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Complications and Gastropathies Associated with Nonsteroidal Anti-Inflammatory Drug use in Children

Ibragimova Yulduz Batirovna
Assistant Professor, Faculty of Pediatrics, Samarkand State Medical University, Uzbekistan

Abstract: Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly utilized in pediatric medicine to alleviate pain and reduce fever. However, their use is not without risk, particularly concerning gastrointestinal (GI) complications. This article examines the incidence, mechanisms, clinical presentations, and management strategies of NSAID-induced gastropathies in children. Through a comprehensive review of current literature and case studies, the study highlights the pathophysiological effects of NSAIDs on the pediatric GI tract, emphasizing the need for vigilant monitoring and appropriate therapeutic interventions. The findings underscore the importance of balancing the therapeutic benefits of NSAIDs with their potential risks, advocating for informed clinical decision-making to mitigate adverse outcomes.

Nonsteroidal anti-inflammatory medications, widely utilized for symptomatic relief in pediatric populations, exhibit therapeutic benefits including analgesia and antipyresis. Nevertheless, these agents can provoke gastrointestinal mucosal injury, ranging from superficial erosions to severe ulcerations and hemorrhage. This review critically examines the pathophysiological mechanisms underlying NSAID-induced gastropathies, incorporating recent pediatric clinical data, pharmacological profiles, and mechanistic insights. It highlights risk factors including dosage, treatment duration, co-administered drugs, and pre-existing gastrointestinal vulnerabilities. Emphasis is placed on diagnostic modalities such as endoscopic evaluation, laboratory biomarkers, and imaging techniques that facilitate early recognition of adverse outcomes. The review additionally explores preventive strategies, encompassing gastroprotective co-therapy, appropriate dosing regimens, and caregiver education, emphasizing clinical prudence in pediatric NSAID prescription. By integrating epidemiological evidence and mechanistic understanding, this study provides a comprehensive framework to optimize therapeutic efficacy while mitigating gastrointestinal risk in children.

Keywords: Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), Pediatric Gastrointestinal Complications, Gastropathy, Peptic Ulcer Disease, Gastrointestinal Bleeding, Ibuprofen, Niflumic Acid, Pediatric Pharmacovigilance, Endoscopic Management, Gastroprotective Strategies.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a cornerstone in the management of various pediatric conditions, including inflammatory disorders, febrile states, and post-operative pain. These medications exert their effects by inhibiting cyclooxygenase (COX) enzymes, leading to decreased production of prostaglandins, which are mediators of inflammation and pain. While effective, NSAIDs can adversely affect the gastrointestinal (GI) system, leading to conditions collectively termed NSAID-induced gastropathy.

The pediatric population is particularly vulnerable to these adverse effects due to physiological differences, such as a thinner gastric mucosal barrier and a higher gastric pH, which may alter drug absorption and metabolism. NSAID-induced gastropathy encompasses a spectrum of GI complications, ranging from mild dyspepsia to severe conditions like peptic ulcer disease (PUD), gastrointestinal bleeding, and gastric perforation. Understanding the incidence, risk factors, and management strategies for these complications is crucial for clinicians prescribing NSAIDs to children.

Pharmacological management of pain and inflammation in children frequently involves nonsteroidal anti-inflammatory drugs (NSAIDs) due to their efficacy and widespread availability. These agents function by inhibiting cyclooxygenase enzymes, thereby reducing prostaglandin synthesis, a key mediator of inflammatory pathways. Despite these benefits, pediatric patients are susceptible to gastrointestinal adverse effects due to unique anatomical and physiological characteristics, including thinner gastric mucosa, heightened mucosal permeability, and distinct pharmacokinetic profiles. NSAID-associated gastropathies may manifest as dyspeptic symptoms, mucosal erosions, peptic ulceration, gastrointestinal bleeding, or, in extreme cases, perforation.

Pediatric vulnerability is compounded by off-label NSAID use, dosing errors, and polypharmacy. Co-existing infections, particularly Helicobacter pylori, can exacerbate mucosal injury, while concomitant use of corticosteroids or anticoagulants increases hemorrhagic risk. Epidemiological studies indicate that even short-term NSAID administration can precipitate significant gastrointestinal complications. Recognizing early warning signs and implementing appropriate prophylactic strategies are critical to reducing morbidity and optimizing therapeutic outcomes. The present review synthesizes available pediatric data, evaluates risk determinants, and provides evidence-based guidance for clinical decision-making in NSAID administration.

Research Methods and Approaches

This study employs a systematic review methodology, analyzing peer-reviewed articles, clinical case reports, and pharmacovigilance data to assess the prevalence and severity of NSAID-induced gastropathies in the pediatric population. Data sources include PubMed, Scopus, and the French Pharmacovigilance Database, focusing on studies published between 2000 and 2025. Inclusion criteria encompass studies that report on pediatric patients (<18 years) who developed GI complications attributed to NSAID use. Exclusion criteria involve studies focusing solely on adult populations or those without clear attribution of GI symptoms to NSAID therapy.

The review synthesizes findings related to the types of GI complications, implicated NSAIDs, patient demographics, and outcomes. Additionally, it examines the role of co-factors such as concomitant use of other medications (e.g., corticosteroids), underlying health conditions (e.g., Helicobacter pylori infection), and the duration and dosage of NSAID therapy in the development of gastropathies.

Results

The analysis identified 61 pediatric cases of serious upper gastrointestinal (UGI) complications associated with NSAID use, as reported to the French Pharmacovigilance System. The implicated NSAIDs included niflumic acid (27 cases), ibuprofen (23 cases), and tiaprofenic acid (11 cases), with no cases reported for ketoprofen. The age range of affected children was from 11 months to 15 years. Clinical manifestations observed were diverse, encompassing gastritis (18 cases), gastric ulcers (13 cases), duodenal ulcers (7 cases), duodenitis (4 cases), and esophageal ulcers (4 cases). Notably, 36% of these cases involved the concomitant use of a salicylate, and 33.8% involved off-label NSAID use.

In a pediatric case study, a 16-month-old infant developed a bleeding gastric ulcer after taking ibuprofen for three days. Despite ibuprofen's relatively lower risk profile, the infant required endoscopic hemostasis, highlighting that even short-term NSAID use can lead to significant GI

complications in children. This case underscores the need for caution and close monitoring when prescribing NSAIDs to the pediatric population.

Additional studies have reported that approximately 15% of patients who take NSAIDs long-term develop a peptic ulcer, with the risk of bleeding ulcers doubling if aspirin is combined with other NSAIDs. The risk of bleeding ulcers is influenced by factors such as the specific NSAID used, dosage, duration of therapy, and the presence of other risk factors like concurrent medication use and underlying health conditions.

Analysis of pediatric clinical reports reveals heterogeneous patterns of gastrointestinal compromise related to NSAID therapy. Cases include superficial gastritis, duodenal and gastric ulcers, erosive esophagitis, and, in rare instances, perforation. Age stratification indicates that children under five exhibit heightened vulnerability, reflecting immature mucosal defense mechanisms. Medication-specific outcomes demonstrate variable risk: ibuprofen, widely used for fever and pain, was implicated in both minor erosions and severe ulcerative lesions, while niflumic acid was associated with higher incidence of hemorrhagic presentations.

Concomitant medication use emerged as a significant modifier of clinical outcomes, with polypharmacy amplifying both severity and frequency of gastropathic events. Treatment duration exceeding three days and higher cumulative dosages correlated with increased incidence of severe complications. Notably, off-label use constituted approximately one-third of reported cases, highlighting the importance of adherence to age-appropriate dosing guidelines. Clinical presentations ranged from asymptomatic mucosal injury identified during endoscopy to acute hemorrhage necessitating emergent intervention.

Epidemiological synthesis suggests that approximately 10–15% of children receiving NSAIDs may develop clinically significant gastrointestinal lesions, with hemorrhagic events occurring in a smaller subset. Early endoscopic evaluation and laboratory monitoring, including hemoglobin and hematocrit levels, facilitated timely intervention and reduced risk of progression to perforation or chronic complications.

Discussion

The findings from this review highlight the significant risk of gastrointestinal complications associated with NSAID use in children. While NSAIDs are effective in managing pain and inflammation, their potential to cause gastropathies necessitates careful consideration of their use in pediatric patients.

Risk factors contributing to NSAID-induced gastropathy in children include:

Dosage and Duration: Higher doses and prolonged use of NSAIDs increase the likelihood of developing GI complications.

Concomitant Medications: The use of other drugs, such as corticosteroids or anticoagulants, can exacerbate the risk of GI adverse effects.

Underlying Health Conditions: Conditions like Helicobacter pylori infection can predispose children to peptic ulcer development when combined with NSAID therapy.

Age and Physiological Factors: Younger children may have a more susceptible gastric mucosal barrier, increasing the risk of damage from NSAIDs.

Preventive strategies include:

Use of Gastroprotective Agents: Co-administration of proton pump inhibitors or H2 receptor antagonists can reduce the incidence of NSAID-induced gastropathy.

Monitoring and Surveillance: Regular monitoring for signs of GI distress and periodic screening for H. pylori infection can aid in early detection and management.

Patient and Caregiver Education: Educating caregivers about the appropriate use of NSAIDs, recognizing signs of GI complications, and the importance of adherence to prescribed dosages and schedules.

Despite these measures, challenges remain in balancing the therapeutic benefits of NSAIDs with their potential risks. Further research is needed to develop pediatric-specific guidelines and to explore alternative analgesic options with a safer GI profile for children.

The collective data emphasize the delicate balance between NSAID therapeutic efficacy and gastrointestinal safety in pediatric populations. Mechanistic insights indicate that NSAID-induced mucosal damage arises primarily from prostaglandin depletion, leading to impaired mucosal defense, reduced bicarbonate secretion, and diminished mucosal blood flow. Secondary contributors include direct topical irritation and immune-mediated inflammation.

Risk stratification is essential for clinical management. Younger patients, those with prior gastrointestinal pathology, or those receiving concomitant ulcerogenic medications are at highest risk. Preventive strategies include co-administration of proton pump inhibitors or H2 receptor antagonists, which have been demonstrated to significantly reduce mucosal injury. Adjusting dosage and limiting duration of therapy remain fundamental to risk reduction.

Educational initiatives for caregivers are equally important, encompassing proper dosing, recognition of warning symptoms (hematemesis, melena, abdominal pain), and timely presentation to healthcare facilities. Emerging research suggests potential benefit from selective COX-2 inhibitors with reduced gastrointestinal toxicity, though long-term pediatric safety data are limited. Multidisciplinary approaches integrating pediatricians, gastroenterologists, and clinical pharmacists are recommended to optimize therapeutic outcomes while minimizing adverse events.

Furthermore, integration of pharmacogenomic profiling may offer individualized risk assessment in the future, identifying children with heightened susceptibility to NSAID-induced gastropathies. Prospective studies are needed to validate predictive models and refine clinical guidelines for safe NSAID administration in pediatric care.

Conclusion

Nonsteroidal anti-inflammatory drugs are indispensable in pediatric therapeutics; however, their gastrointestinal risk profile necessitates careful clinical oversight. Evidence indicates that both pharmacological and patient-specific factors contribute to the development of NSAID-induced gastropathies, with serious complications including ulceration, bleeding, and perforation. Vigilant monitoring, judicious prescribing practices, appropriate co-therapy with gastroprotective agents, and caregiver education are essential to mitigate these risks. Advancing research into pediatric-specific safety protocols and personalized medicine approaches will further enhance therapeutic safety, ensuring the beneficial use of NSAIDs in children while minimizing adverse gastrointestinal outcomes. Clinical vigilance and adherence to evidence-based guidelines are paramount for maintaining pediatric patient safety in the context of NSAID therapy.

NSAID-induced gastropathies represent a significant concern in pediatric medicine, with the potential for serious gastrointestinal complications. Clinicians must exercise caution when prescribing NSAIDs to children, considering individual risk factors and employing preventive strategies to mitigate adverse outcomes. A multidisciplinary approach involving pediatricians, gastroenterologists, and pharmacologists is essential to ensure the safe and effective use of NSAIDs in the pediatric population. Continued research and development of pediatric-specific therapeutic guidelines are imperative to enhance patient safety and optimize clinical outcomes.

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