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Case Study

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TAPENTADOL INDUCED HYPOGLYCEMIA: A CASE REPORT

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ABSTRACT

Tapentadol is a centrally acting opioid analgesic with a dual mode of action that combines inhibition of noradrenaline reuptake and agonism of the mu-opioid receptor in one molecule. It is a helpful analgesic for treating acute, chronic, and neuropathic pain because to its dual mechanism of action. Side effects associated with tapentadol are often under reported and further studies and literatures are to be necessitated to establish causality. In this report, we discuss one of the rare adverse effects of Tapentadol-hypoglycemia. The use of Tapentadol as an analgesic have been increasing worldwide for pain relief, hence these life-threatening adverse effects of Tapentadol are to be monitored and borne in mind during its use in any treatment.

KEYWORDS: Tapentadol, Hypoglycemia, Opioids, Pain.

INTRODUCTION

Tapentadol is an opioid analgesic used to treat severe pain not responding to non-opioid medicines. It was approved by the FDA on Nov 20, 2008. It has been found to be an effective medication for a wide variety of chronic pain conditions, including back pain, cancer-related pain, and arthritic pain. Immediate release formulations of tapentadol is indicated for moderate to severe acute pain whereas its long acting formulation provides round the clock analgesic effect for relief for moderate to severe chronic pain.[1] It has also been found to have fewer gastrointestinal side effects than more traditional opioid-based therapies. More recently, tapentadol extended release has also been demonstrated to be effective in the management of painful diabetic neuropathy, an often debilitating condition affecting approximately one-third of all patients with diabetes.[2] It has a bioavailability of 32%, well distributed throughout the body, 97% is metabolised by glucuronidation and other enzymes and are 99% exclusively eliminated via kidneys through urine. The most common adverse reactions (>10%)include was nausea, dizziness, vomiting and somnolence along with various life threatening adverse reactions. As an opioid, tapentadol also exposes users to the risks of addiction, abuse, and misuse. Rare but serious side effects include serotonin syndrome and increased seizure risks.[3] There have been limited case reports describing hypoglycemia induced by opioids and resolved upon its discontinuation.[4] These incidents occurred in both patients with and without diabetes. Hypoglycemia ADR is of great concern since it can lead to many serious complications including neurocognitive dysfunction, retinal cell damage and vision loss, risk of falls, and other complications affecting health and quality of life.[5]

Hypoglycemia in non-diabetic patients is glucose <55 mg/dL [3.0 mmol/L][6]

Here we present a case report on tapentadol induced hypoglycemia.

CASE REPORT

A 87 year old female patient presented to the emergency department in the hospital with sudden onset decreased responsiveness and increased sweating since evening. Patient was found to have hypoglycemia (48mg/gl) on initial evaluation. While taking the medical history, patient had said that she had a similar episode on the previous day and went to nearby hospital where she was symptomatically management with IV fluids. She had also went to a nearby palliative centre for consultation where she was prescribed Tab. Tapentadol 50mg BD for 2 days for supposed relief from body pain and fatigue she had suffered back then. Patient had taken the medication in the morning as prescribed by the previous center after which she had experienced profuse sweating with fatigue which resulted in her admission at our hospital. Hence 25% dextrose and 1 pint dextrose with normal saline was given after which GRBS was 237 mg/dL. Patient also had a history of old cerebrovascular disease, systemic hypertension and dyslipidemia on treatment with oral clopidogrel, amlodipine and atorvastatin. Routine evaluation of Hba1c was 5.9% (prediabetes). USG abdomen scanning was done to rule out insulinomas or pancreatic lesions. GTT was done

post prandially and the results indicated prediabetes (Table 1). The FBS level was found to be within the normal limit (97 mg/dl). Tapentadol was found to be the sole cause of hypoglycemia.

Table 1:

Parameters (mg/dl)	Values	Normal range
Fasting blood glucose	97	70-99
Gtt 1 hr pp glucose	210	90-140
Gtt 2 hr pp glucose	190	90-140
Gtt 3 hr pp glucose	130	90-140
Gtt 4 hr pp glucose	108	90-140
Gtt 5 hr pp glucose	91	-

DISCUSSION

Tapentadol has dual mechanism of action; mu-opioid receptor agonism (MOR) and noradrenaline reuptake inhibition. It inhibits the ascending pain pathway due to mu- receptor agonism in the peripheral tissue, spinal cord and brain. It also potentiates the descending pain pathway by noradrenaline reuptake inhibition which in turn leads to analgesia through inhibition of alpha-2-receptors, through which it provides relief in patients with diabetic neuropathy. This dual mechanism contributes analgesia and opioid sparing effects. Its analgesic effect begins around 30 minutes for both acute nociceptive and chronic neuropathic pain. Till now the pathophysiology associated with opioids induced hypoglycemia remains poorly understood. It may be caused by increased glucose central utilisation as a result of stimulation of mu-receptors and certain serotonergic receptors. Some studies have been done to analyse and conclude possibility of opioid induced hypoglycemia, but most of them had not included tapentadol.[7][8]

Hypoglycemia ADR is of great concern since it can lead to many serious complications including neurocognitive dysfunction, retinal cell damage and vision loss, risk of falls, and other complications affecting health and quality of life. There are only 16 case reports of tapentadol induced hypoglycemia in Vigiaccess till date. The safety of tapentadol in real-world conditions remains poorly documented, particularly in at-risk patient subgroups and also in the ability to assess the risk associated with its residual serotonergic activity.

CONCLUSION

This case presents a unique incidence of hypoglycemia caused by Tapentadol. Thus if a patient is suspected to have an hypoglycemic episode, whether pre-diabetic or diabetic with medications, and is treated with an opioid analgesic, specifically tapentadol, it could be considered an hypoglycemia inducing agent after ruling out other organic causes. Hence in a growing trend of using opioid analgesics especially in elderly patients for pain relief of any cause, these life threatening adverse effects should be suspected and proper plasma glucose monitoring is essential. More studies are needed to establish causality.

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Conflicts of interest

There are no conflicts of interest.

Abbreviations

FDA: Food and Drug Administration
ADR: Adverse Drug Reaction
BD: Twice daily
GRBS: Glucose Random Blood Sugar
GTT: Glucose Tolerance Test
PP: Post Prandial
MOR: Mu-opioid receptor agonism

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