What are the new pain medications, COX-2 Inhibitors?

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Citation

T Glauser. *What are the new pain medications, COX-2 Inhibitors?*. The Internet Journal of Health. 1999 Volume 1 Number 1.

Abstract

Parts of the willow tree have been used since ancient times to relieve pain and inflammation (swelling) (Rehman and Sack 1999). In 1897 the active compound in these willow herbal remedies was isolated, and Bayer began marketing it as aspirin in 1899 (Rehman and Sack 1999). Not until the 1960's were other synthetic nonsteroidal anti-inflammatory drugs (NSAIDs) produced. NSAIDs are widely prescribed for many musculoskeletal disorders. Unfortunately, the use of these drugs is associated with a significant risk of gastrointestinal (GI) complications, including dyspepsia, ulcers, and bleeding. In addition, they can cause generalized bleeding, liver and kidney dysfunction and organ failure, and skin reactions. There has recently been concern that they may actually accelerate the process of cartilage destruction in osteoarthritis . Because of these adverse effects, a great deal of effort has been spent developing new NSAIDs without these drawbacks.

Why are the new NSAIDs so much better than the original NSAIDs? All of the NSAIDs developed before 1990 exert their anti-inflammatory and analgesic (pain-relieving) activity by inhibiting an enzyme, cyclooxygenase (COX). This enzyme converts a substance called arachidonic acid into various biologically active substances, with the most significant ones being the prostaglandins (Vane and Botting 1998). Prostaglandins are potent molecules that help regulate processes in the GI tract, the platelets, and the kidneys. Prostaglandins also promote inflammation and pain in certain diseases and after injury .

In 1991 it was discovered that at least 2 distinct forms ("isoforms") of the COX enzyme exist. There is a constitutive (constantly produced) isoform, COX-1, and an inducible (produced after a stimulus) isoform, COX-2 (Rehman and Sack, Vane and Botting). These isoforms have different distributions throughout the body and play different roles in body functions. COX-1 is constitutively expressed in normal tissues, especially in the GI tract, kidneys, and platelets, and produces prostaglandins that perform a number of functions. Most importantly, these prostaglandins protect the GI tract from corrosive digestive acids, regulate platelets, and maintain kidney function. COX-2—the inducible COX isoform—is rapidly produced in response to tissue injury and produces prostaglandins that act as powerful mediators of pain and inflammation in various tissues. Conventional NSAIDs nonselectively inhibit both COX-1 and COX-2.

It was clear that NSAIDs that could inhibit COX-2 without suppressing COX-1 might provide anti-inflammatory and analgesic effects with a reduced risk of GI and other adverse events. There are already 2 COX-2 inhibitors available by prescription, and a third will be available soon. To find out if one of these new NSAIDs are appropriate for you, please speak with your doctor.

References

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