TRENDS IN NON STEROIDAL ANTI-INFLAMMATORY DRUG UTILIZATION IN THE ORTHOPAEDIC OUTPATIENT UNIT OF A TERTIARY CARE HOSPITAL IN INDIA

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Summary

A cross-sectional study was conducted to study the pattern and quality of prescribing NSAIDs in a unit of the Orthopaedic out patient department in a tertiary care hospital in India. Prescriptions were collected from a unit of the Orthopaedics out patient department for a period of six months. NSAID utilization was analysed using the Drug Utilization 90% (DU 90%) method. 1008 prescriptions were analysed. NSAIDs were prescribed in 804 prescriptions. 989 NSAID preparations were prescribed. The average number of drugs per prescription was 2.13 and the average cost of each prescription was Rs.129.13 (approximately US$ 2.7). Fourteen NSAIDs among 29 different NSAIDs used, were found in the DU 90% segment. Eight preparations were single drug preparations and six were fixed drug combinations. Diclofenac topped the list with 21.2% prescriptions containing it, followed by Diclofenac + Serratiopeptidase with 11.1%. Among the selective COX-2 inhibitors only Etoricoxib (4.15%) figured in the list. Diclofenac was the most common NSAID prescribed. Despite reports of the relative gastrointestinal safety of Ibuprofen, it is being under-prescribed. Selective COX-2 inhibitors are being used only occasionally. Though topical Diclofenac was used commonly, it was not used alone; it was always combined with an oral NSAID.

Key words: NSAIDs, COX-2 inhibitors, Prescriptions, Drug Utilization-90%, Orthopaedics.

Introduction

Drug utilization studies are pre-requisites for the formulation of drug policies. They also offer useful methods for teaching and training in drug therapy. It is well known that indiscriminate use of drugs results in unwanted adverse effects and drug interactions and poses difficulties in diagnosis. Manufacturers create artificial demands of unwanted drugs and drug combinations through competitive sale promotions. Drug utilization studies identify the problems that arise from drug usage in healthcare delivery system and highlight the current approaches to the rational use of drugs (1). A drug utilization review is defined as an authorized, structured and continuing program that reviews, analyses and interprets the pattern of drug use against pre-determined standards (2). The prescribing behavior of clinicians is usually shaped by academic literature, professional colleagues, government regulations and commercial publicities (3). Hence, drug utilization reviews like these would help in this direction.

Non steroidal anti-inflammatory drugs (NSAIDs) make up one of the largest groups of pharmaceutical agents used world wide. NSAIDs, used by more than 20% of the population (4), are also one of the most common causes of adverse drug reactions (ADRs) reported to drug regulatory agencies as well as in many clinical and epidemiological studies. The most common ADRs are those pertaining to the gastrointestinal system, notably dyspepsia and bleeding. Though selective COX-2 inhibitors have better gastrointestinal safety, clinical (5) and experimental data (6) as well as reviews suggest that their use is associated with increase in systolic blood pressure and cardiovascular morbidity and mortality due to myocardial infarction. The risk of gastrointestinal complications varies widely among individual NSAIDs and so does the cost. Study of NSAID preference pattern among practitioners is interesting because some trials have revealed that there is no substantial difference in the responses to equivalent doses of NSAIDs, so the choice of first line treatment should be based on their relative toxicity and cost (7). There exist significant differences in the usage pattern and preferences of NSAIDs among different practice categories in India (8).

Hence we decided to study the pattern and quality of prescribing NSAIDs in the Orthopedic out patient department of a tertiary care hospital in India.

Methods

A cross-sectional study was conducted at a tertiary care hospital in India. Prescriptions were collected from the Orthopaedics out patient department for a period of six months. The Institutional Ethics Committee's approval was obtained before starting the study. Relevant information was entered into a preformed proforma. Patient details such as age, sex, diagnosis and the drugs prescribed were recorded. Prescriptions were analyzed using the Drug Utilization (DU) 90% method. The DU 90% is an inexpensive, flexible and simple method for assessing the quality of drug prescribing in routine health care. The number of products in the DU 90% segment and adherence to prescription guidelines may serve as general quality indicators. The method may be adopted to provide comparative data between primary health centers, hospitals or regions and may be cross sectional or longitudinal (9).

- Quality indicators of drug use included:
  - Average number of drugs per prescription (encounter).
  - Percentage of drugs prescribed by generic name.
  - Average drug cost per encounter.
- NSAID utilization was analyzed by accounting for the drugs used in the 90% segment [Drug utilization (DU) 90%].
- Drug utilization pattern of NSAIDs in three common orthopaedic conditions: chronic low backache, soft tissue injury and fracture were analyzed.

Results

A total of 1008 prescriptions were analysed, out of which 515 were for male and 493 were for female patients. Two thousand one hundred and forty five drugs were prescribed in these 1008 prescriptions. Eight hundred and four patients received NSAIDs either as oral formulations, topical applications, injections or a combination of these. Most of the prescriptions were for five to ten days. Of the 2,145 drugs prescribed, 989 were NSAID preparations, of which 778 were oral, 190 topical and 21 parenteral preparations. The oral preparations were prescribed as single drug preparation or fixed dose combinations (FDC). The other commonly used drugs were Calcium preparations, Vitamin supplements, anti-ulcer drugs, Tramadol (either alone or combined with an NSAID) and antibiotics for open wounds and fractures. Among the anti-ulcer drugs, Proton pump inhibitors were most commonly used. None of the drugs were prescribed by generic names. The patients' demographic characteristics, NSAID formulations prescribed, quality indicators of drug use and concomitant medications are shown in **Table 1.**

Fourteen NSAIDs among 29 different NSAIDs used, were found in the DU 90% segment. Eight preparations were single drug preparations and six were FDCs. Diclofenac topped the list with 21.2% prescriptions followed by Diclofenac + Serratiopeptidase with 11.1%. Among the selective COX-2 inhibitors only Etoricoxib (4.15%) figured in the list. Diclofenac sodium gel was the most commonly prescribed topical preparation. The number of NSAIDs that accounted for 90 % use is shown in the **Table 2.**

In the geriatric age group Diclofenac was the most common drug used, followed by Naproxen. Among the FDCs the most commonly used combination was Paracetamol + Tramadol. Ibuprofen was mainly prescribed in the paediatric age group. There were 171 prescriptions for chronic low backache, 164 for soft tissue injuries, and 79 for fractures. The most commonly prescribed NSAID for chronic low backache and soft tissue injuries was Diclofenac. For fracture, Diclofenac and a combination of Tramadol + Paracetamol were the most preferred preparations.

Table 1: Patient's Demographic Characteristics and Quality Indicators of Drug Use

Total number of prescriptions screened	1008
Males	515 (51.09%)
Females	493 (48.91%)
Age (Years)	**n (%)**
1 - 16	47 (04.67%)
17 – 30	213 (21.14%)
31 - 49	405 (40.17%)
50 - 59	178 (17.65%)
> 60	165 (16.37%)
Total number of drugs prescribed	2145
Total number of prescriptions with NSAIDs	804 (79.76%)
Number of NSAID preparations	989 (46.10%)
▪ Oral NSAID formulations	778 (78.67%)
Single drug preparation	458 (58.87%)
Fixed Drug Combination	320 (41.13%)
▪ Topical NSAID gels	190 (19.21%)
▪ Parenteral NSAID formulations	21 (02.12%)
Quality indicators of drug use :	
• Average number of drugs per prescription	2.13
• Percentage of drugs prescribed by generic name	Nil
• Average drug cost per encounter	Rs.129.13
Concomitant medications :	
• Anti-Ulcer Drugs	301 (14.03%)
• Calcium salts	152 (07.09%)
• Vitamin supplements	249 (11.61%)
• Others	454 (21.17%)

Table 2: NSAIDs accounting for 90 %(DU-90%) prescriptions

Drug	**Prescriptions n (%)**
1. Diclofenac	165 (21.20)
2. Diclofenac + Serratiopeptidase	86 (11.10)
3. Paracetamol + Tramadol	84 (10.80)
4. Naproxen	65 (08.35)
5. Aceclofenac	56 (07.20)
6. Nimesulide	47 (06.04)
7.Etoricoxib	32 (04.15)
8. Diclofenac + Paracetamol+ Chlorzoxazone	32 (04.15)
9.Piroxicam	29 (03.73)
10.Aceclofenac + Paracetamol	28 (03.60)
11.Diclofenac + Paracetamol	25 (03.21)
12.Nimesulide + Chlorzoxazone	21 (02.70)
13.Paracetamol	20 (02.57)
14.Indomethacin	20 (02.57)
DU 90 % of drugs (1 – 14)	**91.37 %**
15.Ibuprofen	19 (02.44)
16.Ibuprofen+Paracetamol	11 (01.41)

Discussion

NSAIDs have proven analgesic, anti-inflammatory and antithrombotic properties but also have significant gastric toxicity. The gastrointestinal toxicity appears to be related to cyclooxygenase-1 (COX-1) inhibition. Identification of the COX-2 protein rekindled the efforts of the pharmaceutical industry to produce safer analgesic and anti-inflammatory drugs via selective inhibition of COX-2 and this class of agents was introduced in 1999. Only a few clinical trials have compared the relative efficacy of the NSAIDs. These trials have not found any substantial differences in the responses to equivalent doses of NSAIDs (7). An individual patient may respond better to one NSAID than another even with equivalent doses because of individual patient differences and/or disease state fluctuations. The analgesic activity of NSAIDs is apparent in a few hours, while the onset of anti-inflammatory effect usually takes 7 days with peak effects occurring in 2-3 weeks. A minimum of one week trial of an NSAID should be given before it is considered ineffective and then the dose may be increased or another NSAID tried.

A study conducted in a north Indian tertiary care hospital in 2003 has shown five NSAIDs in the DU-90% segment, namely Rofecoxib, Valdecoxib, Diclofenac, Nimesulide and a fixed drug combination of Ibuprofen and Paracetamol (10). The present study has found a paradigm shift in the pattern of NSAID utilization. COX-2 inhibitors which were the two most frequently prescribed NSAIDs five years back seem to have been consciously avoided. Etoricoxib makes up less than 5% of the oral NSAID preparations in the present study. Non-selective COX inhibitors have predominantly been preferred over selective COX-2 inhibitors. In patients with a risk of gastrointestinal toxicity, anti-ulcer agents have been combined with conventional NSAIDs. Studies associating the use of selective COX-2 inhibitors with increased cardiac events might have brought down the usage of selective COX-2 inhibitors (5,6). The anti-ulcer agents most preferred were Proton pump inhibitors and among them, Pantoprazole.

Though Ibuprofen has been rated as the safest conventional NSAID (7), in this drug utilization review, Ibuprofen does not figure in the DU 90% segment. Its use has been mainly confined to the paediatric age group. In another study conducted in Mumbai and its suburbs to evaluate the usage pattern of NSAIDs in diverse clinical practice settings among general practioners to specialists, the first choice NSAIDs were Ibuprofen, Aspirin, Diclofenac, Paracetamol, Piroxicam and Ibuprofen+Paracetamol (8). In the present study though, Diclofenac is the most frequently used analgesic, probably due to our study being restricted to a tertiary care set up. However it is difficult to explain why Ibuprofen was under-prescribed.

The use of topical Dicofenac is also quite common; however topical NSAID therapy was not given alone, it was, in every case accompanied by an oral NSAID, which implies that the efficacy of topical NSAID therapy as perceived by the clinician appears to be suspect, except as a counterirritant (due to the presence of other irritant ingredients in the formulation) and placebo. In contrast, published randomized controlled trials have shown that topical NSAIDs are more efficacious than placebo (11). However more studies are required to prove that topical NSAIDs are as effective as oral NSAIDs in acute and chronic pain.

The three commonest NSAIDs (single drug preparation or FDC) used for chronic low backache were Diclofenac, Paracetamol and Aceclofenac; for soft tissue injuries

were Diclofenac, Paracetamol and Nimesulide; and for fractures were Diclofenac, Paracetamol (most were in combination with Tramadol), and Aceclofenac. Diclofenac was the most preferred NSAID irrespective of the diagnosis.

The average cost per prescription was Rs.129.13 (approximately US$ 2.7), which is a little too high for a developing country like India. Using H_2 blockers instead of Proton pump inhibitors may have helped in reducing the costs to a certain extent.

Conclusion

Diclofenac was the most common NSAID prescribed. Despite reports of the relative gastrointestinal safety of Ibuprofen, it is being under-prescribed. Selective COX-2 inhibitors are being used only occasionally. Though topical Diclofenac was used commonly, it was not used alone; it was always combined with an oral NSAID.

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