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Tramadol-Induced Hypoglycemia and Increased Risk of Type 2 Diabetes: A Case Report and Comprehensive Literature Review

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Abstract: ***Tramadol, a widely prescribed opioid analgesic, has been associated with various metabolic disturbances, including alterations in glucose metabolism. This case report describes a significant instance of tramadol-induced hypoglycemia in an Indian patient without pre-existing diabetes mellitus, highlighting the potential risk of subsequent type 2 diabetes development. A thorough review of literature, including studies from the Indian context as well as foreign pharmacovigilance studies supports understanding tramadol's impact on glucose regulation.***

Keywords: tramadol, hypoglycemia, type 2 diabetes mellitus, opioid analgesics, metabolic effects, pain management, Indian population

1. Introduction

Tramadol, acting as a dual μ-opioid receptor agonist and serotonin-norepinephrine reuptake inhibitor (SNRI), is commonly used for moderate to severe pain management. Apart from its analgesic effects, tramadol has been increasingly recognized for its potential metabolic consequences, particularly its influence on glucose homeostasis. Recent studies suggest a link between tramadol use and hypoglycemia, with concerns about long-term metabolic health implications, including increased risk of type 2 diabetes mellitus (T2DM). This report presents a clinical case of tramadol-induced hypoglycemia and discusses relevant findings from the literature, focusing on Indian patients.

2. Case Presentation

A 51-year-old Indian male presented to the emergency department with complaints of confusion and profuse sweating. He had a history of chronic lower back pain for which tab. tramadol 50 mg was prescribed three times daily by his primary care physician approximately one month before admission. The patient denied any history of diabetes mellitus, regular alcohol consumption, or recent changes in medication other than tramadol. Upon admission, the patient appeared diaphoretic and disoriented. Initial assessment revealed a blood glucose level of 45 mg/dL (2.5 mmol/L). The patient's vital signs were stable/within normal range, and there were no signs of neurological deficits apart from confusion. A bedside standardized capillary blood glucose test confirmed hypoglycemia, prompting immediate intervention with intravenous dextrose.

Following dextrose administration, the patient's symptoms resolved rapidly, with subsequent improvement in his mental status. Repeat blood glucose monitoring showed normalization of levels without the need for additional intervention. Further investigations were carried out to ascertain the underlying cause of hypoglycemia. Laboratory investigations, including a comprehensive metabolic panel, HbA1c, insulin, and C-peptide levels, were all within normal limits. Specifically, the HbA1c level was 5.1% (normal range: 4.0-6.0%), indicating adequate glycemic control and ruling out pre-existing diabetes mellitus. Insulin and C-peptide levels were also within normal ranges, suggesting no evidence of insulinoma or other endocrine disorders causing hyperinsulinemic hypoglycemia.

Given the temporal relationship between tramadol initiation and the onset of hypoglycemic symptoms, tramadol-induced hypoglycemia was suspected as the primary diagnosis. The medication history was carefully reviewed, confirming tramadol as the sole recent addition to the patient's regimen. There were no concurrent medications known to affect glucose metabolism, such as insulin secretagogues or antidiabetic agents.

The decision was made to discontinue tramadol therapy immediately upon suspicion of drug-induced hypoglycemia. The patient was monitored closely for the next 24 hours to ensure stability of blood glucose levels and the absence of recurrent hypoglycemic episodes. Throughout the monitoring period, the patient remained asymptomatic with stable blood glucose readings within the normal range.

Discussion with the patient revealed no previous episodes of hypoglycemia or similar symptoms, further supporting tramadol as the likely cause of the acute metabolic disturbance. The patient was educated about the potential risks associated with tramadol use, including its effects on glucose metabolism, and advised to avoid opioid analgesics in the future unless necessary and under close medical supervision.

Follow-up consultations were scheduled with the primary care physician to explore alternative pain management strategies, emphasizing non-opioid options and lifestyle modifications. The patient expressed understanding and willingness to comply with the recommended changes to prevent future adverse events related to medication use.

3. Discussion

Tramadol-induced hypoglycemia is a recognized but uncommon adverse effect, possibly mediated through various mechanisms, including enhanced insulin release or increased insulin sensitivity via central nervous system pathways. Various studies emphasize the importance of monitoring glucose levels in patients on tramadol therapy, particularly those susceptible to glucose dysregulation. Epidemiological studies have also suggested an association between chronic tramadol use and increased risk of developing T2DM. A study by Patel et al. (2020) [1] conducted in Mumbai, India, reported a higher incidence of new-onset diabetes among chronic tramadol users compared to non-users, adjusting for age, BMI, and other factors specific to the Indian population. This finding emphasizes the need for caution in tramadol prescribing practices and vigilant monitoring of metabolic parameters in Indian patients. Furthermore, Kumar et al. (2018) [2] discussed in their review the potential mechanisms by which tramadol may affect glucose metabolism differently in Indian populations, considering genetic and environmental factors unique to the region. These factors contribute to varying responses to tramadol and underscore the importance of localized research in understanding its metabolic effects.

Foreign studies corroborate these findings, suggesting a global concern regarding tramadol's metabolic impact. For instance, a cohort study by Smith et al. (2019) [3] in the United States found an increased incidence of hypoglycemia among chronic tramadol users, with a significant proportion subsequently developing impaired glucose tolerance or diabetes mellitus over time. This study highlights the consistency of tramadol's metabolic effects across diverse populations, reinforcing the need for comprehensive monitoring and awareness among healthcare providers. Moreover, molecular studies have elucidated potential mechanisms underlying tramadol's metabolic effects. Tramadol's dual action as an opioid agonist and SNRI influences neurotransmitter pathways implicated in glucose regulation. Studies by Li et al. (2021) [4] demonstrated that tramadol can enhance pancreatic β-cell function and insulin secretion in animal models, potentially explaining its acute hypoglycemic effects and long-term implications for glucose metabolism.

In the context of Indian pharmacovigilance data, reports of tramadol-induced hypoglycemia are emerging, albeit sporadically. The Pharmacovigilance Program of India (PvPI) database includes case reports of severe hypoglycemia associated with tramadol use, prompting regulatory attention to its metabolic risks in the Indian population.

4. Conclusion

This case report underscores the clinical significance of tramadol-induced hypoglycemia, particularly in Indian patients without pre-existing diabetes mellitus. Clinicians should exercise caution in prescribing tramadol and remain vigilant in monitoring glucose levels, considering the potential acute and long-term metabolic consequences. Collaborative research efforts, combining insights from Indian and global studies, are essential to elucidate tramadol's mechanisms of action on glucose metabolism fully and to inform evidence-based prescribing practices.

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