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ORIGINAL ARTICLE

## Trends in Prescribing Gastroprotective Agents with Non Steroidal Anti-Inflammatory Drugs in an Orthopaedic Outpatient Unit of a Tertiary Care Hospital

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### ABSTRACT

**Background:** Non steroidal anti-inflammatory drugs (NSAIDs) are the most common drugs prescribed the world over. However, they have many adverse effects, especially gastrointestinal toxicity, which is the reason for their frequent co-prescription with gastroprotective agents. Misoprostol has been specifically approved for prevention of NSAID-induced ulcers in high-risk patients. Proton pump inhibitors too have been used with outstanding efficacy for this indication.

**Aim:** This drug utilization study was conducted to study the co-administration of NSAIDs with gastroprotective drugs in an Orthopaedic Outpatient Unit of an urban, tertiary care, teaching hospital.

**Settings and Design:** A prospective drug utilization study

**Patients and Methods:** This was a prospective study conducted in the Orthopaedic Outpatient Unit of an urban, tertiary care, teaching hospital, for six months. Prescriptions were collected from patients attending the Orthopaedic Outpatients Department. The co-prescription of NSAIDs with gastroprotective agents was analyzed.

**Results:** A total of 1008 prescriptions were studied; 884 prescriptions contained NSAIDs, out of which 288 (32.58%) were co-prescribed with gastroprotective agents. The most common gastroprotective agents combined with NSAIDs were Proton pump inhibitors (81.19%). H<sub>2</sub> receptor blockers were a distant second (17.81%), while Misoprostol was not used at all.

**Conclusion:** NSAIDs are commonly co-prescribed with gastroprotectives. Diclofenac is the most commonly co-prescribed NSAID, while Naproxen was least commonly co-prescribed with gastroprotectives. Proton pump inhibitors were most frequently used, while Misoprostol was not used at all, probably because of its higher costs, frequent side effects and the need for multiple daily dosing.

### Key Messages

- NSAIDs are commonly co-prescribed with gastroprotectives.
- Diclofenac is the NSAID which is most commonly co-prescribed with gastroprotectives.
- Proton pump inhibitors are the gastroprotectives which are most frequently co-prescribed with NSAIDs.
- Misoprostol was not used at all, probably because of its higher costs, frequent side effects and the need for multiple daily dosing.
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**Key words:** NSAIDs, gastroprotectives, drug utilization study

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## Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used medicines in the world. They have a wide variety of indications for use, ranging from treatment of acute pain to more chronic conditions such as rheumatoid arthritis. These agents exert their effect by inhibiting the activity of the enzyme cyclooxygenase, with a resultant reduction in prostaglandin synthesis and an alleviation of the inflammatory response [1]. Their association with gastrointestinal toxicity – dyspepsia, peptic ulcers and gastrointestinal bleeds is well known [2].

The demonstration of two unique isoforms of cyclooxygenase (designated COX-1 and COX-2) has led to a greater understanding of the mechanism of action of NSAIDs and has also provided an explanation for their toxicity [1]. Selective COX-2 inhibitors were developed with the aim of minimizing gastrointestinal toxicity, while maintaining anti-inflammatory activity [3]. However, clinical and experimental data, as well as reviews suggest that the long term use of selective COX-2 inhibitors is associated with an increase in systolic blood pressure and cardiovascular morbidity and mortality due to myocardial infarction[4],[5].

The use of NSAIDs is an important predisposing factor for peptic ulcer disease in the community. Approximately 10-20% of patients who receive long-term NSAID therapy develop asymptomatic peptic ulceration and ulcer-related complications (bleeding and perforation) develop in 1-2% of persons per year[6]. This warrants a cautious use of NSAIDs in high risk individuals who include the elderly, those already receiving gastro-toxic agents and those with a history of gastro-intestinal

diseases[7]. So, the best alternative in such individuals would be the co-administration of NSAIDs with gastroprotective drugs. Misoprostol, an analog of prostaglandin E<sub>1</sub>, has been specifically approved for the prevention of NSAID-induced ulcers in high-risk patients. Proton pump inhibitors too, have been used with outstanding efficacy for this indication.

Drug utilization studies are continuing programmes that review, analyze and interpret the pattern of drug use against pre-determined standards. This drug utilization study was conducted to study the co-administration of non-steroidal anti-inflammatory drugs (NSAIDs) with gastroprotective drugs in an Orthopaedic Outpatient Unit of an urban, tertiary care, teaching hospital.

## Patients and Methods

A prospective study was conducted in the Orthopaedic Outpatient Unit of an urban, tertiary care, teaching hospital, during July and August 2006. Prescriptions were collected from patients attending the Orthopaedic Outpatients Department. The co-prescription of NSAIDs with gastroprotective agents was analyzed. The Institutional Ethics Committee's approval was obtained before starting the study.

The use of gastroprotective agents with the 12 most commonly prescribed NSAID preparations, either as monotherapy or Fixed Dose Combinations (FDC), was analyzed in detail.

## Results

Total number of prescriptions: 1008  
 Number of prescriptions with oral NSAIDs: 884  
 Number of prescriptions with gastroprotective agents: 303  
 Number of prescriptions with oral NSAIDs and gastroprotective agents: 288 (32.58%)

The gastroprotective agents prescribed were proton pump inhibitors (PPIs) (81.19%), H<sub>2</sub> antagonists (17.82%) and antacids (0.99%). None of the other gastroprotective agents

were used. The different drugs used in these groups are shown in [Table/Fig 1].

(Table/Fig 1) Gastroprotective Agents prescribed

<b>Proton Pump Inhibitors:</b>	246 (81.19%)
• Panteprazole	69
• Rabeprazole	126
• Omeprazole	41
• Esomeprazole	05
• Lansoprazole	05
<b>H<sub>2</sub> antagonists:</b>	54 (17.82%)
• Rantidine	53
• Famotidine	01
<b>Antacid preparations:</b>	03 (0.99%)

The use of gastroprotective agents along with the 12 commonly used NSAIDs, either as monotherapy or FDCs, is shown in [Table/Fig 2]. The NSAID which was most commonly used with gastroprotectives was Diclofenac. Naproxen was the least used NSAID with a gastroprotective agent.

(Table/Fig 2) NSAIDs co-prescribed with Anti-Ulcer agents

NSAID	No. of prescriptions (n)	Co-prescription with anti-ulcer agents		
		N (%)	PPIs <sup>a</sup>	H <sub>2</sub> Antagonists
Diclofenac	165	109(66.1)	95	14
Diclofenac + serratiopeptidase	86	42(48.84)	32	10
Paracetamol + Tramadol	84	41(48.81)	29	12
Naproxen	65	01(1.54)	01	00
Acceclofenac	56	18(32.14)	15	03
Nimesulide	47	07(14.9)	07	00
Etoricoxib	32	06(18.8)	05	01
Diclofenac+Paracetamol + Chlorzoxazone	27	05(18.5)	04	01
Piroxicam	29	01(3.45)	01	00
Acceclofenac + Paracetamol	20	08(40)	06	02
Diclofenac + Paracetamol	25	10(4)	06	04
Nimesulide + Chlorzoxazone	18	02(11.11)	02	00

<sup>a</sup>PPI – Proton pump inhibitors

## Discussion

When gastric side effects are a cause of concern, non selective COX inhibitors are co-prescribed with an anti-ulcer agent. The use of selective COX-2 inhibitors seems to have decreased after the cardiac adverse effects which were observed with these drugs [4], [5].

Diclofenac was the most commonly co-prescribed NSAID with a gastroprotective

agent - 69.60%. Naproxen was least commonly co-prescribed with a gastroprotective agent - 1.96%.

Proton pump inhibitors were the most commonly used gastroprotective agents, followed by H<sub>2</sub> antagonists. Literature too suggests that Proton pump inhibitors produce more sustained acid suppression as compared to H<sub>2</sub> blockers [8] and promote ulcer healing despite continued NSAID therapy [6]. Antacids were rarely 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 [9]. Misoprostol, the drug indicated for the prophylaxis of high risk individuals, was not used at all [7]. This may be because of various reasons including the higher cost, frequent side effects and the need for multiple daily dosing of Misoprostol. In any case, similar or even better efficacy is obtained by Proton pump inhibitors in preventing and/or treating NSAID-induced peptic ulcers.

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