

FROM TOOTHACHE TO NEPHROPATHY: EXPLORING THE RENAL RISKS OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN DENTAL PRESCRIPTIONS

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Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently endorsed in dentistry practice for their effectiveness in analgesia and anti-inflammation, especially in managing odontogenic pain. The growing data connecting NSAID usage to adverse renal effects, such as acute kidney injury, exacerbation of chronic kidney disease, and electrolyte disturbances, prompts significant concerns, particularly regarding indiscriminate use or administration in at-risk populations. This narrative review examines the pathophysiological mechanisms underlying NSAIDs-induced nephrotoxicity, evaluates clinical evidence regarding renal outcomes associated with NSAIDs use, and highlights the risk factors that exacerbate renal impairment. It highlights the importance of enhanced awareness, patient screening, and interdisciplinary communication to mitigate nephrotoxic risks by connecting pharmacological insights with dental prescribing practices. The findings advocate for prudent NSAIDs application in dental care and recommend updating guidelines to address renal safety considerations.

Key Words: NSAIDs, nephrotoxicity, dental prescription, acute kidney injury, chronic kidney disease, odontogenic pain, COX inhibitors.

1. Introduction:

Dental pain represents a complex public health concern, transcending age, geographic boundaries, and socioeconomic status. Its etiology is multifactorial, arising from a combination of clinical pathologies such as dental caries and periodontal disease, as well as psychological factors like dental anxiety and broader social determinants including access to medical care. Evidence from diverse populations underscores the widespread nature of this issue. In Mexico, studies have reported dental pain prevalence rates of 34.0% and 28.0% among school-aged children aged 6 to 12 years (1,2). Among the same age population and adolescents in Brazil, the reported prevalence ranges from 31.6% to 35.7%, with higher rates observed in

individuals from socioeconomically disadvantaged backgrounds and those with dental fear (3,4). Adult populations exhibit a varied burden, with prevalence rates of 18.0% in Brazil with higher rates observed in younger adults (23.9%) compared to older adults (10.4%) (5) and 36.42% in South Korea, where pain was significantly linked to diminished quality of life and mental health challenges (6). While dental pain tends to decline with age, it remains a notable issue in vulnerable populations. For instance, among homeless individuals in Brazil, prevalence reaches an alarming prevalence of 50%, frequently characterized by severe pain and reliance on self-management strategies such as over-the-counter medication or tooth extraction (7).

These findings illustrate the widespread impact of dental pain and highlight the need for targeted interventions. Building upon this foundation, it is essential to recognize that dental pain does not occur in isolation but is deeply rooted in a matrix of contributing factors. Among these, sociodemographic determinants such as socioeconomic status, education, and gender play a pivotal role in shaping individual experiences of dental pain and access to care. A lower socioeconomic position is robustly associated with higher prevalence rates of dental pain, often due to structural barriers such as limited access to oral healthcare services, reduced utilization of preventive measures, and greater exposure to risk factors (1,4). Educational attainment also plays a pivotal role; individuals with lower levels of education are disproportionately affected, potentially due to lower oral health literacy and reduced engagement in health-promoting behaviors (4,5). Gender differences have similarly been documented, with women more frequently reporting dental pain than men, a trend observed in both Brazilian and South Korean cohorts, potentially reflecting differences in health-seeking behavior and pain perception (6,8).

Understanding these underlying determinants is crucial for prevention and also for guiding effective treatment strategies. As such, clinical management plays a vital role in mitigating the impact of dental pain, particularly in acute scenarios. Nonsteroidal anti-inflammatory drugs have become a cornerstone in the management of dental pain and inflammation, particularly for acute odontogenic pain. Their widespread use is attributed to their efficacy and established role as first-line treatments in various dental procedures.

The World Health Organization (WHO) has recommended NSAIDs as the primary medications for alleviating pain and inflammation in oral conditions (9).

While NSAIDs are indispensable in dental pain management due to their anti-inflammatory and analgesic properties, their use is not without clinical concern, particularly regarding renal safety. An increasing amount of evidence has underscored the potential nephrotoxic effects of NSAIDs, including diminished glomerular filtration rate (GFR), advancement of chronic kidney disease (CKD), and, in severe instances, renal papillary necrosis (10). These renal risks warrant particular attention in dental settings, where NSAIDs are frequently prescribed without routine assessment of renal function or awareness of cumulative exposure.

This narrative review aims to evaluate the renal implications of NSAIDs use in dental care, focusing on NSAIDs induced nephropathy mechanisms, risk profiles of various NSAIDs used in dentistry and practical implications for clinicians. To construct this review, a comprehensive literature search was undertaken across PubMed, Scopus, and Embase databases from their inception through 2025, by synthesizing data from narrative and systematic reviews, clinical trials, observational studies, and pharmacological analyses.

2. Non-Steroidal Anti-Inflammatory Drugs Pharmacology

2.1.Mechanism of Action

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a class of medications widely used for their anti-inflammatory, analgesic, and antipyretic properties (11). Their primary mechanism of action involves the inhibition of cyclooxygenase (COX) enzymes, which are key players in the synthesis of prostaglandins and thromboxane (12). These lipid compounds are central to the inflammatory response and various physiological processes (13).

The COX pathway begins with the conversion of arachidonic acid into prostaglandin H₂ (PGH₂) by COX enzymes. This step is followed by the action of specific synthases that produce various prostaglandins (e.g., PGE₂, PGD₂) (14) and thromboxane A₂ (TXA₂) (15). These molecules mediate inflammation, pain, fever, and other physiological responses.

Two main isoforms of COX have been identified: COX-1 and COX-2. COX-1 is constitutively expressed in most tissues and is responsible for maintaining physiological homeostasis, such as protecting the gastric mucosa and regulating renal function (16). COX-2, on the other hand, is inducible and is primarily associated with inflammatory responses. It is upregulated by pro-inflammatory stimuli, such as cytokines and growth factors, at sites of inflammation (14,17).

NSAIDs exert their therapeutic effects by inhibiting the COX enzymes, thereby reducing the production of prostaglandins and thromboxane. This inhibition occurs through the binding of NSAIDs to the active site of the COX enzymes, preventing the conversion of arachidonic acid into PGH₂. The anti-inflammatory effects of NSAIDs are primarily attributed to the inhibition of COX-2, while their

gastrointestinal and other side effects are largely due to the inhibition of COX-1 (17). While COX inhibition remains the primary mechanism of action for NSAIDs, research has identified several COX-independent pathways through which these drugs exert their effects. These include modulation of nuclear factor- κ B (NF- κ B), activation of peroxisome proliferator-activated receptor gamma (PPAR γ), and effects on ion channels and mitochondrial function.

The NF- κ B pathway is a key regulator of inflammation and is activated in response to pro-inflammatory stimuli. NSAIDs, such as aspirin and ibuprofen, have been shown to inhibit the activation of NF- κ B, thereby reducing the expression of pro-inflammatory genes (18).

PPAR γ is a nuclear receptor that plays a role in regulating inflammation and cellular differentiation. Certain NSAIDs, such as indomethacin and diclofenac, have been shown to activate PPAR γ , leading to anti-inflammatory effects and the induction of apoptosis in cancer cells (19).

NSAIDs have been found to modulate the activity of various ion channels, including transient receptor potential melastatin 7 (TRPM7) and acid-sensing ion channels (ASICs). For instance, naproxen and ibuprofen inhibit TRPM7 channels through cytosolic acidification, while aspirin and diclofenac inhibit ASICs, which are involved in pain perception (20,21). NSAIDs, particularly aspirin and salicylates, have been shown to affect mitochondrial function. These effects include the induction of mitochondrial membrane permeabilization and the generation of reactive oxygen species (ROS), which can contribute to apoptosis in cancer cells (22).

2.2. Non-Steroidal Anti-Inflammatory Drugs Classification

Chemically, nonsteroidal anti-inflammatory drugs (NSAIDs) encompass a broad array of structural classes, which can be systematically categorized into derivatives of benzoic acid, phenols, pyrazoles, acetic acid, propionic acid, 4-hydroxybenzothiazines, naphthylalkanones, quinazolinones, and diaryl heterocycles. Among these, benzoic acid derivatives are further subdivided into salicylic acid and anthranilic acid compounds, reflecting distinct pharmacophores within the same core structure. Acetic acid derivatives exhibit greater diversity and can be subclassified into phenylacetic acid, indoleacetic acid, indeneacetic acid, and pyrroleacetic acid groups, each contributing to nuanced differences in biological activity and selectivity profiles. Diaryl heterocycles can be classified into furanones, isoxazoles, and pyridine derivatives, underscoring the structural innovation aimed at enhancing COX-2 selectivity while minimizing adverse effects (23).

Nonsteroidal anti-inflammatory drugs, while generally sharing a common chemical profile as relatively lipid-soluble weak acids, display considerable variability in their pharmacokinetic characteristics. Most NSAIDs are efficiently and completely absorbed with minimal first-pass hepatic metabolism, exhibit high affinity for serum protein binding, and possess relatively small volumes of distribution. Despite these shared features, their metabolic pathways diverge, primarily involving hepatic cytochrome P450 enzymes, specifically CYP3A and CYP2C isoforms, as well as conjugation through

glucuronidation. A key distinction among NSAIDs lies in their elimination half-lives, which allows for classification into short-acting agents (with half-lives less than six hours) and long-acting agents (with half-lives exceeding six hours), a pharmacokinetic parameter that influences both dosing frequency and therapeutic duration (24).

The relative selectivity of NSAIDs is determined by their affinity for cyclooxygenase isoforms COX-1 and COX-2, allowing for their classification into four principal groups based on inhibitory potency toward each enzyme (14). These classes include selective COX-1 inhibitors, which predominantly target the constitutive isoform involved in physiological functions (Mofezolac), preferential COX-1 inhibitors, which exhibit a higher but not exclusive affinity for COX-1 (Aspirin, Diflunisal, Indomethacin, Naproxen, Ketoprofen, Flurbiprofen, Piroxicam), preferential COX-2 inhibitors, which favor the inducible isoform associated with inflammation and pain (Mefenamic acid, Meclofenamate, Nimesulide, Diclofenac, Carprofen, Etodolac, Aceclofenac, Tolmetin, Meloxicam, Nabumetone) and non-selective COX inhibitors, which exhibit comparable inhibitory activity against both isoforms (Flufenamic acid, Tolfenamic acid, Salsalate, Sulphasalazine, Sodium salicylate, Salicyl salicylate, Salicylamide, Methyl Salicylate, Olsalazine, Mesalamine, Magnesium Salicylate, Paracetamol, Phenacetin, Phenylbutazone, Sulfapyrazone, Oxyphenbutazone, Mofebutazone, Ramifenazone, Propiphenazone, Phenazone, Proglumetacin, Oxametacin, Sulindac, Zomepirac, Ibuprofen, Ketorolac,

Suprofen, Meclofenamic acid, Loxoprofen, Fenoprofen, Vedaprofen, oxaprozin, Tiaprofenic acid Tenoxicam, Sudoxicam, Proquazone) (23).

Furthermore, NSAIDs can also be categorized based on their interaction kinetics with the COX isoenzymes into reversible and irreversible inhibitors. Reversible inhibitors, such as ibuprofen, indomethacin, diclofenac, and celecoxib, bind non-covalently to COX-1 and/or COX-2, allowing enzymatic activity to resume once the drug dissociates or is metabolized. In contrast, aspirin represents the primary example of an irreversible inhibitor (23,25).

3. Non-Steroidal Anti-Inflammatory Use in Dentistry

3.1. Overview of NSAIDs in Dentistry

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used as first-line agents for managing pain and inflammation in oral health settings (26), as recommended by the World Health Organization (WHO) (27). Their pharmacological versatility has established their application across nearly all branches of dentistry, including conservative dentistry, endodontics, oral and maxillofacial surgery, orthodontics, periodontology, and the treatment of oral mucosal diseases.

In oral and maxillofacial surgical practice, NSAIDs such as ibuprofen, naproxen, and diclofenac are frequently prescribed for the effective reduction of postoperative pain, swelling, and trismus following procedures like third molar extractions and dental implant placements (28,29). For example,

ibuprofen 400 mg administered every eight hours for up to three days is a common regimen for managing surgical pain (28).

In endodontics, NSAIDs also play a crucial role in alleviating post-treatment pain. A single preoperative dose of piroxicam (20 mg) has been demonstrated to significantly reduce discomfort following root canal therapy on non-vital mandibular molars (30), and diclofenac potassium has shown superior analgesic efficacy over ibuprofen in cases of irreversible pulpitis (29).

Within periodontal therapy, NSAIDs, especially ibuprofen and diclofenac, are used as alternatives to surgical procedures to minimize inflammation and enhance clinical outcomes (31), although some studies have raised concerns regarding their potential to interfere with periodontal wound healing and osseointegration when COX-2 selective inhibitors are employed (32).

Dental implantology further supports the role of NSAIDs in postoperative care, with naproxen sodium found to be more effective than acetaminophen in controlling pain and systemic inflammation (33), while transdermal NSAID delivery has shown promise for reducing adverse effects compared to oral administration (34).

Lastly, in orthodontic settings, NSAIDs are routinely used to mitigate pain associated with bracket placement and archwire adjustments, thereby improving patient comfort and compliance during treatment (27).

Studies comparing COX-2 inhibitors with traditional NSAIDs have shown that both classes of drugs are effective in managing dental pain. For example, a meta-analysis of randomized clinical trials found no statistically significant differences in pain relief between selective COX-2 inhibitors

and ibuprofen at 6, 8, and 12 hours post-medication. However, patients treated with COX-2 inhibitors required less rescue analgesia after 24 hours, suggesting a longer duration of action for COX-2 inhibitors (35). Another study comparing lumiracoxib and diclofenac found that both drugs were effective in controlling postoperative pain, but lumiracoxib offered better pain control (36).

3.2. Prescribing Trends of NSAIDs in Dentistry

The prescribing landscape for non-steroidal anti-inflammatory drugs (NSAIDs) in dental practice has evolved significantly over the past two decades, reflecting a global shift toward safer, evidence-based analgesic strategies. NSAIDs such as ibuprofen and naproxen are now widely recognized as first-line agents for managing acute dental pain due to their superior efficacy over opioids and their anti-inflammatory action at the site of tissue trauma.

In Germany, for instance, ibuprofen has emerged as the dominant nonsteroidal anti-inflammatory drug (NSAID) prescribed for dental pain management, substantially displacing other agents in the class. In 2012, NSAIDs accounted for 65.9% of all analgesic prescriptions in dentistry, a figure that rose sharply to 80.1% by 2021, with ibuprofen comprising the vast majority of this increase. Specifically, ibuprofen's share of total dental pain prescriptions surged from 60.4% in 2012 to 79.0% in 2021, underscoring its central role in contemporary dental pharmacotherapy. In contrast, other NSAIDs such as diclofenac and dexketoprofen experienced a marked decline in usage, collectively representing

only 1.0% of analgesic prescriptions in 2021. Similarly, the use of combination therapies involving codeine significantly decreased from 5.1% to just 1.0% over the same period, reflecting a broader trend toward minimizing opioid use in routine dental care. Additionally, the proportion of unclassified analgesics dropped from 25.9% in 2012 to 15.0% in 2021, further highlighting the consolidation of ibuprofen as the preferred analgesic in dental practice (37).

Similar patterns have been observed in Australia, where NSAIDs were consistently the most prescribed analgesics from 2001 to 2012, emphasizing their central role in dental pharmacotherapy (38). Due to increased awareness of opioid-related harms, practice guidelines now recommend NSAIDs use first and opioids only for severe, intractable pain (39).

3.3. Patient Awareness and NSAIDs Epidemiology

The epidemiology of NSAIDs use in dentistry highlights a growing public health concern, particularly regarding over-the-counter accessibility and misuse. Studies indicate a high prevalence of NSAIDs self-medication among dental patients, reporting widespread unsupervised use, especially for dental pain relief (40).

The widespread use of NSAIDs in dental pain management has significant public health implications. Improving access to preventive dental care and promoting oral health education can reduce the incidence of dental pain and the subsequent need for NSAIDs. Public health strategies should also focus on minimizing the risks associated with NSAIDs use through

appropriate prescribing practices and patient education (40,41).

4. Non-Steroidal Anti-Inflammatory Drugs and Renal Interactions

4.1. Renal Physiology and NSAIDs Interactions

COX-1 and COX-2 are isoforms of the cyclooxygenase enzyme, with distinct roles in renal physiology. COX-1 is constitutively expressed in the kidney and is involved in maintaining basal prostaglandin production, which regulates renal blood flow and glomerular filtration rate (GFR) (42,43). COX-2, on the other hand, is inducible and plays a role in pathophysiological conditions, such as inflammation and hypertension (44).

Prostaglandins are lipid compounds derived from arachidonic acid and play a critical role in maintaining renal homeostasis. In the kidneys, prostaglandins, particularly PGE₂ and PGI₂, act as vasodilators, counteracting the effects of vasoconstrictors such as angiotensin II and norepinephrine. This vasodilatory action is essential for maintaining renal blood flow and glomerular filtration rate (GFR) (45).

COX inhibition can lead to acute changes in renal hemodynamics. Nonselective COX inhibitors, which block both COX-1 and COX-2, reduce renal blood flow and GFR by inhibiting prostaglandin synthesis (43). This effect is more pronounced in conditions of reduced renal perfusion, such as volume depletion or heart failure (46). Selective COX-2 inhibitors, such as celecoxib, also reduce renal blood flow but to a lesser extent compared to nonselective inhibitors (42). This is because COX-2-

derived prostaglandins play a smaller role in maintaining basal renal hemodynamics under normal conditions (47).

COX-2 plays a critical role in the regulation of the renin-angiotensin system. COX-2-derived prostaglandins modulate renin release from the macula densa, a specialized structure in the renal cortex that senses changes in luminal sodium chloride concentration (44). Studies have shown that COX-2 inhibitors reduce plasma renin activity, particularly in conditions of high renin states, such as sodium restriction or ACE inhibitor therapy (48,49). Additionally, COX-2 inhibition can blunt the pressor response to angiotensin II by reducing the production of vasoconstrictive prostaglandins, such as PGF_{2α} (50,51).

COX inhibition can alter electrolyte balance by affecting sodium and potassium excretion. COX-2 inhibitors reduce sodium excretion by decreasing PGE₂ production, which normally inhibits sodium reabsorption in the renal tubules (44,49). This effect is more pronounced in conditions of low sodium intake or reduced nitric oxide synthesis (47,52). COX inhibition can also lead to hyperkalemia, particularly in patients with preexisting renal insufficiency. This occurs because PGI₂, a COX-2-derived prostaglandin, stimulates potassium secretion in the distal nephron (46).

4.2. NSAIDs induced Nephrotoxicity

The use of nonsteroidal anti-inflammatory drugs is associated with significant renal risks, including acute kidney injury (AKI), exacerbation of chronic kidney disease (CKD), acute interstitial nephritis, renal papillary necrosis, and various electrolyte disturbances.

NSAIDs are known to cause AKI primarily through their inhibition of prostaglandin synthesis, which leads to intrarenal vasoconstriction and reduced glomerular filtration rate (53). Prostaglandins play a critical role in maintaining renal blood flow, especially in patients with pre-existing kidney disease or those in volume-depleted states. AKI associated with NSAIDs typically presents as a rapid decline in renal function, often accompanied by hyperkalemia, hyponatremia, and fluid retention (54,55). The risk of AKI is higher in elderly patients, those with pre-existing kidney disease, and individuals using high doses or long-term NSAID therapy (56). While AKI is generally reversible, prolonged use or delayed discontinuation can lead to more severe and potentially irreversible renal damage (57).

Chronic use of NSAIDs can exacerbate chronic kidney disease by causing persistent renal ischemia and fibrosis. This is attributed to the long-term suppression of prostaglandin synthesis, which disrupts the balance between vasodilatory and vasoconstrictive forces in the kidney (58). Patients with pre-existing CKD are particularly vulnerable, as their kidneys are already compromised, making them less able to compensate for the loss of prostaglandin-mediated renal protection (59). The progression of CKD in NSAID users is often insidious, with manifestations such as proteinuria, hypertension, and a gradual decline in GFR (60).

Acute interstitial nephritis (AIN) is an inflammatory condition characterized by immune-mediated damage to the renal interstitium (61). Patients with NSAID-induced AIN often present with acute renal

failure, fever, rash, and eosinophilia. Proteinuria and hematuria may also be present, and in some cases, nephrotic syndrome can develop (60).

Renal papillary necrosis is a severe complication of long-term NSAIDs use, particularly in patients with a history of analgesic abuse. The condition is characterized by ischemic necrosis of the renal papillae, leading to chronic kidney disease and, in some cases, end-stage renal disease (57).

NSAIDs may also impair renal tubular function, resulting in distal renal tubular acidosis (RTA), typically marked by hyperchloremic metabolic acidosis and hypokalemia (55,61). Furthermore, NSAIDs can worsen hypertension by promoting sodium and water retention and increasing renal vascular resistance, particularly in individuals with existing hypertension or cardiovascular conditions (62).

4.3. Risk Factors

Several risk factors contribute to NSAID-induced renal injury, which can be broadly categorized into patient-related, drug-related, and clinical scenario-based factors. Patient-related risks include advanced age, existing kidney disease, heart failure, liver dysfunction, diabetes mellitus, and states of volume depletion.

Drug-related risks involve the use of high NSAID doses, prolonged duration of use, and the concurrent administration of other nephrotoxic medications.

Clinically, individuals with multiple comorbidities, those using NSAIDs for chronic pain management, or patients with a known history of analgesic nephropathy

are particularly vulnerable to developing renal complications (1,4).

4.4. Evidence from Literature

A 44-year-old male presented with nausea, vomiting, and generalized weakness, having recently used nonsteroidal anti-inflammatory drugs (NSAIDs) for back pain. Laboratory tests revealed elevated serum creatinine and eosinophilia, prompting a renal biopsy, which confirmed granulomatous interstitial nephritis (GIN). After excluding infectious and autoimmune causes, the condition was attributed to NSAIDs use. This case highlights the importance of early recognition and corticosteroid intervention in NSAIDs-induced acute GIN to prevent progression to chronic kidney disease (63).

While NSAIDs-induced granulomatous interstitial nephritis is rare, as demonstrated in the adult case of a 44-year-old male who responded positively to corticosteroid therapy, similar nephrotoxic risks can also manifest in pediatric populations. Two adolescent cases further underscore the renal danger of unsupervised high-dose ibuprofen use. A 17-year-old male developed acute kidney injury (AKI) after consuming 4 g/day (41 mg/kg/day) for four days, and a 16-year-old female presented with similar symptoms after taking around of 46 mg/kg/day to relieve menstrual cramps. Both patients exhibited elevated serum creatinine and inflammatory markers, though imaging showed no structural abnormalities. With timely intravenous hydration and NSAIDs discontinuation, both adolescents achieved full recovery (64).

These cases highlight the spectrum of NSAIDs-induced renal complications

across ages and the critical need for careful monitoring and patient education regarding over-the-counter analgesic use.

5. Risk Mitigation and Safe Prescribing

5.1. Prescribing Guidelines

Prescribing nonsteroidal anti-inflammatory drugs (NSAIDs) in dental practice necessitates a careful balance between efficacy and renal safety, particularly in vulnerable populations. Clinical guidelines emphasize avoiding NSAIDs in patients with known renal disease, favoring alternative analgesics where possible (40). Furthermore, specific recommendations for dental patients with chronic kidney disease or transplants advocate for individualized analgesic plans and stress the importance of interprofessional collaboration to prevent acute kidney injury (65).

Although the US Food and Drug Administration recommends the use of NSAIDs beyond 10 days to be accompanied by a consultation with a health care provider, the use of NSAIDs may be considered relatively safe when prescribed at the most effective dose and for the shortest duration of time, which was defined as 10 days or fewer. Exceptions would be for patients at risk of developing NSAIDs-exacerbated respiratory disease, patients with prior myocardial infarction who are receiving antithrombotic therapy, patients with asthma, and patients with a history of renal disease (66).

While short-term use of NSAIDs is generally considered safe in dental practice, according to FDA and Aminoshariae et al. (66), their prescription should be limited to 10 days at the lowest dosage, especially in

patients predisposed to complications, such as exacerbated respiratory disease, asthma, prior myocardial infarction with concurrent antithrombotic therapy, or renal impairment.

Risk stratification plays a critical role: patients with chronic kidney disease, acute kidney injury (AKI), or comorbidities like hypertension, heart failure, or diabetes require pre-prescription evaluation of serum creatinine and estimated glomerular filtration rate (eGFR) to prevent nephrotoxicity (67,68). Dehydrated patients or those with volume depletion (e.g., from vomiting or diarrhea) are also more susceptible to renal injury (69,70). Special populations such as the elderly and pregnant women (71) require heightened caution due to physiological vulnerability, with NSAIDs contraindicated in late pregnancy and used only under close monitoring in geriatric and CKD patients (68). Management of NSAIDs-induced renal dysfunction includes immediate discontinuation of the drug, correction of fluid/electrolyte imbalances, and supportive care to control complications like edema and hypertension (57,72). These guidelines highlight the importance of not only therapeutic efficacy but also the renal safety of NSAIDs use in modern dental care.

5.2. Alternatives to NSAIDs

Given the potential renal risks and contraindications associated with NSAIDs use in certain patients who experience dental pathology, exploring alternative analgesics becomes essential for safety and effectiveness of pain management.

Acetaminophen (paracetamol) is widely recommended as a first-line substitute,

especially for individuals with renal impairment or cardiovascular comorbidities. Although it provides reliable analgesia, it lacks the anti-inflammatory efficacy of NSAIDs, limiting its utility in cases requiring inflammation control (73).

For more severe pain scenarios, opioids may be cautiously employed. However, their prescription should adhere strictly to short-term use due to significant risks, including dependence, sedation, and gastrointestinal or respiratory side effects (74,75).

Non-pharmacologic methods, such as physiotherapy, exercise, and local therapies, can be effective in managing pain and reducing reliance on NSAIDs, thereby minimizing renal risks (76).

5.3. Patient counseling and Monitoring

Effective patient counseling and vigilant monitoring are indispensable when prescribing NSAIDs in dental settings, particularly to mitigate renal risks. Patients should be informed of the potential for NSAIDs-induced kidney injury and the importance of reporting symptoms such as reduced urine output or swelling.

Clinicians are advised to monitor renal function markers, including serum creatinine, estimated glomerular filtration rate (eGFR), and urine output, especially in high-risk groups (67). Additionally, NSAIDs may induce or worsen hypertension, necessitating regular blood pressure checks during treatment (69). Electrolyte disturbances such as hyperkalemia and hyponatremia as consequences of altered renal tubular function, also warrant periodic monitoring of serum potassium and sodium levels,

particularly in elderly or comorbid patients. Prevention strategies include using the lowest effective NSAIDs dose for the shortest appropriate duration, avoiding co-administration of other nephrotoxic medications and opting for alternative analgesics in patients with compromised renal profiles (59). Incorporating these monitoring and counseling measures into dental practice enhances patient safety and optimizes therapeutic outcomes when NSAIDs are indicated.

6. Conclusions

Nonsteroidal anti-inflammatory drugs remain important in the management of dental pain due to their proven efficacy, but their use is not without risk, particularly due to renal safety.

NSAID-induced nephrotoxicity, including acute kidney injury, exacerbation of chronic kidney disease, and electrolyte disturbances, represents a significant concern. These adverse effects are primarily mediated through the inhibition of renal prostaglandin synthesis, which disrupts glomerular hemodynamics and sodium-water homeostasis.

It would be helpful for dental practitioners to ask for renal function assessment into their routine prescribing protocols and adhere to the guidelines that prioritize the lowest effective dose for the shortest duration, in light of these risks. In patients with underlying renal vulnerability, such as those with CKD, diabetes, or elderly ones, careful screening, patient counseling and post-prescription monitoring are essential. Alternative analgesics may offer renal safety advantages, but their efficacy and safety profiles have to be carefully checked. Looking forward, the development and implementation of AI-driven risk stratification tools could transform NSAIDs prescribing by enabling personalized risk assessment in real time. Moreover, targeted clinical trials represent an area that can be more developed in order to investigate the renal safety of NSAIDs, specifically within dental suffering populations. Lastly, the balance between analgesic benefit and renal safety requires a personalized approach. Responsible prescribing and continued research into the renal effects of NSAIDs will be useful to optimize dental pain management while minimizing harm.

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