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A STUDY OF PRESCRIPTION PATTERN OF NON STEROIDAL ANTI-INFLAMMATORY DRUGS IN MEDICINE OUT-PATIENT CLINIC OF A RURAL TEACHING HOSPITAL

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ABSTRACT: Non Steroidal anti-inflammatory Drugs (NSAIDs) are most commonly prescribed drugs constituting more than 20% of all drug prescriptions. Prescription pattern study of NSAID was conducted in Medicine OPD of a rural teaching hospital with the objective of analyzing prescribing trend of NSAIDs, to evaluate co-prescription of Gastro-protective agents (GPAs) with NSAIDs and to determine number of prescribed NSAIDs falling within Drug utilization (DU) 90% segment. Overall 200 NSAID prescriptions were analysed. Prevalence of NSAID prescription was 25.71%. Paracetamol (36%) was the commonest drug prescribed. In general non-selective NSAIDs were more commonly prescribed (79.5%) and selective COX-2 inhibitors were least prescribed (1%). High prevalence of nimesulide prescription (19.5%) was a significant finding. Co-prescription of GPAs was high (61%). Four drugs (paracetamol, diclofenac, nimesulide and aceclofenac) fall within DU90% segment. In general prescription pattern requires further rationalization of NSAID usage as more number of drugs constitutes DU90% segment.

KEY WORD: Prescription pattern, NSAID, DU90%, GPAs co-prescription.

INTRODUCTION: The treatment of pain and inflammation is an important area of therapeutics. Over the past two decades, non steroidal anti-inflammatory drugs (NSAIDs) have played a central role in these indications. NSAIDs constitute the largest single group of drugs used worldwide, constituting more than 20% of all drug prescriptions[1]. In India over 400 formulations of NSAIDs are marketed, resulting in wide spread exposure of patients to this class of drugs and its adverse effects[2]. For all these reasons, studies that evaluate the pattern, extent and frequency of NSAID prescriptions are valuable.

The demonstration of two unique isoforms of cyclooxygenase (designated as COX-1 and COX-2) has led to a greater understanding of the mechanisms of action of NSAIDs and their toxicity[3]. The beneficial anti-inflammatory effect of the NSAIDs had been attributed to inhibition of COX-2, while the gastrointestinal (GI), renal and anti-platelet adverse effects were attributed to COX-1 inhibition[4]. Prescription pattern of NSAID changed frequently over a period of time. With the introduction of the selective COX-2 inhibitors, it has been suggested that they may be more cost–effective because of their improved GI tolerability and a reduction in concomitant prescription of antiulcer agents. This has led to an increase of almost 50% in the total number of NSAID prescriptions dispensed, with COX-2 drugs accounting for two thirds of this increase[3].

Before withdrawal of Rofecoxib, the prescriptions of COX-2 selective inhibitors had accounted for 37% of the total NSAID prescriptions dispensed. After its withdrawal in 2004, following the emergence of evidence of increased cardiovascular morbidity in the APPROVe (Adenomatous Polyp Prevention on Vioxx) study, COX-2 inhibitors represented less than 16% of the

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NSAID prescriptions. Subsequently the number of non-selective NSAID prescriptions increased to almost 33%[4, 5].

NSAIDs are generally prescribed with gastro-protective agents to prevent gastrointestinal side effects. Gastro-protective agents (GPAs) are more frequently prescribed with non-selective NSAIDs; they are also more frequently prescribed in older patients and in those with history of acid peptic disorders[6]. Selective COX-2 inhibitors promise better gastrointestinal tolerance, but various studies[6, 7] have shown that selective COX-2 inhibitors do not decrease the frequency of GPAs co-prescription. Precise role of GPAs co-prescription with NSAIDs is still widely debated.

For a developing country like India, where nearly 70% of the population resides in rural areas, a national drug policy is needed to rationalize drug usage. To achieve this it is very important to determine drug use pattern and monitor drug use profile over a period of time. Several studies of NSAID prescription patterns are available[8, 9], but very few studies were conducted in rural areas. Thus this present study attempts to describe NSAID prescription pattern and its utilization in a rural setup. Furthermore in this regard we used innovative approach to assess NSAID prescribing and its rational usage with the help of DU 90% (Drug Utilization 90%) methodology.

DU (Drug Utilization) 90%: DU 90% is an innovative approach to assess drug prescribing. Using this approach, the drugs that represent 90% of the drug prescription/sales volume are identified[10]. The rationale behind the development of DU90% rests on an assumption that a low number of products prescribed is associated with more rational prescribing practice.

DU90 identifies the number of drugs making up to 90% of the total volume, measured in Defined Daily Dose (DDD) or number of Prescriptions (NP), during a certain period of time.

According to DU90% concept a physician using few, well known and proved drug alternatives in the daily practice, would provide a more rational prescribing and hence a higher quality of care. It is a purely descriptive prescription indicator[8].

Size of the DU90% segment helps us to assess rational prescribing. A very large number of drugs in the DU90% segment indicate less rational prescribing. On the other hand, a small number of drugs in DU90% could suggest a more rational prescribing. The assumption that less is better is used as prescribing indicator in DU90%[11].

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. It will only be assigned for drugs that already have an Anatomical Therapeutic Chemical (ATC) classification code. DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose[12]. Drug consumption data presented in DDDs only give a rough estimate of consumption and not exact picture of actual use. The DDD provides a fixed unit of measurement that is independent of price and formulation, and makes it easier to compare drug utilisation across studies. The major benefit of studying drug utilization using DDD is that the dosage and the duration of use are both factored in to the calculation. The dosage, frequency and duration of use are variable in different patients, and these differences can be overcome by using the DDD as a measure of drug consumption[13].

METHODOLOGY: A prospective, non Interventional, cross sectional (observational) study was carried out in Medicine Out-patient Department (OPD) for a period of 5 months (July 2010 to Nov 2010).

Institutional ethical committee clearance was taken for the conduct of study. Data collection

was done at Medicine OPD registration counter where the prescriptions were recorded in the department records. Here investigator used to screen prescriptions of NSAIDs. Prescriptions containing NSAID were documented in an ethically approved specialized drug utilization proforma. Prescriptions not containing NSAIDs or Inpatient NSAID prescriptions were excluded from the study. Here Defined daily dose is calculated as DDD/1000/day and the formula used was:

$$DDD/1000/day = \frac{\text{Total no of dosage units prescribed X Strength of each dosage unit X 1000}}{\text{DDD X duration of study X total sample size}}$$

STATISTICAL ANALYSIS: Descriptive statistical procedure and evaluation were done to analysis the result. Analysis was done in frequency and tabular form. All the relevant statistical methods were carried out using SPSS for windows (version 11.0).

RESULTS: Demographic profile and prescription indices are mentioned in table-1. Of 778 prescriptions screened over a study period, 200 patients received NSAIDs. Frequency of NSAID prescription was 25.71%. Overall Paracetamol (36%) was the commonest drug prescribed followed by Diclofenac (22.5%), nimesulide (19.5%), aceclofenac (13.5%), ibuprofen (4%), ibuprofen + paracetamol (3.5%) and etoricoxib (1%). Non selective NSAIDs (79.5%) were more commonly prescribed, followed by preferential COX-2 inhibitors (19.5%). Selective COX-2 inhibitors were least prescribed (1%). Etoricoxib was the only drug prescribed in this class (table-2). Fever is the commonest indication (33% cases) for NSAID prescription, followed by others like headache, low backache and myalgia (due to viral infections, respiratory tract infections, chest pain etc). Ibuprofen + paracetamol, was the most commonly prescribed fixed dose combination (FDC). GPAs were prescribed in 61% cases. Ranitidine (51.6%) was the most frequently prescribed GPA (table-3). Four drugs (Paracetamol, diclofenac, nimesulide and aceclofenac) fall within DU90% segment (table-4).

Table-1: Demographic profile and prescription indices

Demographic Profile	
Total sample size	200(n)
Male	115
Female	85
Age	
➢ 01 to 20 yr	49
➢ 21 to 40 yr	78
➢ 41 to 60 yr	40
➢ More than 60 yr	33
Prescription Indices	
Total number of drugs prescribed	673
Average Number of drugs per prescription	3.36
Number of NSAIDs given in parenteral form	18
Number of FDCs prescribed	61
Number of antibiotics prescribed	74
Number of analgesic gel prescribed	12
Average cost of NSAID per prescription	Rs 20.75p

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Table-2: Class details of various NSAIDs prescribed in medicine OPD

NSAID class	No of prescription	Percentage (n=200)
Non selective COX inhibitors	**(159)**	**(79.5)**
➤ Paracetamol	72	36.0
➤ Diclofenac	45	22.5
➤ Aceclofenac	27	13.5
➤ Ibuprofen	08	04.0
➤ Ibuprofen+paracetamol	07	03.5
Preferential COX2 inhibitors	**(39)**	**(19.5)**
➤ Nimesulide	39	19.5
Selective COX2 inhibitors	**(02)**	**(01.0)**
➤ Etoricoxib	02	01.0

Table-3: Details of GPAs co-prescription

Frequency of GPAs prescribed	122 (61%)
Average cost of GPAs /prescription	15.5 rs

GPAs prescribed in Medicine	No of prescription	Percentage (n=122)
Ranitidine	63	51.64
Omeprazole	40	32.79
Pantoprazole	11	09.01
Antacids	08	06.56

Table-4: Drug constituting DU90% in Medicine OPD

S.No	Drugs	ATC Code	DDD	No. of prescriptions	DDD/1000/ days
1.	Paracetamol	NO2BE01	3000mg	72	03.96
2.	Diclofenac	MOIAB05	100mg	45	05.00
3.	Nimesulide	MOIAX17	200mg	39	03.90
4.	Aceclofenac	MOIAB16	200mg	27	02.70
DU 90% constituted by first four drugs (1 to 4)				**183 (91.5%)**	
5.	Ibuprofen	MOIAE01	1200mg	8	00.73
6.	Ibuprofen + Paracetamol	NO2BE01	400 + 500mg	7	00.70
7.	Etoricoxib	MOIAH05	60mg	2	00.33

DISCUSSION: Overall frequency of NSAID prescription in this study was 25.71%, which is slightly high when compared to various other studies done in urban setup, which has showed varied NSAID prevalence pattern. In St. John's Medical College and Hospital Bangalore, frequency of NSAID prescription was 24.52%[14]. Study conducted in Madurai, concluded that prescription prevalence of NSAID is more in rural setup (>25%) than in urban setup (21%) [15]. This present study being conducted in rural setup shows similar trend.

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Prevalence of prescriptions containing parenteral (IM route) preparations of NSAIDs in this study is 9%, which is almost similar when compared to study conducted in Manipal where parenteral preparation of NSAID prevalence was 8.6%[16]. In present study Fever was the commonest indication for NSAID prescription. Similarly Fever and musculoskeletal pain were the commonest indications for NSAID prescription in Saudi Arabia[17] and Dhaka study[18].

Traditional non-selective NSAIDs constitute nearly 80% of all NSAID prescriptions which is similar to prescribing trends observed in various other prescription pattern studies[14, 19, 16]. Findings in our study is similar to findings observed in Dhaka Bangladesh prescription study, where paracetamol is most commonly prescribed drug in Medicine department, followed by other non-selective NSAIDs like diclofenac[18].

COX-2 selective inhibitors were negligibly prescribed (1%) in our study. In contrast studies conducted prior to rofecoxib withdrawal showed high prevalence of selective COX-2 inhibitor prescription, like Study in Calicut showed upward trend in prescription of selective COX-2 inhibitor during the year 2000 to 2003[20]. Similarly study in Chandigarh also showed high prescription of selective COX-2 inhibitors (32.8%) [21].

High frequency of non-selective NSAID prescription in this study points towards the changing trends observed in the prescriber's preference for NSAID prescription after the withdrawal of rofecoxib[22]. This trend is quite evident in a study conducted in New York, which showed that selective COX-2 inhibitors constituted 37% of NSAID prescription before the withdrawal of rofecoxib. After withdrawal, their frequency decreased to 16% within one year and progressively decreased further in follow up studies[23].

Similarly study conducted in Ireland after withdrawal of rofecoxib showed less prescription of selective COX-2 inhibitors. Simultaneously Prescription of non-selective NSAIDs was on the rise and also preferential COX-2 inhibitors were more preferred as replacement to selective COX-2 inhibitors[22]. Similar finding is observed in this present study where significant numbers of prescriptions containing preferential COX-2 inhibitor were prescribed. Nimesulide was the only preferential COX-2 inhibitor prescribed in our study. In spite of controversy surrounding its prescription, especially with regard to its safety profile[24] it is still widely prescribed in our study (19.5%). It is also a part of DU90% segment. Similar trends were also observed in Irish General Hospital, where nimesulide was the commonest preferential COX-2 inhibitor prescribed[25].

CONCLUSION: In this study non-selective NSAIDs (79.5%) were commonly prescribed, followed by preferential COX-2 inhibitors (19.5%). Prescription frequency of selective COX-2 inhibitors (1%) was significantly low. Exclusion of selective COX-2 inhibitors from the DU90% segment further confirms this finding. Findings in our study was in accordance with general trend observed in NSAID prescription pattern where non-selective NSAIDs constitute the major bulk of prescription and also with the decline of selective COX-2 inhibitors, rise in preferential COX-2 inhibitors prescription was noted as probable alternative (in terms of GI safety) to COX-2 inhibitors. In spite of controversy surrounding nimesulide use, its prescription was significantly high (19.5%) in this study. High prevalence of GPAs co-prescription was noted here as non-selective NSAIDs were more commonly prescribed, which are less gastro-protective. Of seven different NSAIDs prescribed, four were part of DU90% segment. Prescription pattern needs further rationalization of NSAID usages as more than half of the various NSAIDs prescribed here were part of DU90% segment.

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LIMITATION AND RECOMMENDATIONS: The study has got few limitations. Duration of study was short (five months) hence effect of seasonal variation on NSAID prescription pattern could not be determined. Study was conducted only in medicine department (due to rural set up, this department handles maximum patient load) and other clinical departments were not involved, hence true prevalence of NSAID prescription and its pattern may show subtle variations.

Further large scale research is required for detail evaluation of NSAID prescription pattern, especially in rural setup where data regarding its rational utilization is lacking. Continuing medical education regarding appropriate use of NSAIDs, knowledge of its potential adverse effects and standard prescription guidelines will play pivotal role in rational prescription of NSAIDs.

Conflict of interest: None declared.

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