A Critical Review of Piroxicam: From Mechanism to Adverse Effects in Clinical Use

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Abstract: Piroxicam is medications primarily used to treat pain and help relieve symptoms of arthritis (e.g. osteoarthritis, rheumatoid arthritis), such as inflammation, swelling, stiffness, and joint pain. They can be given orally and rectal route. Piroxicam, akin to other nonsteroidal anti-inflammatory drugs (NSAIDs), functions via the inhibition of tissue cyclooxygenases (Cox-1 and -2), resulting in a reduction in the synthesis of pro-inflammatory prostaglandins, which are influential mediators of pain and inflammation. Piroxicam exhibits analgesic properties alongside antipyretic and anti-inflammatory effects. Piroxicam is a monocarboxylic acid amide.

Keywords: Piroxicam, NSAIDs, COX-1 & COX-2, Pharmacokinetics, Adverse effects.

INTRODUCTION

Piroxicam is a nonsteroidal anti-inflammatory drug (NSAID) commonly employed for the management of pain and inflammation associated with various musculoskeletal disorders. It belongs to the oxicam class of NSAIDs, which is characterized by a distinctive chemical structure that includes a 1,2-benzothiazine ring.

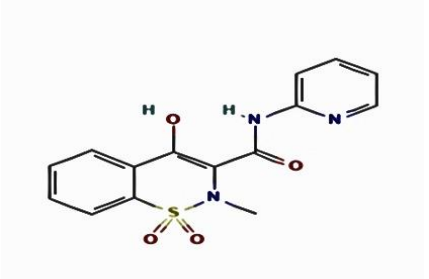

Fig 1: Structure of Piroxicam

This structural feature contributes to piroxicam's potency and prolonged duration of action. Notably, piroxicam is recognized for its sustained therapeutic effect, allowing for once-daily administration. It is available in multiple formulations, including oral, topical, and injectable forms, offering versatility in treating conditions such as arthritis, bursitis, tendinitis, and other inflammatory diseases.

Piroxicam was developed in the 1970s by the pharmaceutical company Merck as part of a broader initiative to create new NSAIDs that could provide effective analgesia with a reduced incidence of side effects. In 1981, the drug received regulatory approval in several countries, marking its introduction to the pharmaceutical market. Piroxicam quickly gained recognition for its efficacy in treating various inflammatory conditions, including osteoarthritis and rheumatoid arthritis. Numerous clinical trials conducted during the 1980s and 1990s assessed the safety and efficacy of piroxicam. These studies demonstrated its effectiveness in managing chronic pain linked to arthritis and other musculoskeletal disorders. However, concerns regarding its long half-life and potential gastrointestinal toxicity necessitated careful monitoring and appropriate dosing strategies. Following its market introduction, piroxicam became widely prescribed; however, growing concerns about adverse effects prompted increased scrutiny. Consequently, medical guidelines began to stress the importance of prescribing the lowest effective dose for the shortest duration necessary. Today, piroxicam remains an important option within the NSAID class for treating inflammatory conditions, particularly for patients requiring long-term management. Its various formulations ensure its utility in clinical practice. Ongoing research is focused on its long-term safety profile, optimal dosing strategies, and potential drug interactions, thereby ensuring that piroxicam continues to be a relevant and effective treatment option in contemporary medicine.

Fig 2: Piroxicam tablet

Mechanism of Action

Piroxicam exerts its therapeutic effects by inhibiting the enzyme cyclooxygenase (COX), which is crucial in the biosynthesis of prostaglandins, mediators involved in the processes of inflammation, pain, and fever. Specifically, piroxicam inhibits both the COX-1 and COX-2 isoforms. While suppression of prostaglandin production alleviates inflammation and pain, the inhibition of COX-1 can result in adverse effects on the gastrointestinal system and kidneys, as this enzyme also plays a protective role in maintaining the integrity of these organs.

Indications and Uses

Piroxicam is primarily indicated for the management of the following conditions:

a) Osteoarthritis: A degenerative joint disease characterized by chronic pain and stiffness resulting from cartilage degradation.
b) Rheumatoid arthritis: An autoimmune disorder that causes inflammation of the joints, leading to pain, swelling, and stiffness.
c) Ankylosing spondylitis: A chronic inflammatory condition affecting the spine, which may lead to reduced mobility and persistent pain.
d) Acute musculoskeletal disorders: Conditions such as tendinitis, bursitis, and other inflammation-related musculoskeletal disorders.

Dosage and Administration

Piroxicam is generally administered once daily, owing to its extended half-life, with the recommended adult dosage ranging from 10 to 20 mg per day. It may be taken with or without food; however, administering it with food can help mitigate gastrointestinal adverse effects.

The available formulations of piroxicam include:

a) Oral tablets or capsules: The most commonly prescribed form, suitable for the long-term management of chronic pain.
b) Topical gels or creams: Applied to localized areas to target inflammation or pain directly.
c) Intramuscular injections: Utilized for the relief of acute pain when oral administration is not appropriate.

Pharmacokinetics

Piroxicam exhibits a relatively slow onset of action, with peak plasma concentrations attained within 3 to 5 hours following oral administration. The drug demonstrates extensive binding to plasma proteins, which contributes to its prolonged half-life of approximately 30 to 50 hours, thereby facilitating once-daily dosing. Piroxicam undergoes hepatic metabolism, primarily via cytochrome P450 enzymes, and is subsequently excreted through both urine and bile.

Adverse Effects

Like other nonsteroidal anti-inflammatory drugs (NSAIDs), piroxicam is associated with potential adverse effects, particularly when used over extended periods. Common side effects include:

a) Gastrointestinal effects: Symptoms such as nausea, dyspepsia, and abdominal pain are frequently observed, with more severe outcomes such as gastric ulcers or gastrointestinal bleeding occurring in some cases. The risk of these complications increases with higher doses and prolonged use.
b) Renal impairment: Piroxicam may decrease renal perfusion, potentially leading to kidney damage, particularly in patients with pre-existing renal conditions or those concurrently using nephrotoxic agents.
c) Cardiovascular risks: Piroxicam, like other NSAIDs, has been associated with an elevated risk of cardiovascular events, including myocardial infarction and stroke, particularly when used in high doses or for long durations.
d) Cutaneous reactions: Although rare, severe skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported.

Contraindications

Piroxicam is contraindicated in the following populations:

a) Patients with a history of hypersensitivity reactions to NSAIDs, including those with aspirin-induced asthma or other allergic reactions.
b) Individuals with active gastrointestinal bleeding or peptic ulcer disease.
c) Patients with severe heart failure, as NSAIDs may exacerbate fluid retention and worsen cardiovascular conditions.
d) Pregnant women, particularly during the third trimester, due to the risk of foetal complications, including the potential closure of the ductus arteriosus.

e) Individuals with severe hepatic or renal impairment.

Drug Interactions

Piroxicam has the potential to interact with various medications, which may result in enhanced side effects or diminished therapeutic efficacy. Significant drug interactions include:

a) Anticoagulants (e.g., warfarin): There is an increased risk of bleeding due to the additive effects of anticoagulation.
b) Corticosteroids: Concurrent use increases the likelihood of gastrointestinal ulcers and bleeding.
c) ACE inhibitors or angiotensin receptor blockers (ARBs): Piroxicam may reduce the antihypertensive effects of these agents and elevate the risk of renal impairment.
d) Diuretics: The effectiveness of diuretics may be diminished, leading to an increased risk of nephrotoxicity.

Special Considerations

a) Elderly Patients: Older adults are at an increased risk for gastrointestinal, renal, and cardiovascular adverse effects associated with NSAIDs, including piroxicam. Therefore, vigilant monitoring and potential dose adjustments may be warranted.
b) Pregnancy and Lactation: Piroxicam is categorized as a Category C medication during pregnancy, indicating that its safety profile has not been adequately established. Its use should be avoided, especially in the third trimester. Additionally, it is not advised for use in breastfeeding mothers.

CONCLUSION

Piroxicam is a potent nonsteroidal anti-inflammatory drug (NSAID) characterized by its long duration of action, rendering it particularly effective in the management of chronic inflammatory conditions such as arthritis. While the drug provides substantial relief from pain and effectively reduces inflammation, its administration necessitates careful consideration of potential adverse effects, especially concerning gastrointestinal and cardiovascular risks. Given these concerns, it is essential to prescribe piroxicam at the lowest effective dose for the minimal duration necessary to achieve symptom control. This approach helps to mitigate the likelihood of side effects while ensuring therapeutic efficacy. Additionally, clinicians must engage in regular monitoring of patients undergoing piroxicam therapy to detect any adverse reactions early. Awareness of the drug's contraindications and possible drug interactions is also crucial in minimizing the risk of adverse effects. By adopting these practices, healthcare providers can optimize the management of patients with chronic inflammatory conditions while safeguarding their overall health and well-being. Ultimately, the careful and judicious use of piroxicam can contribute to improved quality of life for individuals suffering from painful inflammatory disorders.

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Conflicts of interest
There are no conflicts of interest.

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Authors contribution
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