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Research Article

A STUDY OF ADVERSE DRUG REACTIONS IN PATIENTS ADMITTED TO ORTHOPAEDIC WARDS IN TERTIARY CARE TEACHING RURAL HOSPITAL

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ABSTRACT

Adverse drug reaction (ADR) is one of the major problems associated with pharmacotherapy. The aim of the present study was to find out the incidence rate of ADR and investigate its various aspects in orthopaedic patients admitted to a tertiary care teaching rural hospital. A prospective-observational study, involving 521 patients over one and half year, was carried out to find the incidence rate of ADR, and its various aspects like types, grades, drugs causing them, organs/systems involved, onset and duration and management strategy with outcome. Structured and pre-tested format was used for compiling the data.Thirty one of the 521 patients developed ADR which yielded an incidence rate of 5.95%. Twenty seven 87.09% ADR were Type A (Augmented) reactions. Causality assessment, using WHO-UMC method revealed that 45.16% and 48.38% ADR were of "probable" and "possible" grades respectively while 6.42% were certain in nature. Majority of ADRs 23 (74.19%) occurred due to Non-steroidal anti-inflammatory drugs, followed by opioid analgesics, antibiotics and blood or blood products. None of the ADR was fatal. Suspected drugs were discontinued in 22.58% while they were replaced with other drug in 22.58% of cases. Some other drug was added in 29.03% of cases. This study shows the importance of ADR monitoring. Hospital based reporting is good method of detecting ADRs which can be followed by timely reporting. The health care providers should make an attempt for early detections of ADRs and be vigilant about safety profile monitoring of the prescribed medicines. This will not only decrease the morbidity and mortality but also the health care cost.
Keywords: Adverse drug reactions, Orthopaedic, Causality assessment, Rational drug therapy, Pharmacovigilance.

INTRODUCTION:

An 'adverse drug reaction'(ADR), as defined by the World Health Organization, is a noxious, unintended effect of a drug, which occurs at normal doses in humans for the prophylaxis, diagnosis, or the therapy of the disease or for the modification of its physiological function[1]. ADRs are considered as the 4th to 6th leading causes of death among hospitalized patients.

These are associated with significant morbidity, mortality and permanent disability and are a huge economic burden on the patients due to prolonged hospitalization [2]. It has been estimated that the incidence of ADRs throughout the world is 5% and 5-6% of all the hospital admissions which are caused by drug - induced problems [3].

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An important risk factor for developing ADR is the previous occurrence of ADR. Re-exposure to offending drugs due to poor documentation can cause the patient to experience the same ADR again, thus emphasizing the importance of the accurate documentation of ADR at the time of the event and providing relevant information to the patient about the ADR will help prevent its further occurrence.

It is important to note that most of these data related to the studies are decades old. With the changing demographics, the well-knownpredisposition of the elderly to ADRs, and the changes in medicalpractice that have occurred over the last few decades, there is aneed for more data on the ADR burden in patients admitted in the hospital. So the current study was planned with the objectives of:

1. Finding the incidence rate of adverse drug reactions in patients admitted to orthopaedic wards of Dhiraj Hospital, a tertiary care teachingrural hospital, Piparia, Gujarat.
2. Characterize the types of adverse drug reactions, the drugs causing them, thenature of reactions and their outcome.

MATERIALS AND METHOD:

This was a prospective, cross sectional study and was observational in nature that was conducted at a tertiary care teaching hospital, attached to S.B.K.S. Medical Institute & Research Centre (SBKSMI&RC), Sumandeep Vidyapeeth, Piparia. Prior approval for carrying out the study was obtained from the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC).

All the participants were examined on the day of admission and relevant details were noted in the structured format.Subsequently the patients were visited everyday till their discharge from the orthopaedic ward. Each day the patients were inquired and examined for development of possible ADR. In case of patients who developed an ADR, appropriate details were collected in the structured format.

Patients of either sex and above the age of 10 yearsserially admitted to orthopaedic wards during the study period and those willing to sign the informed consent form were included in the study. However, patients admitted with diagnosed ADR, those referred by or transferred from other departments, patients discharged or transferred to other departments within 24 hrs, patients unable to communicate i.e., patients on ventilators or suffering from serious diseases etc., and those who were not willing to participate in the study were excluded from the study.

Information of all the patients including relevant history, examination details, investigations and drug therapy was collected and recorded by visiting them daily from the day of admission till discharge from the hospital.Any adverse drug reaction reported by the patient or observed by the investigator or treating surgeon, were noted in structured format form.

OBSERVATIONS AND RESULTS:

A total of 521 patients admitted to the orthopaedic wards, during 1st January 2011 to 31st may 2012 were enrolled in the study. Out of 521 patients, 305 (58.54%) were male patients and 216 (41.46%) were female patients.

Out of 521 patients who participated in the study, 31 patients developed adverse drug reactions while the remaining were not affected with any kind of adverse reactions, that yielded an incidence rate of 5.95 per cent. Out of which,20 (64.51%) were male

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patients and remaining 11 (35.49%) were female patients. Total incidence of ADR among the male patient is 6.55%, where as 5.09% in female patients. [Table 1].

The patients were grouped into five groups (including both the genders) based on their age and the percentage of ADR were observed.Total percentage of ADRs in different age group was as follows: Group-I(18-30) 22.58%, Group-II(31-40) 25.80%, Group-III(41-50) 9.67%, Group-IV(51-60) 22.58% and Group-V (>60)19.33% [Table 2]. Of the 31(5.95%) patients belonging to various age groups and to either sex suffered with ADRs, 87.09% of the reactions were of Type A reaction (predictable) and 12.91% of the reactions were of Type B reaction (unpredictable).The most commonly recorded ADRs were from gastro-intestinal system 83.87% followed by immune 9.67%, genito-urinary 3.22% and vestibulo cerebellar 3.22%. [Table 3]. The admitted patients were treated with various groups of drugs in orthopaedic wards. Therefore involvement of different class of drugs causing the adverse drug reaction were observed for and percentage of ADR was calculated.Ofthe different groups of drugs that were administered to the patient at the time of treatment in the orthopaedic ward NSAIDs were the most common drugs involved in causing ADRs, followed by opioid analgesics, antimicrobials, blood and blood products, vitamins and minerals. [Table 4].

Among the recorded cases of ADRs most common were nausea and vomiting followed by retrosternal burning pain, diarrhoea, transfusion related reaction, abdominal pain, epigastric distress, rash, dizziness, vertigo, headache and hematuria. [Figure 1]. According to WHO criteria when the causality was assessed we found that of 31 patients who suffered withADRs, 2(6.42%) were certain, 14(45.16%) were probable and 15(48.38%) were possible in nature. [Table 4]. When the severity of ADR was assessed by Hartwig's scale we observed that of 31patients who suffered with ADRs 3(3.22) were in level-1, 15(48.38) were in level-2 and 13(41.93) were in level-3.Whereas with the help of Naranjo's scale we observed that from the ADR suffered 16(51.61%) were probable in nature while 15(49.39) were possible in nature.

However, all the patients had recovered without any sequel and none of the drugs causing ADR led to mortality among the recorded cases.

Management of suspected adverse drug reaction varied greatly. In 25.80% of patients suspected drug causing ADR were continued , no dose adjustment was made and in 22.58% of cases suspected drug causing ADR was discontinued. While some other drug was added in 51.61% of cases. [Table 5].

Table 1.Percentage of adverse drug reaction gender wise

Sex	**Patients with ADR n (%)**	**Patients without ADR n (%)**	**Total n (%)**
Male	20(6.55)	285(93.45)	305(100.00)
Female	11(5.09)	205(94.11)	216(100.00)
Total	31(5.95)	490(94.05)	521(100.00)

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Table 2.Total Percentage of ADRs in the patients grouped according to their age

Groups of patients according to age	Number of patients with ADRs (gender wise)		Total number of patients with ADR(%)
	Male	Female	
Group-1(18-30)	5	2	7(22.58)
Group-2(31-40)	6	2	8(25.80)
Group-3(41-50)	2	1	3(9.67)
Group-4(51-60)	4	3	7(22.58)
Group-5(>60)	3	3	6(19.33)
Total	20	11	31(100)

Table 3. System associated with adverse drug reaction:

No.	System	Numbers of ADRs (n=31) (%)
1	Gastro intestinal system	26(83.87)
2	Immune	3(9.67)
3	Genito-Urinary	1(3.22)
4	Vestibulo cerebellar	1(3.22)
	Total	31(100)

Table.4: Drug classes and drugs involved in adverse drug reaction

No.	Drug classes	Drugs	Number (%) of ADR
1	Non-steroidal anti-inflammatory drugs	Paracetamol	9(29.03)
		Mefenamic Acid	2(6.45)
		Naproxen	2(6.45)
		Diclofenac sodium	11(35.48)
2	Opioids analgesics	Tramadol	9(29.03)
3	Antibiotics	Ceftriaxone	9(29.03)
		Cefuroxime	4(12.90)
		Amikacin	8(25.6)
		Metronidazole	2(6.45)
4	Blood and blood products	Whole blood	2(6.45)
5	Vitamin	Multivitamin	1(3.22)

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Figure 1: Adverse drug reaction recorded for suspected drug

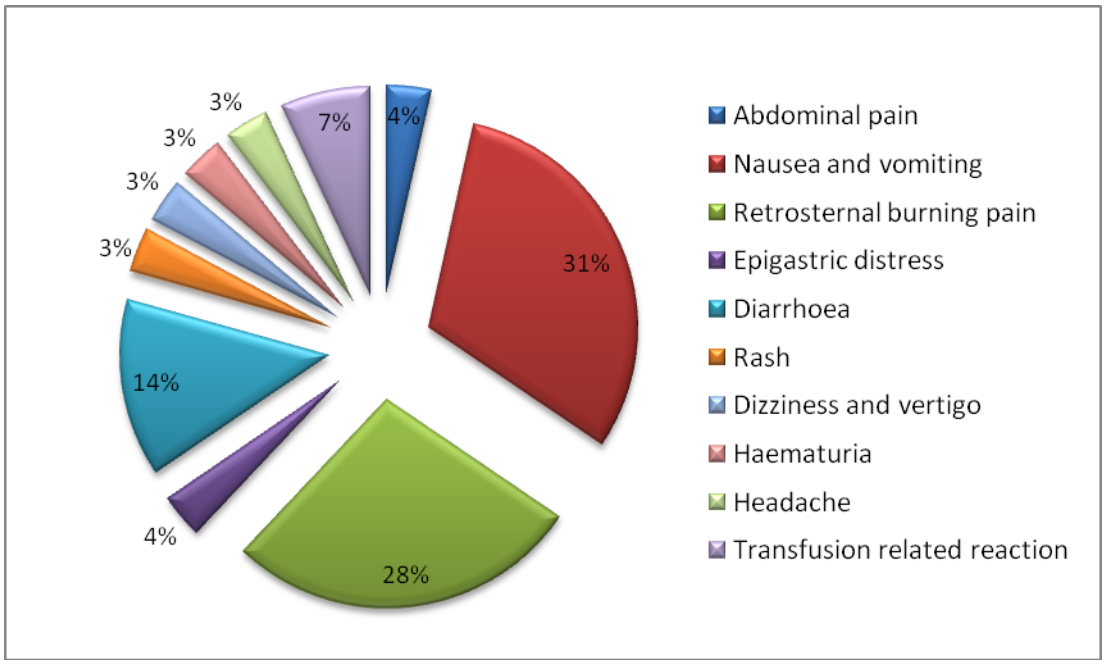

Table 4.Causality assessment of adverse drug reaction according to WHO criteria

Causality	Number of reactions n(%)
Certain	2(6.42%)
Probable	14(45.16%)
Possible	15(48.38%)
Unlikely	0

Table 5. Management of reported adverse drug reactions

Management of ADR	No. of ADRs(%)
Treatment with suspected drug causing ADRs was continued	8(25.80)
Treatment with suspected drug causing ADRs was discontinued	7(22.58)
Dose of the suspected drug causing ADR was reduced	0
Replacement of the suspected drug causing ADRs	7(22.58)
Addition of some other drug	9(29.03)
Total	31(100)

DISCUSSION:

Adverse drug reactions (ADRs) are global problems and are of major concern, affecting the patients of either sex and patients belonging to all age groups. They impose considerable economic burden on society and already stretched healthcare system. The attitude towards adverse reactions used to be, to avoid the use of apparently offensive drugs. Therefore, in the era of modern clinical therapeutics

understanding the mechanism by which the drug causes the adverse effects is also highlighted so that health care providers may avoid ADRs in their patients and maximize efficacy of their therapeutic regimens.

Orthopaedic ailments are very common in patients at all age groups. The non-steroidal anti-inflammatory drugs have always been the most widely used class of drugs in the treatment orthopaedic cases. They are often prescribed for musculoskeletal pain. Use of these drugs for a prolong period makes them more susceptible to ADRs. The major adverse effect caused by class of drug is gastro intestinal toxicity. There are number of studies that describe NASIDs as the leading cause of adverse drug reactions (ADRs). Study done by Sivasankari Venkatachalam et al, at Chennai, Tamilnadu showed the incidence of ADR to be 5.5% in patients admitted in orthopaedic wards[4]. However other study done by Karine Dal-Pazet al at Soa Paulo, Brazil reported total incidence of ADR as 1.45% in all patients admitted in hospital following orthopaedic trauma [5].

The adverse events with administered drugs commonly occur in the hospitalized patients and are frequently associated with human errors.

The post marketing surveillance of drugs is very important in analyzing and managing the risks associated with drugs once they are available for the use of the general population. Spontaneous reporting of ADRs has contributed significantly to successful pharmacovigilance. The health professional's contribution in this regard, has encouraged ongoing ascertainment of the benefit risk ratio of some drugs [6, 7] as well as detection of unsuspected and unusual ADRs those were previously undetected during the initial evaluation of a drug [8,9]. In spite of these, under-reporting of the adverse drug reactions remains a major draw-back. It is estimated that only 6-10% of all ADRs are reported [9,10].

The absence of organized continuing medical education programs and problematic physician attitude are other problems that add to under reporting of the adverse drug reaction [11].

The ADRs in the orthopedic wards were more in male patients (6.55%) than in female patients (5.09%). They occurred more commonly in patients of the age group 31-40 years (25.80%), followed by patients of the age group 18-30 years and 51-60 years (22.58%) each.

With multiple drugs used for patients admitted in orthopedic ward, the ADR were more common with NSAIDs followed opioid analgesics, antimicrobials, blood and blood products and vitamin.

In the present study, it was found that diclofenac, paracetamol, naproxen, mefenamic acid were top four orally taken NSAIDs. The most common reported adverse drug reaction due to these drugs is retrosternal burning pain, epigastric distress and abdominal pain. In this study tramadol was the only analgesic prescribed to the patient for postoperative pain management; however it was associated with high incidence of nausea and vomiting. We also found a case of rash induced by diclofenac. In this study we also reported four cases of diarrhea, which might be attributed to the simultaneous prescription of broad spectrum antibiotics like cefuroxime. Other reported ADRs were dizziness, vertigo, epigastric distress, headache, hematuria, transfusion related reaction etc. Most of the adverse drug reactions affected gastro intestinal system followed by immune, genito-urinary and vestibulo-cerebellar and central nervous system.

Of the reported ADRs the treatment with the some of the suspected drugs causing ADRs were continued 22.80%, and some of the suspected drugs causing ADRs were discontinued 22.58% while some other drugs is added in 51.61% of cases.

It was observed that none of those who suffered with ADR were left behind with any kind of sequel or mortality

CONCLUSION:

Adverse drug reactions are the important Public health Problems which are brought to medical attention by subjective reports and patients complaints. So, with focus to increase the awareness and understandings of health care professionals in reporting of ADRs and to integrate the various elements in comprehensive and constructive manner, the prospective study was undertaken.

The problem of ADRs could be remediable if the health care professionals employing pharmacotherapy understand that most of ADRs are preventable reflect the errors in management or misconception on the part of medical teams and patients.

Despite proper prescription and administration, any course of drug therapy is associated with potential risk of ADRs. According to law it is shared responsibility of both the physician and pharmaceutical industries, since each drug course may be as unique as individual taking medication. It might be difficult to determine with certainty the risk-benefit ratio of drugs.

There continues to be need to explore the mechanism underlying ADRs with the aim of understanding and decreasing their frequency.

Identifying the adverse drug events, recording them meticulously and reporting them to the concerned authority is a valuable to skin medical profession. This practice will prove to be very valuable in making the drug therapy safer and rational. This study has paved the way to carry out further studies on a large population in the future.

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