

## Prescription pattern of non-steroidal anti-inflammatory drugs in patients with acute musculoskeletal pain

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### ABSTRACT

**Background:** Without the knowledge on how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use and to suggest measures to change prescribing habits for the better information on the past performance of prescribers is linchpin of any auditing system. The objective of the study was to assess the NSAIDs prescription pattern in patients with MS pain.

**Methods:** Prospective study of prescriptions of 306 patients with MS pain presenting in orthopedic outpatient department (OPD) of Owaisi Health and Research Centre during the period of January 2014 to August 2015. Patient particulars, history and clinical findings were obtained using the study proforma. Data collected was analyzed by frequency, and percentage.

**Results:** Overall frequency of NSAIDs prescription in this study was 96%. Diclofenac (70.7%) was the commonest NSAID prescribed. Selective COX-2 inhibitors were not prescribed. Combination of paracetamol and tramadol (77%) was the commonest FDC prescribed among the 92 FDC prescriptions. High frequency of GPAs co-prescription (94%) was noted. Of 7 different NSAIDs prescribed, 2 drug (diclofenac, and paracetamol) falls within DU90% segment-mainly constituted by non-selective NSAIDs.

**Conclusions:** Overall, the prescription pattern was in accordance with standard guidelines, as suggested by the fact that the DU90%, segment was constituted by only few drugs.

**Keywords:** NSAID, Prescription pattern, Patients

### INTRODUCTION

The International Association for the Study of Pain (IASP) defines pain as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.<sup>1</sup> Pain is universally understood as signal of disease, it is the most common symptom that brings a patient to a physician's attention. The function of the pain sensory system is to protect the body and maintain homeostasis. Since different diseases produces characteristic patterns of tissue damage, the quality, time, course and location of a patient's pain complaint, location of tenderness, provide diagnostic clues and are used to evaluate the response to treatment.<sup>2</sup> Pain is generally classified according to its location, duration, type, frequency, underlying cause and intensity. The anatomical pain classification system identifies sites of

pain. In contrast, the body system of pain classification method focuses on the classical body systems (e.g. Musculoskeletal (MS), neurologic, vascular).<sup>3</sup> MS pain is the deep, somatic pain that originates in skeletal muscles, facial sheaths, tendons (myogenous pain), bone and periosteum (osseous pain), joint capsules, ligaments (arthralgia pain) and in soft connective tissues.

Musculoskeletal pain (MS) conditions are extremely common and have important consequences or the individual and the society. Population surveys show that low back ache is the most common site of regional pain in younger and middle aged adults, knee pain in aged people. The prevalence of physical disability is higher in women than men. It rises with age; 60% of women aged over 75 years living in the community report some physical limitations. Among older people Rheumatoid arthritis, OA

and Osteoporosis are associated with loss of independence and a need for more support in the community or admission to residential care.<sup>4</sup> Prevalence of MS pain was found to be 25.9% in a recent study conducted in India. High prevalence of MS pain is observed in UK, Sweden, Netherlands, The Philippines, and Indonesia.<sup>5</sup>

Non-steroidal anti-inflammatory drugs (NSAIDs) play an important role in management of MS pain. Most currently available traditional NSAIDs (tNSAIDs) act by inhibiting cyclo-oxygenase (COXs) enzyme. The inhibition of cyclo-oxygenase-2 (COX-2) is thought to mediate, the antipyretic, analgesic, and anti-inflammatory actions of tNSAIDs, while the simultaneous inhibition of cyclo-oxygenase-1(COX-1) largely but not exclusively accounts for unwanted adverse effects in the gastrointestinal tract. NSAIDs are one of the most commonly prescribed medications. More than 70 million prescriptions for NSAIDs are filled in the United States (US) each year. Some investigation has estimated that 5% to 10% of the adults in the U. S. (approximately 15 to 25 million people) use NSAIDs regularly. More than 30 billion over the counter (OTC) NSAIDs tablets are sold annually in the U.S.<sup>6</sup>

Without the knowledge on how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use and to suggest measures to change prescribing habits for the better information on the past performance of prescribers is linchpin of any auditing system.

Thus drug utilization study of NSAIDs for the management of MS pain will help us assess the pattern, quality, determinants in the outcomes of usage.

## METHODS

A prospective study was carried out among 306 patients from orthopedics department presenting with musculoskeletal pain from January 2014 to August 2015. Both males and females above the age of 18 years and below the age of 65 years who were admitted with complaints of MS pain and treated in Owaisi Health and Research Centre (OHRC), Hyderabad were included in the study. Ethical committee clearance and informed consent from patients was obtained for the conduct of the study. Data privacy and confidentiality were maintained at all times. Patient particulars, history and clinical findings were obtained using the study proforma.

### Inclusion criteria

- Patients above the age of 18 years and below 65 years
- Patients of either gender
- Patients who have been treated for back pain (dorsalgia/ lumbago), Rheumatoid arthritis, OA , Spondylosis, Tenosynovitis, Tennis elbow, Sciatica, Myalgia, Polyarthralgia

### Exclusion criteria

- Patients below the age of 18 years and above 65 years
- Patients with diagnosis of gastro-esophageal reflux disease and peptic ulcer
- Pregnant women
- Patients with cardiovascular problems

### Data analysis

Data collected was analysed by frequency and percentage.

## RESULTS

**Table 1: WHO core prescribing indicators.**

Prescribing indicators	
Average number of drugs per encounter	2.61
Percentage of drugs prescribed by generic name	32%
Percentage of encounters with injections prescribed	9.2%
Percentage of drugs from EDL formulary	63%

A total of 800 drugs were prescribed in 306 patients and the average number drugs per prescription were  $2.61 \pm 0.955$ . Of the 800 drugs 256 (32%) were prescribed by generic name. 77 of the 800 drugs (9.2%) were administered parenterally. The drugs prescribed from EDL were 505 (63%).

**Table 2: Pattern of drug usage.**

Class	Total	% N=800
NSAIDs	397	49.6
GPA's	287	31.9
Multivitamins and Minerals	67	6
Anti-anxiety	15	1
Muscle relaxant	15	1.9
Opioid analgesics	11	1
Disease modifying anti rheumatoid drugs	8	9
Total	800	

800 drugs used in 306 patients of which were 397 (49.6%) NSAIDs and were the most frequently prescribed drugs in the patients of MS pain in this study followed by 287 GPA's (35.9%), 67 multivitamins and minerals (8.4%), 15 (1.9%) of anti-anxiety and muscle relaxant each, opioid analgesics (1.4%) and Disease Modifying Anti Rheumatoid Drugs (DMARDs) (1%).

Out of the 306 patients, 296 (96%) were prescribed NSAIDs. A total of 416 NSAIDs were prescribed in the 296 prescriptions together with drugs constituting the FDCs. Average number of NSAIDs per prescription expressed as mean  $\pm$  standard deviation was  $1.36 \pm 0.67$ .

214 NSAIDs (51%) were prescribed in generic name. 376 (90.38%) were from the essential drug list formulary. All the NSAIDs prescribed were non selective. Out of the 416 drugs 92 (22.1%) were FDCs and the most common FDC of analgesic was paracetamol with an opioid analgesic (tramadol). It was observed that in 68 (22.2%) of the total prescription the same drug was repeated in a different formulations (e.g.: oral and topical; oral and injection; injection and topical). Out of the 406 drugs 275 (69%) were administered orally, 58(15%) were administered parenterally and 64 (16%) were administered topically. 10 (3%) patients of MS pain were not prescribed NSAID, monotherapy was followed in 199 patients 65 % and the rest had more than one drug in their prescription (32%).

**Table 3: Pattern of NSAIDs usage.**

	Number	%
Total patients with MS Pain	306	
Total Number of patients prescribed NSAIDs	296	96%
Number of NSAIDs prescribed	416	
Average number of NSAIDs per prescription	1.36 ± 0.67	
Number of NSAIDs prescribed in generic name	214	51%
Number of drugs from EDL formulary	376	90.4%
Number of FDCs prescribed	92	22.6%
Number of oral medications	275	69%
Number of topical medications	64	16%
Number of injections	58	15%
<b>Number of NSAIDs prescribed per prescription</b>		
0	10	3.3%
1	199	65%
2	75	24.5%
3	21	6.9%
4	1	0.3%
Total	306	

**Table 4: Details of NSAIDs prescription and drugs constituting DU90%.**

Drug	Number	% N=416
Diclofenac	294	70.7%
Paracetamol	99	23.8%
DU 90% of drugs 1-2: 393 (94.5%)		
Indomethacin	14	3.4%
Ibuprofen	5	1.2%
Nimesulide	2	0.5%
Lornoxicam	1	0.2%
Naproxen	1	0.2%
Total	416	

Overall 7 different NSAIDs were prescribed in the patients. Diclofenac was the most commonly prescribed

agent (70.7%) followed by paracetamol (23.8%), indomethacin (3.4%), ibuprofen (1.2%), nimesulide (0.5%), (0.2%) and naproxen (0.2%). Diclofenac and paracetamol constituted of DU 90%.

**Table 5: Fixed dose combinations.**

FDCs	No of prescription	%N=92
Tramadol + Paracetamol	70	77%
Diclofenac + Paracetamol	17	18%
Nimesulide + Tizanidine	2	2%
Lornoxicam + Paracetamol	1	1%
Ibuprofen + Paracetamol	1	1%
Paracetamol + Dextropropoxyphene	1	1%
Total	92	

**Table 6: Routes of administration.**

Route of administration	Number	% N=416
Oral	282	68%
Topical	71	17%
Parenteral	18	4%
	Stat only 45	11%
Total	416	

**Table 7: Pattern of management with other approaches.**

Management	Number of cases	% N=306
Analgesics and physiotherapy	220	71.8
Only analgesics	79	26
Only physiotherapy	4	1.3
No physiotherapy or analgesics	3	0.9
Total	306	

Overall 30% of the patients were prescribed FDCs. 22% of the NSAIDs prescribed were FDCs of which most preferred was combination of NSAID with opioid, paracetamol + tramadol (77%) followed by combination of two NSAIDs, diclofenac + paracetamol (18%), NSAID and muscle relaxant, nimesulide + tizanidine (2%), 2 NSAID lornoxicam + paracetamol (1%), ibuprofen + paracetamol (1%) and paracetamol + dextropropoxyphene (1%). Almost 20% of the FDCs constituted of two NSAIDs.

Systemic route was most preferred (83%) for administration of NSAIDs. Oral route (68%) was the

most frequently used for drug administration followed by topical (17%) and then parenteral (15%). The parenteral formulation was mostly used only for stat administration (11%).

Among the 306 patients 224 (73.2%) patients received physiotherapy. In the patients who received physiotherapy 220 received concomitant pharmacological measures (analgesic) and only 4 were managed with physiotherapy alone.

Out of the remaining 82 patients who did not receive physiotherapy, 79 patients were managed with analgesics alone for MS pain and 3 patients were not prescribed medication or were given non pharmacological therapy.

## DISCUSSION

In this study the average number of drugs per encounter was  $2.614 \pm 0.955$  similar to other studies in Uttaranchal<sup>7</sup> and Chandigarh.<sup>8</sup> The average (mean) number of drugs per prescription is an important parameter while doing a prescription audit; it helps understand the degree of polypharmacy.<sup>9</sup>

Percentage of drugs prescribed by generic name was 32% which is much higher than other studies like in Nepal but still there is scope of improvement.<sup>10</sup>

Parenteral formulations were prescribed in 9.2% of patients similar to prescription pattern studies in Nepal.<sup>10</sup> Parenteral formulations are usually overused and expensive form of drug therapy.

63% of the drugs were prescribed from EDL formulary of India indicating that the drugs confine to the national drug policy.

NSAIDs (49.6%) were the commonest class of drugs prescribed in the patients suffering from MS disorders followed by GPAs (35.9%). Similar to in studies in Uttaranchal GPAs, multivitamins, minerals and anti-anxiety and muscle relaxants were the other classes of drugs prescribed.<sup>11</sup>

Analgesics were prescribed in 296 patients and 416 NSAIDs were prescribed. Average number of NSAIDs per prescription expressed as mean  $\pm$  standard deviation was  $1.36 \pm 0.67$  similar to a prescription study of NSAID use in South Delhi.<sup>8</sup>

Prescription with selective NSAID was nil in this study, this shift is due to the reports of Cardiovascular toxicity. Reduced prescribing trends have also been seen in other studies.<sup>12,13</sup>

Fixed dose combination (FDC) term is used generically to mean a particular combination of actives irrespective of the formulation or brand. It may be administered as single

entity products given concurrently or as a finished pharmaceutical product.<sup>14</sup>

In India, a variety of NSAID combinations are available, often as over the counter products. Ibuprofen and paracetamol combination does not offer added advantage as both have same target of action. Combination of NSAIDs with muscle relaxant has got questionable efficacy and further research is needed in this regard. NSAIDs combination with antispasmodic can be dangerous, hence it is not recommended.<sup>15</sup> Some of the combinations are irrational, for instance diclofenac plus serratiopeptidase do not offer any particular advantage over the individual drugs.<sup>16</sup> Despite the claim that serratiopeptidase promotes more rapid resolution of inflammation, but on the other hand, the patient is exposed to greater risk of GI adverse effects and increased cost.<sup>17</sup>

In the present study 22.1% were fixed dose combinations and the most common fixed dose combination analgesic was paracetamol with an opioid analgesic – tramadol where as other studies has shown > 40% of FDC usage.<sup>11</sup> Other combinations were of 2 NSAIDs like diclofenac + paracetamol, lornoxicam + paracetamol, ibuprofen + paracetamol, and NSAID along with muscle relaxant, nimesulide + tizanidine. Though NSAID and muscle relaxant combinations are high often in orthopedic department prescription studies,<sup>14</sup> here we observe that muscle relaxant was mostly given as a single drug rather than in combination.

Combination of two different NSAIDs as FDCs is not recommended as the combination will not give any additional advantage than individual drugs being prescribed alone. No drug synergism takes place when two drugs have same mechanism of action. Furthermore the combination can increase the chances of adverse events and overall cost of prescribing.<sup>18</sup> However some useful analgesic combinations do exist, such as combination of tramadol with paracetamol. They synergize with each other as site of actions are different for both the drugs.<sup>19</sup> In the present study, FDCs were not the bulk of overall NSAIDs prescription.

The most commonly prescribed NSAID was diclofenac 70.7% similar in a study in Uttaranchal.<sup>11</sup>

Systemic prescriptions of NSAIDs comprised of 84% of which oral was 69% and 15% were administered parenterally. 16% of the NSAIDs were prescribed in topical formulation. This observation is comparable to the study in South Delhi.<sup>8</sup>

High prevalence of GPA co-prescription was noted in this study (94%). High frequency of GPAs prescription can be attributed to prescriber's preference for non-selective NSAIDs prescription, which is more prone to gastritis and peptic ulceration. Similar trend was also observed in Spanish study where frequency of GPAs co-prescription was 64%.<sup>20</sup> Antacids were not prescribed in this study.



In the present study, non-selective NSAIDs were the major component of DU 90% segment. Out of 7 different NSAIDs prescribed in present study, two drugs (diclofenac and paracetamol) falls within DU90% segment. Contrary to our result COX-2 inhibitors were the major constituents of DU90% in Korean study.<sup>21</sup>

NSAIDs prescription pattern appears to be rational in this study as only two drugs falls within DU90%. This finding is in contrast to trend seen in Queensland Australia, where COX-2 inhibitors form the major component DU90% segment (before rofecoxib withdrawal).<sup>22</sup> After the withdrawal of rofecoxib (2004), prescribers increasingly replaced COX-2 inhibitors with non-selective NSAIDs and preferential COX2 inhibitors, considering it as a class effect and not as individual drug effect.<sup>12</sup>

This observation can very well be noted in our study as DU90% segment is mainly constituted by non-selective NSAIDs.

## CONCLUSION

Overall frequency of NSAIDs prescription in this study was 96%. Seven different types of NSAIDs were prescribed. Diclofenac (70.7%) was the commonest NSAID prescribed followed by paracetamol (23.80%), indomethacin (3.4%), ibuprofen (1.2%), nimesulide (0.5%), lornoxicam (0.2%), and naproxen (0.2%). Selective COX-2 inhibitors were not prescribed. Combination of paracetamol and tramadol (77%) was the commonest FDC prescribed among the 92 FDC prescriptions. Diclofenac + paracetamol, ibuprofen + paracetamol, lornoxicam + paracetamol combinations were the FDCs containing two different NSAIDs prescribed in this study; it accounts for 20% of overall FDC prescriptions. High frequency of GPAs co-prescription (94%) was noted in this study. Of 7 different NSAIDs prescribed in this study, 2 drug (diclofenac, and paracetamol) falls within DU90% segment- mainly constituted by non-selective NSAIDs. Overall, the prescription pattern was in accordance with standard guidelines, as suggested by the fact that the DU90%, segment was constituted by only few drugs.

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