

A SHORT-TERM PROSPECTIVE STUDY ON DRUG UTILIZATION EVALUATION & RELATED PROBLEMS OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AT A TERTIARY CARE HOSPITAL**Dr. V. M. Chandrashekhar*², Dr. Madhu Patil¹, Dr. Sabarinath H.¹, Dr. Rhema Sara Jose¹, Dr. Ancil Babu¹, Dr. Achu Girish¹**¹Department. of Pharmacy Practice, BVVS Hanagal Shri Kumareshwar College of Pharmacy and HSK Hospital and Research Center, Bagalkote.²H.O.D Department of Pharmacology, BVVS Hanagal Shri Kumareshwar College of Pharmacy and HSK Hospital and Research Center, Bagalkote.***Corresponding Author: Dr. V. M. Chandrashekhar**

Department. of Pharmacy Practice, BVVS Hanagal Shri Kumareshwar College of Pharmacy and HSK Hospital and Research Center, Bagalkote.

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ABSTRACT

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are used all over the world for their analgesic, anti-inflammatory, and antipyretic effects. NSAIDs are among the most commonly prescribed classes of medications globally and account for approximately 5–10% of all medications each year. The use of NSAIDs increased the risk of Gastro-Intestinal complications in 55 – 75% of healthy volunteers. **Objectives:** To study the drug utilization, evaluation, and drug-related problems of NSAIDs used in in-patients at tertiary care hospitals. **Methods:** This was a prospective and observational study conducted in the inpatient department of a tertiary care hospital. The study was conducted by reviewing and collecting the case sheets of patients who were administered NSAIDs. The collected data were analyzed to study the prescribing pattern; drug-related problems of NSAIDs and assess the usage of gastroprotective agents among chronic NSAIDs users and identification of adverse drug reactions. **Results:** Among 110 patients who satisfied eligibility criteria and were prescribed NSAID, drugs 73(66.37%) participants received monotherapy, 31(28.18%) participants received two-drug therapy, and a three-drug combination was given to 6 (5.45%). Patients were prescribed NSAIDs with/without Gastroprotective Agents, out of 110 patients - 105 patients were prescribed Gastroprotective Agents in combination (95.45%) and 5 patients were given NSAIDs alone (4.55%). Among Drug-Related Problems, there were 4 (6.452%) adverse drug reactions, 38 (61.29%) clinically significant drug interactions, a subtherapeutic dose in 2(3.22%), and an overdose of NSAIDs in 18 (29.032%) was observed. **Conclusions:** We conclude that drug-related problems associated with NSAIDs continue to be a major barrier to effective treatment and management of inflammation. And our results reflect the same. A broader study is needed to further study analyze and address this concern. The study supports the actions to implement pharmaceutical care programs that could positively affect healthcare and prevent complications in in-patients associated with NSAIDs.

KEYWORDS: Drug Utilization; Nonsteroidal Anti-inflammatory Drugs; Drug-Related Problems; Prescribing Pattern; Gastroprotective Agents.

INTRODUCTION

Drug utilization evaluation is “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences is defined as the drug utilization.^[1]” Studies on prescription pattern monitoring are a type of drug utilization research, with their main focus on rational prescribing of drugs.^[2] It compares the observed patterns of drug use with current recommendations and guidelines.^[1] Rational use of medicines mandates that “patients receive medications according to their clinical needs, in doses that meet their

requirements, for an adequate period, and at the lowest cost to them and their community.^[3]” Irrational use of medicines is a major problem and the World Health Organization (WHO) also estimates that more than half of all medicines are prescribed, dispensed, or sold inappropriately. Therefore, irrational use of drugs can lead to ineffective treatment, adverse drug reactions, and an economic burden on patients and society. To overcome this, rational use of drugs should be imperative in the healthcare system.^[3] Drug utilization data can help in the formulation of guidelines on the clinical use of the drugs and facilitate their rational use and it also helps us to

know the epidemiology of the disease, the pattern of drug use, indications, contraindications, and appropriate dosage of drugs to ensure its rational use.^[3]

Non-steroidal anti-inflammatory drugs (NSAIDs) are used all over the world for their analgesic, anti-inflammatory, and antipyretic effects.^[4] NSAIDs are among the most commonly prescribed class of medications globally and account for approximately 5–10% of all medications each year.^[5] For obvious reasons, the elderly was among the frequent users of NSAIDs^[6-8], and the fact that this sub-population is highly involved in prescription and non-prescription medications^[9], they are highly susceptible to polypharmacy, drug-drug interactions and ultimately drug-related complications and even death.^[10-12] Serious/fatal gastrointestinal problems including ulcers and bleeding have been frequently reported with chronic use of NSAIDs^[13] and thus, co-prescription of gastroprotective agents has paramount importance in preventing such risks.^[14] In the elderly, it was estimated that 29% of fatal peptic ulcer complications were possibly due to NSAIDs.^[15] Despite this fact, gastroprotective agents were poorly co-prescribed along with NSAIDs^[16] and the other serious adverse effects reported with NSAIDs even amplify this concern. The use of multiple drugs per prescription (polypharmacy) is recognized as an independent risk factor for serious adverse drug reactions in the elderly.^[17-18]

NSAIDs and Gastrointestinal (GI) adverse effects Drug Interaction

METHODS

Ethical committee clearance and formal permission from Institutional Ethics Committee were obtained before the initiation of the study. This study was considered with the prospective intervention by student pharmacists. All the intervention was subjected to verification by consultation with the academic clinical pharmacist (staff) of the department of clinical pharmacy. This was a prospective cross-sectional, observational study of 6 months duration conducted in the in-patient departments (IPDs) of our tertiary care teaching hospital. All outpatients, pregnant and lactating women, and those who were not willing to participate were excluded from the study. The study was conducted by reviewing and collecting the case sheets of patients who were administered NSAIDs. During the study period, patients were reviewed on daily basis, and any change in medication orders or laboratory details was collected and updated in the patient data collection form. All the collected patient data and medical data were subjected to independent review by pharmacists including a staff member to identify the drug-related problems. Each drug-related problem was categorized based on Hepler and Strand as follows:

- Untreated indication
- Drug use without indication
- Adverse drug reaction
- Drug interaction

- Subtherapeutic dosage
- Overdose
- Failure to receive drug
- Medical condition resulted from unindicated drugs

Statistical analysis

Data analysis was done using statistical methods like percentages to find the significant differences.

RESULTS

A total of 110 prescriptions were analyzed, which had NSAIDs prescribed of which 71(64.5%) were male and 39(35.5%). Seven different classes of NSAIDs were prescribed from which paracetamol was mostly prescribed 98 (60.12%). During the 6 months of study, drugs were given as monotherapy 73 (66.37%), two-drug combinations 31(28.18%), and three-drug combination 6 (5.45%). Among the patients prescribed with/without Gastroprotective Agents along with NSAIDs. 105 patients were prescribed Gastroprotective Agents in combination (95.45%) and 6 patients were given NSAIDs alone (4.55%). Furthermore, in the identification and assessment of various DRPs prescribed with NSAIDs of which four drug-related problems like adverse drug reactions, drug-drug interactions, subtherapeutic dose, and overdose were assessed in patients.

NSAIDs are one of the most common causes of adverse drug reactions.^[24] As patients age, and the number of medications increases, NSAIDs in the elderly should be prescribed with caution. NSAIDs concomitantly used with specific medication can alter the risk of gastrointestinal ulceration and/or bleeding. These drugs include selective serotonin reuptake inhibitors (SSRIs), corticosteroids, digitalis glycosides, diuretics, beta-blockers, calcium antagonists, angiotensin-converting enzymes, warfarin, clopidogrel, aspirin, and other anticoagulants.^[22,25,26,27] Some specific NSAIDs were found to reduce the renal clearance of methotrexate, a commonly used medication for rheumatoid arthritis.^[28] There were 4 (6.452%) adverse drug reactions, clinically significant drug interaction of 38 (61.29%), a subtherapeutic dose of 2(3.22%) and an overdose of NSAIDs 18 (29.032%) also obtained.

During the study, 4 ADRs were found, out of which 2 (50%) are Diclofenac-induced pain, 1 (25%) is Diclofenac-induced vomiting and the other is 1(25%) Mefenamic acid-induced constipation.

From the study conducted, 62 DRPs were found, out of which 38 were drug interactions, in which 27(71.053%) were found as major drug interactions.

FIGURES AND TABLES

Table 1: Monotherapy and combination therapy of NSAIDs.

SL.NO:	THERAPY	NUMBER OF PATIENTS	PERCENTAGE (%)
1	MONOTHERAPY	73	66.37
2	TWO-DRUG COMBINATION	31	28.18
3	THREE-DRUG COMBINATION	6	5.45

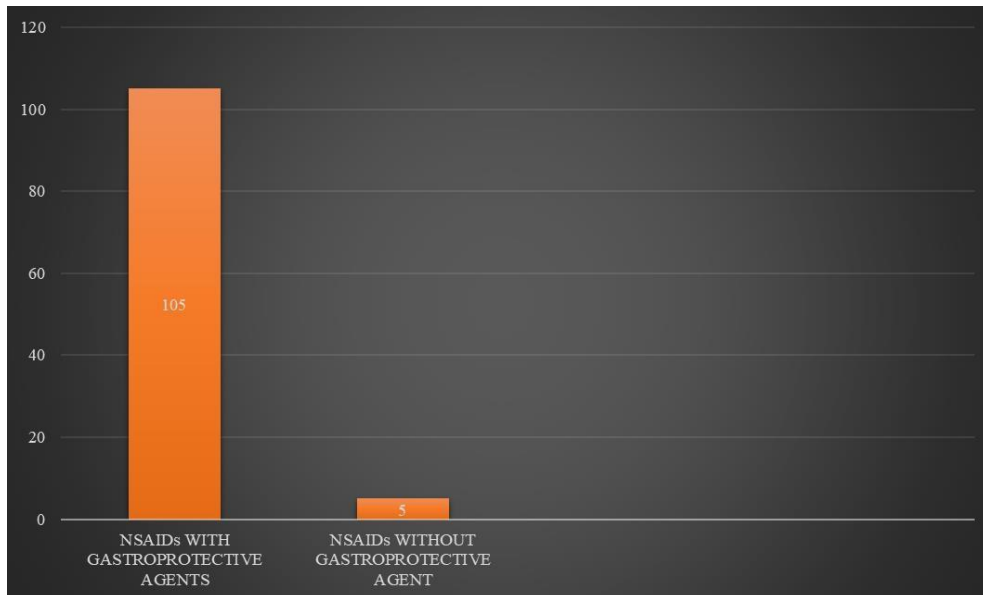


Fig 1: Patient prescribed with/without gastroprotective agents along with NSAIDs.

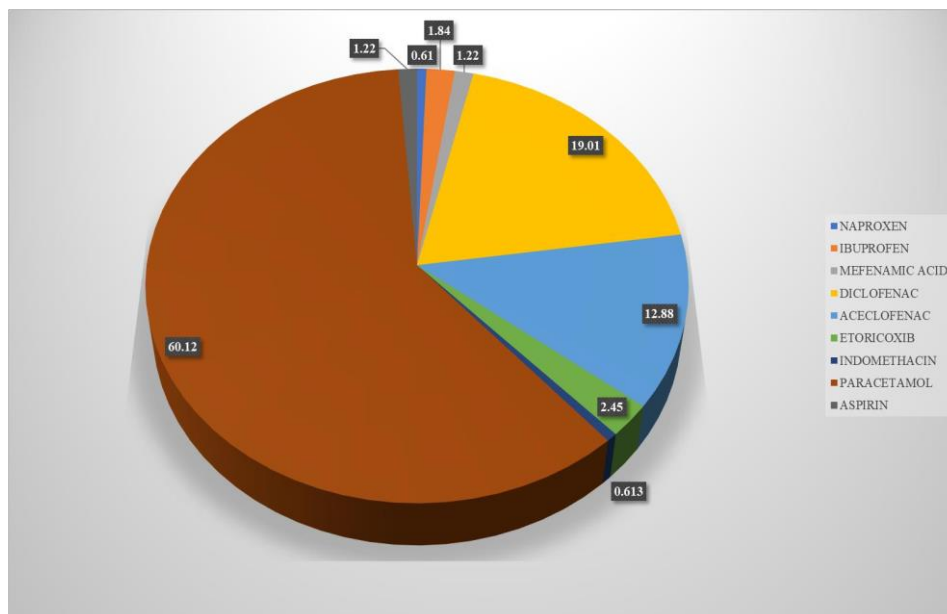


Fig 2: Class of NSAIDs prescribed among the in-patients.

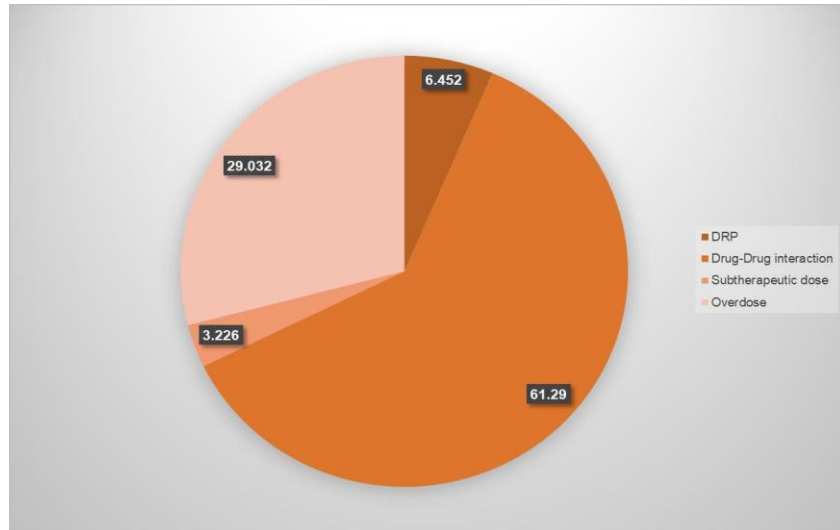


Fig 3: Identification and Assessment of DRPs among in-patients.

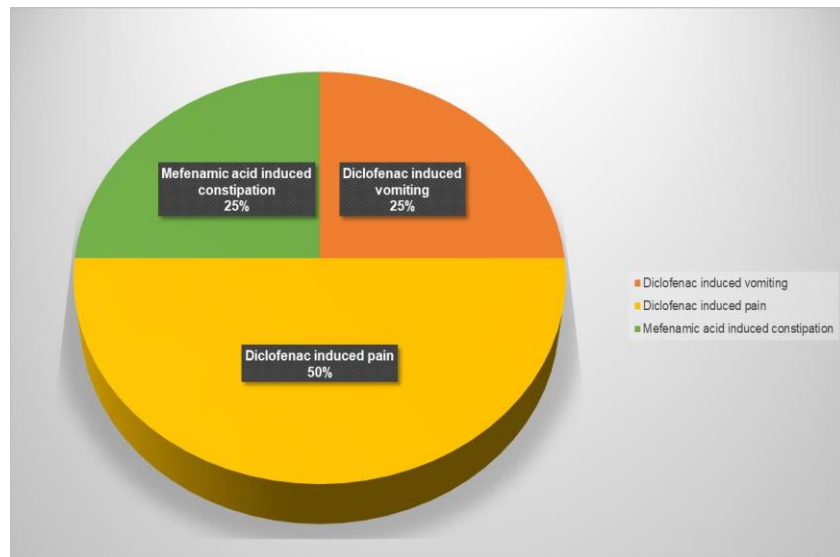


Fig 4: ADR identified in patients prescribed with NSAIDs visiting tertiary care patients.

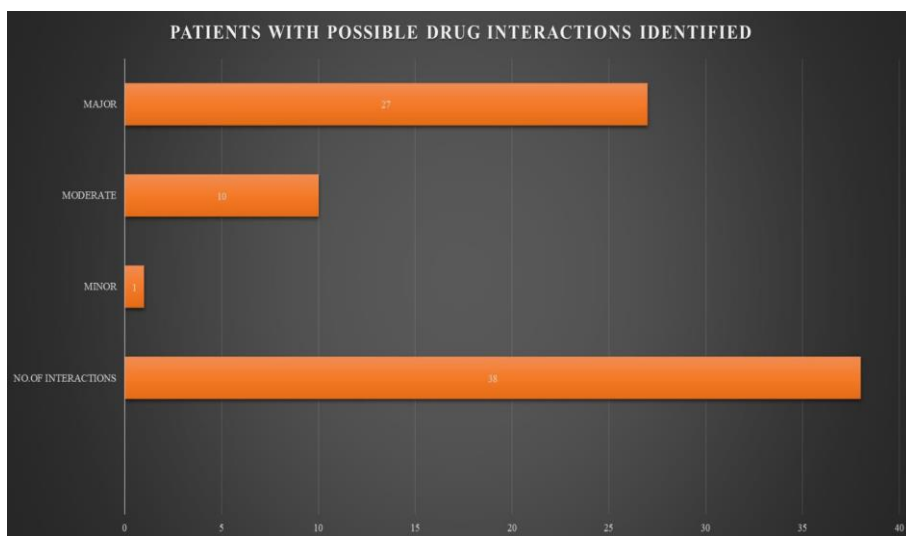


Fig 5: Patient with possible drug interactions identified.

ABBREVIATIONS AND SYMBOLS

ADD	Adverse Drug Reaction
COX-2	Cyclooxygenase – 2
DDI	Drug-Drug Interaction
DRP	Drug Related Problems
GI	Gastrointestinal
H2RA	H2 receptor antagonists
IPD	Inpatient Department
NSAID	Non-Steroidal Anti-Inflammatory Drugs
OPD	Outpatient Department
PPI	Proton Pump Inhibitors
SSRI	Selective Serotonin Reuptake Inhibitors
WHO	World Health Organization

DISCUSSIONS

NSAIDs are one of the most common causes of adverse drug reactions.^[24] As patients age, and the number of medications increases, NSAIDs in the elderly should be prescribed with caution. NSAIDs concomitantly used with specific medication can alter the risk of gastrointestinal ulceration and/or bleeding. These drugs include selective serotonin reuptake inhibitors (SSRIs), corticosteroids, digitalis glycosides, diuretics, beta-blockers, calcium antagonists, angiotensin- converting enzymes, warfarin, clopidogrel, aspirin, and other anticoagulants.^[22,25,26,27] Some specific NSAIDs were found to reduce the renal clearance of methotrexate, a commonly used medication for rheumatoid arthritis.^[28] This study was undertaken to analyze the drug utilization pattern of NSAIDs. Out of 110 patients who were prescribed NSAIDs visiting tertiary care hospitals, the total number of males was more, n= 71(65%) participants compared to female participants n=39(35%). In orthopedics, surgery, pediatrics, and medicine, NSAIDs were commonly prescribed. In a similar study done by Isswariya Anandan et al, the percentage of NSAIDs prescription was 42.4% which was higher when compared to a study conducted in Karnataka (11.3%).

In our study, 95% of the NSAIDs were co-prescribed with gastroprotective agents which was higher in comparison with findings from a similar study (24.32%), and 5% were prescribed alone. In a study among chronic NSAID users, the use of gastroprotective agents was found to be very poor which is against international guidelines and recommendations. Our finding was higher than the finding of a similar study in the UK (10%) and lower than that reported in the US (99.8).

The results of a similar study conducted in Chhattisgarh showed that no COX-2 selective NSAIDs were prescribed. The study conducted by Niyaz Alam et al reported Aceclofenac and diclofenac were the most frequently used drugs (5.26 & 40.66%). In the present study, paracetamol was mostly prescribed at 60.12% followed by Diclofenac at 19.01% and Aceclofenac at 12.88%.

Among 110 patient's monotherapy was prescribed at 66.37% followed by two-drug combination and three-

drug combinations at 28.18% and 5.45% respectively. Drug-related problems like adverse drug reactions, drug-drug interactions, subtherapeutic doses, and overdoses were assessed in patients. Adverse drug reaction was reported in 15 patients, Maximum ADRs were due to Ibuprofen (66%) followed by Diclofenac (33.33) which is similar to the study by Pragnesh A et al. In the present study there were 6.452% adverse drug reactions, in which ADRs were due to Diclofenac and Mefenamic Acid. Clinically significant drug interaction of 61.29%, a subtherapeutic dose of 3.22%, and an overdose of NSAIDs at 29.032% were also found. Major drug interactions were mostly found followed by moderate and minor drug interactions.

An increase in several drugs per encounter results in polypharmacy which leads to an increased incidence of adverse drug reactions and drug-drug interactions which interfere with achieving desired goals of therapy. Implementation of pharmacist intervention and other healthcare professionals will help improve patients' quality of life by individualizing therapy regimens and monitoring parameters during patients' stay in tertiary care hospitals.

CONCLUSION

The study can be concluded as Paracetamol was mostly prescribed compared to other NSAIDs as monotherapy and two-drug combinations are prescribed more among polytherapy. And the fact that it is commonly available and does not have commonly seen immediate anaphylactic reactions further facilitates the uncontrolled abuse of NSAIDs, we identified erosions of gastrointestinal mucosa and ulcers in patients who are chronic abusers of NSAIDs, 4 ADRs, 38 DDIs, two subtherapeutic doses, and, 18 overdoses were the DRPs found in the current study.

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