Assessment of nonsteroidal anti-inflammatory drug use pattern using World Health Organization indicators: A cross-sectional study in a tertiary care teaching hospital of Chhattisgarh

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Abstract:

OBJECTIVE: The objective of this study is to assess drug utilization pattern of nonsteroidal anti-inflammatory drugs (NSAIDs) in a tertiary care teaching hospital, Raipur, Chhattisgarh.

MATERIALS AND METHODS: A prospective, cross-sectional observational study was conducted in the outpatient department during 2-month period. After informed consent, the patients visiting pharmacy shop with a prescription were enrolled in the study. Their demographic details and prescription data were recorded in a case record form. The data were analyzed to determine the drug utilization pattern of NSAIDs, using the World Health Organization (WHO) prescribing indicators.

RESULTS: A total of 600 prescriptions were analyzed. Of them, NSAIDs were prescribed in 30.83% encounters. In general, nonselective COX inhibitors were most commonly prescribed. The most commonly prescribed form of NSAID was paracetamol (39.45%). The percentage of NSAIDs prescribed with generic names were almost identical (91.15%), whereas the percentage of NSAIDs prescribed from the National List of Essential Medicine (India) – 2015 (49.72%) was not identical with the WHO standard (100%) which serves as an ideal. In 13.51% encounters, a fixed-dose combination (FDC) of NSAIDs was prescribed. Co-administration of gastroprotective agent with NSAIDs was observed in 24.32% encounters.

CONCLUSION: The prescribing practices of NSAIDs indicate some deviation from the WHO standard. In addition, FDCs of NSAIDs with gastroprotective agents as well as other NSAIDs was also prescribed, which are irrational. This baseline data will be useful to plan further targeted research and to improve prescribing practices at the center. Various strategies such as face-to-face periodic training programs of prescribers, establishing drug and therapeutic committee; drug information centers; and drug bulletins can serve beneficial in improving prescribing practices.

Keywords: Drug utilization, essential medicine, fixed-dose combinations, gastroprotective agents, nonsteroidal anti-inflammatory drugs, World Health Organization indicators

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely prescribed drugs for pain, fever, and inflammation. Worldwide, over 73 million prescriptions of NSAIDs are written yearly, and approximately 30 million people take NSAIDs daily.¹,² The data of global and Indian studies showed that
the total number of NSAIDs prescription ranges from 15% to 40%.\cite{3-5}

As per the World Health Organization (WHO), rational use of medicines is defined as, “patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period, and at the lowest cost to them and their community.”\cite{6} To address the irrational use of medicines, practices such as prescribing and dispensing of drugs as well as patient should be regularly monitored in terms of types, amount, and reasons for irrational use.\cite{7}

It is important to identify and quantify the problem to promote rational use of NSAIDs. This can be done by focusing drug utilization studies concerning the use of particular medicines in question. WHO prescribing indicators are one of the most widely accepted tools which can be used to identify general prescribing practices in health-care facilities.\cite{8}

In spite of few drug utilization studies of NSAIDs in India, there is a paucity of data in that respect, pertaining to tertiary care centers of Central India, especially Chhattisgarh. To promote rationale prescribing practices, we must identify the gaps. Hence, there is a need to quantify drug utilization pattern of NSAIDs using standardized WHO prescribing indicators in each health-care settings. Therefore, this study was planned to assess the drug utilization pattern of NSAIDs in a newly established tertiary care teaching hospital in Raipur, Chhattisgarh and to compare various prescribing indicators with the WHO prescribing indicators.

**Materials and Methods**

This was a prospective cross-sectional, observational study of 2-months duration, conducted during the period in May and June 2016, in outpatient departments (OPDs) of a tertiary care teaching hospital of Raipur, Chhattisgarh, India, after obtaining Institute Ethics Committee approval. WHO document “How to investigate drug use in health facilities?” recommends to include at least 600 encounters (prescriptions) in a cross-sectional survey. Therefore, considering this as a standard, we screened 600 OPD prescriptions in our cross-sectional study during 2-month period.

The patients visiting pharmacy shop (situated within the hospital premises) with OPD prescription during peak hours (between 10.00 AM and 1.00 PM) were enrolled in the study after obtaining their written informed consent. The patients who dissented, seriously ill, and the patients who were advised indoor admission were excluded from the study. The demographic details and prescription data of enrolled patients were recorded in a case record form. The data collected during this study was kept confidential and was utilized only for the study purpose.

The data were entered in Microsoft Excel sheet (Microsoft office 2007) and analyzed using WHO prescribing indicators.\cite{8} The following prescribing indicators were adopted and modified as per the objectives of the study:

- 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)
- Percentage of encounter with fixed-dose combination (FDC) of NSAIDs prescribed
- Percentage of encounters with NSAIDs and gastroprotective agent prescribed.

In addition, the data were also analyzed for following parameters:

- Most commonly prescribed COX-2 selective NSAID
- Most commonly used gastroprotective agent along with NSAIDs
- Most commonly prescribed NSAIDs from NLEM
- Most commonly prescribed injection form of NSAID.

**Results**

A total 600 patients were interviewed, and their OPD prescriptions were screened and analyzed for core prescribing indicators [Table 1].

Of 600 prescriptions, NSAIDs were prescribed in 185 encounters (30.83%). Nonselective COX inhibitors were the most commonly prescribed, with the highest frequency for paracetamol (27.03%) followed by diclofenac, aceclofenac, ibuprofen, and ketorolac. Pantoprazole (64.44%) was the most commonly prescribed gastroprotective agent followed by ranitidine, rabeprazole, and omeprazole.

A total of 45 FDCs of an NSAID and gastroprotective agent followed by ranitidine, rabeprazole, and omeprazole. All the gastroprotective agents were prescribed in combination with NSAIDs as FDC and not separately [Table 2].
A total of 25 FDCs of two NSAIDs (13.51%) were prescribed and the most commonly prescribed FDC was of diclofenac and paracetamol [Table 3]. In five encounters, an FDC of mefenamic acid and dicyclomine was prescribed.

Of 185 prescriptions of NSAIDs, 92 (49.72%) were of NSAIDs listed in NLEM–2015. The most common prescribed NSAID as per NLEM was paracetamol while aceclofenac was the most common NSAID prescribed other than those listed in NLEM. In the remaining prescriptions, prescribed NSAIDs are not listed in NLEM [Table 4].

In few prescriptions, the dose, duration, indication, dosage form of NSAIDs, and instructions to patients were not mentioned [Table 5].

### Discussion

The prescribing practices of NSAIDs in our study indicated some deviation from the WHO standard. The average number of drugs per prescriptions in our study, 3.15 (range: 1–8 drugs/prescriptions), is not acceptable as compared to standard (1.6–1.8) derived as ideal. Yet, in a study of prescribing practices among urban and rural general practitioners (GPs), the average number of drugs per prescriptions were 5.05 (urban) and 4.03 (rural) with an average of 4.54. The figures in our study were lower than the finding of this study which could be because of different clinical setting. Our survey was undertaken in a tertiary care government hospital, whereas above-referenced study was carried out among GPs.

In our study, one-third of the prescriptions in outpatient setting comprise NSAIDs. This finding is consistent with the previous drug utilization study conducted by Kulkarni et al., where the frequency of NSAIDs prescriptions was 25.71%. The frequency of prescription of an injection form of NSAID in our study (4.32%) is consistent with another study conducted in South Delhi hospital (2.2%), which indicates less prevalence of parental use of NSAIDs in OPD settings. The uncontrolled use of NSAIDs by parenteral route in OPD setting is not justified when more convenient options, such as oral dosage form are available and it shall be reserved for severe painful conditions.

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 comorbidities, diabetes, or patients with a previous history of GI bleeding or peptic ulcer disease.
both, the most frequently prescribed NSAIDs, paracetamol and diclofenac, are listed in NLEM. However, the overall percentage of NSAIDs prescribed from NLEM is not identical (47.92%) with the WHO standard (100%) which serves as an ideal. This indicator reflects that prescribers are noncompliant with NLEM and awareness regarding this is urgently necessitated.

In our study, five prescribed NSAIDs, namely, aceclofenac, ketoprofen, indomethacin, ketorolac, and nepafenac, are not listed in NLEM. Aceclofenac, as well as diclofenac, was preferred for osteoarthritis, which is a degenerative condition with minimal inflammation. The efficacy of aceclofenac and diclofenac is comparable. The only advantage offered by aceclofenac is in terms of good GI tolerability. Although diclofenac is cost-effective as compared to aceclofenac, the better GI tolerability with aceclofenac could be the reason for its preference. However, it was observed in our study that aceclofenac was prescribed as a FDC with a gastroprotective agent (pantoprazole and ranitidine). This FDC is not justified, and the reasons for the same are mentioned in the following discussion. Moreover, Osteoarthritis Research Society International (OARSI) recommended paracetamol for long duration in osteoarthritis patients with mild-to-moderate pain. Traditional NSAIDs can be considered in symptomatic patients in low dose for shorter period.

In this study, 91.15% prescriptions containing NSAIDs were prescribed with generic names which is almost identical with the WHO standard (100%). This observation is a good indicator for rational prescribing practices. In a similar study conducted among urban and rural practitioners, nearly 71% of urban GPs prescribed the drugs by generic name, but only 52% of the rural GPs did so. The percentage of prescribing by generic names in a study of 12 developing countries was observed to be low in Nigeria (58%) and Sudan (68%) whereas it was observed encouraging in Tanzania (82%) and Zimbabwe (94%).

FDCs evaluated in our study were of two types: combination of two NSAIDs and combination of an NSAID and a gastroprotective agent. A total of 45 encounters of such FDCs were observed which account for one-third of the total NSAID encounters. Proton-pump inhibitors (PPIs) were the most commonly used gastroprotective agents with NSAIDs in such FDCs.

It is a known fact that PPIs are always administered 30 min before the breakfast as its therapeutic effectiveness decrease if taken after meal. In contrast, NSAIDs are known to cause GI side effects; hence, they are usually taken after meal. The administration a PPI with NSAID as an FDC does not make any rationale because of many reasons. First, at any point of time, one of the components (either PPI or NSAID) will be useless (either less therapeutic effectiveness or more prone to GI side effects). Second, pantoprazole is taken only once daily, whereas diclofenac is usually taken twice or thrice daily. Hence, such combination offers pharmacokinetic incompatibility. Third, co-administration of a gastroprotective agent with NSAIDs is justified only in certain circumstances. The overall rate of bleeding with NSAID use, in general population, is low (1:6000 users or less). The conditions which warrant co-administration of a gastroprotective agent with NSAIDs include elderly population, duration of NSAIDs therapy more than consecutive 3 months, previous history of peptic ulcer with or without haemorrhage or perforation, history of alcoholism, concomitant use of anticoagulant or corticosteroids, and concomitant Helicobacter pylori infection. Thus, it is important for a physician to determine the risk category of the patient for NSAID-induced GI toxicity before prescribing a gastroprotective agent along with NSAIDs. In such situations, gastroprotective agent should be prescribed separately as a single agent and not as a FDC. Instead, selective COX-2 inhibitors can be considered in high risk. Nevertheless, various studies suggested that selective COX-2 inhibitors are also prone to increased cardiovascular risk. Targownik and Thomson have discussed a decision algorithm for gastroprotective strategies for NSAID users. Hence, the ultimate choice
of agent for gastroprotection depends on risk factors, preference of patients and physician, and cost of therapy.

Another observation from the study, combination of paracetamol and a gastroprotective agent is also irrational. It is needless to mention that paracetamol is safe in terms of GI side effect. Indeed, paracetamol is preferred NSAID in a patient with acid peptic disease.

There were 25 encounters (13.51%) of FDCs of two NSAIDs. Paracetamol was usually one of the components such FDCs. Wide marketing of such combinations is often practiced by the medical representatives with a justification that other NSAIDs have anti-inflammatory action, while paracetamol has antipyretic action. On many occasions, the prescribers fall easy prey of such marketing strategies and often prescribe such irrational combinations. It is essential for prescribers to apply their scientific knowledge and analyze the claim produced by medical representatives. It is important to note that both, paracetamol and other NSAIDs, act by the same mechanism, i.e., inhibition of COX and thus, combination is not synergistic. Such irrational combinations do not improve efficacy of treatment and can only increase the cost of therapy and adverse effects. Hence, to rationalize the use of NSAIDs, paracetamol shall be used only when antipyretic and analgesic action is required while other NSAIDs shall be used when antipyretic, analgesic, and anti-inflammatory actions are required.

Another concern with the use of NSAIDs is analgesic nephropathy, and this risk is more after prolonged and regular use in high doses and when used in combination with other NSAID. In our study, NSAID combinations prescribed over a wide range of age from 16 to 68 years. This warrant precaution while using NSAIDs, especially in extremes of age, patient with poor renal functions, type 2 diabetes patients, hypovolemia, heart failure, ascites, concurrent administration of nephrotoxic drugs, and concurrent administration of angiotensin-converting-enzyme inhibitors/angiotensin–receptor blockers. Therefore, combinations of two NSAIDs should be avoided. Similarly, increase incidence of adverse effect, could be related to dose and duration of NSAIDs therapy. In our study, few encounters did not have any mention of dose, duration, or dosage form of NSAIDs. In addition, few encounters did not mention instructions to patients regarding its use after the meal. The patients often take these medications for prolonged period, without food, may lead to increased incidence of GI adverse effects.

There are other combinations available in the market containing NSAID with antihistamine, antacid, antispasmodic (like dicyclomine), sedative-hypnotic (like diazepam), and serratopeptidase. These combinations do not offer any therapeutic benefit, prone for pharmacokinetic incompatibility, and adverse effects. In our study, we also observed five encounters in which FDC of mefenamic acid and dicyclomine was prescribed. Mefenamic acid, as an antipyretic promotes sweating while dicyclomine, an anticholinergic-antispasmodic drug, inhibits sweating. Thus, this combination is not only irrational but also dangerous and may lead to dangerous elevation of the body temperature.

Overall, the results of this study showed a varied prescription pattern of NSAIDs in a tertiary care teaching hospital of Chhattisgarh. The prescribers were compliant with few parameters, whereas noncompliance was also observed with reference to rational use of medicine. NSAIDs, which constitute 30% of total prescriptions, almost equate with a prescribed percentage of antibiotics. Injudicious use of NSAIDs can add to the cost of therapy and unnecessary exposure to adverse effects. The results of this study identified a few areas where corrective measures can be taken to improve prescribing practices. We are determined for the periodic sensitization of prescribers apropos to concept of essential medicine, rational use of NSAIDs, standards for writing prescriptions, to reinforce healthy practices and create awareness. Furthermore, this study highlighted the prescription pattern of NSAIDs in one of the teaching hospitals of Raipur district in Chhattisgarh. This data does not represent the prescription pattern of NSAIDs in entire Chhattisgarh. To map the data for entire state, we need similar studies from different areas and different health-care settings such as other teaching hospitals, private hospitals, district hospitals, and primary health-care centers.

**Conclusion**

The prescribing practices of NSAIDs indicate some deviation from the WHO standard. This baseline data will be useful to plan further targeted research and to improve prescribing practices at the center. Various strategies such as face-to-face periodic training programs of prescribers, establishing drug and therapeutic committee; drug information centers; and drug bulletins can serve beneficial in improving prescribing practices.

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**Conflicts of interest**

There are no conflicts of interest.

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