NSAIDS: The Double Edge Sword- Pharmacovigilance In A Tertiary Care Hospital

[1]Rahul Saini, [2]Bhawna Sharma, [3]Prem Kumar Verma, [4]Garima Bhutani, [5]Seema Rani,
[1]Assistant Professor, [2]Techinical Associate Pharmacovigilance, [3]Professor, [4]Assistant Professor,
[5]Associate Professor, BPS, GMC, Khanpur Kalan University of Health Sciences, Rohtak, Haryana

ABSTRACT

Background: There is no other group in pharmacology which truly can replace the role of NSAIDs in daily life as far as pain, inflammation and fever are concerned. But it is also true fact that NSAIDs are associated with lots of ADRs like gastritis, gastric ulcer, gastric perforations, obstructions. The other reported ADRs are cardiac, psychological, dermatological and renal in a small number of patients. **Method:** This Pharmacovigilance study was conducted for assessing the ADRs that occur due to NSAIDS in the BPS Hospital, Khanpur Kalan, Sonepat. The study period was of 8 months duration, from April, 2015 to February, 2016. The patients with any adverse event due to NSAIDS, of both genders and all age groups were included in the study. Detailed history of ADR (drug name, dose and frequency, date of onset, pattern), nature of illness for which the drug was taken and recorded. WHO-UMC Causality Assessment scale and Naranjo Algorithm was used for the causality assessment of the ADRs due to NSAIDS. **Results:** Out of 163 ADRs observed (from April, 2015 to February, 2016) 27 ADRs were due to NSAIDS administration. Out of 27 ADRs, 17 (62.96%) were due to Diclofenac, followed by 6 (22.22%) due to paracetamol, 2 (7.40%) due to Ibuprofen and 1 (3.70%) due to a combination of Diclofenac and Paracetamol. No ADR was found due to nimuslide and etoricoxib, that were prescribed less frequently as compared to Diclofenac and paracetamol. Along with NSAIDs gastroprotective agents, i.e. ranitidine and pantoprazole were prescribed in 9 out of 27 patients. Antibiotics were prescribed to 4 patients along with NSAIDS. Causality assessment was done by WHO UMC Causality Assessment scale and Naranjos algorithm Scale revealed that out of 27 ADRs, 20 were possible and 7 were probable in nature. **Conclusion:** There is need of continuous vigilance over the adverse drug reactions due to NSAIDs otherwise would result in an unnecessary increase in morbidity and mortality.

Keywords: NSAIDs, ADR, Pharmacovigilance, adverse drug reaction, causality assessment.

Corresponding Author: Dr. Rahul Saini, Assistant Professor, BPS, GMC, Khanpur Kalan University of Health Sciences, Rohtak, Haryana Mail: drrahulnanu@gmail.com Mob: 9416837647.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDS) are one of the most commonly used medications available for the treatment of pain, fever and inflammation. They are easily available over the counter drugs. The main symptom which compels the patients to reach to doctors is pain and no doubt NSAIDS are the most commonly used drugs in this aspect. But it is also true that these are one of the most notorious drugs showing ADR. NSAIDS acts by inhibiting the activity of Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) enzymes that are responsible for the formation of

prostaglandins and thromboxane. Inhibition of COX-2 inducible enzyme produced under specific condition like inflammation leads to anti inflammatory, analgesic and antipyretic effect of NSAIDS. But inhibition of COX-1, which is constitutively expressed in GIT is responsible for undesirable side effects. NSAIDS induced adverse drug reactions (ADRs) are one of the leading causes of increase in morbidity, mortality of the patients. And no doubt these ADR are also responsible for an unnecessary increase in hospital stay and affect the quality of life. The most common ADR observed due to NSAIDs use are gastrointestinal effects. Studies have shown that NSAID induced gastric perforations, obstructions and ulcers were responsible for the 16,000 deaths that occurred in the US and 10,000 deaths in Canada in a year.[1] The other reported ADRs are cardiac, psychological, dermatological and renal in a small subset of patients.[2] Other rare ADRs associated with NSAIDS are agranulocytosis and aplastic anaemia with phenylbutazone,[3,4] and Stevens Johnson and Lyell's Syndromes and other severe skin reactions with isoxicam and piroxicam.[5,6] The identification, assessment and prevention of ADR is an important mandatory process of hospitals. This is the general basic concept of pharmacovigilance. It is also true that the eyes only see what the mind knows. So we conduct the study to assess the ADR, which are related to NSAIDS, so that these can be prevented further. NSAIDs is like a double edge sword as we have no better option than these drugs and also have to deal with its ADRs. Therefore present study was carried to monitor and evaluate the various adverse events occurring due to NSAIDS in BPS Hospital, Khanpur Kalan, Sonepat for a specified period.

MATERIAL AND METHODS

This Pharmacovigilance study was conducted for assessing the ADRs occurring due to NSAIDS in the BPS Hospital, Khanpur Kalan, Sonepat, Haryana. The study period was of 8 months duration, from April, 2015 to February, 2016. Patients with any adverse event due to NSAIDS, of both genders, under all age groups were included in the study. Detailed history of ADR (drug name, dose and frequency, date of onset, pattern), nature of illness for which the drug was taken and recorded. WHO-UMC Causality Assessment scale and Naranjo Algorithm was used for the causality assessment of the ADRs due to NSAIDS. No follow-up was done.

RESULTS

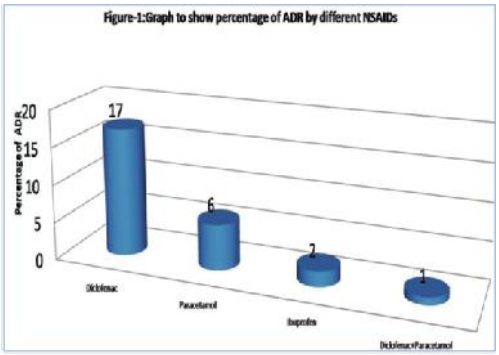
Out of 163 ADRs observed (from April, 2015 to February, 2016) 27 ADRs were due to NSAIDS administration. Out of 27 patients who suffered from ADRs 33.33% were males and 66.66% were females (Table-1).

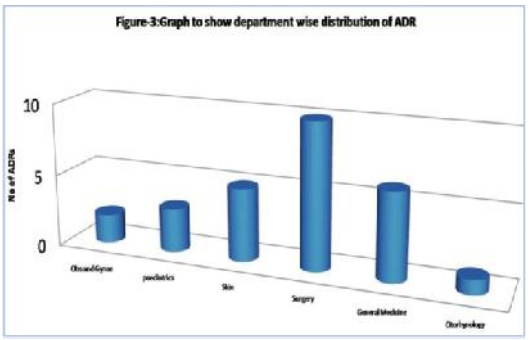
Table 1: Age and Gender of the patients

Interval	No. of patients	Male	Female
0-15	5	3	2
16-30	7	3	4
31-45	6	1	5
46-60	5	0	5
61-75	4	2	2
Total	27	9	18

The distribution of different drug causing various ADRs is shown in figure 1.

Causality assessment was done by WHO UMC Causality Assessment scale and Naranjos algorithm Scale revealed that out of 27 ADRs, 20 were possible and 7 were probable in nature.(Figure2) Most of the cases of ADRs due to NSAIDS were reported from surgery department. Diclofenac is the commonly prescribed drug used as analgesic in the surgery department. Least number of cases was there from ENT Department. (Figure3)



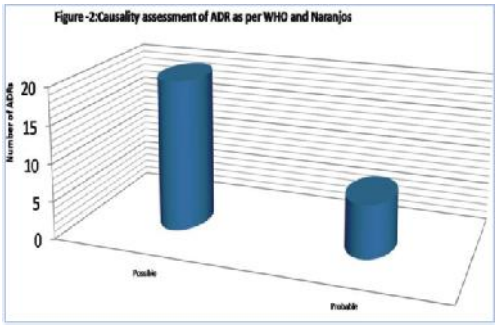


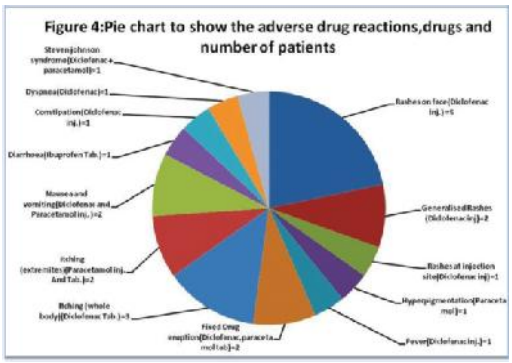
Most common ADR was related to the skin, including skin rashes, erythema, itching, Steven Johnson Syndrome, fixed drug eruption and hyperpigmentation (17 out of 27) followed by gastrointestinal disorders like nausea, vomiting, diarrhea, constipation and flatulence with abdominal pain (7 out of 27) which is followed by 1case each of fever, swelling on the whole body and exaggeration of Asthma. (Figure4)

DISCUSSION

NSAIDS are among the most frequently prescribed drugs worldwide, no doubt these are commonly associated with number of ADRs.[7] In the present study, we received 27 (16.56%) cases of ADRs due to NSAIDs out of 163 total cases in 8 months duration. Out of these ADR, 18 occurred in females and 9 occurred in males. The study done by Gallelli et al, showed that NSAIDs caused >55% of the ADRs detected in patients.[8] Mujahid et al also showed that number of the female patients suffering from ADRs due to NSAIDS were more than males as per study.[9] Most of the cases reported by our study are between 16-60 years of age and only 4 cases reported are above 60 years of age. But some studies showed the highest percentage of ADRs in the older age group >61 years.[10-14] The reason for this difference may be sample difference depending on the prevalence and underestimation as it is difficult to detect ADR in older patients because these ADR may be due to their age related problems. ADRs reported during combination therapy (NSAIDS with anitibiotics/ gastroprotective agents) were 49% against 51% in monotherapy (only NSAIDS) as per our study. This data contradicts other data in which percentage of ADRs caused are more when NSAIDs were given in combination with other drugs.[15]

The Causality assessment in our study is done by using both WHO-UMC Probability scale and Naranjo ADR probability scale. Both scoring have shown the possible relationship between NSAIDs and ADRs in 74% of the patients. Diclofenac is the commonly prescribed drug for pain. Some studies have shown





that Diclofenac and Ibuprofen have less side effects as compared to indomethacin, piroxicam and naproxen.[16] But in our study, out of 27 patients, 17 developed ADRs due to Diclofenac. Out of these 18 patients, 10 developed skin related symptoms (like rash, erythema, fixed drug eruption and face oedema), 6 developed GI related symptoms (severe constipation, diarrhea, nausea & vomiting), 1 developed fever and in 1 patient exaggeration of Asthma. Actually, in our study the number of patients who received Diclofenac was more in comparison to the number that received other NSAIDs, so the number of ADRs were also more with Diclofenac. Studies have shown about 20% of patients experience side effects with Diclofenac, but only 2% have to discontinue the drug.[17] Paracetamol was the second most common drug prescribed as per our the study among NSAIDS and 6 cases of drugs reactions were seen due to paracetamol, 5 cases were related to skin reactions (Hyperpigmentation, itching and fixed drug eruption), and 1 related to GI Symptom (flatulence with abdominal pain)]. One case of Steven Johnson syndrome was seen due to fixed drug combination of Diclofenac and Paracetamol (Diclopara). Ibuprofen tablet was seen to cause 2 drug reactions (rash with angioedema and severe gastritis with vomiting). One case of aspirin tablet causing constipation was also observed. No adverse drug reaction case was observed due to COX-2 inhibitors like etoricoxib, nimesulide, etc. Being a selective inhibitor etoricoxib has less adverse drug reactions as compared to other drugs.[18]

CONCLUSION:

This is a pharmacovigilance observational study in an aspect of NSAIDS. In this study, we have shown, the prevalence of ADR, type of ADR, various types of NSAIDS, concomitant medicines with NSAIDS showing ADR. This information will be helpful in planning of rational use of drugs in long term basis. There is need of continuous monitoring of these ADR and also sensitization of doctors to record the ADR meticulously. So that it will be helpful in prevention, assessment and management of ADR for future purpose.

Conflict of interest : No

Funding: No

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