Original Article

The Effect of Selectivity of Inhibitors to Cox-2 Enzyme on Hepatobiliary and Platelet Function in Patients with Osteoarthritis

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Summary:

Background: The development of non steroidal anti-inflammatory drugs (NSAIDs) was based principally on inhibiting cyclooxygenases (COX) activity. However, the identification of two COX- isoforms (i.e., COX-1 and COX-2) with different physiological effects has led to the development of COX-2 specific NSAIDs, with fewer adverse effects than traditional NSAIDs. Therefore, They are expected to produce anti-inflammatory activity with minimal adverse effects on GI mucosa, as well as, other structures and cells such as platelets. The aim of this study is to evaluate the effect of selectivity of COX-2 inhibitors on many organs and systems function such as the hepatobiliary system, platelets function, as well as, serum uric acid levels.

Patients and methods: Thirty six patients with osteoarthritis participated in this study. Twenty – four of them were treated with 400 mg celecoxib/day. The remainder received 15 mg meloxicam daily for 3 months .In addition to twelve apparently healthy subjects as a control . Measurement of serum alanine transaminase , serum alkaline phosphatase activity ,total serum protein, and serum albumin to evaluate hepatobiliary system . In addition to the estimation of bleeding time to evaluate the effect of selectivity of inhibitors to COX-2 on platelets function.

Results: The results showed minor variations in their effects on liver function tests. However, meloxicam, the relatively selective COX-2 inhibitor affects bleeding time more than does celecoxib, the purely COX-2 selective. Whereas, celecoxib elevated serum levels of uric acid more than meloxicam.

Conclusion: We could conclude that selectivity to COX-2 enzyme has different odds of risks on platelets function, such effects that could add more risk factors to patients due to their pharmacological action.

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Introduction:

Selective cyclooxygenase (Cox)-2 inhibitors that are widespread in clinical use , were developed to avoid side effects of conventional NSAIDs, including gastrointestinal and renal toxicity (1). These agents offer potentially significant advantages because of their relative lack of gastrointestinal irritation (2). Because of this, it is likely that these medications will be frequently used in the management of dental and other medical conditions (3). Traditional nonsteroidal antiinflammatory drugs (NSAIDs) inhibit both isoforms of the enzyme cyclooxygenase (Cox). The first, Cox-1, is constitutively expressed in most cells throughout the body, and its inhibition has been associated with gastrointestinal bleeding and ulceration (2). In contrast, Cox-2 expression is induced in the presence of inflammation and its inhibition results in the therapeutic effects of NSAIDs.

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Thus, the development of selective Cox-2 inhibitors brought about a new way to produce potent antiinflammatory actions with a decreased risk of significant gastrointestinal adverse effects (4). Celecoxib is a NSAID reported to be a selective inhibitor of cyclo-oxygenase-2 (Cox-2). It is used in the treatment of rheumatoid arthritis and osteoarthritis and as adjunctive treatment of adenomatous colorectal polyps (5). Meloxicam selectivity for Cox-2 is dose dependent and is reduced at higher doses. Therefore meloxicam has been labeled a "preferential" inhibitor instead of a "selective" inhibitor of Cox-2(6).The enzyme Cox-2 is not found in platelets, but in endothelial cells induces prostacyclins synthesis, which prevents platelet aggregation and promotes vasodilatation (7). Thus Cox-2 inhibitors block endothelial prostacyclin synthesis, which leads to platelet aggregation and vasoconstriction (8). Unlike the traditional NSAIDs , celecoxib inhibited Cox-1 derived thromboxine A2 (TXA2) coincident with its impact on prostcycline (PGI2) , the