ABSTRACT

The present study was aimed to appropriateness of NSAIDs use with secondary objectives of assessment of co-prescription with gastro-protective agents, the nature and severity of adverse drug reactions and drug-drug interactions with an intention to prevent the inappropriate use of NSAIDs. A prospective study was carried out in 400 In-patients of various departments of the hospital during the 6 months period. Results: Out of 400 patients, 237 were male and 163 were females, in which most of the patients (63.5%) were belonging to age group of 21-50 years. The major complaint of the patient was arthritic pain (25.5%). Most of the patients (77%) were prescribed single NSAID as monotherapy in different dosage forms, although some patients were prescribed with combination of Aceclofenac + Paracetamol (13.75%). The preferential COX-2 inhibitors were widely prescribed (84.5%) as compared to non-selective COX inhibitor (15.5%). Among various NSAIDs prescribed, Diclofenac (45.90%) and Aceclofenac (15.96%) were mostly prescribed. NSAIDs were mostly prescribed by parenteral route (36.31%). Most of the patients were co-prescribed NSAIDs with gastro-protective agents (80.5%). In the study, moderate drug interactions were found between NSAIDs and antibiotics and no adverse drug reactions were reported during the study. The study concluded that, prescription of NSAIDs was found to be rational. Education program, counselling program, alertness of community pharmacy regarding OTC drugs can be helpful to minimize harmful effect of the drug to patients.

Key words: Appropriateness, Cox inhibitors, Drug-drug interactions, NSAIDs, Prescribing Pattern.

INTRODUCTION

Currently, irrational/inappropriate prescribing has become worldwide problem of the health care delivery system.\(^1\) It may be due to improper diagnosis, lucrative advertisements of pharmaceutical company or production of large extent of brand drugs by different names. In recent years, studies on prescribing pattern, drug utilization evaluation, drug related problems are found to be useful tool to facilitate rationality of prescribing as it provides suggestion/feedback on drug use and/or constitute guidelines on prescribing.\(^2,3,4\)

Non-steroidal anti-inflammatory drugs (NSAIDs) are used widely since its discovery as analgesics, anti-inflammatory and anti-pyretic and became necessary choice for most of patients visiting hospital as pain is the common symptom for most of illness. Over the past two decades, they became first line class of drug and played central role in management of pain. NSAIDs are highest selling OTC drugs throughout the country.\(^5\)

It was found that parenteral routes (IV/IM) are preferred routes of administration for the patients in emergency, ICU and other In-patient wards like orthopaedics, surgery. Similarly, oral routes are preferred during later days of recovery. NSAIDs in spraying form are popular in athletic injury.\(^6\) Several studies concluded that, in India, more than 400 formulations of NSAIDs are marketed in either single or combination form, resulting in wide spread exposure of patients to this class of drugs and its adverse effects.\(^7,8,9\) Recently, many fixed dose combinations of NSAIDs are banned by Health Ministry of India due to concurrent drug-drug interactions and adverse effects.

Alterations in renal function, hepatic injury,
effect on blood pressure and platelet inhibition which may result in bleeding and gastrointestinal (GI) problems are the most common side effects associated with NSAID use. NSAID use has been shown to increase the risk of peptic ulcer disease by 3-5 folds. Approximately, 15% of NSAID users will have dyspepsia and 1-4% will have significant GI complications each year (e.g., perforated ulcers or GI bleeding requiring hospitalization). Cardiovascular adverse events are significant with Cox-2 inhibitors which need attention to prescriber before prescribing.

For all these reasons, studies that evaluate the pattern, extent and frequency of NSAID prescriptions are valuable. Hence, this study is proposed to promote safe use of NSAIDs. Reducing the risks for NSAID-induced adverse effects, especially GIT, CVS related side effects and preventive co-therapies, will lead to safer & more effective treatment.

MATERIALS AND METHODS

Type of study: Prospective observational study

Sample size: 400 patients

Study Duration: 6 months

Data Collection: Data were collected from General Medicine, Pediatric, OBG, Orthopedic and Surgery ward using structured data entry form.

Study Site: Navodaya Medical College Hospital and Research Center, Raichur, Karnataka, India.

Inclusion criteria: Patients prescribed with NSAIDs from the wards such as General medicine, Pediatric, OBG, Orthopedic and Surgery.

Exclusion criteria: Patients who were prescribed with NSAIDs in Casualty, ICU and wards other than mentioned in inclusion criteria.

Data Evaluation:

The data was collected using structured data entry form and was evaluated for parameters such as patient’s demographics, types of NSAIDs prescribed, route of administration, and average number of NSAIDs per prescription, monotherapy and combination therapy, concurrent drugs prescribed and ADRs associated with prescribed NSAIDs. The data was evaluated using standard guidelines and Micromedex 2.0® software system for information regarding the number of drug-drug interactions in a prescription, their severity and management. Data were expressed as percentage and as it was a descriptive study, statistical analysis was not done.

RESULT AND DISCUSSION

Although most of studies have shown that more female patients use NSAIDs than male. However present study showed that more males 237 (59.25%) are using NSAIDs than females 163 (40.75%) out of 400 patients. Majority of patients using NSAIDs were between the ranges of 41-50 years (22.5%), 31-40 years (22%) and 21-30 years (19%). It shows that NSAIDs are used mainly in middle age group. Similar results have been reported in study done by Niyaz Alam et al. (2013).

Fig. 1: Age Distribution of Study Population

Out of 400 patients, majority were from general medicine (35%), orthopedic (32.5%) and surgery department (25.75%). However, only 2 patients were from pediatric department. Arthritic pain was the major clinical complaint of the patients (25.5%), besides abdominal pain (20.75%), low back ache (17.5%), swelling (17%), traumatic injury (7%) and 9 months gestation delivery pain (6.25%).

Among 400 patients, 153 patients were prescribed with more than 7 drugs followed by 78 patients with 4 drugs and 77 patients with 5 drugs per prescription. These results indicates high incidence of polypharmacy and this discrepancy in prevalence may be due to the patient’s expectation and demand of quick relief, incorrect diagnosis and the influence of the lucrative promotional programs of the pharmaceutical companies. As the amount of illness increases, the amount of prescription medication use often increases as well. As this happens, it becomes ever more challenging to achieve an ideal balance.
between the risks and benefits of medications. This can lead to an increased risk of adverse drug events. It has been reported that the probability of an adverse drug event is 13% in patients taking 2 drugs, and increases to 82% in those taking more than seven concluded by study of Goldberg et al., (1996). In patients taking 10 medications or more, this probability nears 100% concluded by study of Nolan and O’Malley (1988). (Fig. 2)

**Fig. 2: Number of Drugs per Prescription**

In current study, most of the patients (77%) were prescribed with single NSAIDs as monotherapy, although some patients (23%) were prescribed with combination of Aceclofenac + Paracetamol (13.75%) and Diclofenac + Paracetamol (6.65%). (Table 1)

<table>
<thead>
<tr>
<th>S. N.</th>
<th>NSAIDs</th>
<th>No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac</td>
<td>207</td>
<td>45.90</td>
</tr>
<tr>
<td>2</td>
<td>Aceclofenac</td>
<td>72</td>
<td>15.96</td>
</tr>
<tr>
<td>3</td>
<td>Ibuprofen</td>
<td>42</td>
<td>9.44</td>
</tr>
<tr>
<td>4</td>
<td>Mefenamic acid</td>
<td>16</td>
<td>3.60</td>
</tr>
<tr>
<td>5</td>
<td>Aspirin</td>
<td>10</td>
<td>2.25</td>
</tr>
<tr>
<td>6</td>
<td>Paracetamol</td>
<td>6</td>
<td>1.33</td>
</tr>
<tr>
<td>7</td>
<td>Naproxen</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>8</td>
<td>Lornoxicam</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>9</td>
<td>Indomethacin</td>
<td>1</td>
<td>0.22</td>
</tr>
<tr>
<td>10</td>
<td>Nimesulide</td>
<td>1</td>
<td>0.22</td>
</tr>
<tr>
<td>11</td>
<td>Aceclofenac + Paracetamol</td>
<td>62</td>
<td>13.75</td>
</tr>
<tr>
<td>12</td>
<td>Diclofenac + Paracetamol</td>
<td>30</td>
<td>6.65</td>
</tr>
</tbody>
</table>

Table 1: Distribution of Prescribed NSAIDs

It is observed from the study that, most of the patients (83.37%) were prescribed with preferential COX 2 inhibitors and the remaining patients (16.63%) were prescribed with non-selective COX inhibitors. However the selective COX 2 inhibitors were not prescribed. Although traditional NSAIDs including preferential COX 2 inhibitors and non-selective COX inhibitors are associated with high rate of GI complications, but possess low risk of cardiovascular complications than that of selective COX 2 inhibitors. Moreover several studies have concluded that, Coxibs have to be used with caution to avoid the risk of CVS disorders. Besides, the cost of Coxibs is also higher than traditional NSAIDs. Hence the non-prescription of selective COX 2 inhibitors observed from the study is rational. The duration of NSAIDs use were found 124(31%) for more than 7 days.

It is observed from the study that, Diclofenac (45.90%) and Aceclofenac (15.96%) were mostly prescribed and least prescribed NSAIDs were Indomethacin and Nimesulide. The other study, Niyaz Alam et al. (2013), has reported that aryl acetic acid derivatives like Diclofenac and Aceclofenac were most commonly prescribed, followed by combination of aceclofenac or diclofenac with paracetamol. (Table 1) Most of the patients were co-prescribed NSAIDs with gastroprotective agents (80.5%) followed by antibiotics (65.25%) and vitamins supplements (32.5%). (Table 2)

Table 2: Concurrent Drugs Prescribed

<table>
<thead>
<tr>
<th>S. N.</th>
<th>Concurrent Drugs</th>
<th>No. of Patients</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gastroprotective agents</td>
<td>322</td>
<td>80.5</td>
</tr>
<tr>
<td>2</td>
<td>Antibiotics</td>
<td>257</td>
<td>64.25</td>
</tr>
<tr>
<td>3</td>
<td>Vitamins</td>
<td>130</td>
<td>32.5</td>
</tr>
<tr>
<td>4</td>
<td>Calcium</td>
<td>62</td>
<td>15.5</td>
</tr>
<tr>
<td>5</td>
<td>Antihypertensives</td>
<td>50</td>
<td>12.5</td>
</tr>
<tr>
<td>6</td>
<td>Bronchodilators</td>
<td>39</td>
<td>9.75</td>
</tr>
<tr>
<td>7</td>
<td>Antiemetics</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>Anxiolytics</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>9</td>
<td>Antidiabetics</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>Others</td>
<td>196</td>
<td>49</td>
</tr>
</tbody>
</table>

In this study, most of the NSAIDs were prescribed via parenteral route (36.31%), oral route (35.12%) and combination of parenteral and oral route (15.48%). However the topical NSAIDs (11.31%) and topical + parenteral NSAIDs (1.78%) were least prescribed. Topical route causes a high local concentration in
cutaneous and subcutaneous area of the body with low systemic delivery, thereby significantly improving therapeutic efficacy and minimizing systemic side effects. (Fig.3)

**Fig. 3: Route of Administration of NSAIDs**

To manage NSAIDs associated GI adverse effects, a PPI, H2 antagonist or local acting antacids must be co-prescribed with NSAIDs. In the present study more than 80% of patients were co-prescribed with gastroprotective agents along with NSAIDs, out of which 45.75% were prescribed with proton pump inhibitors and 34.75% with H2 receptor antagonist. The other concurrently prescribed drugs include antibiotics (64.25%) and multivitamins (32.5%). (Fig. 4)

**Fig. 4: Class of Gastro-protective Agents Prescribed**

In the study, moderate drug interactions were found between NSAIDs and antibiotics and no adverse drug reactions were reported during the study.

Elderly patients its successful therapy for the pain relieving symptoms of arthritis and moderate pain related to musculoskeletal disorders, it relieves just symptoms not disease should be kept in mind. Unfortunately prevalence of irrational prescribing increasing day by day people came in health department actually are not aware about their medication and its reason of prescribing. The important findings about practice of using more than one NSAID reveal some basic facts:

- Irrational prescribing habits of physicians.
- Not supported/visible role of the pharmacist.
- Patient adherence with medication from a long period and with physician.
- People have no awareness concerning their medications that they used more than one NSAIDs came from the same therapeutic class.
- One reason may also possible that they don’t get pain relief due to inadequate pain management of NSAIDs by their physicians.

**CONCLUSION**

In this study, NSAIDs were more prevalently used in middle age group of male patients. The diclofenac and aceclofenac were most frequently prescribed for the management of pain, inflammation and traumatic injury. The monotherapy with single NSAID was preferred mode of therapy via parenteral and oral therapy.

NSAIDs are vital for clinical management of wide range of pain and inflammatory condition, but it is mostly accompanied by gastrointestinal complications. In the present study, the gastro protective agents were widely prescribed for prevention and healing of NSAIDs associated ulcers or other GI complications.

The study concluded that the prescription of NSAIDs was found to be rational. However to ensure safe, effective and well balanced therapeutic management of this NSAIDs, both patients and prescribers should be more sensitized regarding the appropriate dose, dosage regimen and overall indications. Education program, counseling program, utilization survey, alertness of community pharmacy regarding OTC drugs can be helpful to minimize harmful effect of the drug to patients.
ACKNOWLEDGEMENT

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