Prescribing pattern of gastroprotective agents with non-steroidal anti-inflammatory drugs

Sir,

Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used drugs for management of pain and inflammation. They represent a most widely prescribed class of medications and are used as over the counter drugs. NSAIDs work by interfering with cyclooxygenase (COX) pathway, which involves the conversion of arachidonic acid by the enzyme COX to prostaglandins. COX is available in two isoforms i.e., COX-1 and 2. Despite wide clinical use of classical NSAIDs as analgesics, anti-pyretic, and anti-inflammatory agents, their gastro-intestinal toxicity is a major clinical limitation. This adverse effect is associated with their ability to inhibit COX-1 in the gastrointestinal tract.[1] Subsequently, the selective COX-2 inhibitors emerged as potentially gastro-friendly NSAIDs and it was conceptualized that sufficient therapeutic benefits are achieved by selective COX-2 inhibition. At first glance these COX-2 inhibitors looked like a solution to NSAIDs related GI complication. However, Post marketing experience unmarked various adverse cardiovascular effects. Recent evidences of adverse cardiovascular events with the use of COX-2 selective inhibitors have created a sense of insecurity not only among prescribers but also among consumers.[2]

With a variety of NSAIDs that are presently available, it is difficult at times to select a particular NSAID. Keeping present scenario in mind this prospective study was planned and conducted during a six months period from December 2010 to May 2011. All the prescriptions from newly registered patients suffering from rheumatoid arthritis, osteoarthritis and low back pain were collected once the patients had been attended by the doctors, in the outpatient unit. A specially designed form was used to record and analyze the following information; Total number of prescriptions: 440, number of oral NSAIDs: 620, number of prescriptions with gastroprotective agents: 260, number of prescriptions with oral NSAIDs and gastroprotective agents: 260 (41.93%).

A total of 620 NSAIDs were prescribed, 55.96% as monotherapy and 44.04% as fixed dose combination (FDC). Among these 596 (96.12%) were non-selective and 24 (3.87%) were selective NSAIDs. Diclofenac sodium 228 (36.77%) followed by ibuprofen and etodolac were the conventional older NSAIDs commonly used and among newer selective COX-2 inhibitors Etoricoxib 24 (3.87%) was prescribed [Table 1].

The gastroprotective agents prescribed were proton pump inhibitors (PPIs) (94.61%) and H_2 antagonists (5.38%). The NSAID which was most commonly used with gastroprotectives was diclofenac 70.0%. Etoricoxib was the least used NSAID with a gastroprotective agent 1.92% [Table 2].

COX-2 selective inhibitors were developed with assumption of better safety profile (renal and gastrointestinal) than non-selective NSAIDs and became very popular few years

Table 1: Pattern of non-steroidal anti-inflammatory drugs used in orthopaedics

Total number of prescriptions	*n*=440
Total number of drugs used	1,000
Average number of drugs per prescription	2.27
Total number of NSAIDs	620 (62.0%)
As Monotherapy	55.96%
As FDC*	44.04%
Total number of non-selective NSAIDs	596 (96.12%)
Diclofenac	228 (36.77%)
Ibuprofen	132 (21.29%)
Etodolac	105 (16.93%)
Piroxicam	075 (12.09%)
Nimesulide	056 (09.03%)
Total number of selective NSAIDs	
Etoricoxib	024 (3.87%)
Total number of gastroprotective agents	260 (26.0%)
Concomitant medications (Calcium Salts, vitamin D3 and vitamin E)	120 (12.0%)

*Fixed dose combinations, NSAIDs=Non-steroidal anti-inflammatory drugs

Table 2: Pattern of gastroprotectives prescribed along with non-steroidal anti-inflammatory drugs

Drug	Numbers prescribed	Percentage
Proton pump inhibitors		
Pantoprazole	230	88.46
Rabeprazole	016	06.15
H_2 Blocker		
Ranitidine	014	05.38
Along with different NSAIDs		
With Diclofenac in monotherapy and FDC*	182	70.0
With Etoricoxib	005	01.92
With others	073	28.07

*Fixed dose combinations, NSAIDs=Non-steroidal anti-inflammatory drugs

back. However, the results of present study points towards the reversal of trends back to the use of conventional NSAIDs. This shift might have come with the recent reported cardiovascular toxicity with the use of selective COX-2 inhibitors. Recent reports from population based studies indicate increased risk of myocardial infarction and congestive cardiac failure in patients prescribed with rofecoxib and celecoxib. Similarly, thromboembolic phenomenon with parecoxib and valdecoxib use has been reported after cardiac surgery.[3]

Gastric side effects are a cause of concern with non-selective COX inhibitors and hence are co-prescribed with an anti-ulcer agent. In this study proton pump inhibitors were the most commonly used gastroprotective agents, followed by H_2 antagonists. Literature too suggests that proton pump inhibitors produce more sustained acid suppression as compared to H_2 blockers and promote ulcer healing despite continued NSAID therapy. Antacids were not used, and rightly so, since they are indicated only for symptomatic relief of pain and are associated with a number of drug interactions, thereby restricting their rational indication.[4] Misoprostol, the drug used prophylactically with NSAIDs to prevent NSAID-induced ulcers,[5] was not used at all. This may be because of various reasons including the higher cost, frequent side effects and the need for multiple daily dosing of misoprostol.[4]

To conclude, the present study points towards the reversal of trends back to the use of conventional NSAIDs. Since proton pump inhibitors produce more effective acid suppression despite continued NSAIDs therapy; they should be preferred over H_2 antagonists in chronic inflammatory conditions like rheumatoid arthritis and osteoarthritis as seen in our study.

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