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Original Research Article

Prescription pattern of non-steroidal anti-inflammatory drugs among patients admitted with fever in a tertiary hospital

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ABSTRACT

Background: WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately. Nonsteroidal anti-inflammatory drugs are a group of drugs that are commonly prescribed for the treatment of fever associated with pain and inflammation. The objective was to assess the prescribing pattern of NSAIDs in fever patients. Along with this, we looked at the clinical indications for prescribing and the pattern of prescribing with respect to use of generic or trade names.
Methods: This observational study was conducted in a tertiary care teaching hospital in Malappuram district of Kerala, India by extracting data of inpatients retrospectively from medical records for a six-month period. The reported prevalence of NSAID use in previous study was 20%, with a relative precision of 18% the sample size required was 500. The data was analyzed and expressed as absolute numbers and/or percentages.
Results: Out of these 500 patients, Dengue fever was the most common diagnosis (86.6%) followed by Typhoid (2.8%) and Leptospirosis (2.4%). Among these, 392 (78.4%) received any of the NSAIDs. The most commonly prescribed drug was Paracetamol (77.04%). Among to the prescriptions, 91.7% were prescribed with generic names. As concomitant medications, antibiotics were prescribed at 21.2% cases, gastro protective agents were prescribed to 24.23% and vitamins were prescribed in 72.6% cases.
Conclusions: This study has shown that the prescribing, usage and preferences of NSAIDs practiced rationally. No over use, under use or misuse of drugs was noticed.

Keywords: Rational drug use, Non-steroidal anti-inflammatory drugs, Prescribing pattern, Fever, Generic name

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are medications that are widely used to relieve pain, reduce inflammation and bring down a high temperature.[1] They are among the most widely used drugs around the world, in the treatment of fever associated with pain and inflammation.[2] India being a tropical country, due to increased probability of acquiring infection, either viral or bacterial acute fever, an elevation in core body temperature above the normal range of 98.6°F is one of the most common presenting complaints to primary as well as to tertiary care centers. Some of the common causes contributing to fever are viral fevers, respiratory infections, malaria and dengue, which are the most prevalent febrile illness seen in the Indian population.

Since 20 to 30% of patients admitted to any general hospital may be with fever symptoms, treatment of fever cases is an important area of therapeutics. For the treatment of fever, pain and inflammation, NSAIDs play an important role. Worldwide prescription audit studies reported that NSAIDs prescriptions constitute more than 20% of all drug prescriptions.[1] Among this group, paracetamol was a very commonly prescribed drug. Paracetamol also known as acetaminophen is a good and promptly acting antipyretic and analgesic coming under this class of drugs. To manage fever and associated myalgia in dengue fever WHO and US CDC (United States centre for disease control) recommends the use of paracetamol because of its safety profile over other NSAIDs. Also, poor response to paracetamol was predicted as a proxy of more serious infections.[3] Aspirin and other NSAIDs are contraindicated because of the risk of bleeding with thrombocytopenia and renal toxicity. But at the same time paracetamol associated hepatotoxicity were reported due to over prescription.[3] Pharmacologically NSAIDs act by interfering with the production of prostaglandins by inhibiting the enzyme cyclooxygenase (COX), this results in reduction of inflammation and pain as desired effect while at the same time reducing protection to gastric mucosa, renal and platelet function as an undesired effect. Even though Prostaglandins are mediators of pain, inflammation and fever, they also play a very important role in protecting gastric mucosa, renal function and platelet activity. Cox enzyme exists in a constitutive (COX-1) and an inducible (COX-2) isoforms. Most NSAIDs inhibit COX-1 and Cox-2 non selectively, but selective COX-2 inhibitors have also been developed. With the introduction of the selective COX-2 inhibitors, it has been suggested that they may be more cost–effective because of their improved gastro intestinal (GI) tolerability and a reduction in concomitant prescription of anti-ulcer agents. This has led to an increase of almost 50% of NSAID prescriptions, with COX-2 inhibitors accounting for two thirds of this increase.[4] The prescription pattern of NSAIDs changes frequently over a period of time. Before the withdrawal of Rofecoxib in 2004, the prescriptions of COX-2 selective inhibitors had accounted for 37% of the total NSAID prescriptions dispensed[5]. After the withdrawal following the evidence of increased cardiovascular morbidity in the APPROVe (Adenomatous Polyp Prevention on Vioxx) study, COX-2 inhibitors represented less than 16% of the NSAID prescriptions. Subsequently, the number of non-selective NSAID prescriptions increased to almost 33%.[5-7] Wide spread use of NSAIDs and its adverse effects are due to the availability of different formulations. In India, more than 400 formulations of NSAIDs are available with different brand names[3]. For a developing country like India, where the drug market is not strictly regulated, drug prescriptions are not monitored, a national drug policy is needed to rationalize drug usage. To attain this purpose, understanding the drug prescriptions, and drug use pattern and its trends in time and place is important. Even though studies of NSAID prescription patterns are available from other parts of the country, very few studies are conducted in this part.[8-9] Thus, this present study attempts to describe the NSAIDs prescription pattern in fever and its utilization in a tertiary hospital.

METHODS

This observational study was conducted in Government medical college Manjeri -a public-sector thousand-bedded tertiary care teaching hospital in Malappuram district of Kerala, India by reviewing the patients' records of those who have undergone treatment from the hospital. Data was collected retrospectively from medical records of adult patients who were having symptoms of fever, with any diagnosis and were admitted to medicine wards during the study period. Patients who were admitted with fever with obvious infections and were discharged or died within 24 hours were excluded. The duration of study was 6 months, starting from July to December 2017.

Sample size and sampling technique

The sampling technique was universal sampling. The reported prevalence of NSAID use in the previous study was 20%.[1] Hence, by using the formula mentioned below:

$$N = 4PQ/E2$$

where a relative precision of 18% was considered, the sample size was calculated to be 500.

Data collection

The list of patients with fever symptoms and have undergone inpatient treatment from the hospital was collected. The case records of the patients who had undergone inpatient treatment for fever symptoms from the medical wards during the study period were retrieved from the record library. Information regarding the demographic details like age and sex of the patients, socioeconomic status and the details of diagnosis and drug therapy were recorded from the day one of admission to the discharge day from the case sheets, by using standard data collection forms by the investigators. Principle mode of analgesic antipyretic use, dose, and other concomitant drugs like antibiotics, gastro protective drugs, vitamins were noted. The WHO prescription indicators were also collected. The total duration of the hospital stay was also recorded.

Data analysis

The data was numerically coded and entered into MS EXCEL, analyzed and the frequencies of qualitative variables were expressed as absolute numbers and/or percentages.

RESULTS

As per the hospital records available during our study period of six months, 2800 patients were admitted and

underwent treatment from this hospital, out of which 620 (22.14%) had the symptoms of fever. From the fever case records, 500 cases were selected consecutively and data collection and analysis were done. Sex wise 55.2% were males and the rest were females. Their age and sex distribution are given below (Table 1).

Table 1: Demographic characteristics of patients (n=500).

Demographic factors	Categories	N	%
Age (years)	Below 30	239	47.8
	30-60	120	24
	Above 60	141	28.2
Gender	Male	276	55.2
	Female	224	44.8

Table 2: Distribution of NSAID prescriptions (n=392).

NSAID	N	%
Paracetamol	302	77.04
Diclofenac	28	7.14
Meftal	26	6.63
Dexona	20	5.10
Tramadol	16	4.08
Total	392	100

Out of this total, 392 (78.4%) received any of the NSAIDs. Among them, non-selective COX inhibitors were most commonly prescribed and the most commonly used drug was Paracetamol (77.04%) followed by diclofenac sodium (7.14%) and Meftal (6.63%) (Table 2). The percentage of NSAIDs prescribed with generic names was almost identical (91.07%), with the National list of essential medicine (India) 2022 (94.39%), which was also almost identical to the WHO standard of prescriptions. Diagnosis wise, dengue fever was the most common clinical condition (86.6%) followed by Typhoid (2.8 %) and Leptospirosis (2.4%) and the rest were uncategorized (Table 3).

Table 3: Clinical indication (n=500).

Clinical indication	N	%
Dengue (viral)	433	86.6
Leptospirosis (bacterial)	12	2.4
Typhoid (bacterial)	14	2.8
Others	41	8.0

Table 4: Distribution of antibiotic prescription.

Antibiotic	N	%
Ceftriaxone	32	30
doxycycline	26	24.5
Moxiclav	13	12.3
Azithromycin	12	11.3
Total	106	100
generic	66	62.26

We have also collected the details of concomitant medications like antibiotics, gastro protective agents and vitamins and the details were as given below.

Antibiotics

Antibiotics were prescribed in 106 (21.2%) cases, out of which the most common was Ceftriaxone 30% followed by Doxycycline 24.5% (Table 4). This in proportional to bacterial disease like typhoid and leptospirosis. Among the antibiotics 66 (62.26%) of drugs have been prescribed with generic names.

Gastro protective agents

Gastro protective agents like pantoprazole, ranitidine, omeprazole were co-prescribed to 95 (24.23%) patients.

Vitamins

Vitamins were prescribed in 363 (72.6%) of cases. In which the vitamin B complex constitutes 298 (82%), vitamin C 38 (10.5%), Folic acid 13 (3.6%) and vitamin D3 in 2 cases. Category wise 45.1% were prescribed generic and the majority were in brand names (Table 6). The mean number of hospital stays was 4.3 days ranged from 2 days to 16 days.

Table 5: Distribution of patients according to gastroprotective agent use.

Gastro protective agent	N	%
Prescribed	95	24.23
Not prescribed	297	75.76

Table 6: Vitamin use.

Vitamin	N	%
Prescribed	363	72.6
Not prescribed	137	27.4
Generic	164	45.1

DISCUSSION

The evaluation of drug prescribing patterns is considered to be one of the essential tools for improving clinical and economic outcomes.[10] The main aim of these type of studies are providing information to the prescribers and create consciousness about the proper use of drugs.[11] In the above context, a retrospective observational study was conducted in a tertiary care teaching hospital in Malappuram, Kerala with the aim of assessing the prescribing pattern of NSAIDs. Along with this, we also observed other WHO specific prescribing indicators such as the pharmacological sub-classes of NSAIDs prescribed, the clinical indications and an assessment of prescriptions with respect to use of generic or trade names. Gender wise, 55% of our patients were males, approximately corresponds to the sex ratio of this part of the state. Age wise in our study (n=500) 47.8% were below the 30-year

age group, that shows most of the patients admitted were in the economically productive young age group and exposure to infectious diseases is very common in this population. In our study, NSAIDs were found to be prescribed irrespective of age. Similar to what was observed in previous studies (62.6%), in the present study 78.4% (392) of the patients have been prescribed any other NSAID group of drugs.[12] Among them are Paracetamol/acetaminophen (77.04%) was the most widely used drug followed by Diclofenac (7.14%). Ibuprofen was least prescribed which may be due to contraindications in conditions like Dengue and leptospirosis which were prevalent in this area. At the same time the proportional increase in paracetamol prescriptions compared to other NSAIDs like Diclofenac may be due to the increased incidence of Dengue and leptospirosis where paracetamol is the safer drug. The preference of paracetamol, as frequently prescribed NSAID, can be attributed to its safety profile over other NSAIDs in people at increased risk of NSAID-related adverse effects. For example, children or older patients, patients with gastrointestinal (GI) bleeding, renal co morbidities, diabetes, or patients with a previous history of GI symptoms, bleeding disorder, or NSAID hypersensitivity as well as pregnancy.[3] Asprin is also found to be the least prescribed drug here. In patients with viral fever, intake of aspirin may be associated with Reye's syndrome.[3,13]

The most frequently prescribed drugs that are listed in the National list of essential medicines (NLEM), were prescribed in their generic names (91.07%) which are also similarly reported in other studies.[14,15] Since our hospital is a teaching hospital, the doctors are following this pattern of prescription, which may not be generalised in this part of the state. In studies conducted on prescribing patterns in 12 developing countries, reported that the generic-name prescription was low in Nigeria (58%) and Sudan (68%) and was observed high in Tanzania (82%) and Zimbabwe (94%).[16-19] These observations are good indicators for rational prescribing practices practised by the health care workers in the health care system of those regions. The majority of the fever cases were either clinically or by laboratory diagnosed as Dengue fever (86.6%), followed by typhoid (2.8%) and leptospirosis (2.4%). In the year 2017 the state experienced a huge epidemic of dengue in all districts. In dengue infection, paracetamol is given for high fever if the patient is uncomfortable and the interval of dosing is not less than six hours. Our study period was from July to September, which corresponds to the monsoon season and seasonality was associated with the highest incidence of dengue outbreak and other water or vector born infections.[20] The uncategorized cases were mostly due to viral etiology, since viral fevers were prevalent during this season.

Concomitant medication

Antimicrobial agents are used to prevent, control and treat infectious diseases. Rational use of antibiotics is the cornerstone for preventing the development of antimicrobial resistance (AMR). Inappropriate use of antibiotics, such as unnecessary use or sub optimal antibiotic choice, dose or duration is a major contributor to AMR.[21] So we also looked for antibiotic prescription pattern among fever patients. In our study only 21.2%, patients received any kind of antibiotics and the majority did not receive any antibiotics which indicates optimal use of antibiotics. Diagnosis wise, among the patients, there was a high prevalence of dengue which was a viral infection where antibiotics are contraindicated. Among antibiotics ceftriaxone was mostly prescribed among 30%, followed by 24.5% doxycycline. Among our patients, 3% were diagnosed as typhoid. Ceftriaxone, a third-generation cephalosporin, is highly effective against *S. typhi* and has become the standard of care for the treatment of typhoid fever in many parts of the world and Doxycycline for Leptospirosis.[22] This pattern corresponded with our diagnosis as typhoid and leptospirosis among our patients. So, the prescription of the above-mentioned antibiotics pattern were rational. Anywhere in the world, east or west, irrational use of drugs is a universal problem. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly also. The misuse, over use or under use of drugs not only results in wide-spread health hazards but also leads to wastage of scarce resources in countries like India. In that sense, any measure promoting rational use of drugs is an essential step which has global relevance.

Despite wide clinical use of classical NSAIDs as analgesics, anti-pyretic, and anti-inflammatory agents, their gastro-intestinal toxicity is a major clinical limitation. This adverse effect is associated with their ability to inhibit COX-1 which act as gastro protective in the gastrointestinal tract.[23] Hence, gastric side effects are a cause of concern with non-selective COX inhibitors and hence are co-prescribed with an anti-ulcer agent. In a published study conducted in north India proton pump inhibitors were the most commonly used gastro protective agents, followed by H_2 antagonists.[24] Similarly in the present study gastro protective agents prescribed were 24.23%. In other studies, conducted in other parts, more than 40% use of H2 antagonists were seen.[17-19] Thus, it is important for a physician to determine the risk category of the patient for NSAID-induced GI toxicity before prescribing a gastro protective agent along with NSAIDs. Finally, the physician should consider the risk factors in patients, cost of the drug and patients preferences before prescribing a gatroprotective drugs along with NSAIDs. In the present study vitamins use was found to be 72.6%. Out of which, 82% was B complex, followed by vitamin C 10.5%. Types of vitamin B complex (thiamine, pyridoxine, and cyanocobalamin) have been studied for many years for their pain-relieving properties at doses higher than nutritional doses when given along with NSAIDs in patients with lumbago, polyneuropathies, rheumatic diseases, and pain after tonsillectomy.[25] In this context, it was found to be rational to prescribe routinely

vitamins along with NSAIDs in conditions associated with pain, inflammation and fever. Also, vitamins are prescribed for infections to boost immunity along with antimicrobial agents. Rational drug prescribing can be defined as the right drugs being prescribed at the right dose, at the right time intervals for a sufficient duration.[26] The purpose of a drug utilization study is to provide feedback to the prescriber and to create awareness about the rational use of medicines.[27-30] In this sense, our study has enlightened our knowledge about the prescription pattern of NSAIDs.

Limitations

Limitations of current study were; it was conducted in a single center, a tertiary care teaching hospital for a duration of a six-month period. So, it will not represent the prescription pattern of the whole doctor population at the primary, secondary centers in the area. Our study also included only inpatients case reports, not out patients. So, for extrapolation, a study including all levels of health care centres with a larger sample size is needed.

CONCLUSION

This study has shown that the prescribing pattern, usage and preferences of NSAIDs and concomitant medications like antibiotics, gastro protective agents, and vitamins that are practiced rationally, and it also shows that among NSAIDs, paracetamol was the most commonly utilized drug. No overuse, under use or misuse of drugs were noticed in any one of the case records also. Periodic evaluation of drug utilization 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.

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