Tramadol Induced Hypoglycaemia: A Case Report

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ABSTRACT

Tramadol is most commonly used opioid analgesic. It has a very rare and serious endocrine metabolic side effect as hypoglycaemia. The reason behind hypoglycaemia is still unclear but it may lead due to increased insulin concentration and utilization of glucose by muscles. In this report, a patient is prescribed tramadol for toothache. This report focuses on hypoglycaemia due to tramadol administration. Clinical Pharmacists should be at bedside to alert regarding any Adverse Drug Reaction. Regular monitoring of patients can decrease the mortality rate which is occurring due to ADR.

Keywords: Tramadol, Opioid Analgesic, Suspected Adverse Drug Reaction, Hypoglycaemia, Toothache.

Key Message: This case highlights rare consequences of the Opioid Analgesic administration. This can be fatal if not monitored on time.

INTRODUCTION

Tramadol is a synthetic analogue of codeine and its acts as a pure opioid agonist. Analgesia results also by inhibition of reuptake of nor-epinephrine and serotonin, endogenous neurotransmitters that modulate pain.[1] By suppressing the neuron signal to transmit the sensation of pain to the brain, it is centrally functioning synthetic opioid analgesic, the action by μ-opioid receptors. The approved indication of tramadol is for pain relief. Generally, non-steroidal anti-inflammatory drugs (NSAIDS) are known to cause gastric irritation. But we came across a rare adverse drug reaction hypoglycaemia. Published reports are available for other NSAIDS such as aspirin, indomethacin, Ibuprofen, naproxen. So far in our case we found tramadol to cause hypoglycaemia. Various other adverse drug reactions of tramadol mentioned in Table 1.

CASE HISTORY

A 56-year-old male patient admitted in tertiary care hospital for sudden onset of perspiration with uneasiness while working in office. The patient reported these symptoms while taking the first dose of Tab. Tramadol (50mg) (0-1-0). It was prescribed for toothache by the dentist. He was a known case of hypertension since 3 years. He is on a regular medicine Tab. Amlodipine (5mg) (1-0-0). On examination the vitals were found to be normal except random blood sugar (50mg/dL). The ECG and Troponin-I found to be normal. For the complaints he was started with intravenous D50W (dextrose 50%), IV. Pantoprazole (40mg) (stat) and IV. Ondansetron (2ml). After initiation of therapy his regular blood sugar level recovered within 30 min (110 mg/dL) and the patient was discharged.

DISCUSSION

Generally, NSAIDs are known to cause gastric irritation but we came across a rare adverse drug reaction hypoglycaemia. Previous reports are available for aspirin, indomethacin, ibuprofen, and naproxen. There are few reports of hypoglycaemia due to Tramadol. The mechanism of ADR is not clear till date but in our case, we found it by

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temporal relationship. The proposed mechanism of ADR is a reduction in hepatic gluconeogenesis and increased insulin secretion. Apart from that, it enhances insulin signalling which leads to hepatic sensitivity to insulin and stimulates glucose utilization by body muscles.[3] Various other drugs are also responsible to cause hypoglycaemia such as ondansetron, ramipril, propranolol, ciprofloxacin and other antibiotics.[4] As in our case ondansetron has been given as prophylactic treatment but it can increase chances of hypoglycaemia. It is mandatory to monitor diabetic patient who are on above mentioned drugs. A causality assessment has been performed to confirm the ADR which is mentioned in Table 2.

We should also monitor patient for their IV drugs which are given simultaneously to monitor for drug-drug interactions. However clinical pharmacists can play a significant role in such cases to aware patients about drug induced ADR and its monitoring. We can aware patients for non-pharmacology treatment: Eat or drink 15 to 20 g of fast-acting carbohydrates**.** These are sugary foods without protein or fat those are easily converted to sugar in the body. Try glucose powder, fruit juice, honey, and sugary candy. Recheck blood sugar levels after 15 min of treatment.[5] Clinical Pharmacists are also aware about PvPI (Pharmacovigilance Programme of India) where such ADRs are reported and used for signal generation. In this report, when a patient presents in the emergency department, he is treated with intravenous 50% dextrose. After this treatment the random blood sugar of the patient is under control. The combined drug of amlodipine (calcium channel blocker) for hypertension with tramadol significantly enhances the antinociceptive activity of tramadol. It helps to reduce toothache pain. From the case it can be concluded that the tramadol drug thought to be a safe drug for pain management can also lead to severe hypoglycaemia.

Table 1: Adverse Drug Reactions of Tramadol.[2]

Common Adverse Drug reactions	
Dermatologic	Flushing (7.7% to 15.8%), Pruritus (3% to 11.9%)
Gastrointestinal	Constipation (10% to 46%), Nausea (13% to 40%), Vomiting (3% to 17%), Xerostomia (1% to 10%)
Neurologic	Dizziness (7% to 33%), Headache (3% to 32%), Insomnia (1% to 10.9%), Somnolence (4% to 25%)
Serious Adverse Drug reactions	
Cardiovascular	Myocardial infarction (0.5% to less than 1%)
Endocrine	Hypoglycaemia (Very rare)
Gastrointestinal	Pancreatitis (0.5% to less than 1%)
Immunologic	Allergic reaction, Anaphylaxis
Neurologic	Seizure (Less than 1%)
Respiratory	Difficulty breathing, Dyspnoea (Less than 5%), Respiratory depression
Others	Serotonin syndrome (Less than 1%)

Table 2: Causality Assessment.

Scales	Stage
WHO	Probable
Naranjo's algorithm	Probable
Karch and lasagna algorithm	Probable
Predictability	Predictable
Severity	Severe (level 4B)

CONCLUSION

Appropriate counselling is required for treatment implementation and successful outcomes. It is necessary to perform and monitor dose titration. Close monitoring of any detrimental effects, as well as the potential for safety, should be done with caution. This also indicates that the clinical pharmacist has a broad role to play in therapeutic evaluation.

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CONFLICT OF INTREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

ADR: Adverse drug reaction; **NSAIDs:** non-steroidal anti-inflammatory drugs; **IV:** intravenous; **PVPI:** Pharmacovigilance Programme of India.

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