



A STUDY ON MONITORING ADVERSE DRUG REACTIONS ASSOCIATED WITH THE USE OF OPIOID ANALGESICS IN POST OPERATIVE PATIENTS

Mohammed Fareedullah^{1*}, Syeda Zuleqaunnisa¹, Fathma Mohammed¹, Ghousiya Noorie¹, Mir Moinuddin Ali Khan¹, Mohammed Sohail Ali¹ and Syed Nusrath Farees²

¹Department of Pharmacy Practice, Deccan School of Pharmacy, Hyderabad.

²Department of General Surgery, Owaisi Hospital & Research Center, Hyderabad.

***Corresponding Author: Mohammed Fareedullah**

Department of Pharmacy Practice, Deccan School of Pharmacy, Hyderabad.

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ABSTRACT

Opioid analgesics are the most frequently used drug for the management of pain in post-operative and expected to have increased risk of adverse drug reactions during the hospitalization. A prospective observational study was carried out in a teaching hospital over a period of 4 months and 100 patients were enrolled. Tramadol (100 mg/ml, IV, BD or TID) and Fentanyl (100 mg/ml, IV, TID or BD) were administered in the patients. Detection of the ADR was done using Naranjo's causality assessment scale. The severity of the ADRs was assessed using the Hartwig and Siegel scale. ADRs were identified in 16% of patients. Majority of the ADRs were seen in the young patients of age group 21-40 years. The most common ADR among the patients is nausea (18.75%) followed up by the gastric irritation, nausea and vomiting, purities, dyspnea, urinary retention which are 12.5% each. In this study majority of the ADRs were because of the use of the tramadol 15 (based on the causality assessment Naranjo scale 8 (50%) were probable, 5 (31.25%) doubtful, 2 (12.5%) possible, 1 (6.25%) probable. The severity appeared to be mild in 11 (68.75%), moderate in 3 (12%) & severe in 2 (12.5%) patients. ADRs were managed by reduction in dose or by drug withdrawal. Mortality or disabilities due to ADRs are not identified in our study. All patients recovered and discharged at stable condition. The present finding provides the perspective with regard to the ADRs reported with the opioid analgesics. This would help the healthcare practitioners for safe and more rational use of it in the management of the pain in the post-operative patients.

KEYWORDS: Adverse drug reaction (ADR), opioid analgesics, post-operative patients, causality assessment, severity assessment, rational use of opioids, pain.

INTRODUCTION

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem.^[1]

WHO's definition of an ADR, is "a reaction to a drug that that is noxious and unintentional and happens at doses commonly utilized in man for the prophylaxis, diagnosis or therapy of disease, or for change of physiological function."^[2]

Opioid analgesics

World Health Organization defines ache as "an unsightly sensory or emotional enjoy related to real or capability tissue damage, or defined in phrases of such damage

The time period opioid comes from the Greek phrase for stupor

Morphine is the maximum critical of the opioid analgesics

Opioid analgesics are the drugs that relieve pain/discomfort by binding to opioid receptors, which

are present in the central and peripheral nervous system.^[3]

Opioid analgesics relieve ache, however, additionally produce variety of aspect results. Opioid receptors also are responsible for several detrimental results that limits opioid ache therapy. Activation of μ -receptors can result in breathing depression, constipation, sedation, nausea, vomiting, and dependence/withdrawal.

Activation of δ -receptors can purpose convulsions and may contribute to worthwhile results of different pills of abuse.

Agonists of κ -receptors exert aversion, sedation, and diuresis (i.e., expanded urine output). Each of those signs represents a complicated phenomenon with more than one cell and molecular mechanisms.^[4]

METHODOLOGY

A prospective observational study was conducted to

identify and monitor the adverse drug reactions related to the use of opioid analgesics at inpatient unit of department of surgery in a tertiary teaching hospital. This study was carried out in 100 patients who had undergone elective surgery and were prescribed opioid analgesics for the management of the post-operative pain. Following details were recorded from each progress report of the patients

- Patients' demographic details
- Patient's present illness & Comorbidities
- The opioid analgesics given to the patients (dose, frequency, route of administration)
- Post-operative follow-up notes

All the details were then documented in patient profile form which have all the information such as the demographic details, vitals, past medical history, personal history, treatment given to the patients.

The tramadol and fentanyl were the frequently used opioid analgesics for the management of the pain. the most frequently given dose of the tramadol 100 ml and fentanyl was 100 ml and was given thrice a day and was administered intravenously.

All the spontaneous reported ADRS with the tramadol and fentanyl over a period of 4 months were analyzed. The nature and the type of ADRs due to opioid analgesics were analyzed with patient related factors (age, gender, comorbidities, disease conditions, smoking, alcohol.

Only the adult patients of age 18-75 years and patients who were undergoing the elective surgeries were included.

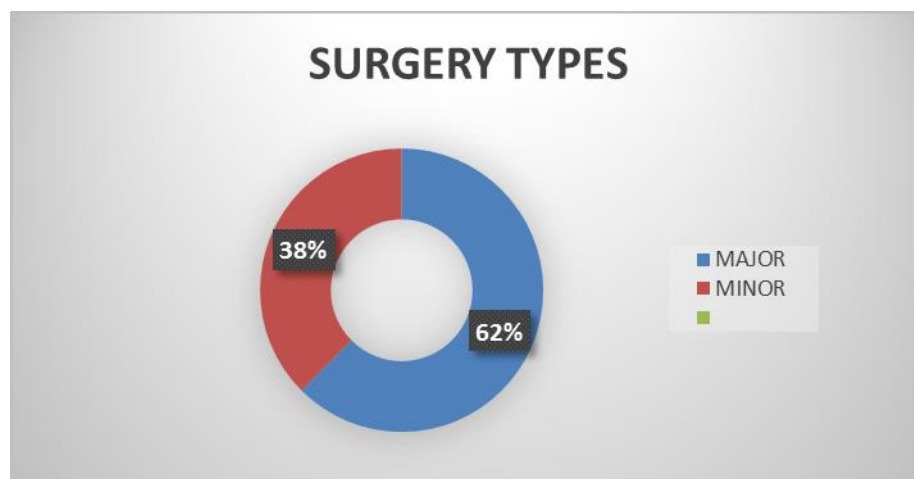
The pregnant, lactating, drug addicts, outpatients were not included in this study The suspected adverse drug reactions were identified among the patients.

The assessment of the ADR was done using the Naranjo scale which helps in describing the relation between the medicine and reactions that occurred to the patient. And the severity assessment was done by using the Hartwig and Siegel scale which describes the extent to which the ADRs influence the everyday life of the patients.^[5,6]

The management of the ADR was done either by decreasing, discontinuing or by using the alternate medicine. A predesigned Performa of Central Drugs Standard Control Organization was used to record the ADRs.

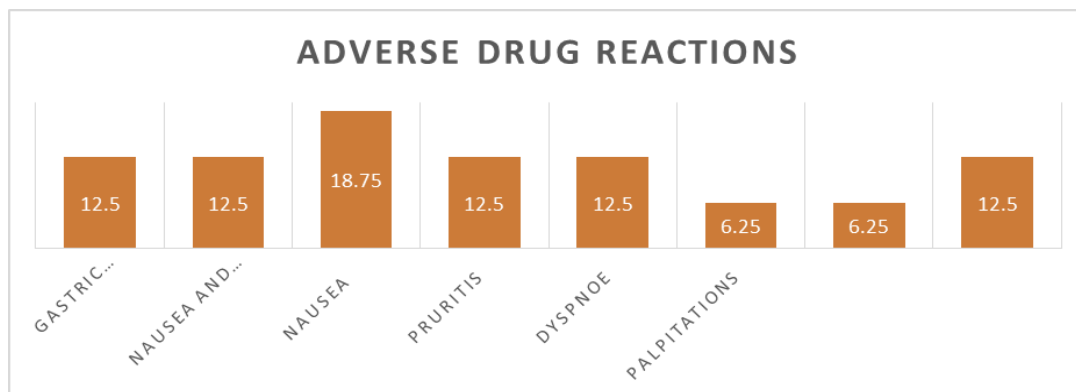
RESULTS

A total of 100 patients above the age of 18 were included in this study. The patient group falls into three categories 21-40, 41-60, 61-80. A total of 16 ADRs were identified, with predominance in males. The highest percentage was seen in the first category. Maximum number of ADRs were reported to be 60% in the age group of 21-40 years followed by 27% in 41 – 60 years & 13% in the age group of 61-80 years. Study participants undergone major surgeries in 62% & minor Surgeries in 38%.



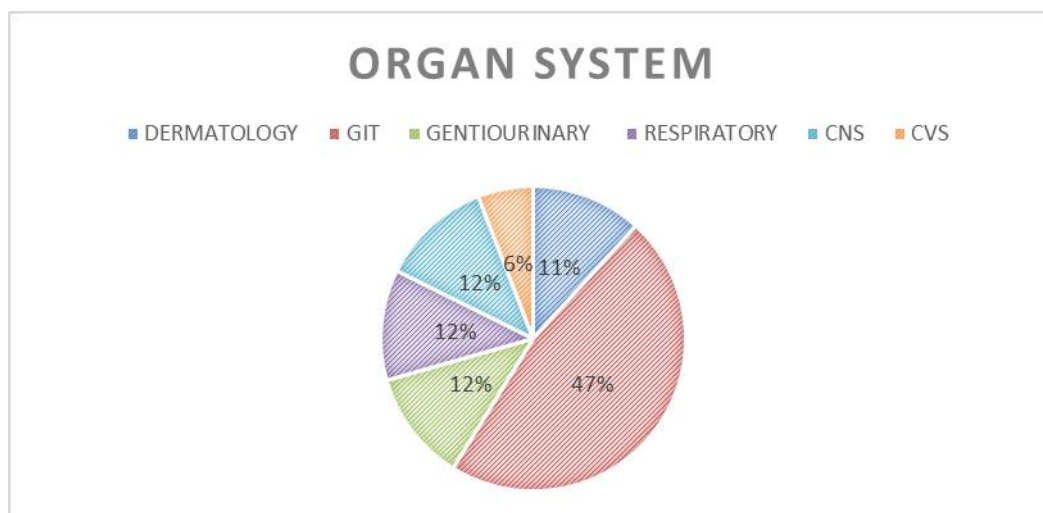
The tramadol and the fentanyl were most frequently used for the management of the pain. More number of ADRs were identified from the tramadol. Out of 16 ADRs, 15 were associated with the use of tramadol & 1 with fentanyl.

The most common Adverse drug reactions found are nausea 3 (18.75%), gastric irritation & constipation 2 (12.5%), Nausea & vomiting 2 (12.5%), pruritus 2 (12.5%), Dyspnoea 2 (12.5%), urinary retention 2 (12.5%), Hypoglycaemia 1 (6.25%), etc.



We observed that most of the ADRs were related to GIT 8 (47%), followed by dermatology 2 (12%),

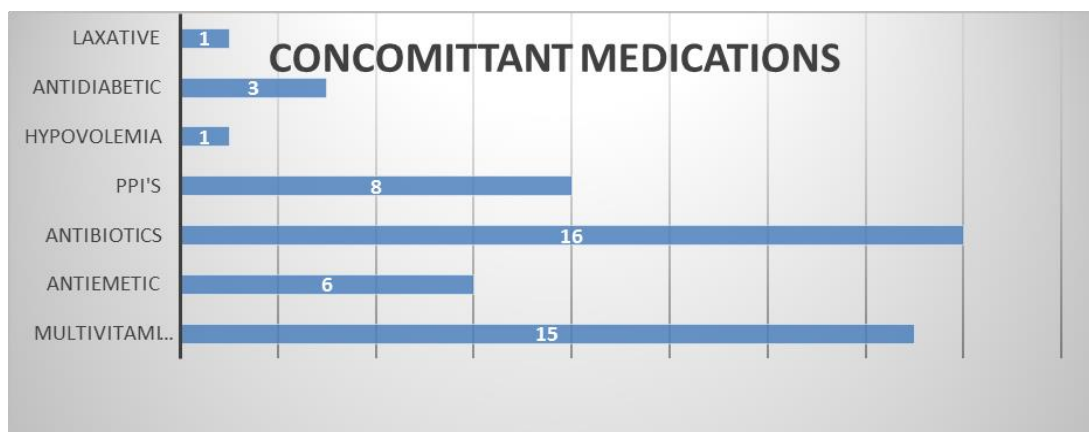
genitourinary 2 (12%), respiratory 2 (12%), CNS 2 (12%) and CVS 1 (6%).



Action taken in a greater number of patients was mostly withdrawal of suspected drug 10 (62%), followed by dose reduction 4 (25%) & dose unchanged 2 (13%). In most of the patients the drug was withdrawn when the ADR was seen in the patients.

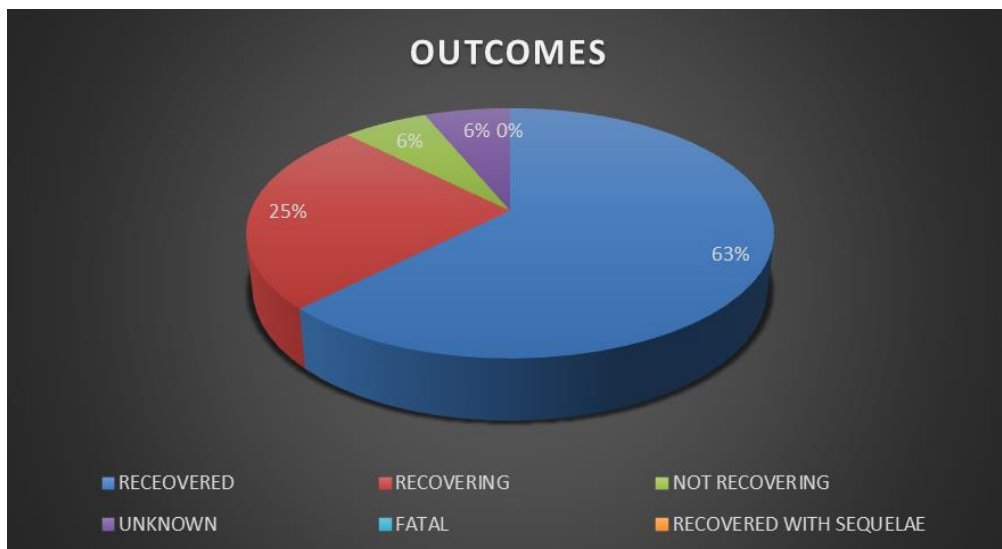
Inhibitors 8, antiemetics 6, antidiabetic 3, laxative 1 and hypovolemia 1. Seriousness of the reaction, out of 16 only 6 patients had serious reactions. 5(83%) of the patients required prolonged hospitalization to recover from the reaction, the rest 1 (17%) has experienced life-threatening reactions. The death, disability, congenital anomaly was not seen in any patients.

In most of patients, concomitant medications used are Antibiotics 16 followed by multivitamins 15, Proton Pump



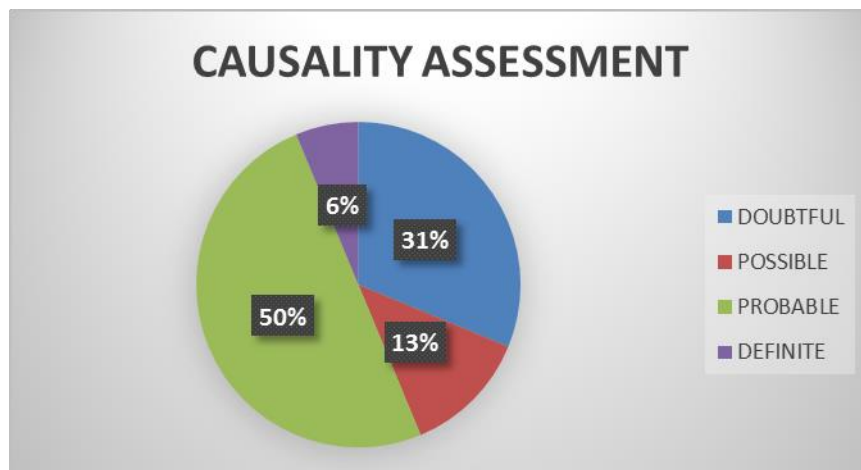
The study revealed that more number of patient are recovered 10 (63%) followed by recovering 4 (25%), not

recovering 1 (6%), fatal 0 (0%), recovered with sequelae 0 (0%) and unknown 1 (6%).



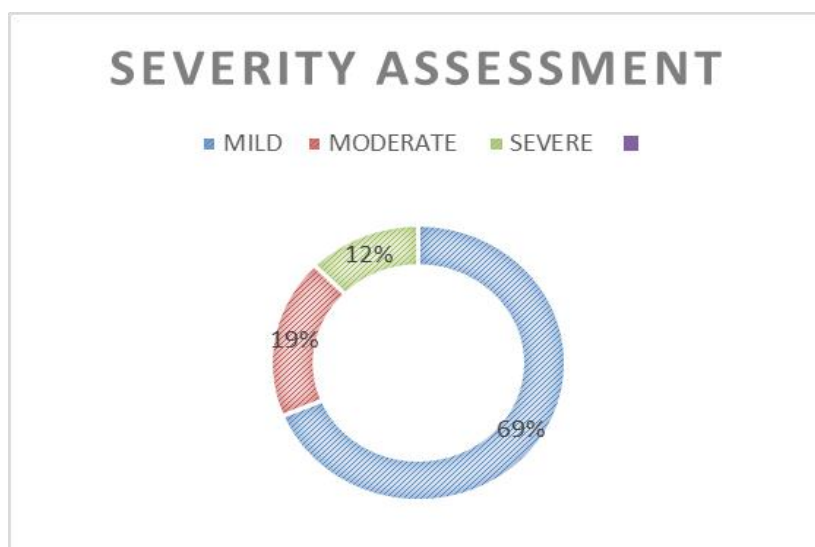
According to Naranjo scale 8 (50%) were probable, 2 (31%) were possible, 1 (6%) was definite and 5 (31%) were doubtful. The most of the ADRS falls into the

category of probable whereas only 1 ADR falls in the definite category.



The severities of the reactions were assessed using Hartwig & Seigel Scale. We identified that the majority

of ADRs were mild 11 (69%) followed by moderate 3 (19%) & severe 2 (12%).



DISCUSSION

In this study, males suffered a greater number of ADRs compared to that of females. The maximum number of ADRs were reported from adults 21-40 years. The number of ADRs with suspected medications were tramadol 15 (94%) and fentanyl 1 (6%). The most common Adverse drug reaction is nausea followed by other ADRs. These findings were consistent with the results of study carried by Gary M. Oderda, et al.^[7] The most common system involved were related to GIT, followed by dermatology, genitourinary, respiratory, CNS and CVS. The findings were consistent with the results of study carried by Walder, et al.^[8]

Management of ADRs were done mostly by withdrawal of suspected drug. In a greater number of patient's concomitant medications used are Antibiotics followed by other drugs. No mortality or disability was observed.

According to Naranjo scale most of the ADR were probable followed by doubtful, possible and definite. The severities of the reactions were done using Hart Wig Scale. Study reveals majority of ADRs were mild reactions followed by moderate reactions, severe.

From this study we observed that out of 16 patients 10 has comorbidity, two patients have diabetes + hypertension, followed by diabetes, hypothyroid, smoker, hypertension and chronic alcoholic. The results were different from study carried out by Monica et al where the majority of ADRs were seen in the cardiovascular patients.^[9]

CONCLUSION

Opioid analgesics play a vital role in the management of the pain in the post-operative patients, hence the use of it must be appropriately monitored so as to prevent or decrease the number of ADRs. The majority of the ADRs were mild and most of the patients recovered early after the withdrawal of drug. The patients were counseled about the proper use of opioid analgesics. The present finding provides the perspective with regards to the ADRs reported with the opioid analgesics. This would help the healthcare practitioners for safe and more rational use of it in the management of the pain in the post-operative patients.

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