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Research Article

PROSPECTIVE ASSESSMENT OF NSAIDs INDUCED ADRs IN ORTHOPAEDIC IN-PATIENTS

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ABSTRACT

Background and Objectives: nonsteroidal anti-inflammatory drugs (NSAIDs) are one among the most widely used medications to treat pain and inflammation condition. But inadvertent use of NSAIDs have resulted in gastric upset and even death. Hence to minimize such consequences and to identify the incidence of the Adverse drug reaction (ADR)s due to NSAIDs in orthopaedic in-patients to promote rational prescribing. **Materials and Methods:** A prospective study was done in one hundred orthopaedic in-patients of a tertiary care hospital for 3 months from June-Augest 2012. The ADRs pattern were noted with respect to age, gender and drugs involved . The causality of ADRs were assessed by Naranjo's Algorithm. **Results:** Among one hundred in- patients 16% developed ADR due to NSAIDs and 1.92% due to Antimicrobial agents (AMAs). The ADRs were more in males (11%) than females (5%). Most prescribed NSAID was Diclofenac (76 %), and least was nimesulide (2%). Others were Paracetamol (16%), Ibuprofen (3%) and Etoricoxib (3%) . Out of 16 ADRs Tablet (Tab) Diclofenac accounted for maximum number {87.5%, (n=14)} of ADRs, followed by Tab. Paracetamol {12.5 % (n=2)}. **Conclusion:** ADR incidence rate in orthopaedic in-patient due to NSAIDs was 16%. Educating, establishment and encouragement of Pharmacovigilance system among medical and non-health professionals including medical undergraduates improve ADRs identification and to identify the drugs causing it, therefore prolonged hospitalization, treatment cost, morbidity and mortalities can be minimized. Hence, further ADRs due to particular drugs can be reduced in other patients with rational prescription.

Keywords: Adverse drug reactions, NSAIDs, Pharmacovigilance, Naranjo's Algorithm, rational prescription.

INTRODUCTION:

In the year 1972 WHO defined Adverse drug reaction (ADR) as a response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.[1]

ADRs are usually associated with significant morbidity, permanent disability, mortality and huge financial burden on the patients to treat the same due to prolonged hospitalization.[2]

NSAIDs are one of the most widely used medications to treat pain and inflammation in patients with various musculoskeletal conditions.

The benefits and adverse effects of NSAIDs are due to the inhibition of either COX-1 or COX-2 enzymes. NSAIDs inhibit both COX-1 and COX-2, but the extent of inhibition differs between NSAIDs.[3]

In general NSAIDs acts by inhibiting both cyclooxygenase-1 (COX-1) and COX-2 involved in prostaglandin synthesis to exert analgesic, anti-

inflammatory and antipyretic effects. Conventional or traditional COX-1 maintains normal gastric mucosa and helps in homeostasis. Inhibition of COX-1 produces undesirable gastric side effects. Inducible COX-2 mediates inflammatory process and selective COX-2 inhibition reduce gastric adverse reactions. Thus, the most "classic" NSAIDs block both isoforms, but the so-called coxibs preferentially inhibits COX-2 and hence better tolerability due to reduction in gastrointestinal side effects.[4, 5]

Various studies have shown that the Gastrointestinal and cutaneous ADRs including hepatic and renal toxicity are the well known ADRs associated with NSAIDs therapy.[6, 7, 8]

However, recent studies have shown an unequivocal increase in risk of cardiovascular thrombotic event even with selective COX-2 inhibitors.

The thalidomide catastrophe and serious adverse drug reactions to high estrogen oral contraceptives around 1960s probably the main reason which led to the establishment of a spontaneous reporting system.[9, 10]

Monitoring and evaluation of ADR reports have become a more important component in hospitals[11]. And ADR related information may be useful for identifying and minimizing the preventable causes of ADR which intern enhances the ability and confidence of prescribers to manage ADRs more effectively.[12, 13]

Hence, with the above background present study was undertaken among orthopaedic inpatients to

i) Determine the frequency of ADRs related to NSAIDs and Antimicrobial agents (AMAs)
ii) Find out the drug causing it.
iii) Report the most common clinical feature associated with these ADRs.

MATERIALS AND METHODS

A prospective study was carried out among one hundred orthopaedic inpatients of District Hospital, Bidar a 350 bedded tertiary care teaching hospital. The study was conducted for 3 months from June 2012 to August 2012 after obtaining institutional ethical clearance. All the patients of either sex, of age group 18 years and above who is being treated with NSAIDs therapy namely diclofenac (50mg), paracetamol (500mg), ibuprofen (200mg), nimusulide (100mg), etoricoxib (90mg) for various musculoskeletal conditions for a minimum of 2 days and patient on AMAs were included in the study . And patients who are having hepatic problems, renal problems, cardiovascular disease, Gastrointestinal problems, patients not willing to give consent; pregnant women and lactating mothers were excluded.

Demographic details, diagnosis, detailed history of ADR and concomitant medication were recorded in the Proforma. Causality assessment for evaluating adverse drug reaction was done by one of the frequently used method, i.e., Naranjos algorithm, which consists of objective type of questions with three types of answer i.e yes/no/don't know. Scores were drawn and total score: > 9; in-between 5 to 8 and 1 to 4 were classified as 'definite', 'probable' and 'possible' respectively. Follow-up of the patients were not done. Data was collected and analyzed by using the Chi-square with two-tailed test. A P value of <0.05 was considered as significant. Numerical values were expressed in percentages.

RESULTS

Among 100 inpatients, 16 patients suffered from ADRs. Male to female ratio was 2.2:1 (table-1). Out of 16 patients who suffered ADRs 14% were males and 2% were females (table-1). With respect to age groups, between 18 and 65 years, 11% of ADRs were noted and 5% of ADRs were above 65 years (table-1) and was found to be statistically significant ($p < 0.05$). In our study gender had no statistical significance ($p > 0.05$) with respect to the occurrence of ADRs caused by NSAIDs prescribed.

Out of 16 ADRs, 15 (93.75%) were due to diclofenac, and one (6.25%) was due to paracetamol. No ADR was found due to ibuprofen, nimesulide and etoricoxib, that were prescribed less frequently compared to diclofenac and paracetamol. Along with NSAIDs gastroprotective agents were prescribed in 76 patients, ranitidine and pantoprazole were prescribed in 74 and 2 patients respectively (table-2). Antibiotics were prescribed in 52 patients and one had developed skin rashes due to ceftriaxone (table-2). Causality assessment by Naranjos algorithm revealed that out of 16 ADRs, 9 were possible, 5 were probable and 2 were doubtful in nature. Most common ADR was Gastritis and GI distress, and 9 patients had experienced it, 3 had abdominal pain, 2 had nausea, one each had vomiting, Skin rashes and were managed symptomatically (table-3).

Table 1:Patients Demographic Profile, Gender, Distribution details of Adverse Drug Reactions.

Age (years)	Males (%)	Females (%)	With ADR (%)	Without ADR (%)
18 to 65	71	14	11	74
>65	12	3	5	10
Total	83	-	14	69
	-	17	2	15

Table 2: Drugs Prescribed And Adverse Drug Reactions.

Class of drugs	Drug name	No.of patients (%)	No.of ADR (%)
NSAIDs	Diclofenac(50mg)	76	15
	Paracetamol(500mg)	16	1
	Ibuprofen(200mg)	3	0
	Nimusulide(100mg)	2	
COX 2 Inhibitors	Etoricoxib(90mg)	3	0
Gastroprotective Drugs	Pantoprazole(40mg)	2	0
	Ranitidine(150mg)	74	0
Antibiotic	Ceftriaxone(1gm)	52	1

Table3: ADRs Detected And Implicated Drugs

ADR	Total no of patients (%)	The drug causing ADR
Nausea	2	diclofenac
Vomiting	1	diclofenac
Gastritis & GI distress	9	Diclofenac, paracetamol
Abdominal pain,	3	Diclofenac
Skin rashes	1	Diclofenac

DISCUSSION

In the present study incidence rate of ADRs in orthopaedic inpatients due to NSAIDs was found to be 16% and was low when compared to other three studies made in Brazil [14], Mumbai [15] and Delhi [16] which reported that 25%, 26% and 26 to 33% of Orthopaedic inpatients respectively developed an ADR. Low incidence of ADR in the present study can be attributed to rational therapy and appropriate NSAIDs selection based on individual illness and medical history.

Age is one of a major risk factor for the occurrence of ADRs[17] and few other important risk factors includes any history of duodenal ulcer or gastric ulcer, indigestion, unnecessary use of corticosteroids and anticoagulants, use of multiple and high dosage of Nonsteroidal anti-inflammatory agents and coexisting illness.[18] Age had significant association with the occurrence of ADRs due NSAIDs in the present study and 5 (%) of 15 patients above 65 years and 11 (%) of 85 patients between 18-65 years who received NSAIDs, experienced ADR. These results were on par with the other studies done in Brazil, Gujarat and Chennai.[14,19,20] And showed adult predominance, but was incongruous with Egger et al study [21], which reported the highest incidence of ADRs in elders.

In our study diclofenac was the most commonly prescribed NSAIDs followed by paracetamol, ibuprofen, nimesulide and etoricoxib. Out of 76 patients who received diclofenac 15 (93.75%) developed ADRs which was in accordance with other 2 studies at Gujarat and Chennai [19, 20] implying that proportion of diclofenac prescribed was more when compared to other NSAIDs. Diclofenac was more easily available and economical with lesser degree of side effects. In addition, a study done in Brazil[14] reported analgesic caused highest ADRs followed by antibiotics.

In the present study besides diclofenac, paracetamol was prescribed for 16 patients, of which one experienced gastritis and one of 52 patients who received antibiotics had a skin rash and the drug responsible was ceftriaxone, which was similar to studies done in north Brazil.[14]

No ADR was found in patient who were receiving ibuprofen, nimesulide, and etoricoxib.

ADR affecting the male was quite higher than female in the present study, but gender factor was statistically insignificant with the occurrence of ADRs.

Totally 76 patients received Gastroprotective agents of which 74 received ranitidine and 2 received pantoprazole.

Limitation of the study was, it was undertaken in a single department, i.e., orthopaedic and the duration was short and the number of patients screened was less. Further studies may take up larger study groups involving various departments. So that pharmcovigilance can be practiced more efficiently.

CONCLUSION

The ADR incidence rate in orthopaedic inpatient due to NSAIDs and antimicrobial agents was 16% and

1.92% respectively. Incidence of ADRs due to NSAIDs was found to be satisfactory when compared to other studies. Strict adherence to the Pharmacovigilance guidelines and practices will reduce ADRs and cuts down the economical burden on patients too. Hence establishment and encouragement of pharmacovigilance system in various specialties helps in reducing the ADRs and improves rational prescribing and good clinical practice.

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