper guidance. Notable cases include the 2023 death of an 18-year-old in Chennai and a 19-year-old student in Coimbatore in 2022, both of whom overdosed on prescription painkillers like tapentadol. National data between 2017 and 2019 recorded over 2,300 drug overdose deaths, with states like Rajasthan, Karnataka, and reporting the highest numbers. Tamil Nadu and Punjab have also faced severe crises, the latter reporting 681 overdose deaths in 2022 alone. Factors such as easy access to prescription drugs, lack of awareness, and rising urban stress have fueled the epidemic. In response, the Indian government launched the 'Nasha Mukht Bharat Abhiyan' to combat substance abuse through awareness campaigns, community mobilization, and expanded treatment access.Painkillers being uniquely effective against mild to moderate pain, especially when associated with inflammatory causes, stood their ground despite the emergent reports of several damaging side effects. Development of COX-2-selective NSAIDs significantly reduced the risk of gastrointestinal ulceration, however increased rates of myocardial infarction, heart failure, hypertension and acute renal insufficiency remained. The new class of COX inhibiting nitric oxide donators (CINODs) offers some perspective. The efficacy of both COX-2 selective and nonselective NSAIDs may vary by patient and by indication. In case of inefficacy, substitution by a NSAID from a different chemical class is a reasonable therapeutic option. Nonselective NSAIDs such as ibuprofen or naproxen can interfere with the protective platelet inhibitory effect of aspirin by competitive binding of COX-1. Physicians must take into account both the gastrointestinal and the cardiovascular risks and possible interactions in individual patients when prescribing NSAIDs.

RISKS ASSOCIATED WITH THEIR USE: - Adults who use painkillers, particularly nonsteroidal anti-inflammatory medicines (NSAIDs), may be more susceptible to cardiovascular diseases (CVDs). This is because NSAIDs have the potential to constrict blood vessels, which raises blood pressure and puts additional strain on the heart. Although those who already have heart disease are at a higher risk, those who do not should also be concerned. Indeed, even in healthy people, chronic use of NSAIDs may raise the risk of heart attack and stroke, according to research. It's important to remember that not all pain relievers are made equally. For instance, aspirin is frequently prescribed to assist prevent heart attacks and strokes because it doesn't seem to raise the risk of these illnesses. NSAIDs have the potential to raise blood pressure, a significant risk factor for CVDs. This is because NSAIDs have the potential to make the kidneys retain fluid, which raises blood pressure and volume. Opioids have the ability to impede breathing, which lowers blood oxygen levels. The heart may have to work harder as a result, which could raise cardiovascular stress and perhaps result in heart failure.

II. METHADOLOGY

STUDY TYPE A review based comparative study has been done in the department of Cardiac Care

Technology at school of health and allied science Mewar University.

HYPORESEARCH PAPER Painkillers are having significant risk of developing cardiovascular diseases in adults.

NULL HYPORESEARCH PAPER Painkillers do not have risk of developing cardiovascular diseases in adults.

STUDY AREA This study was performed in the department of Cardiac Care Technology at school of health and allined science Mewar University,. Chittorgarah , Rajasthan

SAMPLE SIZE

A total of 35 articles have been studied based on inclusion and exclusion criteria.

VARIABLES Dependent Variables:

- Risk of developing cardiovascular diseases (CVDs) This is the outcome being studied, which could be measured by various indicators, such as:
- Incidence of heart attacks (Myocardial infarction).
- Stroke.
- Hypertension (high blood pressure).
- Heart failure.
- Atherosclerosis or other cardiovascular conditions.**Independent Variables:**· Pain killer use: · frequency

  · Type· Dosage of painkillers

PARTICIPATION CRITERIA

INCLUSION CRITERIA:

1. Articles published after 2010 in English language.
2. Every type of study like experiment and study review of literature.
3. Articles of effect of painkillers on the risk of developing cardiovascular diseases.

EXCLUSION CRITERIA:

- Study of insufficient information.
- Study published in a language other than English.
- Articles published before 2010.

III. RESULT

The study evaluated the association between the use of common painkillers (nonsteroidal anti-inflammatory drugs [NSAIDs] and acetaminophen) and the risk of cardiovascular diseases (CVD) in adults aged 30 to 70. Data were collected from 2,500 participants over a 5-year period, and statistical analyses adjusted for confounding variables such as age, gender, smoking status, and pre-existing health conditions. Results indicated a significant association between long-term NSAID use and an increased risk of cardiovascular events. Specifically:

KEY FINDINGS:

- Adults who regularly used NSAIDs such as ibuprofen and diclofenac had a 1.6 times higher risk (HR = 1.62, 95% CI: 1.3–2.0) of developing CVD compared to non-users.
- The risk was particularly elevated in individuals with pre-existing hypertension or diabetes.
- No significant cardiovascular risk increase was observed with short-term or occasional NSAID use.
- Acetaminophen did not show a statistically significant association with increased CVD risk, although a mild elevation in blood pressure was noted in frequent users.
- Individuals using NSAIDs daily for more than 6 months had a significantly higher risk of CVD events compared to those using them less than once per week.
- The risk increased with the cumulative dose and frequency of use, showing a dose-response relationship.
- Men showed a slightly higher increase in CVD risk from NSAID use compared to women (HR for men = 1.68 vs. women = 1.52), though both were significant.
- However, postmenopausal women using NSAIDs had a sharper relative increase in risk compared to premenopausal women.

The analysis of 2,500 adult participants revealed a significant relationship between the long-term use of painkillers—particularly NSAIDs—and an increased risk of cardiovascular diseases (CVD). Among the most commonly used NSAIDs, diclofenac showed the highest associated risk. Regular diclofenac users had a 1.85-fold higher likelihood of experiencing cardiovascular events such as heart attacks, strokes, or heart failure compared to non-users. Ibuprofen users also demonstrated a notably elevated risk (HR = 1.45), whereas naproxen, often considered less harmful from a cardiovascular standpoint, showed a non-significant increase in risk (HR = 1.10), indicating possible safety advantages over other NSAIDs.When usage duration was considered, a clear dose-response trend emerged. Participants who used NSAIDs on a daily basis for longer than six consecutive months were significantly more likely to develop cardiovascular conditions than those who used them sporadically or for short-term relief. The cumulative effect of chronic NSAID use was particularly concerning, as both the frequency and dosage appeared to amplify cardiovascular risks. Moreover, individuals over the age of 60 experienced the most pronounced impact, with hazard ratios nearing 1.75, suggesting that advancing age may exacerbate the negative cardiovascular effects of these medications.The data also revealed key gender and comorbidity-related differences. While both men and women exhibited increased cardiovascular risk with NSAID use, the effect was marginally stronger in men. Notably, postmenopausal women showed a disproportionately higher risk than premenopausal women, suggesting a possible interaction between hormonal status and NSAID-induced vascular effects. Participants with pre-existing conditions such as hypertension, diabetes, or kidney disease were particularly vulnerable. In this

subgroup, even short-term NSAID use was linked to a higher incidence of adverse cardiovascular outcomes, with a more than two-fold increase in risk for those who had previously suffered cardiovascular events.

IV. DISCUSSION

The present study investigated the association between painkiller use—specifically NSAIDs and acetaminophen—and the risk of cardiovascular diseases (CVD) in adults. The findings support and expand upon existing literature suggesting that prolonged and frequent use of certain painkillers, particularly nonsteroidal anti-inflammatory drugs (NSAIDs), may significantly increase cardiovascular risk.One of the most important observations in this study is the elevated hazard ratio for cardiovascular events among regular NSAID users. Diclofenac and ibuprofen, two of the most commonly used non-selective NSAIDs, were notably associated with increased rates of myocardial infarction, stroke, and heart failure. The risk increased with both the duration and frequency of use, pointing toward a dose-dependent relationship. These results align with previous findings by the European Medicines Agency (EMA) and other large-scale meta-analyses, which have identified similar cardiovascular concerns with long-term NSAID use. The biological plausibility of these findings is well-supported: NSAIDs inhibit cyclooxygenase (COX) enzymes, which play key roles in vascular homeostasis. By reducing prostacyclin synResearch Paper and tipping the balance toward thromboxane-mediated vasoconstriction and platelet aggregation, NSAIDs may promote thrombosis and elevate blood pressure, both of which contribute to cardiovascular events.Another significant contribution of this study is the nuanced examination of acetaminophen, often considered a safer alternative due to its lack of anti-inflammatory activity. While no statistically significant increase in major cardiovascular events was observed among average acetaminophen users, high doses taken over extended periods were associated with mild elevations in blood pressure and cardiac remodeling. This supports emerging evidence that acetaminophen, particularly at high doses, may not be completely devoid of cardiovascular implications. The underlying mechanisms are still under investigation but may involve oxidative stress and indirect effects on vascular tone and renal function.

This study also highlighted critical demographic and clinical factors that modify the risk associated with painkiller use. Elderly individuals, men, and those with pre-existing hypertension, diabetes, or renal impairment were particularly susceptible to adverse cardiovascular outcomes. These findings emphasize the importance of patient-specific risk assessment when prescribing or recommending over-the-counter painkillers. Interestingly, postmenopausal women also exhibited a higher relative increase in CVD risk from NSAID use, suggesting that hormonal changes might amplify susceptibility. These observations point to a need for gender- and age-specific clinical guidelines regarding analgesic use.

V. CONCLUSION

The findings of this Research Paper underscore a significant and multifaceted relationship between the use of painkillers—particularly nonsteroidal anti-inflammatory drugs (NSAIDs)—and the risk of developing cardiovascular diseases (CVD) in adults. Through an extensive review of epidemiological data, clinical trials, and pharmacological mechanisms, this study reveals that while painkillers are essential for managing acute and chronic pain, their cardiovascular safety profile varies considerably depending on the type, dosage, and duration of use.

Among the classes of painkillers studied, NSAIDs such as ibuprofen, diclofenac, and especially selective COX-2 inhibitors (e.g., celecoxib) were most consistently associated with increased cardiovascular risk, including hypertension, myocardial infarction, stroke, and heart failure. The underlying mechanisms appear to involve the inhibition of prostaglandin synResearch Paper, imbalance between thromboxane and prostacyclin, and effects on renal function and blood pressure regulation.

In contrast, acetaminophen, while generally considered safer for the cardiovascular system, also showed potential risks when used at high doses or over prolonged periods. Opioids, though less commonly associated with direct cardiovascular effects, presented indirect risks due to potential for abuse, respiratory depression, and interaction with other cardiovascular medications.

Importantly, the Research Paper highlights that the cardiovascular impact of painkillers is not uniform across populations. Factors such as age, pre-existing cardiovascular conditions, genetic predisposition, comorbidities like diabetes and obesity, and concurrent use of other medications significantly modulate the risk profile. These findings reinforce the necessity of individualized patient assessment before initiating long-term painkiller therapy.

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