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PREVALENCE OF GASTROINTESTINAL RISK FACTORS AMONG PATIENTS ON ANALGESICS AT A TERTIARY CARE HOSPITAL IN KERALA, SOUTH INDIA.

Community Medicine

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ABSTRACT

Introduction: Chronic non-cancer pain affects about 19% of the adult population which can be managed by a variety of analgesics. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most common ones used. NSAIDs are associated with a broad spectrum of side effects most common being the risk for upper gastrointestinal (GI) complications.

Objective: This study was conducted to determine the prevalence of GI risk factors among patients on analgesics in clinical practice in a tertiary care hospital in Kerala.

Methodology: It was a cross-sectional study conducted among patients taking analgesics for more than or equal to three months for various diseases in a tertiary care hospital. The study population included 123 patients admitted in different wards. We collected data using GI SCORE (Standardized Calculator of Risk for Events) to assess the GI risk factors of the patients.

Results: The study groups were stratified into four risk groups according to GI SCORE tool, thirteen percent (13%) of the study population belonged to low risk group, forty percent (40%) belonged to moderate risk group, thirty-five percent (35%) of the patients were in high risk group and twelve percent (12%) were in very high-risk group for GI complications.

Conclusion: The prevalence of GI risk factors in our study population was evaluated and percentage of individuals belonging to high or very high-risk groups was found to be 47.15%. From the results it is encouraged that physicians consider each patient's clinical factors before prescribing NSAIDs which could help to decrease the GI complications in patients requiring NSAID treatment.

KEYWORDS

Analgesics, GI SCORE, NSAIDs, Pain, South India

INTRODUCTION

Chronic non-cancer pain affects about 19% of the adult population. [1] Its management requires a range of biopsychosocial approach and involves usage of non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants drugs, anti-convulsant (gabapentin and pregabalin are often used for neuropathic pain), opioids and skeletal muscle relaxants (for more of musculoskeletal conditions than for chronic pain).[2,3]

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the widely prescribed analgesics in the world. It was in 1897 the first NSAID acetylsalicylic acid (ASA) was synthesized by Felix Hoffman.[4] Owing to their variety of actions which include anti-inflammatory, anti-pyretic, analgesic, and anti-platelet effects they find use in managing various diseases like rheumatoidarthritis, osteoarthritis, collagen disease, and ischemic cardiovascular or cerebrovascular disease. [5]

Like many other drugs, however NSAIDs are also associated with a broad spectrum of side effects, including gastrointestinal (GI) and cardiovascular (CV) events, renal toxicity, increased blood pressure, and deterioration of congestive heart failure among others.[6] More common are NSAID-related GI events.[7]Treatment with oral NSAIDs increases the risk for upper GI complications (UGIC) by 3-fold to 5-fold.[8]GI complications occur in 1-5% patients, taking NSAIDs for more than one year and result in high costs and mortality.[9-14]

The GI side effects of NSAIDs are due to local injury and mucosal cyclooxygenase-1 (COX-1) inhibition, which suppresses prostaglandin production. While COX-2 selective agents are associated with fewer GI complications, there is still an increased risk of UGIC. [7,15] Other mechanisms like changes in bacterial microbiome in the gut or the production of free radicals can also be attributed to these adverse effects.[16,17]

Most common GI symptoms due to NSAIDs are gastroesophageal reflux (regurgitation and/or heart burn) and dyspeptic symptoms (including belching, epigastric discomfort, bloating, early satiety and postprandial nausea) and is seen in 40% of users. [18] But presence of these symptoms need not indicate mucosal injury. On the other hand, significant upper GI mucosal lesions, which include subepithelial hemorrhages, erosions, ulcerations, perforation and obstruction is present in 30% to 50% of NSAID users, but these are not associated with any clinical manifestations. [18,19]The lower GI complications resulting due to NSAIDs include bleeding in the large and small bowel, strictures of the small bowel, or exacerbation of existing illnesses such as inflammatory bowel disease.[20]

Identification of the NSAID-related GI risk factors is crucial in determining the proper treatment for each patient. The risk factors for NSAID-related GI complications include older age (age ≥65 years); history of GI ulcer or GI bleed, need for long-term or high dose NSAID use, comorbidities (cardiovascular, renal, liver, diabetes and hypertension), history of NSAID-related GI symptoms, tobacco and alcohol use, concomitant use of drugs like systemic steroids, anticoagulants, antiplatelet agents, selective serotonin reuptake inhibitors (SSRI), health status of disability,rheumatoid arthritis and Helicobacter pylori infection.[6,8,21]

Some studies have already demonstrated the relationship between the clinical factors and the use of the NSAIDs. However, only few domestic studies have been undertaken on GI risks factors of the patients taking NSAIDS upon which the preventive therapies to be given are based on(and not on the occurrence of GI symptoms). In this study, we determined the prevalence of gastrointestinal risk factors among patients on analgesics in real clinical practice at a tertiary care hospital in Thrissur District, South India.

METHODOLOGY

A cross-sectional study was conducted on patients taking analgesics for treatment of various diseases in Amala Institute of Medical Sciences. The study population included 123 patients admitted in different wards, all adults (18 years or older) in the period between June 2018 and October 2018. The sample population was selected using inclusion and exclusion criteria. Patients who were admitted and were on analgesics for a period of three or more months were included. Patients who were unable to comprehend the instructions given and severely ill patients were excluded. Sampling method used was consecutive sampling.

In a face to face interview with the patients admitted in the hospital wards, as per an interview schedule, questions were asked regarding their GI risk factors and a questionnaire was thereby filled with the obtained information. Their case sheets were also checked to verify the data given.

A special tool called GI SCORE (Standardized Calculator of Risk for Events) developed at Stanford University, Division of Immunology and Rheumatology, was employed to assess the GI risk of the

patients.[10,22] The GI SCORE considers six predictors (age, diagnosis of rheumatoid arthritis, current health status, proportion of time taking oral steroids, history of a previous GI side effects when taking NSAIDs, and history of a previous hospitalization for GI bleed or ulcer) which were identified from the interview. A certain number of points were allocated for the responses of each predictor and the GI SCORE was calculated for each patient. The SCORE tool was used to stratify patients according to GI risk factors using patient characteristics that have assigned points. There were four groups as per the risk. A score of 10 or less indicated that risk of a serious GI problem was low; 11-15 points indicated moderate risk; 16-20 points indicated high risk; and more than 20 points indicated very high risk. [8]

RESULTS

This cross-sectional study included 123 in-patients out of which 63 (51.21%) patients were females and 60 (48.78%) were males. When divided into two age subgroups, 46 (37.39%) patients were aged above 65 years. On dividing into various age groups, maximum number of patients were of age group 61-70 years i.e. 45(36.59%) patients and minimum number of patients belonged to age group greater than or equal to 81 years i.e. 10 (8.13%) patients. (Table 1)

Table 1: Distribution of study population based on age and gender

Age (In years)	Male	Female	Total (%)
< 50	5 (4.06%)	13(10.57%)	18(14.63%)
51-60	18 (14.63%)	12 (9.76%)	30(24.39%)
61-70	22 (17.89%)	23 (18.70%)	45 (36.59%)
71-80	9 (7.32%)	11 (8.94%)	20 (16.26%)
> 81	6 (4.88%)	4 (3.25%)	10 (8.13%)
Total	60 (48.78%)	63 (51.22%)	123 (100%)

The most common indication for the usage of analgesics was musculoskeletal diseases and its patients were 48 (39.02%) in number in the study population. 42 (34.14%) patients were suffering from cardiovascular disease which formed the next common indication. This was followed by patients suffering from other diseases which were 21 (17.07%)in number and lastly 12 (9.76%) patients had fractures, which was the least common indication for analgesic usage.

Table 2: GI risk factors in the overall population

GI Risk Factors	Frequency (N=123)	Percentage of Cases
History of GI symptoms	68	55.28 %
Use of Anticoagulants and Anti-platelet agents	64	52.03 %
Comorbidities (HTN, DM, CVD, CKD, CLD)	60	48.78 %
Age above 65 years	46	37.40 %
Poor health status	26	21.13 %
History of steroid use	13	10.56 %
History of GI bleed or ulcer	12	9.75 %
Intake of Alcohol	7	5.69 %
Current Smoking	4	3.25 %
History of H. pylori infection	3	2.44 %
Rheumatoid arthritis	3	2.44 %

Among the GI risk factors identified in the questionnaire, patients with history of GI symptoms were 68 (55.28%) and it was the most prevalent risk factor in the overall study population, followed by use of anticoagulants and anti-platelet agents, a number of 64 (52.03%) patients. Next i row was the presence of comorbid diseases (hypertension, diabetes, CAD, CKD, CLD) 60 (48.78%) patients in this category, followed by age over 65 years and 46 (37.39%) patients satisfied this criteria,poor health status accounted the next common risk factor a number of 26 (21.13%) patients. There were 13 (10.56%) patients withhistory of steroid use, forming the next common risk factor, next in line were patients with history of GI bleed or ulcer,12 (9.75%) patients. The next common risk factor was intake of alcohol and it was found in 7 (5.69%) patients, then current smoking, found in 4 (3.25%) patients and lastly history of H. Pylori infection in 3 patients (2.44 %) and rheumatoid arthritis also in 3 (2.44%) patients in the study population. (Table 2)

Table 3: Distribution based on the comorbid diseases

Comorbidities	Frequency (N=123)	Percentage of cases
Hypertension	71	57.72 %
Diabetes mellitus	71	57.72 %
Cardiovascular Disease	48	39.02 %
Dyslipidemia	37	30.08 %
Other diseases	31	25.20 %
Chronic Kidney Disease	18	14.63 %
Bronchial asthma	14	11.38 %
Chronic Liver Disease	1	0.81 %

Table 3 explains the comorbid conditions of the patients included in the study. The study groups when stratified into four risk groups according to GI SCORE tool, 16 (13.01 %)patients of the study population belonged to low risk group, 49 (39.84 %) belonged to moderate riskgroup, 43 (34.96 %)patients were in high risk category and 15 (12.19 %) were in very high-risk category for GI complications.(Table 4)

Table 4: Percentage distribution of sample population based on GI SCORE

GI Risk as per GI SCORE	Frequency (N=123)	Percentage of cases
Low Risk (<10)	16	13.01 %
Moderate Risk (11-15)	49	39.84 %
High Risk (16-20)	43	34.96 %
Very high risk (>20)	15	12.19 %

On analyzing the data with Chi square test the association between high or very high GI risk with age over 65 years (P value= 0.0001), poor health status (P value= 0.001), history of GI symptom (P value= 0.003) and history of GI bleed or ulcer (P value= 0.001) was found statistically significant. (Table 5)

Table 5: Distribution of study population based on GI SCORE predictors

GI SCORE Predictors		GI Risk				Total	Percentage	P Value (Chi Square test)
		Low	Moderate	High	Very High			
Age	< 65 years	16	45	11	5	77	62.61 %	0.0001
	>65 years	0	4	32	10	46	37.39 %	
Health Status	Well	10	28	9	3	50	40.65 %	0.001
	Fair	5	12	25	6	47	38.21 %	
	Poor	1	9	9	6	26	21.13 %	
Rheumatoid arthritis	Absent	16	49	41	14	120	97.56 %	0.080
	Present	0	0	2	1	3	2.43 %	
Oral Steroid Intake (in months)	0	14	43	38	15	110	89.43 %	0.610
	1 to 3	2	6	4	0	12	9.75 %	
	7 to 10	0	0	1	0	1	0.81 %	
History of GI bleed or ulcer	Absent	16	49	42	4	111	90.24 %	0.001
	Present	0	0	1	11	12	9.75 %	
History of GI Symptoms	Absent	11	17	15	12	55	44.71 %	0.003
	Present	5	32	28	3	68	55.28 %	
Total		16	49	43	15	123		

DISCUSSION

In the study population, the proportion of females was 51.22%. On comparing with similar studies, it was 81.9% in a study conducted by Antappan et al. and 69% in one conducted by Sung-Hun Lee et al. In the given study 37.39% people belonged to the group of age above 65 years. While it was 23.8% in the study conducted by Antappan et al. and formed the majority in case of the study by Sung-Hun Lee (54%). In the studymaximum number of patients were of age group 61-70 years(36.59%) patients and minimum number of patients belonged to age group greater than or equal to 81 years(8.13%).[23,8]

The most common indication for analgesic usage was found to be for musculoskeletal diseases (39.02%) in this study. The next common indication was for cardiovascular diseases (34.15%), followed by for some miscellaneous diseases (17.07%) and lastly for fractures (9.76%). In the study conducted by both Sung- Hun Lee et al. and Antappan et al. the most common indication for analgesics was arthritis (67% and 45.7% respectively).[23,8]

Among comorbidities of patients on analgesics the most common ones were hypertension and diabetes mellitus (57.72%). Next in row was cardiovascular diseases (39.02%), followed by dyslipidemia (30.08%) then miscellaneous diseases (25.2%), chronic kidney diseases (14.63%), bronchial asthma (11.38%) and chronic liver disease (0.81%).

One of the main purposes of this study was to understand and present the GI risk factors of patients on analgesics, thus factors besides those included in the SCORE tool have been included here.[8]The study revealed that the most prevalent GI risk factor among patients on analgesics was history of GI symptoms (55.28%), followed by use of anticoagulants and anti-platelet agents (52.03%),comorbid diseases (hypertension, diabetes, CAD, CKD, CLD) (48.78%), age over 65 years (37.39%),poor health status (21.13%), history of steroid use (10.56%), history of GI bleed or ulcer (9.75%), intake of alcohol (5.69%,) current smoking (3.25%), history of H. Pylori infection (2.44 %) and rheumatoid arthritis (2.43%).

Similar studies conducted by Sung-Hun Lee et al. in Korea and by Antappan et al. in Kerala showed long term NSAID use (79%) and presence of comorbid diseases (55.2%) as the most prevalent risk factor respectively.[8,23]The Korean Knee Society (KKS) also presented comparable results, yielding old age over 65 years (56%), history of GI symptoms (40%), presence of co-morbid disease (25%) were prevalent risk factors in the NSAID-induced GI risk management study in 2009.In our study it was found that 47.15% of the patients belonged to high or very high-risk groups for GI complications. While it was 45% in the study by Sung-Hun and 27.6%in the study by Antappan et al. [8,23]Our study also revealed that statistically significant association was found between gastrointestinal risk factors and age over 65 years, poor health status, history of gastrointestinal diseases and history of gastrointestinal bleeding and ulcers.

A GI bleeding risk model based on Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS) database in 1991 was created by Fries et al.[10] GI SCORE is an updated and refined tool developed by Singh et al. in 1998, and it's a well-accepted, reliable and accurate predictor of serious NSAID-related GI events. [8,24,25]

The GI related adverse effects of analgesics range from mild dyspepsia, abdominal pain to life-threatening complications like ulceration, bleeding and perforation. Various studies conducted in the world have established that use of NSAIDs increases the risk for GI complications from 3.5-fold to 7.8-fold overall. [12, 26, 27] As mentioned earlier the GI symptoms may either not be accompanied with any specific GI lesions neither do all GI complications have related symptoms. While several epidemiological studies have identified the individual risk factors for developing GI complications, the necessity of a multivariate risk factor model to estimate the risk in individual patient and initiation of proper therapeutic measure still remains.

CONCLUSION

The prevalence of GI risk factors in our study population was evaluated and percentage of individuals belonging to high or very high-risk groups was found to be 47.15%. These results were found comparable with other studies. Physicians'considerate prescription of analgesics with well-understanding of each patient's GI risk factors is encouraged. This helps to maximize cost effectiveness as well as to prevent serious GI complications following analgesic treatment.

The study has few limitations. Firstly, the effect of gastroprotectors' usage wasn't studied. Nowadays young medical practitioners tend to prescribe gastroprotective agents in a customary manner without considering patient factors. Secondly, the study design being observational cross-sectional type no effort was made to develop new GI risk factors. [8] If new GI risk factors typical for population in Kerala, degree of patient awareness on adverse effects on analgesics, physician's criteria in choosing the type of analgesic or gastroprotectors it would have taken us a little deeper into the subject.

RECOMMENDATIONS

It is advisable that physicians voluntarily put effort to identify each patient's clinical factors before prescribing analgesics and prescribe accordingly rather than prescribing GI protectors in a customary manner. Gastroprotective agents, anti-secretory agents, alternative NSAID formulations, and non pharmacologic therapies have to be used effectively to curb down the adverse effects. Patient education regarding the adverse effects caused by analgesics is also recommended so as to carry out prompt management of the GI events. Government led-educational campaigns and medical association led educational programs may prove very useful.

REFERENCES

1. Breivik H, Collett B, Ventafridda V et al. Survey of chronic pain in Europe: prevalence, impacton daily life, and treatment. Eur J Pain. 2006 May;10(4):287-333.
2. R Lawrence. Analgesic drugs and the gut- a reciprocal relationship. Journal of the Royal College of Physicians of Edinburgh. 2015, 45 (4): 284-8.
3. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. Lancet. 2011; 377(9784):2226-35.
4. Brune K, Hinz B. The discovery and development of antiinflammatory drugs. Arthritis &Rheumatology. 2004; 15:2391–2399.
5. Yun Jeong Lim, Chang Hun Yang. Non-steroidal anti-inflammatory drug-induced enteropathy. Clin Endosc. 2012 Jun; 45(2): 138–144.
6. Carlos Sostres, Carla J Gargallo, Angel Lanas. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. Arthritis Research & Therapy. 2013; 15(Suppl 3): S3.
7. Jay L Goldstein and Byron Cryer. Gastrointestinal injury associated with NSAID use: a case study and review of risk factors and preventative strategies. Drug Healthc Patient Saf. 2015 Jan 22; 7:31-41.
8. Sung-Hun Lee, Chang-Dong Han, Ick-Hwan Yang, and Chul-Won Ha. Prescription Pattern of NSAIDs and the Prevalence of NSAID-induced Gastrointestinal Risk Factors of Orthopaedic Patients in Clinical Practice in Korea. J Korean Med Sci. 2011 Apr; 26(4).
9. Schlansky B, Hwang JH. Prevention of nonsteroidal anti-inflammatory drug-induced gastropathy. J Gastroenterol. 2009;44(Suppl 19):44–52.
10. Fries JF, Williams CA, Bloch DA, Michel BA. Nonsteroidal anti-inflammatory drug-associated gastropathy: incidence and risk factor models. Am J Med. 1991 Sep;91(3):213-222.
11. Johnson RE, Hornbrook MC, Hooker RS, Woodson GT, Shneidman R. Analysis of the costs of NSAID-associated gastropathy. Experience in a US health maintenanceorganisation. Pharmacoeconomics. 1997 Jul; 12(1): 76-88.
12. Singh G, Rosen Ramey D. NSAID induced gastrointestinal complications: the ARAMIS perspective--1997. Arthritis, Rheumatism, and Aging Medical Information System. J Rheumatol Suppl. 1998 May; 51: 8-16.
13. White TJ, Arakelian A, Rho JP. Counting the costs of drug-related adverse events. Pharmacoeconomics. 1999 May; 15(5): 445-58.
14. 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 Mar;85(1-2):169–182.
15. Warner TD, Giuliano F, Vojnovic I, Bukasa A, Mitchell JA, Vane JR. Nonsteroid drug selectivities for cyclo-oxygenase-1 rather than cyclo-oxygenase-2 are associated with human gastrointestinal toxicity: a full in vitro analysis. Proc Natl Acad Sci U S A. 1999 Jun;96(13):7563–7568.
16. Wallace JL. Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself? Physiol Rev. 2008 Oct;88(4):1547–1565.
17. Lanas A, Scarpignato C. Microbial flora in NSAID-induced intestinal damage: a role for antibiotics? Digestion. 2006;73 (Suppl 1):136–150.
18. Larkai EN, Smith JL, Lidsky MD, Graham DY. Gastroduodenal mucosaand dyspeptic symptoms in arthritic patients during chronic steroidal antiinflammatory drug use. Am J Gastroenterol. 1987 Nov; 82(11):1153–1158.
19. Lanas A, Hunt R. Prevention of anti-inflammatory drug induced gastrointestinal damage: beneficts and risks of therapeutic strategies. Ann Med. 2006; 38(6):415–428.
20. Bjorkman D. Nonsteroidal anti-inflammatory drug-associated toxicity of the liver, lower gastrointestinal tract, and esophagus. Am J Med. 1998 Nov 2;105(5A):17S–21S.
21. Sostres C, Gargallo CJ, Arroyo MT, Lanas A. Adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs, aspirin and coxibs) on upper gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2010Apr ; 24(2):121–132.
22. Fries JF. NSAID GI toxicity: epidemiology. J Musculoskel Med. 1991;8:21–28.
23. Anita P Antappan, Bibin Punnoose Micheal, Merin AntoThelappilly, Thazneem Bagum T.D., Leo Mathew, L. Panayappan, K .Krishnakumar. Prescription pattern of NSAIDS and the prevalence of NSAID-induced gastrointestinal risk factors of orthopaedic patients. Indian J. Pharm. Biol. Res. 2017; 5(3): 17-25.
24. Fries JF, Bruce B. Rates of serious gastrointestinal events from low dose use of acetylsalicylic acid, acetaminophen, and ibuprofen in patients with osteoarthritis and rheumatoid arthritis. J Rheumatol. 2003 Oct;30(10) :2226–223.
25. 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 Oct;30 (10):2241–2244.
26. García Rodríguez LA, BarrealesTolosa L. Risk of upper gastrointestinal complications among users of traditional NSAIDs and COXIBs in the general population. Gastroenterology. 2007 Feb; 132(2): 498–506
27. Koncz TA, Lister SP, Makinson GT. Gastroprotection in patients prescribed non-selective NSAIDs, and the risk of related hospitalization. Curr Med Res Opin. 2008 Dec; 24(12) :3405–3412.