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WHITE PAPER

Cascade with GI Prostaglandin and Use of Topical NSAIDs vs Oral NSAIDs

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for their anti-inflammatory, analgesic, and antipyretic effects.[1] NSAIDs generally work by blocking the production of prostaglandins (PGs) through the inhibition of two cyclooxygenase enzymes. [1] However, their use has been associated with potentially serious dose-dependent gastrointestinal (GI) complications such as upper GI bleeding.[2] GI complications resulting from NSAID use are among the most common drug side effects in the United States, due to the widespread use of NSAIDs.[2] Topical products were developed to provide well tolerated, effective targeted therapies, based on the drug's pharmacokinetics and penetration to the site of action.[3]

Topical therapies are delivered to the site of action, avoiding the first-pass metabolism of oral drugs. [3] Most importantly, topical NSAIDs were developed to reduce the risk of gastrointestinal (GI), cardiovascular (CV), and renal adverse events associated with oral NSAIDs.[3] This route possibly reduces gastrointestinal adverse reactions by maximizing local delivery and minimizing systemic toxicity.[5]

The use of oral NSAIDS increase the risk of gastrointestinal (GI) complications. GI complications are generally thought to be mediated primarily through inhibition of mucosal cyclooxygenase-1 (COX-1) and resultant suppression of prostaglandin production.[2] Oral NSAIDS could inhibit PG-mediated effects on the gastrointestinal tract. This effect includes the inhibition of mucin production, HCO3 secretion, and mucosal proliferation.[1] COX-1 inhibition by the use of NSAIDs causes gastric hypermotility.[1] Gastric lesion that formed eventually because of increased mucosal permeability and myeloperoxidase activity comes up with this enhanced gastric hypermotility.[1]

In one study it was determined that GI adverse events associated with oral ibuprofen use make topical formulation a promising alternative for both human and veterinary medicine.[4] In another study with diclofenac, plasma levels after topical administration have been reported to fall within a range of 0.2% to 8% of those achieved after oral administration.[3] Thus, complications such as GI bleeding and gastric ulcerations associated with oral administration of NSAIDs as well as CV and renal toxicity, are less common following use of topical NSAIDs.[3]

In addition, in a retrospective analysis of a rheumatoid arthritis patient database published in 2000, OTC ibuprofen and naproxen users had a relative risk for serious GI complications of approximately 3.5 compared with NSAID nonusers, and it is estimated that 1%–2% of continuous NSAID users experience a clinically significant upper GI event per year.[2] These findings represent a significant clinical concern, as patients taking NSAIDs experience a relative risk of upper GI bleeding and perforations of up to 4.7 compared with nonusers.[2]

Prescription and OTC non-steroidal anti-inflammatory drugs (NSAIDs) are ubiquitous treatments for pain and inflammation; however, oral administration of these drugs may produce gastrointestinal (GI) side effects.[4] Transdermal (TD) administration of NSAIDs circumvents these adverse events by avoiding the GI tract and, presumably, achieves regional drug levels of therapeutic effect and thereby, fewer off-target complications.[4] Reduction of adverse drug reactions associated with the use of topical preparations of NSAIDs is being well considered to obtain high patient compliance and drug therapy efficacy. [5]

References

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