IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, March 2022
Impact Factor: 6.252

Non-Steroidal Antiinflammatory Drugs

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Abstract: *Nonsteroidal anti-inflammatory drugs, or NSAIDs, are among the most often prescribed pain relievers. NSAIDs are a highly successful medicine class for pain and inflammation, but they are also known to cause gastrointestinal bleeding, cardiovascular side effects, and NSAID-induced nephrotoxicity. The pharmacodynamic action of these medicines is predominantly mediated by COX2 inhibition, whereas COX1 inhibition is largely responsible for the unfavourable effects. The activity of (COX-1) and COX2, and thus the synthesis of prostalglandin and thromboxanes, is inhibited by most NSAIDs. Inhibiting COX-2 is thought to have anti-inflammatory, analgesic, and antipyretic effects, and that NSAIDs that also inhibit COX-1, such as aspirin, may cause gastrointestinal bleeding and ulcers. This review aims to provide a comprehensive overview pharmacodynamic and pharmacokinetics of NSAIDs as well as the medication class and method of action.*

Keywords: Non-steroidal anti-inflammatory drug, NSAIDs, Antiinflammatory, Analgesic, Aspirin.

I. INTRODUCTION

NSAIDs (non-steroidal anti-inflammatory drugs) are a broad category of therapeutic drugs with analgesic and anti-inflammatory characteristics which are known to reduce inflammation by inhibition of COX- 2 and COX- 1 enzymes.[1,2]NSAIDs are one of the most often prescribed pain and inflammatory medications. They are responsible for about 5% to 10% of all prescriptions dispensed each year.[3] They are used for the long- and short-term therapy of a number of medical conditions, including osteoarthritis, rheumatoid arthritis, and musculoskeletal discomfort, and are indicated for the decrease of pain, inflammation, and fever.[4] While NSAIDs have numerous advantages, they have also been linked to an increased risk of gastrointestinal (GI) problems, which may limit their usage in some patients.[5] The demand for novel NSAIDs has led to the realisation that conventional NSAIDs' negative effects are caused by suppression of the COX-1 isoform, while COX-2 is responsible for the good effects such as anti-inflammatory effects and analgesia.[6] COX-2 inhibitors (also known as coxibs) inhibit solely COX-2 enzymes, unlike nonselective NSAIDs, which inhibit both COX-1 and COX-2 enzymes. COX-2 is more involved in prostaglandin-mediated pain and inflammation, whereas COX-1 is more involved in gastric mucosa protection and platelet hemostasis.[7]

1.1 Mechanism of action NSAIDs

Most NSAIDs work as nonselective inhibitors of the carboxylase (COX) enzyme, inhibiting both the COX-1 (COX-1) and COX-2 (COX-2) isoenzymes. In contrast to aspirin, which has an irreversible inhibitory mechanism, this inhibition is competitively reversible. COX catalyses the production of prostaglandin and thromboxane from arachidonic acid, which is obtained by phospholipase from the cellular phospholipid bilayer. Inflammation is mediated by prostaglandins, which operate as messenger molecules. COX-1 is a naturally occurring enzyme that plays a "housekeeping" role in regulating a variety of physiological processes. Prostaglandins provide a protective role in the stomach lining, keeping the mucosal from being destroyed by the stomach's own acid. COX-2 is a facultative enzyme that is expressed in inflammation, and it is COX-2 inhibition that causes the beneficial effects of NSAIDs.[8,9]

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1.2 Pharmacokinetics and Pharmacodynamics of NSAIDs

The capacity of NSAIDs to stop the manufacture of specific prostaglandins (PGs) by inhibiting the cyclooxygenase enzymes (COX-1 and COX-2) is the primary therapeutic activity of these drugs. COX-1 is responsible for the production of prostaglandins and thromboxane A2, which regulate the mucosal barrier in the GI tract, renal balance, platelet aggregation, and other physiological processes. COX-2 creates prostaglandins (PGs), which are linked to inflammation, pain, and fever. Normal cells produce COX-1, whereas inflammatory cells produce COX-2.[10-12] COX-2 inhibition is most likely the expected result of NSAIDs' anti-inflammatory, antipyretic, and analgesic responses, but COX-1 inhibition is a major contributor to unfavourable side effects such GI and renal toxicity. The majority of NSAIDs are well absorbed and have a high bioavailability in the gastrointestinal system. Some medications, such as diclofenac, are subjected to hepatic first-pass metabolism, which reduces bioavailability. While some medications, such as sulindac and parecoxib, are prodrugs that require hepatic metabolism to produce active metabolites, others, like sulindac and parecoxib, are not (sulindac sulphide and valdecoxib, respectively). NSAIDs have a strong affinity for plasma proteins. NSAIDs are processed in the liver and eliminated in the urine in most cases. The half-life of common NSAIDs varies; for example, aspirin's half-life is 0.25-0.3 hours, whereas piroxicam's half-life is 45-50 hours. Because the elderly have less body water than adults, all of these pharmacokinetics factors may change with age. Protein binding may be diminished, and distribution volumes may change.[13,14]

1.3 Analgesic, Antipyretic, Anti-Inflammatory and Anti-Platelet

Swelling, redness, discomfort, and heat have been recognised as clinical symptoms of inflammation since ancient times. The underlying mechanisms that cause these symptoms are intricate, involving a wide range of cells and cell products. A healthy inflammatory response is necessary for fighting infections and is also part of the repair and debris removal process after tissue damage. Inflammation can also lead to disease when healthy tissue is damaged. This can happen if the response is too strong or lasts longer than it should. Furthermore, some diseases, such as atherosclerosis, have an undetected inflammatory component. The inflammatory response occurs in vascularized tissues in response to injury. It's an element of the innate immune system's nonspecific response. Inflammatory responses require the activation of leukocytes such as neutrophils, eosinophils, basophils, mast cells, monocytes, and lymphocytes, albeit not all cell types must be engaged during an inflammatory episode. As the cells go to the site of tissue injury produced by the systemic circulation, they get activated.[15]

1.4 Effects of nsaids:

A. Analgesic and Antipyretic Action

Morphine type drugs are strong analgesics as compared to Aspirin, that is morphine 6mg > codein 60mg > Aspirin 600mg. Inflammatory, tissue injury-related, connective tissue, and integument pain are relieved by aspirin, while severe visceral and ischemia pain are not. The analgesic effect is mostly related to peripheral pain receptors and the inhibition of PG-mediated nerve ending sensitization. A central subcortical activity that raises the pain threshold also plays a role. There is no sedation, tolerance, or reliance. Aspirin works by resetting the hypothalamus thermostat and reducing fever quickly by boosting heat loss (sweating, cutaneous vasodilation), but not by reducing heat production.[16]

B. Cardiovascular Risk of NSAID

Apart from aspirin, NSAIDs, including newer selective COX-2 inhibitors and classic anti-inflammatories, increase the risk of and are not indicated for people who have had a previous heart attack because they increase the risk of death and recurrent MI. Apart from (low-dose) aspirin, which has been linked to a doubled risk of heart failure in those without a history of cardiac disease, evidence suggests naproxen may be the least dangerous of these(overview of nsaid). All NSAIDs (both COX-2 and non-selective) have been linked to an increase in cardiovascular side effects, and the risk/benefit profile of each medicine should be examined before prescribing to particular patients.[17]

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C. Respiratory Action

Respiration is stimulated by peripheral (increased CO2 generation) and central (increased sensitivity of respiratory centre to CO2) action at antiinflammatory dosages. In salicylate poisoning, hyperventilation is common. Increased salicylate levels result in respiratory depression, failure, and death.

D. Gastro-Intestinal Tract Effect

Aspirin and its metabolite salicylic acid produce epigastralgia, nausea, and vomiting by irritating the gastric mucosa.[18] The rationale behind NSAID-induced GI side effects is that these drugs block prostaglandin synthesis, weakening the protective GI mucosal barrier and predisposing one to bleeding.[19]

II. Conclusion

Nonsteroidal anti-inflammatory medicines (NSAIDs) are a drug class that includes medications that act as analgesics (pain relievers) and antipyretics (fever reducers). These medicines have anti-inflammatory properties at higher doses. Analgesic and anti-inflammatory effects are mediated by inhibiting two known isoenzymes of prostaglandin cycl-oxygenase (COX), COX 1 and COX 2. The pharmacodynamic action of these medicines is primarily based on COX2 inhibition, while COX1 inhibition is predominantly responsible for the side effects.

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