

Assessment of Nonsteroidal Anti-inflammatory Drugs Prescription Pattern and Gastrointestinal Risk Factors in a Tertiary Care Hospital of Western Nepal

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ABSTRACT

NSAIDs are commonly prescribed group of drugs with changing frequency of prescription pattern over a period of time and has wide range of adverse effect, mainly on alteration in GI, renal functions and CVS system, which can be life-threatening. Thus, the aim of study was to evaluate the current prescription pattern of non-steroidal anti-inflammatory drugs (NSAIDs) and the prevalence of NSAID-induced gastrointestinal (GI) risk factors in a Tertiary Care Hospital of Western Nepal. A prospective observational NSAIDs induced gastrointestinal risk related study was conducted over a period of two months by clinical pharmacist on which study cohort include 370 patients who are taking or/and prescribed with NSAIDs. A self-administered questionnaire was completed by each patient for knowledge over prescribed NSAID and simplified risk scoring scale (the Standardized Calculator of Risk for Events; SCORE) was used to evaluate patients risk for GI complications with the used of NSAIDs. Data were analyzed by using Statistical Package for Social Science (SPSS) software version 17.0. The study groups were stratified into four risk groups according to GI SCORE tool, 18.4% of the patients belonged to high risk to very high risk groups for gastrointestinal complications. Analysis of prescription pattern revealed that overall frequency of prescription pattern of plain NSAIDs was found to be 60%, among which naproxen 500mg (21.3%) was found to be the most commonly prescribed non-selective NSAIDs (92%). Out of 370 at 105 prescription FDCs were prescribed. The finding conclude that although about more than 70% of patients receiving gastroprotective agents and had knowledge over NSAIDs still patients were at high to very high risk for NSAID-induced gastrointestinal complications and still there is a need of effective education/knowledge towards NSAIDs and their pros and cons on use to the respective healthcare workers and patients in order to promote effective drug utilization.

Key words : Fixed Dose Combination (FDCs), Gastro-protective Agents (GPAs), Gastrointestinal complications, Non-Steroidal Anti-inflammatory Drugs (NSAIDs),

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INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a commonly prescribed group of drugs which are of chemically dissimilar in nature and differ in their antipyretic, analgesic and anti-inflammatory activities.¹ Studies have shown that use of NSAIDs increases the risk of hospitalization and death from gastrointestinal bleeding and perforation.¹⁷ GI complications occur in 1-5% of patients taking NSAIDs for more than one year and result in high costs and mortality.^{1,19} The study also concluded that approximately 30 million people worldwide take NSAIDs on a daily basis, of which 40% are older than 60 years.¹⁴ NSAIDs play an important role in management of inflammation, mild to moderate pain and fever in specific cases they are used in treatment of headaches, arthritis, sports injury and menstrual cramp.^{1,7,14,19} Although NSAIDs are being used with the concept of safe and efficacious in pain management but necessary information regarding utilization

patterns of NSAIDs and NSAIDs induced complications are still not taken as serious note.³ Despite wide clinical use of NSAIDs their gastrointestinal toxicity is a major clinical limitation¹⁴ and the use of NSAIDs is an important predisposing factor for peptic ulcer disease. 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.¹⁵ With the introduction of the selective COX-2 inhibitors the prescription pattern of NSAIDs changed frequently over a period of time.^{4,17} In addition, Age > 65 years - History of PUD or UGI bleeding, concomitant oral glucocorticoids, Concomitant anticoagulants, Smoking - Alcohol consumption these factors are the major things that need to be considered while prescribing NSAIDs. Therefore, it become very important to evaluate the prescribing pattern of NSAIDs, cost per prescription, co-prescribing pattern of

Gastro protective agents with NSAIDs, knowledge of patient towards use of NSAIDs and association of gastrointestinal risk factors with prescribed NSAIDs for the enhancement of rational drug prescribing.

METHODS

A total of 370 patients were randomly enrolled in the prospective observational study carried out in outpatient pharmacy of Manipal Teaching Hospital, Fulbari, Pokhara for a period between August-October 2018. The study was evaluate and approved by Ethical Committee of Pokhara University Research Center (PURC) and Ethics Committee (IHEC) of Manipal Teaching Hospital. Sample population was calculated based on the prevalence of the prescription pattern of NSAIDs (59.9%)¹⁷ and using sample size calculation formula. The samples were randomly selected from the each department of the hospital based on Inclusion Criteria: patients visiting outpatient pharmacy of Manipal Teaching Hospital and prescribed with NSAIDs. Patients prescribed with other pain relief medications without NSAIDs, women at pregnancy or lactation state, those prescription brought to the pharmacy by care giver and patients with difficulty in answering questionnaire and patients who are unwilling to participate in the study are excluded from the study. Initially, inform consent was taken from each patients visiting outpatient pharmacy. The questionnaire provided to the patients was designed in such a way that it reflects the lifestyle the patient with inclusion of WHO prescribing parameters. GI Standardized Calculation of Risk Estimation was done through medical history and patient interview. A specially designed data entry form which includes GI SCORE/ NSAIDs GI risk score card to asses GI risk which contains four different questions with respective scoring system: 1) Patient age in years? 2) Current Health status as rated by the patient? 3) Does patient have rheumatoid arthritis? 4) Use of prednisone or other oral steroids in past year? 5) Hospitalized for GI bleed or an ulcer? 6) Has Patient had GI side effects when taking NSAIDs? and the risk levels were stratified into 4 groups and risk level were interrelated based on NSAID SCORE card; Level 1 (0-10 points) – No risk: May use NSAID, Level 2 (11-15 points) – Moderate risk: May use NSAID, Level 3 (16-20 points) – Significant risk: May use standard NSAIDs for < 30 days, Level 4 (>20 points) – Substantial risk : Do not use standard NSAIDs. The data so obtained were analyzed using SPSS version 17.0 and presented in frequency distribution tables with percentages, the correlation and association between variables were analyzed at 95% level of significance.

RESULTS

A total of 370 prescriptions were screened for the evaluation of NSAIDs prescribing pattern and GI risk factor. There was almost equal distribution between male 179 (48.4%) and female 191 (51.6%) patients. It was noted that most patients were of the age group of 21-40 years (157, 42.4%). Patient with age group >60 years was found to be 69 (18.7%). From the study it was observed that highest number of patients encounter during the research has had an occupation of agriculture (28.9%). The frequency of NSAIDs prescription was highest in orthopedic department 173 (46.8%).

Table 1 shows overall prescribing indicators of the study. In total of 1385 drugs were prescribed in 370 NSAIDs containing prescriptions. Average number of drugs per prescription was 3.74 ± 1.430 . Number of NSAIDs prescribed in monotherapy form was 286 (77.3%). NSAIDs prescribed in FDCs were prescribed to 105 (28.3%) patients, 266 (71.9%) patients received gastro-protective agents (GPAs) co-prescribed. In 81 (21.8%) of the prescription antibiotics were co-prescribed. It was interesting to notice that out of 370, only 11 (3.0%) of prescription found to be prescribed in generic form and average cost per prescription was Rs. 736.949 ± 671.66 .

Table 1: Detail of prescription parameters

Prescribing Indicator	Frequency	Percentage
Total Number of drug prescribed	1385	
Average No of Drug per encounter/Prescription	3.74 ± 1.430	
Number of prescription written in Generic	11	3.0
Number of NSAIDs given in monotherapy form	286	77.3
Number of FDCs prescribed	105	28.3
Number of NSAIDs given in injection form	0	0
Number of Antibiotics Prescribed	81	21.8
Number of NSAIDs gel prescribed	31	5.4
Number of prescription containing GPAs	266	71.9

Overall evaluation shows that non-selective NSAIDs were commonly prescribed (92%). Among non-selective NSAIDs class, naproxen 500mg was the most preferred (79, 21.3%). Selective COX-2 inhibitors were least prescribed (2, 0.5%) which was shown in table 2.

Table 2: Classification of the NSAIDs prescribed to the patients

Class of Drug	Drug Prescribed	No of Prescription	Percentage
Non-Selective NSAIDs	Naproxen, Indomethacin, Aspirin Diclofenac, Mephenamic Acid, Aceclofenac, Ketorolac	343	92.7
Preferential COX2 inhibitor	Tromethamine Nimesulide	25	3.2
Selective COX2 inhibitor	Etoricoxib	2	0.5
Analgesic-antipyretic with poor anti-inflammatory action	Acetaminophen	37	9.9

From table 3, high prevalence of GPAs co-prescription was noted in the study (72%). Among various classes of GPAs, proton pump inhibitor was the commonest drug so prescribed (251, 67.83%). On which Rabeprazole 20mg x OD (35.7%) was most frequently prescribed.

Table 3: Detail of gastro protective agents prescribed to the patients

(Gastro protective Agents) GPAs	Frequency	Percentage	P value
Proton Pump Inhibitor	251	67.83	0.074
H ₂ receptor antagonist	15	4.1	

Table 4: Detail about list of diagnosis mention in the prescription

Diagnosis	Frequency	Percentage
Dysmenorrheal	6	1.6
Ear Infection	1	0.3
Eye Infection	4	1.1
Hyperuricemia/Uric acid	5	1.5
IHD, Systemic Hypertension	12	3.2
Non-traumatic pain	296	80.0
Not Mention	16	4.3
Pharyngitis	2	0.5
Traumatic Pain	28	7.5

Diagnosis by the physician was also studied during the time of survey which shows 296 (80%) of the patients were diagnosed with non-traumatic pain followed by 28 (7.3%) of the prescription include traumatic pain as a diagnosis. It was interesting to notice that 16 (4.3%) did not include the diagnosis in the prescription (Table 4).

Table 5 shows detail about the various factors that were used to analyze the gastrointestinal risk. 77 (20.8%) of patients were prescribed with NSAIDs for long term which can also subsequently increase the GI risk to the patient. It was also noted that 54 (14.6%) of patients fall under the age group of over 65 years. 73 (19.7%) of patients has had a history of comorbid disease, 33 (8.8%) of them show the history of GI symptoms after administration of NSAIDs. As documented Aspirin is the most common NSAIDs that has high frequency of causing GI irritation on long term basis of use so the aspirin administration was also evaluated showed that 28 (7.5%) of patients have been under the aspirin medication, 19 (5.1%) has a habit of smoking in heavy rate followed by 15 (4.1%) used to drink alcohol heavily increasing the risk to GI in concomitant use with NSAIDs. 110 (29.7%) of patients had a steroid use history, 142 (38.4%) indicate that they had poor current health status. In addition, 24 (6.5%) patients has a history of rheumatoid arthritis. Out of 370, 1 (0.3%) of patient had a previous hospitalization history due to GI events as well as Helicobacter pylori infection.

The eligible patients were categorized in 4 different risk level based on the GI SCORE; 216 (58.4%) of the patients fall under the level 1 category showing there was no risk followed by 86 (23.2%) of patients fall into the level 2; they were under the moderate risk and may use NSAIDs, similarly, 48 (13%) of them situated under level 3 that is the patient has a significant risk and may caution should be applied while using NSAIDs. It was interesting to notice that with the supplement use of GPAs there were still 20 (5.4%) of patients lies under level 4 that is there is a substantial risk and it is suggested not to prescribed any class of NSAIDs further (Table 6).

Table 5: Association of GI risk factors with prescribed NSAIDs

GI risk factors	Frequency (n= 370)	Percentage	p value
Need for long-term NSAID use	77	20.8	0.000*
Age over 65 Years	54	14.6	0.000*
Comorbid disease (cardiovascular, renal, liver, diabetes, hypertension)	73	19.7	0.000*
History of GI symptom	33	8.9	0.003*
Aspirin use	28	7.5	
Heavy smoking habit	19	5.1	0.191
Heavy drinking habit	15	4.1	0.005*
History of steroid use	110	29.7	0.000*
Currently poor health status	142	38.4	0.023*
Rheumatoid arthritis	24	6.5	0.000*
Previous hospitalization history due to GI events	1	0.3	0.009*
Selective serotonin reuptake inhibitor (SSRI) use	None	0	
Helicobacter pylori infection	1	0.3	0.000*
Anticoagulant use	3	0.8	0.000*

Table 6: Detail of risk level of the patients

Risk Level	Level 1	Level 2	Level 3	Level 4
Frequency (%)	216 (58.4%)	86 (23.2%)	48 (13.0%)	20 (5.4%)

DISCUSSION

The high frequency of traditional NSAIDs prescription pattern was noted this study which shows consistency with other studies done in similar type of hospital setting, however, they conclude varied NSAIDs prevalence pattern as most of the studied were confined to the orthopedics OPD while in this study data were collected and evaluated from different departments simultaneously. Past study done in Manipal Teaching Hospital showed that the frequency of NSAIDs prescription was 59.9%¹⁷, in sub health post of western Nepal was 27.8%²⁰ and Teaching Hospital, Bharatpur was 11.8%⁶. The pattern of NSAIDs prescribing in dental OPD at tertiary care hospital Chitwan was found to be 66%¹⁶ and described as second most commonly prescribed drug after antimicrobials. Study conducted in Kathmandu valley concluded that prescription prevalence of NSAIDs was 38.29%². In addition, the study conducted in South India concludes 77% of prescription prevalence of NSAIDs¹⁰. In this study the frequency of NSAIDs prescription was highest in orthopedic department as compare to other departments^{1,8,18}. It might be due to higher number patients in encounter in orthopaedic department with the complain of back pain, joint pain/arthritis and prescribed with NSAIDs for management of such clinical condition.

Other study concluded that only 3% of were being prescribed

as generic. Which was found to be very low as compare to the similar study conducted at same setting which was 19.3% at 2007¹⁷, the prescribing pattern of medications showed irrationality in case of generic prescribing thus, generic prescribing is to be encouraged as it works out to be cheaper for the patient and the possibility of drug errors is reduced.

In this study lower back/flank pain (14.9%) and back pain with burning sensation (9.2%) were the commonest clinical conditions for NSAIDs prescription. Similar indications were noted however prevalence of low back pain was 71% in case of previous study conducted Nepal³. As most of the patient encounter were from hilly terrain with source of income/occupation of agriculture and labor thus in such cases person has to perform large work forces, heavy manual work that result in back pain with burning sensation, joint pain, arthritis. On comparing the study with other international studies Arthritis and other non-traumatic pain were concluded as the major reasons for NSAID prescription⁵.

Present study shows high prevalence of non-selective NSAIDs prescription compared to other COX-2 selective inhibitors among which naproxen 500mg x BD (20.8%) and aceclofenac 100mg x BD (16.8%) constitute the bulk of non-selective NSAIDs prescription; together they constitute more than 35% of NSAIDs prescription. On evaluating the duration

of therapy it was seen that 178 (48.1%) of the prescription the drug was prescribed up to 4-7 days. From other studies diclofenac sodium, meloxicam, paracetamol and ibuprofen were the commonly prescribed drugs, however dose was not mention on each of the study^{2,3,4,13, 16,17} it might be due to less side effects from the non-selective group or may be less knowledge over safety of COX-2 selective inhibitors over non-selective group.

In case of frequency of FDCs so prescribed in the study was found to be 28.37% which is much lower when comparing with the study conducted in Chitwan Medical College (49.61%)⁶, in case of other country combination of NSAID with other drug was more preferred than combination with paracetamol but on the contrary in this study such combination was the most common one rather than with other drugs. However other drugs like antihistaminic, skeletal muscle relaxant and serritopeptidase were also prescribed but as in co-prescribing form^{4,10,17}.

A study conducted in 2002 at Manipal Teaching Hospital shows only 5.7% of co-prescribing of GPAs with NSAIDs. Various randomized studied concluded that importance of co-prescribing GPAswith NSAID, especially with non-selective NSAID^{4,6}. Similar trends was also observed in study conducted in Bangalore (72.83%) and two different study conducted in Spain 64% and 85% respectively⁴. In this study rabeprazole followed by pantoprazole sodium sesquihydrate were the most prescribed proton pump inhibitor. Antacid preparation were less commonly prescribe. In some cases the patients themselves ask physician for the addition of GPAs in order to prevent the GI complications and in most of the cases for the prophylaxis doctors co-prescribe GPAs which might results in higher percentage from the previous studies.

Present study concluded that average number of drugs per prescription was 3.74, which was more compared to study conducted in Manipal Teaching Hospital (2007) which was 1.9. On the other hand the drug per prescription was found to be less as compare to study conducted in Bharatpur Teaching hospital (2003) which was 4.34. It might be due to addition of other supplementary medications that results in polypharmacy as well as increase in the cost of the prescription it may be due to addition of various supplementary drugs or due to patient's co-morbid condition.

From the present study it was found that 5.4% of patients are at very high risk level followed by 13% of them situated on the high risk level, 23.2% were at moderate risk group and 58.4% had a low risk for GI complication. Among them male were found to be at higher in risk level as compare to female.

The reason behind higher number of male at risk level although female accounted higher number in the research it might be due to alcohol intake and smoking habit of the male patients. The present study shows comparable data with a study conducted to orthopedic patients at India concluding, 8.6 % of the patients were in very high risk followed by 19% are in high risk groups, 34.3% of the patients belonged to moderate risk and 38.1% belongs to low risk for GI complications and Korea describe that pattern of NSAID utilization, showing more frequent use of COX- 2 selective inhibitor in higher risk groups (6% [low] < 28% [moderate] < 51% [high] < 56% [very high]) and more common use of non-selective NSAIDs in less risk groups¹⁹. Here Nepali found to have low risk then other country it might be due to differ in personal habit and lifestyle of the population. The other reason might be due to differ in therapeutic treatment guideline and prescribing pattern of NSAIDs in context of other country.

CONCLUSION

The finding concludes that despite the safest group of NSAIDs are prescribe with gastro protective agents (above 70%) by physician such as, paracetamol, nimesulide, naproxen and still patients were at high (13%) to very high risk (5.4%) for NSAID-induced GI complications, the number of drug per prescription is also higher due to addition of supplementary drugs which ultimately results in increase in cost per prescription. Thus, proper consideration over prescription of NSAIDs with well-understanding of each patient's GI risk factors is strongly encouraged in order to maximize cost effectiveness as well as to prevent serious GI complications in western region. In addition age, comorbid condition, need for long term NSAIDs, history of aspirin and steroid use, rheumatoid arthritis and personal habit of patients also found to have significant relation with GI risk in some cases these factors were not considered while prescribing NSAIDs. Data obtained from this study cannot be generalized as whole context of Nepal. Thus, further drug utilization studies over a longer period of time are recommended to provide a baseline data NSAIDs prescription pattern and GI risk factors associated with NSAIDs. Strategic efforts such as physician's voluntary attention to estimate individual patient's risk factor, patient's self-awareness on the adverse effects caused by NSAIDs would help in minimization of GI risk factors associated with NSAIDs.

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