



DRUG UTILIZATION PATTERN IN PRESCRIBING GASTROPROTECTIVE DRUGS WITH NON STEROIDAL ANTI-INFLAMMATORY DRUGS IN AN ORTHOPAEDIC OUTPATIENT UNIT OF A TERTIARY CARE HOSPITAL OF RAJASTHAN

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ABSTRACT

Despite wide clinical use of NSAIDs as analgesics, anti-pyretics, and anti-inflammatory agents their gastro-intestinal toxicity is a major clinical limitation, which is the reason for their frequent co-prescription with Gastroprotective drugs like Proton Pump Inhibitor, H₂ blocker, misoprostol. To study drug utilization pattern of co-administration of NSAIDs with gastroprotective drugs and identify points for future intervention to improve outcomes. About 1000 prescriptions collected during Sep 2011 to Feb 2012 from patients visiting to Outpatient Department of Orthopedics, S.R.G. Hospital, Jhalawar and co-prescriptions of NSAIDs with gastroprotective agents were analyzed. 712 out of 1000 prescriptions contained NSAIDs, out of which 338 (47.5%) were co-prescribed with GP drugs. The most common GP drug combined with NSAIDs were H₂ receptor blockers (61%). Proton pump inhibitors were a distant second (38%), while Misoprostol was not used at all. The NSAID most commonly & least commonly used with gastroprotectives was Diclofenac & Naproxen respectively. 241 (33.8%) Prescriptions with FDC were prescribed but none of them are included in National Essential Drug List of India.

Keywords: NSAIDS, Gastroprotective drugs, Proton Pump Inhibitor, COX Inhibitor.

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used drugs for years for management of pain and inflammation with good efficacy and represent most widely prescribed class of medications in the world and are used as over the counter drugs, but their use increases the risk of upper-gastrointestinal (UGI) toxicity.

Data suggest that in England, nearly 20 million NSAIDS treatments were prescribed in 2004 alone and more than 111 million prescriptions were written in the United States in 2000 for NSAIDS¹.

The incidence of serious UGI adverse events is approximately 1.5–2.0% per year of therapy, four times higher than in nonusers². According to a published report nearly 100,000 patients were hospitalised in the United States in the year 1999 due to NSAIDS induced gastropathy which resulted in 16500 deaths³. Similar studies from the United Kingdom suggest nearly 12000 annual admissions and 4000 deaths resulting from NSAIDS-induced gastropathy⁴.

If deaths from gastrointestinal toxic effects of NSAIDs were tabulated separately in the National Vital Statistics reports, these effects would constitute the 15th most common cause of death in the United States⁵. In general, at least 10 to 20 percent of patients have dyspepsia while taking an NSAID, although the prevalence may range from 5 to 50 percent. Within a six month period of treatment, 5 to 15 percent of patients with rheumatoid arthritis can be expected to discontinue NSAID therapy because of dyspepsia⁶. According to prospective data from the

Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS), 13 of every 1000 patients with rheumatoid arthritis who take NSAIDs for one year have a serious gastrointestinal complication. The risk in patients with osteoarthritis is somewhat lower (7.3 per 1000 patients per year)⁷.

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. Selective COX-2 inhibitors were developed with the aim of minimizing gastrointestinal toxicity, while maintaining anti-inflammatory activity⁸. 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 risk of cardiovascular morbidity and mortality⁹⁻¹³.

So the strategies for the primary prevention of adverse GI outcomes in NSAID users include co-therapy with Proton pump inhibitors (PPIs), H₂ blockers, Prostaglandin analogue, Antacids.

Drug utilization studies are continuing programmes that review, analyze and interpret the pattern of drug use against predetermined standards. This research was conducted to study the co-administration of NSAIDs with gastroprotective drugs in an Orthopaedic Outpatient Unit of an urban, tertiary care, teaching hospital of Rajasthan.



MATERIALS AND METHODS

A prospective drug utilization study of 1000 prescriptions collected during Sep 2011 to Feb 2012 from patients attending the Orthopaedic out patients department S.R.G. Hospital, Jhalawar. The co-prescriptions of NSAIDs with gastroprotective agents were analyzed. The Institutional Ethics Committee's approval was obtained before starting the study. Details regarding Patient's demographic features were obtained and the frequency & trends of use of gastroprotective agents with the 13 most commonly prescribed NSAID preparations, either as monotherapy or Fixed Dose Combinations (FDC), was analyzed in detail. Only those prescriptions were included which had printed prescribers name, qualifications and status. Only new patient with new prescriptions were included in study. Generic formulations of all preparations were determined and charted in an excel sheet. Simple frequencies and percentages were obtained for various variables.

RESULTS

Males were 2.1 times more frequent than female. Most common age group encountered was between 21 – 39 yrs (41.8%). Out of total 1000 prescriptions, number of prescriptions with oral NSAIDs were 712 and out of which only 338 (47.5%) prescriptions were co-prescribed with gastroprotective. 241 (33.8%) Prescriptions with FDC were prescribed but none of them are rational according to National Essential Drug List of India. The demographic parameter has been described in Table 1.

The gastroprotective agents prescribed were H₂ blockers (61%), PPIs (38%), and antacids (< 1 %). The frequency of GP drugs used is shown in Table 2.

Table 1: Demographic characteristics

Patient Characteristics	Number	(%)
Age Group (years)		
<20	131	13.1
21- 39	418	41.8
40- 59	327	32.7
>60	124	12.4
Sex		
Male	678	
Female	322	
M:F Ratio	2.1 : 1	
Prescribing Indicators		
Total no. of prescriptions	1000	
Total no. of drug used	2736	
Average no. of drugs per prescription	2.7	
Total no. of prescription with NSAIDS	712	
Total no. of prescription with GP agents	338	
Total no. of prescription with FDCs	241	
Miscellaneous Drugs		
Antibiotics	78	
Vitamin B-Complex	67	
Calcium	53	
Thiocholchicoside	33	

Table 2: Gastroprotective drugs prescribed

H₂ Antagonists	206 (61%)
Ranitidine	191
Famotidine	15
Proton Pump Inhibitors	128 (38%)
Omeperazole	97
Rabeperazole	26
Pantoperazole	09
Antacids	4 (<1%)

The use of gastroprotective agents along with the 13 commonly used NSAIDs, either as monotherapy or FDCs, is shown in Table 3. The NSAID most commonly & least commonly used with gastroprotectives was Diclofenac & Naproxen respectively.

Table 3: NSAIDS co-prescribed with GP drugs.

NSAIDS	No. of prescriptions (n)	Co- prescribed with GP agents		
		N (%)	H ₂ Antagonists	PPIs
Diclofenac	214	152 (71%)	98	54
Diclofenac + Paracetamol	82	48 (58.5%)	32	16
Ibuprofen	77	31 (40%)	20	11
Ibuprofen + Paracetamol	52	35 (67.3%)	18	17
Diclofenac + Serratiopeptidase	49	21 (42%)	13	07
Diclofenac + Chlorzoxazone	41	18 (43%)	7	11
Etoricoxib	39	01 (12%)	01	0
Aceclofenac	37	08 (21%)	05	03
Naproxen	33	06 (18%)	04	02
Aceclofenac + Paracetamol	17	05 (29%)	03	02
Nimesulide	16	09 (56%)	04	05
Tramadol + paracetamol	14	04 (28.5%)	02	02
Diacerin	4	01 (25%)	01	0



DISCUSSION

NSAID-associated gastropathy remains a significant source of morbidity and mortality, especially in high-risk patients. Evidence suggests that the appropriate use of concomitant therapy with a H₂ blockers, PPIs or misoprostol, in high-risk patients will reduce the incidence of GI ulceration and complications and remain cost-effective.

Because of publicity surrounding the cardiovascular safety of COX-2 selective inhibitors and other NSAIDs, there is a recent shift in emphasis on NSAIDs from GI to cardiovascular toxicity. Treatment recommendations encompassing both cardiac & GI risk stratification have been postulated. Patients at low risk for gastroduodenal complications and without cardiovascular risk are good candidates for NSAID monotherapy, whereas patients at high risk for GI events without cardiovascular risk require addition of misoprostol, H₂ blocker or a PPI, or discontinuation of NSAIDs and initiation of either a non-NSAID analgesic or a COX-2 inhibitor as monotherapy. The subgroup of patients with both high risks of GI and cardiovascular disease, and who take long-term aspirin, require non-NSAID analgesics or a nonselective NSAID plus a gastro-protective drug^{14,15}.

CONCLUSION

The selective NSAIDs are costlier than the non-selective NSAIDs, but the cost of therapy per prescription to the patient sometimes is lower as the selective NSAIDs need not be complimented with concomitant therapy with gastroprotective drugs.

A very high tendency to use NSAIDS exists amongst doctors of all grades. Also the use of multiple NSAIDS and rather haphazard use of GPA by prescribers reflects the inadequacy of the basic understanding in the mechanism of action of these drugs. Large scale efforts are required at different forum, symposia, workshops and conferences to address this serious issue adequately.

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