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Prescription pattern and adverse drug reaction profile of drugs prescribed with focus on NSAIDs for orthopedic indications at a tertiary care hospital

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Abstract

Introduction: The Non-steroidal Anti-inflammatory Drugs (NSAIDs) constitute the largest group of drugs used worldwide for indications like rheumatoid arthritis, osteoarthritis, low back pain etc. Periodic evaluation of drug utilization patterns enable suitable modifications in prescription of drugs to increase the therapeutic benefit and decrease adverse effects.

Objective: To analyze the prescription patterns and adverse drug reaction profile of NSAIDs prescribed in orthopedic outpatient department of Tertiary Care Hospital. Study design: observational, cross-sectional study.

Results: 360 patients enrolled. Average number of drugs per prescription was 3.83. Total 1382 drugs were prescribed, out of which 418 were NSAIDs (30.24%). Ibuprofen was most commonly prescribed agent (62.79%), followed by Diclofenac (40.66%). Ibuprofen was found to be the commonest drug associated with ADRs.

Conclusion: Ibuprofen was most commonly prescribed NSAID and also responsible for majority ADR. There was higher prevalence of irrational prescribing, polypharmacy and under reporting of ADR.

Keywords: Drug utilization study, Ibuprofen, ADR.

Introduction

The Non-steroidal Anti-inflammatory Drugs (NSAIDs) are the most commonly used medications in the world.(1) They constitute the largest single group of drugs used worldwide, constituting more than 20% of all drug prescriptions.(2)

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.(3)

NSAIDs are used in the treatment of disorders associated with pain and inflammation.(4) They have a wide variety of indications for use, ranging from treatment of acute pain to more chronic conditions such as rheumatoid arthritis (RA), osteoarthritis (OA), low back pain (LBP) etc.(5) These agents exert their effect by inhibiting the activity of the enzyme cyclo-oxygenase with a resultant reduction in prostaglandin synthesis and an alleviation of the nociceptive and inflammatory response.(5) Their long term use are associated with gastrointestinal toxicity like dyspepsia, peptic ulcers and gastrointestinal bleeds etc.(6)

NSAIDs action on two unique isoforms of cyclooxygenase (designated COX-1 and COX-2) has led to a greater understanding of the mechanism of action of NSAIDs and has also provided an explanation for their toxicity.(7)

NSAIDs are also associated with certain adverse drug reactions such as allergic reactions, skin reactions, gastrointestinal effects, renal complications, alteration of hepatic enzyme levels and rarely hepatopathies.(8) The prevalence of NSAIDs induced ulcer has been reported to be between 10 to 25% and it causes significant morbidity and mortality.(9)

An 'adverse drug reaction' (ADR), as defined by the World Health Organization, is a noxious, unintended effect of a drug, which occurs at normal doses in humans for the prophylaxis, diagnosis, or the therapy of the disease or for the modification of its physiological function.(10) ADRs are considered as the 4th to 6th leading causes of death among hospitalized patients. These are associated with significant morbidity, mortality and permanent disability and is a huge economic burden on the patients due to prolonged hospitalization.(11) It has been estimated that the incidence of ADRs throughout the world is 5% and 5-6% of all the hospital admissions which are caused by drug - induced problems(12)

The World Health Organization (WHO 2003) addressed drug utilization as the marketing, distribution, prescription and use of drugs in a society, considering its consequences either medical, social or economic.(13)

Periodic evaluation of drug utilization patterns need to be done to enable suitable modifications in prescription of drugs to increase the therapeutic benefit and decrease the adverse effects. The study of prescribing patterns seeks to monitor, evaluate and if necessary, suggest modifications in the prescribing behaviour of medical practitioners to make medical care rational and cost effective.(14)

With this background, present study was planned to analyze the prescription patterns and adverse drug reaction profile of NSAIDs prescribed in orthopedic outpatient department of a Rural Tertiary Health Care Hospital, Ambajogai, Maharashtra.

Aims and Objectives

1. To analyze prescription pattern of drugs prescribed at orthopedics Out Patient Department (OPD) with

focus on NSAIDs.

2. To evaluate adverse drug reaction (ADR) profile of drugs prescribed at orthopedic OPD.

Materials and Methods

An observational cross-sectional study was conducted for 2 months in 360 patients after the approval of Institutional Ethics Committee at tertiary care teaching hospital. Written Informed Consent was taken from all patients visiting the orthopedic OPD who were willing to participate in study before their prescription were analyzed.

The case sheet of patients was analyzed for prescription pattern using WHO core drug use indicators. Simultaneously development of any ADR to drug prescribed was observed with present visit and follow-up visit after 3 days. ADR was analysed using WHO-UMC causality assessment scale and Hartwig's Severity Assessment Scale. Data was analyzed using descriptive statistics with Mean and percentages as applicable.

Results

Out of 360 patients enrolled, 224 (62.22%) were female and 136 (37.78%) were male. The most common age group was 41-60 (36%). In present study, average number of drugs per prescription was 3.83 with mean duration of 3 days.

Total 1382 drugs were prescribed, out of which 418 were NSAIDs (30.24%). In 96.66% of prescriptions, gastro-protective agents were used along with NSAID's and most commonly antacids (80%) followed by ranitidine (16.66%). Other drugs prescribed were Multi-Vitamins (22.28%) and Calcium Salts (21.85%). (Fig. 1)

Out of 418 NSAIDs drugs, Musculoskeletal pain and backache were the most common indications for the use of NSAIDs. .Most of drugs were prescribed by oral route (95.22%) followed by parenteral route (4.63) followed by topical route (0.14)**.** Ibuprofen was most commonly prescribed agent among NSAIDs (62.79%), followed by Diclofenac (40.66%). (Table 1) Table 2 shows results of prescription analysis according to WHO core drug use indicators.

Adverse drug reaction profile in NSAID users: 15 patients with ADRs were reported in 360 patients. Most of these patients were old aged who regularly takes NSAIDs for joint pain. Eight ADR were reported with monotherapy while 7 ADR were reported in patients with multiple drug regime. Ibuprofen (09) was found to be the commonest drug associated with ADRs inclusive of single and combination therapy, followed by tablet diclofenac (3), Aceclofenac (1), injection Diclofenac (2). Table 3 shows ADR profile of NSAIDs prescribed.

Drug reactions according to WHO-UMC causality assessment, 2 were certain (13.33%), 3 were probable (20%) and 10 were possible (66.66%). On severity assessment by modified Hartwig and Siegel's scale for adverse drug reactions, 1(6.66%) was mild, 10 (66.66%) were moderate and 4(26.66) were severe.

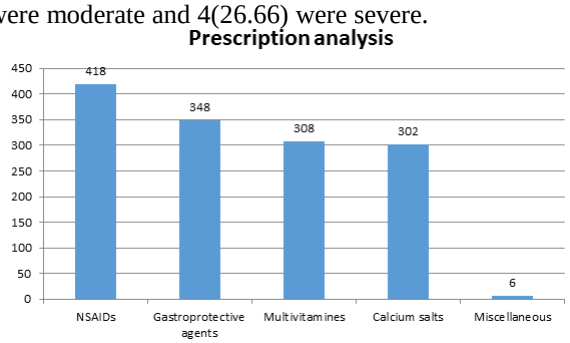

Fig. 1: Analysis of total drugs prescribed in patients. (n= 1382)

Table 1: Pattern of NSAIDs used in Orthopedics outpatient department

Name of Drug	No. of drugs	Percentage Amongs NSAIDs	Percentage in prescription
Tablet Ibuprofen	224	53.58	62.22
Tab Diclofenac	106	25.35	29.44
Inj. Diclofenac	64	15.31	17.77
Tab. Aceclofenac	22	5.26	6.11
Analgesic gel	02	0.5	0.55
Total	418	100	

Table 2: prescription analysis according to World Health Organization core drug use indicators

Parameter	Number (%)
Total no of prescriptions	360
Total no of drugs	1382
Average no of drugs per prescription	3.83
Drugs prescribed by generic name	5.65
Drugs prescribed by brand name	94.35
Drugs from essential drug list	602 (43.56)
Diagnosis not mentioned	310(86.11)
Chief complaints not mentioned	48(13.33)
Duration not mentioned	280(77.77)
Dose not mentioned	322(89.44)
Route not mentioned	352(97.77)
Frequency not mentioned	60(16.66)

Table 3: ADR profile of NSAIDs prescribed (n =418)

Drug	Adverse drug reaction	System Involved	No. of ADRs and percentage
Ibuprofen	Abdominal pain,	Gastrointestinal	09(60)
	G.I.T. irritations	System	
Tablet Diclofenac	1.Gastric discomfort,	Gastrointestinal	02(13.33)
	Vomiting,	system,	
	2. Pruritis	Skin	01(6.66)
Inj Diclofenac	Pruritus,	Skin	02(13.33)
	Hypersensitivity		
	Reaction		
Aceclofenac	Headache	CNS	01 (6.66)

Total	15

Discussion

The assessment of drug utilization is important for clinical, economic and educational purposes. Drug utilization studies aim to provide feedback to the prescriber and to create awareness among them about rational use of medicines.[14]

The average number of drugs per prescription in our study was 3.83. The average (mean) number of drugs per prescription is an important parameter while doing a prescription audit. There was a trend of polypharmacy which create an unnecessary burden on the already exhausted and poorly funded economy of the health system. The mean number of drugs was higher as compared to previous studies done by Shankar et al[15] and Gupta et al.[16]

Rather than moving towards a rational practice, there is trend for 'many pills for a single ill' culture where the prescriber prescribes multiple drugs for a symptom without rationally evaluating the need and necessity for the same. The concept of essential drugs should be evolved precisely to curb this practice.

The population most commonly attending outpatient department was middle aged (21-60yrs). Similar findings also reported by Niyaz alam et al.[17] (31-50age group with 50.2%) As this is a rural based hospital, majority of the patients were farmers, labourers by occupation, explaining the higher orthopedic complaints in this age group.

Ibuprofen (53.58%) was most commonly used NSAIDs in our study while study conducted by Niyaz alam et al[32] reported Aceclofenac and diclofenac were the most frequently used drugs (5.26 & 40.66% respectively) COX-2 selective inhibitors were developed with assumption of better safety profile (renal and GI) than non-selective Non-steroidal anti-inflammatory drugs (NSAIDs) and became very popular few years back. However, the results of present study points towards the reversal of trends back to the use of conventional Non-steroidal anti-inflammatory drugs (NSAIDs). This shift might have come with the recent reported CVS toxicity with the use of selective COX-2 inhibitors.[18] Study conducted by Gupta M.et al.[16] reported use of Selective COX-2 inhibitots (Rofecoxib 30% and Valdecoxib 18%)

Concomitants drugs like Gastoprotective agents were used higher in 96% of prescription due to fear of gastric toxicity associated with use of NSAIDs. Multi-Vitamins (22.28%) and Calcium Salts (21.85%) use were also high which is cause of poly pharmacy. Study conducted by Raghavendra B, Sanji N, et al[19] reported 32% prescription were co- prescribed with gastro protective agents.

Majority of the prescriptions were inadequate in terms of diagnosis, dose, route and frequency of administration i.e., irrational. There is a scope for improvement in writing of prescriptions and educational programmes on proper prescribing habits can be organised for doctors at all levels.

Adverse drug reaction were reported in 15 patient , Maximum ADRs were due to Ibuprofen(66%) followed by Diclofenac(33.33)which is similar to study by Pragnesh A et al.[20] Gastrointestinal system was involved in 73.33% patients followed by Skin(20%). Similar findings were also reported by pharmacovigilance study conducted by Venkatachalam S et al.[12] They reported gastritis as most common adverse drug reaction and main system involved was gastro-intestinal system.

In present study majority ADRs were possible (66.66%) and probable (20%) on WHO-UMC causality assessment scale. Venkatachalam S et al.[12] study reported 63.63% of the adverse reactions were possible and 36.37% were probable on As per Naranjo's Algorithm scale.

Finally to conclude, present study provide baseline data regarding the current prescribing trends of NSAIDs in orthopedic outpatient department in tertiary care hospital. In present study, Ibuprofen was most commonly prescribed NSAID and also responsible for majority ADR. Concomitant medication with gastro protective agents was high. There was higher prevalence of irrational prescribing, polypharmacy and under reporting of ADR. To improve the scenario, programme on the rational use of drugs aims at promoting rational prescribing through a multi-pronged strategy should be organized which includes intervention to correct drug use problems, adoption of essential drug list, development of standard treatment guidelines, hospital formulary. Pharmacovigilance program should be promoted which is highly effective in increasing the reporting of ADRs as well as help to identify infrequent adverse drug reaction caused by drugs.

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