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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/20816
DOI URL: http://dx.doi.org/10.21474/IJAR01/20816

RESEARCH ARTICLE

WORSENING OF NON-DIABETIC HYPOGLYCEMIA IN HEMODIALYSIS-DEPENDENT PATIENT: A CASE REPORT

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Manuscript Info

Manuscript History
Received: 17 February 2025
Final Accepted: 20 March 2025
Published: April 2025

Abstract

Background: Hypoglycemia in non-diabetic hemodialysis patients is a rare but clinically significant phenomenon. Patients with end-stage renal disease (ESRD) are particularly susceptible to glucose dysregulation due to factors such as altered insulin metabolism, impaired renal clearance, and medication effects. Calcimimetic agents, including cinacalcet and etelcalcetide, are widely used to manage secondary hyperparathyroidism in ESRD patients. However, their potential impact on glucose metabolism remains poorly understood. This case report describes a 64-year-old male with ESRD who experienced frequent and severe hypoglycemic episodes following the transition from oral cinacalcet to intravenous etelcalcetide.

Case Presentation: A 64-year-old male with ESRD on hemodialysis three times per week developed recurrent and severe hypoglycemia after switching from oral cinacalcet to intravenous etelcalcetide. Prior to the switch, the patient had a history of infrequent, mild hypoglycemia. However, after initiating etelcalcetide, his blood glucose levels dropped as low as 49 mg/dL, and he experienced a hypoglycemic seizure with a blood glucose level of 53 mg/dL. Following a switch back to oral cinacalcet, the frequency and severity of hypoglycemic episodes returned to baseline.

Conclusion: While a direct causal relationship between intravenous etelcalcetide and hypoglycemia cannot be definitively established, the temporal association and clinical course suggest a potential link. This case highlights the need for vigilant monitoring of glucose levels in hemodialysis patients on calcimimetic therapy, particularly during transitions between formulations. Further research is warranted to explore the mechanisms underlying this association.

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Introduction:-

Hypoglycemia in non-diabetic hemodialysis patients, though uncommon, is a potentially life-threatening condition that requires careful clinical attention. In patients with ESRD, glucose homeostasis is often disrupted due to factors such as altered insulin metabolism, impaired renal clearance, and the effects of medications (1,2). While hypoglycemia is typically associated with diabetes, non-diabetic hemodialysis patients may also experience hypoglycemic events, which are frequently underrecognized or misattributed to other causes (3).

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Calcimimetic agents, such as cinacalcet and etelcalcetide, are integral to the management of secondary hyperparathyroidism in ESRD patients. These medications act by enhancing the sensitivity of the calcium-sensing receptor (CaSR) on parathyroid cells, thereby reducing parathyroid hormone (PTH) secretion and lowering serum calcium levels (4). However, calcium plays a critical role in insulin secretion, and disturbances in calcium homeostasis may influence glucose metabolism. Specifically, hypocalcemia induced by calcimimetics could impair insulin release, potentially leading to hypoglycemia in susceptible individuals (5). Although the association between calcimimetic therapy and hypoglycemia remains unclear, emerging case reports suggest that intravenous formulations, such as etelcalcetide, may be more likely to contribute to hypoglycemic events (6).

This case report describes a 64-year-old male with ESRD who developed frequent and severe hypoglycemia following the transition from oral cinacalcet to intravenous etelcalcetide. We explore the potential mechanisms underlying this phenomenon and discuss the clinical implications for managing hypoglycemia in hemodialysis patients on calcimimetic therapy.

Case Presentation

A 64-year-old male with ESRD on hemodialysis three times per week was referred to the endocrinology clinic for evaluation of recurrent hypoglycemia. His medical history included tertiary hyperparathyroidism, treated with oral cinacalcet, and hypertension, controlled with ACE inhibitors and calcium channel blockers. The patient had no history of diabetes or prior severe hypoglycemic episodes.

Six months prior to presentation, the patient's oral cinacalcet was replaced with intravenous etelcalcetide to improve control of tertiary hyperparathyroidism. Shortly after the transition, he began experiencing frequent episodes of hypoglycemia, with blood glucose levels as low as 49 mg/dL. The patient also experienced a hypoglycemic seizure with a blood glucose level of 53 mg/dL. To mitigate symptoms, he began consuming 8–10 cups of heavily sweetened milk daily.

Laboratory findings at the time of referral included:

- Parathyroid hormone (PTH): 193pmol/L (Reference 1.59-7.23 pmol/L)
- Adjusted calcium (Ca): 2.23 mmol/L (Reference 2.10-2.55 mmol/L)
- Phosphate (PO4): 1.92 mmol/L (Reference 0.74-1.52 mmol/L)
- Magnesium (Mg): 0.83 mmol/L (Reference 0.66-1.07 mmol/L)
- Hemoglobin A1c: 26 mmol/mol (Reference 20.0-42.0 mmol/mol)
- Blood glucose (BS): Recorded as low as 49 mg/dL during dialysis and at home

An intermittent continuous glucose monitoring (iCGM) system was initiated and reviewed to assess glucose trends. The iCGM data revealed significant fluctuations in blood glucose levels, with marked hypoglycemia occurring more frequently after the switch to etelcalcetide.

After consultation with his nephrologist, the patient was switched back to oral cinacalcet. Following this adjustment, the frequency and severity of hypoglycemic episodes returned to baseline, as confirmed by subsequent iCGM readings.*

Discussion:-

Review of Literature: Hypoglycemia in non-diabetic hemodialysis patients is a multifactorial condition influenced by alterations in insulin metabolism, impaired renal clearance, and disturbances in calcium and phosphate balance (1). Calcimimetic agents, such as cinacalcet and etelcalcetide, are commonly used to manage secondary hyperparathyroidism in ESRD patients. These medications reduce PTH secretion and lower serum calcium levels by enhancing CaSR sensitivity (4). However, calcium is a critical regulator of insulin secretion, and hypocalcemia induced by calcimimetics may impair insulin release, potentially contributing to hypoglycemia (5).

Potential Role of Calcimimetic Therapy:

The worsening of hypoglycemia in this patient following the transition to intravenous etelcalcetide suggests a potential link between the medication and glucose dysregulation. Intravenous formulations may exert a more pronounced effect on calcium homeostasis, thereby increasing the risk of hypoglycemia in susceptible individuals (6). This case underscores the importance of considering medication-related effects when evaluating hypoglycemia in hemodialysis patients.

Clinical Implications

This case highlights the need for close monitoring of glucose levels in hemodialysis patients on calcimimetic therapy, particularly during transitions between formulations. Clinicians should be aware of the potential for hypoglycemia and consider alternative therapies or dose adjustments in patients experiencing recurrent episodes.

Conclusion

This case illustrates the complexity of managing hypoglycemia in non-diabetic hemodialysis patients, particularly those receiving calcimimetic therapy. While the association between intravenous etelcalcetide and hypoglycemia remains speculative, the temporal relationship observed in this patient warrants further investigation. Clinicians should remain vigilant when prescribing calcimimetics and consider their potential impact on glucose metabolism.

Declarations

- Acknowledgments: None
- Conflict of Interest: Author declares no competing interests.
- Ethical Statement: This manuscript adheres to the ethical standards of the Helsinki Declaration of 1964 and its later amendments.
- Informed Consent: Written informed consent was obtained from the patient for publication of this case report.

Footnotes

*iCGM data were reviewed and documented during clinic encounters; however, due to a technical malfunction of the iCGM reader, the reports were unavailable at the time of manuscript preparation.

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