Research Paper

A Study of Prescribing Patterns for Non-Steroidal Anti-Inflammatory Drugs in a Tertiary Care Teaching Hospital

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Analgesics including nonsteroidal anti-inflammatory drugs are a commonly prescribed group of drugs in clinical practice for the management of pain and inflammation. This study was carried out to evaluate the prescribing pattern for nonsteroidal anti-inflammatory drugs in the tertiary care teaching hospital. A prospective cross sectional study was conducted in the orthopaedic department of a tertiary care teaching hospital from February to December 2017. The institutional ethical committee approved the study. Patients of both genders were included in the study. Patients treated with at least one nonsteroidal anti-inflammatory drug in the outpatient department of orthopaedics were included. The prescription was compared with World Health Organization drug prescribing indicators to compare selective and non-selective nonsteroidal anti-inflammatory drugs associated with the treatment also concurrent prescription of gastro protective agents. The data collected was analysed by descriptive statistics. Chi-Square test was used to compare the difference between the two groups. A p value of <0.05 was considered significant. Out of 500 prescriptions included in the study, the total number of drugs prescribed was 1098, of which were nonsteroidal anti-inflammatory drugs. Based on the World Health Organization's drug use indicators, the average number of drugs per encounter was 2.19 % and the average number of nonsteroidal anti-inflammatory drugs per encounter was 1.38 %. Out of all the nonsteroidal anti-inflammatory drugs prescribed, 428 (62.20 %) were from National List of Essential Medicine India 2015 and 678 (98.5 %) nonsteroidal anti-inflammatory drugs were prescribed by generic name. Among the study population, only 40 % of patients were prescribed Proton Pump Inhibitors along with nonsteroidal anti-inflammatory drugs. Proton Pump Inhibitors are effective in ulcer prophylaxis in their standard dose. The present study concluded that among cyclooxygenase-1 inhibitors, Diclofenac was the most commonly prescribed nonsteroidal anti-inflammatory drugs from the national list of essential medicine. The most frequently prescribed cyclooxygenase-2 inhibitor in this study was Etoricoxib. The percentage of analgesic prescribed by generic name was excellent. However, the average number of drugs per prescription deviated from the World Health Organization's rational drug use indicator. The use of gastro protective agents needs to be rationalised with nonsteroidal anti-inflammatory drugsy.

Key words: Non-steroidal anti-inflammatory drugs, prescription, world health organisation, indicators

Over the past two decades, non-steroidal anti-inflammatory drugs (NSAIDs) have played a central role in the treatment of pain and inflammation. NSAIDs are the largest single group of drugs used globally, constituting more than 20 % of all prescriptions[1]. It is found that more than thirty million individuals consume NSAIDs daily. Around 400 formulations of NSAIDs are marketed in India, resulting in widespread exposure of patients to this class of drugs and its adverse effects[2]. For all the above reasons, studies evaluating the pattern of prescriptions of NSAIDs are very important.

The cyclooxygenase-2 (COX-2) enzyme helps in controlling gastric mucus production, the water excretion from the kidney. It also induces platelet formation and is involved in producing prostaglandins

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for inflammatory response. Though there is wide clinical use of traditional NSAIDs as analgesics, anti-pyretic and anti-inflammatory agents, their gastro-intestinal toxicity is a major clinical constraint. Subsequently, selective COX-2 inhibitors have emerged as potentially gastro-friendly NSAIDs and it is believed that sufficient therapeutic benefits are achieved by selective COX-2 inhibition[3,4].

Rational drug prescribing has been the subject of several studies[5]. The World Health Organization (WHO) compiled a set of core drug use indicators that are useful for studying the prescribing patterns of drugs in healthcare settings[6,7]. Prescriptions can be used as authorised documents prescribed by a physician and the dispensing pharmacist are responsible for any misconduct in prescribing or dispensing. NSAIDs, including both traditional nonselective NSAIDs and selective COX-2 inhibitors, are among the most widely used drugs for the management of pain. Both prescription and over-the-counter NSAIDs are widely used for their anti-inflammatory and analgesic effects. NSAIDs are the essential choice in pain management because of the combined role of the COX pathway in inflammation[8].

A previous study conducted in Aden in Yemen revealed that non-selective NSAIDs were the most commonly prescribed, with diclofenac sodium being the most frequently prescribed (26.6 %), followed by meloxicam (12.8 %) and ibuprofen the least common (12 %). A combination of two non-selective NSAIDs was also reported. Selective COX-2 inhibitors were much less commonly used. This class of drug was mainly prescribed for infective conditions (29.3 %), fever (9.3 %), orthopaedic pain (8.1 %) and musculoskeletal pain (7.8 %). In general, the study concluded that there was irrational use of NSAIDs and deviation from the WHO standards regarding NSAIDs, with a high rate of NSAID prescription and low practice of prescribing drugs by generic names[9].

Similarly, an Iranian study found that the most prescribed NSAIDs was diclofenac (49.21 %), followed by ibuprofen (28.6 %) and naproxen (8 %). Prescribing two NSAIDs simultaneously was reported in 7 % of the prescriptions. General Doctors tend to prescribe NSAIDs more frequently than specialists-(67 %) and (33 %) respectively. The study reported irrational prescribing patterns in coadministration of NSAIDs and gastroprotective agents as well as NSAID combinations[10].

Another study conducted in Nigeria showed that the most commonly prescribed medicine is Aspirin (62.2 %) followed by Diclofenac potassium (13.7 %), while Tenoxicam and Piroxicam were the least prescribed (0.1 %). In contrast to the previous study, this study showed compliance with the WHO's standards regarding prescribing patterns[11].

Rational use of drugs is essential and it has global importance. Rational drug prescribing can be defined as appropriate drugs prescribed in the right dose, at correct time intervals and for a sufficient duration. Irrational drug use is a common problem in many countries of the world. Therefore, periodic evaluation of drug utilisation patterns needs to be done to enable suitable modifications in the prescription of drugs to increase the therapeutic benefit and decrease the adverse effects in accordance with WHO drug use indicators[12]. The purpose of a drug utilisation study is to provide feedback to the prescriber and to create awareness about the rational use of medicines[13]. Hence, this study aimed to evaluate the use and prescribing pattern of NSAIDs in tertiary care teaching hospitals.

MATERIALS AND METHODS

Study design and setting:

This study used a prospective cross-sectional design, which was carried out in the orthopaedic out-patient department of a tertiary care teaching hospital, Tamilnadu in India, between the February and December 2017.

Study population:

A total of 1695 patients visited the orthopaedic department during the study period. Out of 1695, only 1480 patients were prescribed NASIDs.

Sample size and sampling technique:

The sample size was based on the number of patients visiting the out-patient orthopaedic department (1695) and determined by using a Raosoft sample size calculator (http://www.raosof.com/samplesize.html) with a predetermined margin of error of 5 % and a confidence level of 95 %[14]. In order to minimise erroneous findings and to increase study reliability, the target sample size was set at 314 participants. The number was increased to 500 patients. The institutional ethical committee approved the study. A non-random sampling procedure-i.e. a convenience sampling-was

followed, as selecting a truly random sample was not possible due to the unfeasibility of constructing a sampling frame.

Population criteria:

After obtaining their informed consent, patients of both genders who were prescribed at least one NSAID during the study period. Patients with severe psychiatric disorders, terminal illness and inpatients of any department were excluded from the study.

Patient data collection:

Patient data were collected through data collection forms which consisted of details including the following: age, sex and drug therapy. Additional information was collected from patients' medical records after a direct interview with the patients. The collected data was evaluated for the WHO's prescribing indicators, indication for prescribing NSAIDs and comparison of selective and non-selective NSAIDs.

Evaluation of data:

The prescription was assessed according to the WHO's prescribing indicators[15]. 'Average number of drugs per encounter, Percentage of encounters with NSAIDs prescribed, Percentage of encounters with an injection of NSAID prescribed, Percentage of encounters with nonselective NSAID prescribed, Percentage of encounters with COX-2 selective NSAID prescribed, Percentage of NSAIDs prescribed by generic names, Percentage of encounter with NSAIDs prescribed from National List of Essential Medicine, India (NLEM-2015)[16], Percentage of encounter with fixed-dose combination (FDC) of NSAIDs prescribed, Percentage of encounters with NSAIDs and gastroprotective agent prescribed.

Statistical analysis:

The collected data were cleared, entered and analysed using the Statistical Package for Social Sciences (SPSS) version 24.0 for the windows. Chi-Square test was used to compare the difference between the two groups. A p value of <0.05 was considered significant. Results were described in terms of frequencies. Collected data was analysed by descriptive statistics.

RESULTS AND DISCUSSION

This study set out with the aim of assessing the use and prescribing pattern of NSAIDs in a tertiary care teaching hospital. Out of 1695 who visited the orthopaedic department during the study period, 1480 patients were prescribed NASIDs and 500 patients were enrolled for this study. Out of 500 prescriptions included in the study, the total number of drugs prescribed was 1098, among them 688 NSAIDs. Among the 500 patients, 234 (46.8 %) were male and 266 (53.2 %) were female. The age and gender distribution of the pattern of NSAIDs prescribing is presented in Table 1. About 8.8 % (44) and 4.8 % (24) the patients were smokers and drank alcohol, respectively. The youngest age for which Diclofenac and Ibuprofen was prescribed was 17 y old and this was 22 y for Aspirin. Results showed significant differences ($p<0.0001$) in the frequency of NSAID prescribing according to age groups utilising the Chi-Square test. Diclofenac 148 (21.51 %) and Aceclofenac 104 (15.11%) were prescribed mostly for the adult age group, Aspirin was prescribed only to the adult age group, while Ibuprofen derivatives were prescribed mainly for adults 48 (6.97 %) and to a much lesser extent to children less than 18 y of age (2.32 %). There were no differences ($p=0.193$) in the pattern of prescriptions according to gender.

Similar to what was observed in previous research conducted in the United Arab Emirates[16], the current study shows that the average number of drugs per encounter is 2.19 % and the average number of NSAIDs per encounter is 1.38 %. This is considered high, as the standard value recommended by the WHO for the average number of drugs per encounter is 1.6-1.8[15]. Out of all the NSAIDs prescribed, 428 (62.20 %) were from NLEM India 2015 and 678 (98.5 %) NSAIDs were prescribed by generic name (Table 2 and Table 3). Mirroring the findings observed in a previous study conducted in India[17], the percentage of NSAIDs prescribed from the national essential drug list in the current study is suboptimal (WHO standard value is 100 %)[15]. However, the percentage of NSAIDs prescribed by generic name was satisfactory in the current study. This finding is contrary to the study by Agrawal *et al.* (2016), where 47.26 % of NSAIDs were prescribed by generic name[17].

The route of administration was dominated by the oral route in 360 patients (72 %), followed by oral with topical route of administration in 90 (18 %) patients and topical route in 50 patients (10 %). Thus, the oral route of administration was the most frequently prescribed.

Out of 500 patients, Osteoarthritis 140 (28 %) was the most common condition for which NSAID was prescribed, followed by general pain 90 (18 %), such as post-operative pain, leg pain and joint pain, then

TABLE 1: PRESCRIBING FREQUENCIES OF NON-STEROIDAL INFLAMMATORY DRUGS ACCORDING TO THE AGE GROUP AND SEX OF THE PATIENTS

NSAID	Gender	<18 y	18-49 y	50 or more y	Total
Aspirin	Male	0	2	4	6
	Female	0	2	2	4
	Total	0	4	6	10 (1.45 %)
Ibuprofen	Male	2	9	7	18
	Female	3	19	8	30
	Total	5	28	15	48 (6.97 %)
Diclofenac	Male	3	43	24	70
	Female	0	44	34	78
	Total	3	87	58	148 (21.51 %)
Aceclofenac	Male	0	22	33	55
	Female	0	28	21	49
	Total	0	50	54	104 (15.11 %)
Paracetamol	Male	4	33	28	65
	Female	2	29	24	53
	Total	6	62	50	118 (17.15 %)
Etoricoxib	Male	0	60	32	92
	Female	1	65	40	106
	Total	1	125	72	198 (28.77 %)
Etodolac	Male	1	13	11	25
	Female	0	14	15	29
	Total	1	27	26	54 (7.84 %)
Piroxicam	Male	0	3	2	5
	Female	0	2	1	3
	Total	0	5	3	8 (1.16 %)

NSAID=Non-steroidal Anti-inflammatory drug; Pearson Chi-Square statistic=122.5, p value=0.0001, for NSAID prescription in relation to age; Pearson Chi-Square statistic=9.7, p value=0.193, for NSAID prescription in relation to gender

TABLE 2: WHO CORE PRESCRIBING INDICATORS

WHO core prescribing Indicators	Percentage
Average number of drugs per encounter	2.19
Average number of NSAIDs per encounter	1.38
Percentage of encounters with NSAIDs prescribed	100
Percentage of encounters with an injection of NSAID prescribed	0
Percentage of encounters with nonselective NSAIDs Prescribed	71
Percentage of encounters with selective COX-2 NSAIDs prescribed	29
Percentage of NSAIDs prescribed by generic names	98.5
Percentage of NSAIDs prescribed from NLEM	62.2
Percentage of encounters with a fixed dose combination of NSAIDs prescribed	25.58
Percentage of encounters with NSAIDs and gastroprotective agent co-prescribed	40

WHO-World Health Organisation; NSAIDs-Non steroidal anti-inflammatory drugs; NLEM-National list of essential medicine

TABLE 3: PRESCRIBED NONSTEROIDAL ANTI-INFLAMMATORY DRUGS LISTED AND NOT LISTED IN NATIONAL LIST OF ESSENTIAL MEDICINE 2015[13]

Prescribed NSAIDs, which are listed in NLEM-2015	Number of encounters (%)	Prescribed NSAIDs, which are not listed in NLEM-2015	Number of encounters (%)
Aceclofenac	104 (15.11)	Etoricoxib	198 (28.8)
Diclofenac	148 (21.5)	Etodolac	54 (7.8)
Paracetamol	118 (17.1)	Piroxicam	8 (1.2)
Ibuprofen	48 (6.9)		
Aspirin	10 (1.5)		

NSAIDs-Non steroidal anti-inflammatory drugs; NLEM-National list of essential medicine

rheumatoid arthritis 70 (14 %), impinge syndrome 50 (10 %), spondylosis 60 (12 %), post-viral polyarthralgia 40 (8 %), fibromyalgia 30 (6 %) and gout 20 (4 %) (fig.1). The present study shows osteoarthritis was the most common condition, followed by general pain, rheumatoid arthritis, soft tissue injury, spondylosis, etc.

Consistent with results observed in earlier studies, the current study revealed that the most commonly prescribed NSAID was non-selective COX 1 inhibitors[9,10,18,19,20] i.e. Diclofenac 148 (21.5 %), followed by Paracetamol 118 (17.1 %), Aceclofenac 104 (15.1 %), Ibuprofen 48 (6.9 %), Piroxicam 8 (1.2 %). The most commonly prescribed COX-2 inhibitor was Etoricoxib 198 (28.8 %), followed by Etodolac 54 (7.8 %) and Aspirin 10 (1.5 %). A previous drug utilisation study revealed that 22 % of prescriptions contain paracetamol and diclofenac. However, Aceclofenac accounted for only 1 % of NSAIDs prescription[21].

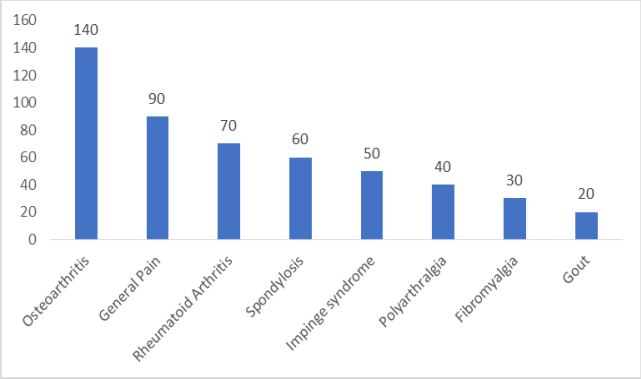

Fig. 1 Shows the number of patients diagnosed in each condition and NSAIDs prescribed for the following indications

TABLE 4: MONOTHERAPY PRESCRIBED AMONG THE STUDY POPULATION

	Number of encounters (%)
Monotherapy	**(n=500)**
Diclofenac	102(20.4)
Paracetamol	12 (2.4 %)
Etodolac	50 (10 %)
Etoricoxib	148 (29.6 %)
Ibuprofen	12 (2.4 %)

TABLE 5: FIXED DOSE COMBINATIONS OF NSAIDs

Fixed Dose combinations of NSAIDs	Number of encounters (%) (n=500)
Aceclofenac + Paracetamol	56 (11.2 %)
Aceclofenac + Paracetamol + Rabeprazole	48(9.6 %)
Diclofenac &Ibuprofen	34 (6.8 %)
Etoricoxib & Diclofenac	22 (4.4 %)
Etoricoxib & Ibuprofen	2 (0.4 %)
Etoricoxib & Aspirin	8 (1.6 %)
Etoricoxib &Piroxicam	6(1.2 %)
Total	176 (35.2 %)

Monotherapy was given to 324 (65 %) patients, whereas a fixed dose combination of two NSAIDs was given to 176 (35 %) (Table 4 and Table 5). Among the most commonly prescribed monotherapy was Etoricoxib 148 (29.6 %), followed by Diclofenac 102 (20.4 %). However, the most commonly prescribed drug among fixed dose combinations was Aceclofenac+Paracetamol followed by Aceclofenac+Paracetamol+Rabeprazole. Fixed dose combination contributes to improved patient adherence due to the reduction in the number of pills taken by the patient[22].

Among the study sample, only 40 % of patients were prescribed proton pump inhibitors (PPIs- Pantoprazole 22 %, Rabeprazole 14 %, Omeprazole 4 %) along with NSAIDs, whereas the remaining 60 % of patients were not prescribed any gastro-protective agent. Out of these 60 %, 28 % of the patients were prescribed COX-2 inhibitors. Thus, 32 % of patients were prescribed COX-1 inhibitors without any gastro-protective agent (Table 6). Consequently, the chances of developing gastro-intestinal complications in these patients is high[23]. Inappropriate prescribing of NSAIDs in diabetes mellitus patients led to significant gastrointestinal and cardio vascular adverse events[24]. Hence, rational use and safe prescription of NSAIDs with other drugs is necessary in order to prevent or minimise the adverse effects.

The current study concludes that, among COX-1 inhibitors, Diclofenac was the most commonly prescribed NSAIDs from NLEM, and Etoricoxib was found to be the most commonly prescribed among COX-2 inhibitors. The percentage of analgesics prescribed by generic name was appropriate, but the average number of drugs per prescription deviated from the WHO's rational drug use indicator. The use of gastro protective agents along with NSAIDs needs to be rationalised.

A limitation of this study is that the sample was

TABLE 6: GASTRO PROTECTIVE AGENTS CO-PRESCRIBED WITH NSAIDs

Co-prescribed Drugs	Number of patients (%) (n=500)
Pantoprazole	110 (22 %)
Rabeprazole	70 (14 %)
Omeprazole	20 (4 %)

selected using a non-random sampling method, and this may have resulted in a biased sample as the intended population did not have equal sampling probability. Therefore, the study finding cannot be extrapolated to all patients prescribed NSAIDs.

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Conflict of Interest:

The authors declare no conflict of interest.

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