CODEN (USA): IJPB07 ISSN: 2320-9267

Indian Journal of Pharmaceutical and Biological Research (IJPBR)

Journal homepage: www.ijpbr.in

Research Article

Prescription pattern of NSAIDS and the prevalence of NSAID-induced gastrointestinal risk factors of orthopaedic patients

Anita P Antappan[1], Bibin Punnoose Micheal,[1] Merin Anto Thelappilly[1], Thazneem Bagum T.D[1],Leo Mathew[2*], L.Panayappan[3] ,K .Krishnakumar[4]

[1]Pharm D Interns, Department of pharmacy practice , St,James college of Pharmaceutical Sciences, KUHS University, Chalakudy, Kerala, India
[2]Assistant Professor, Department of Pharmacy Practice, St,James college of Pharmaceutical Sciences, KUHS University, Chalakudy, Kerala, India
[3]Head of the Department, Department of Pharmacy Practice, St,James college of Pharmaceutical Sciences, KUHS university, Chalakudy, Kerala, India
[4]Principal, St, James college of Pharmaceutical Sciences, KUHS University, chalakudy-680307, Kerala, India

ARTICLE INFO:

Article history:
Received: 14 July 2017
Received in revised form:
18 August 2017
Accepted: 28 August 2017
Available online: 30 September 2017

Keywords:
Anti-Inflammatory Agents, Non-Steroidal;
GI risk factor;
Cyclooxygenase 2 Inhibitors;
SCORE

ABSTRACT

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly used medications in the world. NSAID-induced adverse reactions involve upper gastrointestinal (GI) tract complications, which can be life-threatening. **Objectives:** The study was conducted to explore the current prescription pattern of non-steroidal anti-inflammatory drugs (NSAIDs) and the prevalence of NSAID-induced gastrointestinal(GI) risk factors of orthopedic adult inpatient.**Materials and methods**: A prospective observational NSAIDs induced GI risk related study was conducted over a period of 6 months by clinical pharmacist. Study cohort included 105 orthopaedic inpatients who are taking or will be taking NSAIDs for more than a week. A self-administered questionnaire was completed by each patient. A simplified risk scoring scale (the Standardized Calculator of Risk for Events; SCORE) was used to measure patients' risk for GI complications. The pattern of NSAIDs prescription was identified from medical recordings.**Results:** The study groups were stratified into four risk groups according to GI SCORE tool, 27.6% of the patients belonged to high risk or very high risk groups for GI complications. Analysis of prescription pattern revealed that 11.4% of the patients aged over 65 yr, 19% with co morbid disease were prescribed with COX-2 selective inhibitor.
Conclusion: In this study assessment of prescription pattern and GI risk factors for NSAIDs were evaluated and in conclusion, physician's considerate prescription of NSAIDs with well-understanding of each patient's GI risk factors is strongly encouraged to prevent serious GI complications

Introduction

Although there are many definitions of an ADR, an internationally accepted description is that of the World Health Organization (WHO): ''A response to a drug that is noxious and unintended, and that occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease or for the modification of physiological function". The NSAIDs are a group of chemically dissimilar agents that differ in their antipyretic, analgesic, and anti-inflammatory activities. GI complications occur in 1%-5% of patients taking NSAIDs for more than one year and result in high costs and mortality. Rates of GI complications may vary substantially depending on each patient's clinical characteristics. Identification of the NSAID-related GI risk factors is therefore crucial in determining the proper treatment for each patient. Many studies already reported that the development of serious GI complications are highly correlated with certain factors, including health status of disability, increasing age, concomitant use of systemic steroids or anticoagulants, history of a GI ulcer of bleed, diagnosis of rheumatoid arthritis, certain patterns of prior NSAID use, history of cardiovascular disease, smoking status, and NSAID-related GI symptoms .

Prior to market release of the first cyclooxygenase-2 enzyme(COX-2) selective inhibitor (celecoxib), northern California health maintenance organization (HMO) developed

***Corresponding Author: Leo Mathew,** Assistant Professor, Department of Pharmacy Practice, St James college of pharmaceutical sciences. KUHS University, Chalakudy, Kerala, India

a treatment guideline for the use of NSAIDs based on the Standardized Calculator of Risk for Events (SCORE) program developed at Stanford University, Division of Immunology and Rheumatology. The SCORE tool stratifies patients by risk of developing serious GI complications using patient characteristics that have assigned points. It is desirable that physicians consider each patient's clinical factors before prescribing NSAIDs. In this study, we evaluated the current prescription pattern of NSAIDs and the prevalence of NSAID-induced GI risk factors of orthopaedic patients.

Materials and methods

The study was conducted in a multispecialty tertiary care hospital, in the department of orthopedics. A total of 105 patients were enrolled in the study. The study was designed to be a prospective observational study, carried out in single center for a period of 6 months. The sample population was selected by inclusion–exclusion criteria. Adult in-patients of orthopedic department who have used or will be using NSAIDs for more than a week were included Patients with difficulty in answering questionnaire and patients who are unwilling to participate in the study are excluded from the study.The protocol of the study was submitted to Institutional Human Ethics Committee (IHEC) of hospital. The protocol was approved by the committee with the approval number SJPCEC/P25/PP/2014/034 and the hospital approval number SJCP/DIR/A.20/2015-2016.

The study was conducted by collecting the data from the patient's medical records from orthopedics department. GI Standardized Calculation of Risk Estimation was done through case sheets and patient interview. A specially designed data entry form which includes GI SCORE (GI Standardised Calculation of Risk Estimation) calculator to asses GI risk. The GI SCORE was made and validated by Dr.Prof. G. Singh Department of Immunology and Rheumatology, Stanford university California. The tool was used after obtaining permission from its creators.

Results

This prospective observational study on "*Prescription pattern of NSAIDs and the prevalence of gastrointestinal risk in orthopaedics patients*" has assessed the prescribing pattern of NSAIDs for orthopaedic problems and the occurrence of GI risk events in the same patients. A total of 105 patients who were admitted in the orthopaedic department were enrolled in the study, in which Women accounted for 81.9% of the patients [Table 1] and the average age for the group was 54.32(21-95) yrs. When dividing into two age subgroups 37(23.8%) patients were aged over 65 years[Table 2]. Arthritis was the most common indication for NSAIDs (45.7%) followed by spinal diseases (18.1%) and fracture (14.2%).[Table 4]Among the GI risk factors identified, the presence of co morbid diseases(cardiovascular, renal, hepatic diseases, diabetes mellitus, hypertension etc) [55.2%] was the most prevalent risk factor in the overall study population, followed by current poor health status (34.28%), old age (≥65 yrs) [23.8%] ,history of steroid use (14.2%), history of GI symptom (13.3%),heavy drinking habit (13.3%),anticoagulant use (12.3%), SSRI use (10.4%),aspirin use (8.5%), heavy smoking habit (8.5%),long term NSAID use(3.8%), rheumatoid arthritis(1.9%), previous hospitalization history due to GI events(1%). [Table no.3].When the study groups were stratified into four risk groups according to GI SCORE tool,38.1% belongs to low risk,34.3% of the patients belonged to moderate risk 8.6 % of the patients were in very high risk and 19% are in high risk groups for GI complications [Table 7]. When the type of prescription was analyzed in overall study groups, Lornoxicam was the most commonly used NSAID, comprising 51.4% of the patients. Etoricoxib (32.3%), Diclofenac (14.2%), Aceclofenac(11.4%), Piroxicam (3.8%), Ibuprofen (2.8%), Aspirin (2%) were followed consecutively. [Table 5].Analysis of prescription pattern revealed that only 19% of patients with co morbid diseases(cardiovascular, renal, hepatic diseases, diabetes mellitus, hypertension etc) , 11.4% of patients aged over 65 yrs , 7.6% of patients with current poor health status ,6.6% of patients with concomitant anticoagulant use, 3.8 % of patients with history of GI symptom, 2 % of patients using SSRIs , 1 % of patients with heavy smoking and drinking habit to decrease the risk of GI complications by prescribing selective COX-2 inhibitors.[Table 6].Analysis of the measures taken to reduce the GI risk shows 89% of patients were prescribed with proton pump inhibitor and the rest 11% were on H_2 receptor antagonist [Table 8]

Distribution Based On Gender

Table 1: Distribution of the sample population based on gender

Study population	Frequency (N=105)	Percentage (%)
Male	**19**	**18.10**
Female	**86**	**81.90**

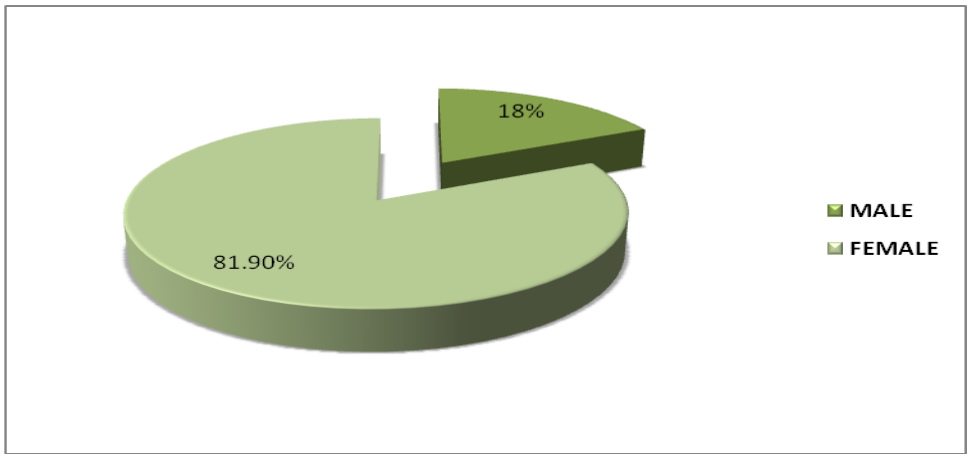

Fig 1: Percentage distribution based on gender

The figure shows the percentage distribution of the study population based on gender

Distribution of the sample population based on age:

Table2: Distribution based on age

Age	No. of patient	Percentage of patient
<20	0	0
20-29	9	8.57
30-39	8	7.61
40-49	24	22.85
50-59	25	23.8
60-69	26	24.76
70-79	9	8.57
80-89	3	2.85
90-99	1	0.95

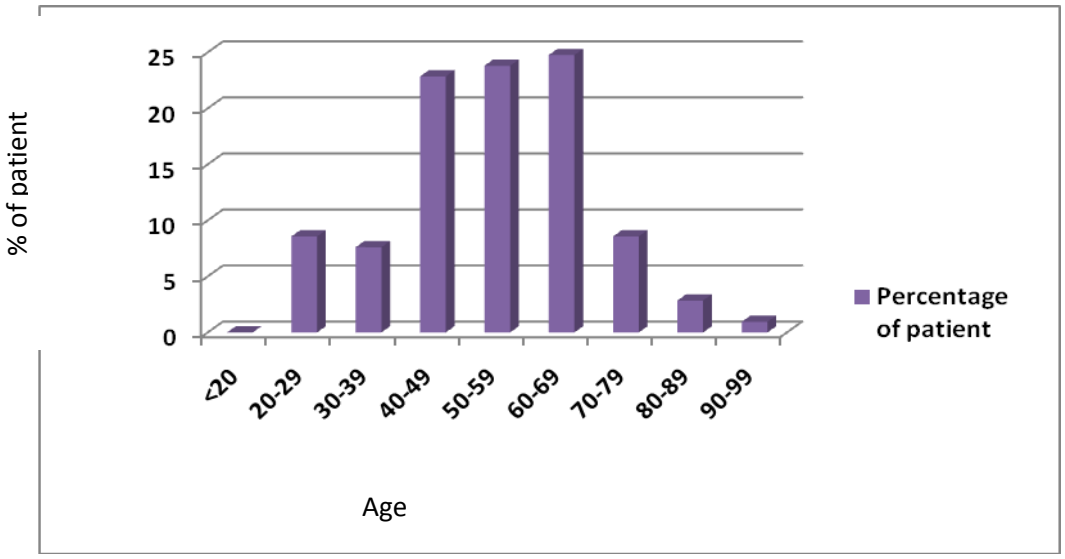

Fig 2: Percentage distribution based on age

The figure depicts the percentage distribution of the study population based on age .

Distribution based on gastrointestinal risk factors

Table 3: Gastrointestinal (GI) risk factors in the overall study population

GI risk factors	Percent of cases (%)
Need for long-term NSAID use	3.8
Age over 65 yr	23.8
Comorbid disease (cardiovascular, renal, liver, diabetes,hypertension)	55.2
History of GI symptom	13.3
Aspirin use	8.5
Heavy smoking habit	8.5
Heavy drinking habit	13.3
History of steroid use	14.2
Currently poor health status	34.28
Rheumatoid arthritis	1.9
Previous hospitalization history due to GI events	1
Selective serotonin reuptake inhibitor (SSRI) use	10.4
Anticoagulant use	12.3

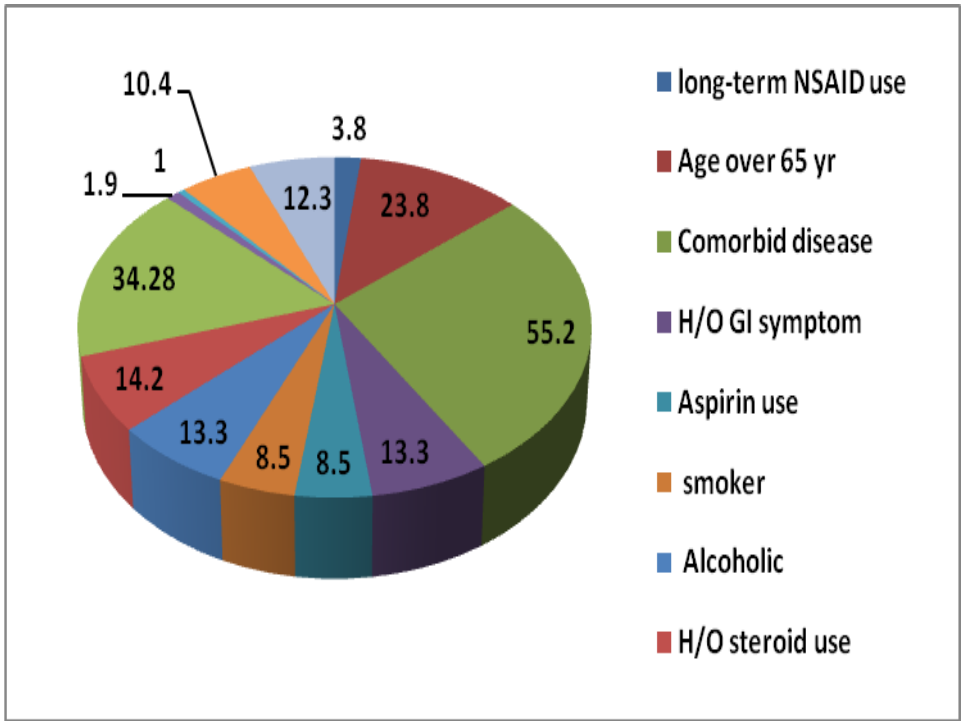

Fig 3: Percentage distribution of gastrointestinal risk factors

The figure shows the percentage distribution of the Gastrointestinal(GI) risk factors in the overall study population

Distribution based on the diagnosis at the time of hospital visit

Table 4: List of diagnosis at the time of hospital visit

Diagnosis	Total	Gender		Age (yr)	
		Male(n = 19)	Female(n = 86)	< 65(n = 80)	≥ 65(n = 25)
Arthritis	45.7%	6	42	38	10
Knee arthritis	26.6%	1	29	21	9
Periarthritis	9.5%	3	7	10	
Rheumatoid arthritis	1.9%		2	2	
Spinal disease	18.1%	3	16	15	4
Spondylosis	3.8%	1	3	3	1
Fracture	14.2%	8	7	12	3
Wrist/hand fracture	4.7%	4	1	4	1
Foot/ankle fracture	6.6%	1	6	6	1
Femur fracture	1.9%	1	1	2	
Other diseases	21.9%	2	21	15	8

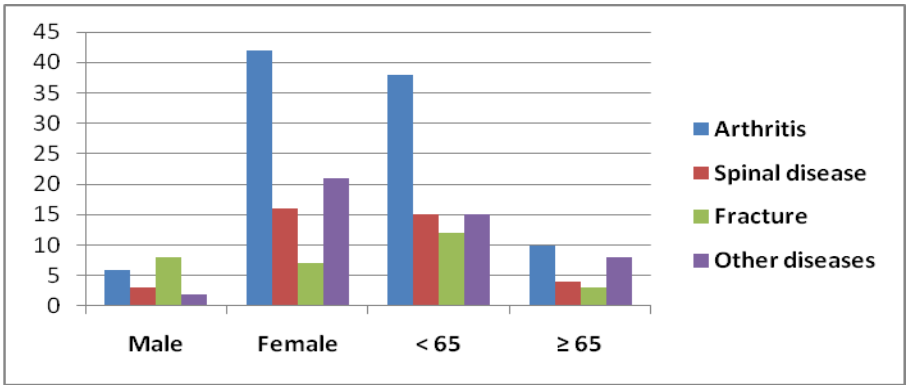

Fig 4: Distribution based on diagnosis

The figure depicts the diagnosis at the time of hospital visit

Distribution based on the prescription pattern of NSAIDs

Table 5: The type of prescription in overall study population

Drugs	Total	Male	Female	<65	>65
Lornoxicam	51.4	5.7	45.7	37.1	14.2
Aceclofenac	11.4	2	6.6	8.5	2.8
Diclofenac	14.2	2	12.3	11.4	2.8
Etoricoxib	32.3	4.7	27.6	25.7	6.6
Aspirin	2	1	1	-	2
Ibuprofen	2.8	-	2.8	2	1
Piroxicam	3.8	-	3.8	3.8	-

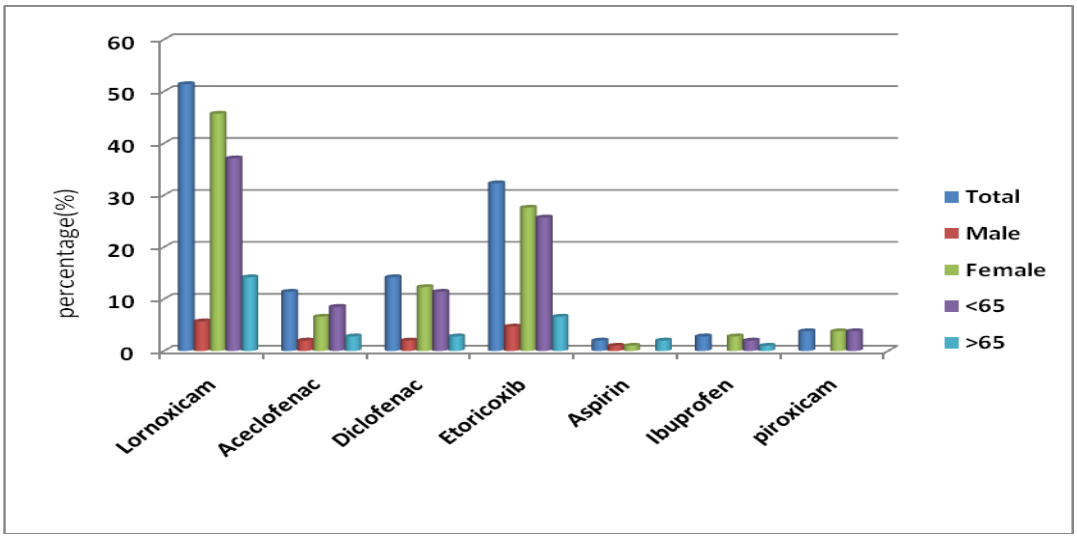

Fig 5: Percentage distribution of prescription patterns of NSAIDs

The figure depicts the prescription pattern of NSAIDs

Distribution based on Prescription pattern of COX-2 inhibitor according to the GI risk factors

Table 6: Prescription pattern of COX-2 inhibitor according to the GI risk factors

GI risk factors	Selective COX-2 inhibitor use(units in %)	Age	
		<65yr	>65yr
Anticoagulant use	6.6	6	1
Age over 65yrs	11.4	0	12
Selective serotonin reuptake inhibitors(SSRI) use	2	1	1
Co morbid disease	19	16	4
Currently poor health status	7.6	5	3
History of GI symptom	3.8	2	2
Heavy smoking habit	1	0	1
Heavy drinking habit	1	0	1

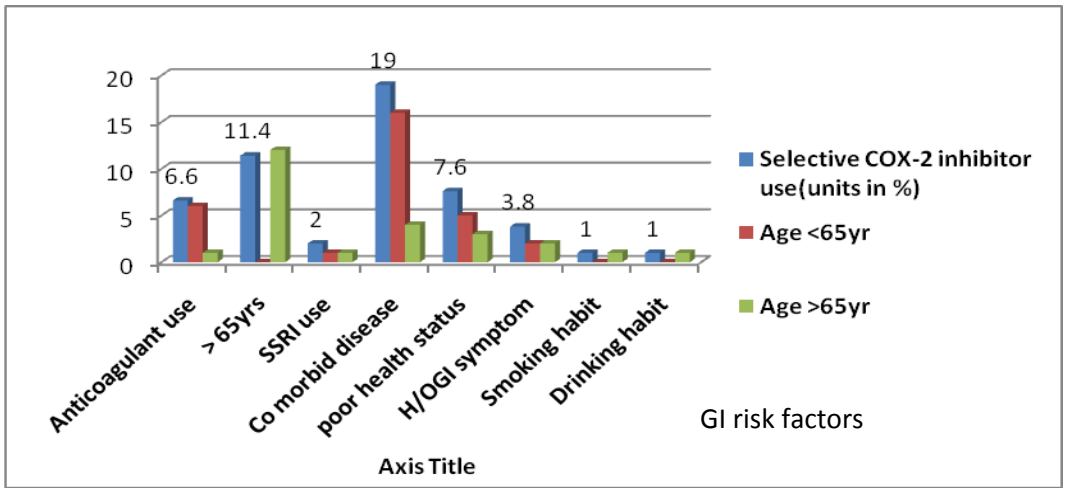

Fig 6: Distribution based on prescription patterns of COX-2 inhibitor according to GI risk factors

The figure depicts the prescription patterns on COX-2 inhibitors based on GI risk factors

Distribution of sample population based on GI score

Table 7: Distribution of sample population based on GI score

Risk level	Level 1 (<10 points)	Level 2 (11-15)	Level3 (16-20)	Level 4 (>20 points)
NO: of patients (%)	38.1	34.3	19.0	8.6

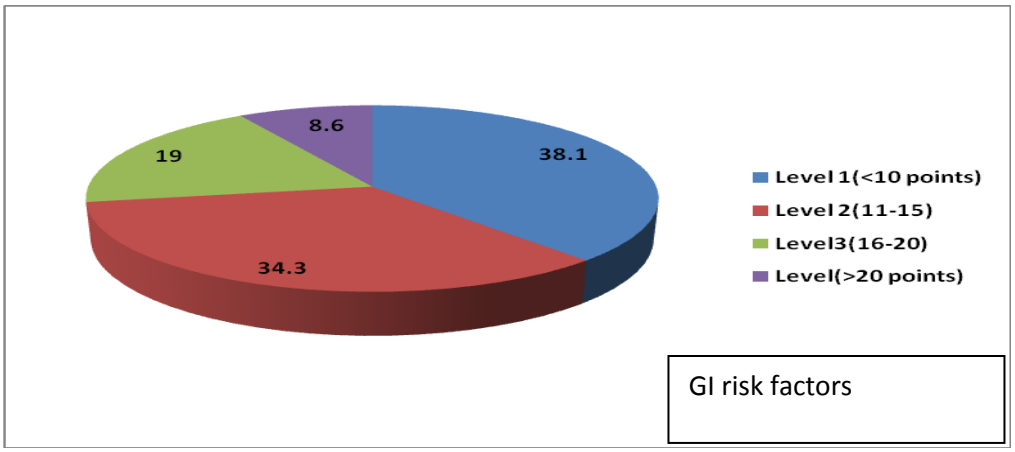

Fig 7: Percentage distribution of sample population based on GI score

This figure shows the percentage distribution of the study population based on the GI score

Distribution based on drugs prescribed to reduce NSAID induced GI risk

Table 8: Distribution of sample population based on drugs used to prevent NSAID induced GI risk

Drugs	Percentage of patients(%)
Proton pumP inhibitor	89
H_2 receptor antagonist	11

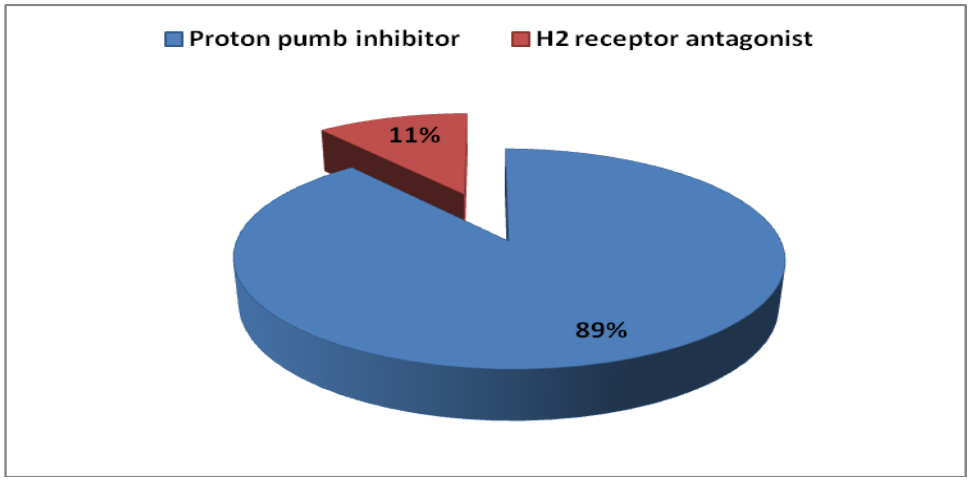

Fig 8: Percentage distribution of sample population based on drugs used to prevent NSAID induced GI risk

This figure shows the percentage distribution of the study population based on the drugs used to prevent NSAID induced GI risk

Discussion

All the individuals participated in the study (105) were grouped according to their gender for analysis as Table 1 & Figure 1.The majority of the people of the study population were female, i.e. about 81.9% remaining 18.1% was male populations.

The respondents were grouped according to their age into 9categories for analyzing as table 2 and figure 2.The majority of patients belongs to category 60-69 i.e.26 (24.76%) with a mean age of 64.About 20-29 patients were belongs to category 9(8.57%),30-39 patients belongs to category 8(7.61%),40-49 belongs to category 24(22.85%),50-59 belongs to category 25 (23.8%),70-79 belongs to category 9(8.57%),80-89 belongs to category 3 (2.85%),90-99 (0.95%) (Table 2 &Figure 5). This study revealed that co morbid disease was the most prevalent risk factor in orthopaedic patients, which is followed by currently poor health(34.28%) ,age over 65 yrs(23.8%),history of steroid use(14.2%),history of GI symptoms(13.3%), anticoagulant use(12.3%) and SSRI use(10.4%) (table 3 & figure 3) .a similar study conducted shows long term NSAID use is the most prevalent risk factor From table 4 & figure 4 , Arthritis was the most common cause of taking NSAIDs (45.7%), followed by other diseases (21.9%),spinal disease (18.1%) and fracture (14.2%).When the type of prescription was analyzed in overall study groups, Lornoxicam (51.4%) was the most commonly used NSAIDs. Etoricoxib (COX-2 selective inhibitor)(32.3%), Diclofenac(14.2%) ,Aceclofenac (11.4%) were followed consecutively in table 5 and figure 5.

Analysis of prescription pattern revealed that only 6.6% of patients with concomitant anticoagulant use, 11.4% of the patients aged over 65 yr, 19% with comorbid disease were prescribed COX-2 selective inhibitor to decrease the risk of developing GI complications (table 6 and figure 6). In table 7 and figure 7, the study groups were stratified into four risk groups according to GI SCORE tool, 38.1% belongs to low risk,34.3% of the patients belonged to moderate risk, 19% belongs to high risk and 8.6% belongs to very high risk.In table 8 and figure 8 ,the study groups were stratified based on drugs prescribed to reduce NSAID induced GI risk.89% of patients were prescribed with proton pump inhibitor and the rest 11% were on H_2 receptor antagonist.

Conclusion

During the study period, most of the risk factors which caused NSAID induced GI problems were analyzed and the prescription pattern of both selective and non-selective COX inhibitors is analyzed. According to the GI SCORE tool 27.6% of patients falls in high risk or very high risk category, the use of selective COX -2 inhibitors are strongly encouraged. A well-understanding of each patient's GI risk factors is necessary in order to maximize cost effectiveness and to prevent serious GI complications.

Acknowledgment

We would like to express our sincere gratitude towards Dr. Prasad Varkey and team Department of orthopaedics, St.James Hospital for his assistance and kind co-operation during the research work. We convey our heartfelt thanks to the Principal and faculty of St.James College of Pharmaceutical Sciences, for their encouragement and support during our work.

References

1. Koncz TA, Lister SP, Makinson GT. Gastroprotection in patients prescribed non-selective NSAIDs, and the risk of related hospitalization, Curr Med Res Opin 2008; 24: 3405-12.
2. Patterson MK, Castellsague J, Walker AM, Pharmaco epidemiol Drug Saf.,2008;17(10):982-8
3. García Rodríguez LA, BarrealesTolosa L. Risk of upper gastrointestinal complications among users of traditional NSAIDs and COXIBs in the general population Gastroenterology 2007; 132: 498-506
4. Vonkeman HE, Fernandes RW, van der Palen J, van Roon EN, van de Laar MA.Arthritis Res Ther. ,2007;9(3):R5
5. Ray WA, Chung CP, Stein CM, Smalley WE, Hall K, Arbogast PG, Griffin MR.m8.Gastroenterology. 2007 ;133(3):790-8. Epub 2007 Jul 3
6. Arroyo M, Lanas A. NSAIDs-induced gastrointestinal damage,Minerva GastroenterolDietol. 2006;52(3):249-59.
7. Goldstein JL, Huang B, Amer F, Christopoulos NG.ClinTher., 2004;26(10):1637-43.
8. Cheetham TC, Levy G, Spence M. Predicting the risk of gastrointestinal bleeding due to nonsteroidal antiinflammatory drugs: NSAID electronic assessment of risk. J Rheumatol 2003; 30: 2241-4
9. El-Serag HB, Graham DY, Richardson P, Inadomi JM.Arch Intern Med. 2002;162(18):2105-10.
10. Bull SA, Conell C, Campen DH. Relationship of clinical factors to the use of COX-2 selective NSAIDs within an arthritis population in a large HMO. J Manag Care Pharm 2002; 8: 252-8.
11. Tramèr MR, Moore RA, Reynolds DJ, McQuay HJ. Quantitative estimation of rare adverse events which follow a biological progression: a new model applied to chronic NSAID use. Pain 2000; 85: 169-82.
12. White TJ, Arakelian A, Rho JP. Counting the costs of drug-related adverse events. Pharmacoeconomics1999; 15: 445-58
13. Singh G, Rosen Ramey D. NSAID induced gastrointestinal complications: the ARAMIS perspective--1997. Arthritis, Rheumatism, and Aging Medical Information System. J RheumatolSuppl 1998;51: 8-16.
14. Singh G. Recent considerations in nonstero;idal anti-inflammatory drug gastropathy. Am J Med 1998; 105: 31S-8S.

15. Gutthann SP, García Rodríguez LA, Raiford DS. Individual nonsteroidal antiinflammatory drugs and other risk factors for upper gastrointestinal bleeding and perforation. Epidemiology 1997; 8: 18-24.
16. Johnson RE, Hornbrook MC, Hooker RS, Woodson GT, Shneidman R. Analysis of the costs of NSAID-associated gastropathy. Experience in a US health maintenance organisation. Pharmacoeconomics 1997; 12: 76-88.
17. Silverstein FE, Graham DY, Senior JR, Davies HW, Struthers BJ, Bittman RM, Geis GS. Ann Intern Med 1995; 123: 241-9.
18. Fries JF, Williams CA, Bloch DA, Michel BA. Nonsteroidal anti-inflammatory drug-associated gastropathy: incidence and risk factor models. Am J Med 1991; 91: 213-22.
19. Gabriel SE, Jaakkimainen L, Bombardier C. Risk for serious gastrointestinal complications related to use of nonsteroidal anti-inflammatory drugs. A meta-analysis. Ann Intern Med 1991; 115: 787-96
20. Sung-Hun Lee, Chang-Dong Han, ICK-Hwan, Yang &Chul Won Ha prescription patterns of NSAIDs and the prevalence of GI risk in orthopedic patient.JKMS J Korean med sci 2011;26; 561-56
21. Laura E. Targownik, MD, MSHS and Peter A. Thomson, PHARMD gastroprotective strategies among NSAID users.CFP-MFCCan Fam Physician. 2006 ; 52(9): 1100–1105.

Cite this article as: **Anita P Antappan, Bibin Punnoose Micheal, Merin Anto Thelappilly, Thazneem Bagum T.D[1],*Leo Mathew*, *L.Panayappan*, *K .Krishnakumar*.Perceived Stress among Undergraduate Medical Students and its Determinants: A Cross-Sectional Study in a Teaching Hospital in West Bengal. Indian J. Pharm. Biol. Res.2017; 5(3):17-25.**