Ketamine-Induced Syndrome of Inappropriate Antidiuretic Hormone Secretion: A Case Report

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Abstract

Ketamine is a phencyclidine-derived dissociative anaesthetic used in the UK currently for the Induction and maintenance of anaesthesia for procedures and diagnostic manoeuvrers. The prevalence of ketamine misuse in England and Wales was at an all-time high in 2019 - 2020, at 0.8%.[1] The younger age group (16 to 24 years of age) seems to be the most avid users: 3.2% of them used ketamine in that period. Despite its clinical utility, ketamine possesses a significant potential for abuse and dependence, which may precipitate a spectrum of adverse outcomes, including neurotoxicity, psychiatric disturbances, multisystem dysfunction, and alterations in biochemical homeostasis. This report is based on the case of a 30-year-old healthy male who developed severe hyponatremia, confusion, and seizures following recreational ketamine use. Laboratory findings confirmed SIADH, and the patient was treated successfully with fluid restriction and hypertonic saline. This case highlights the potential of ketamine to disrupt water and sodium balance, through central mechanisms involving ADH dysregulation. Clinicians should consider ketamine as a possible cause of acute hyponatremia, especially given its increasing medical and recreational use

Keywords: SIADH (Syndrome of Inappropriate Antidiuretic Hormone), ADH (Antidiuretic hormone, Hyponatraemia, Ketamine, NMDA Receptor agonist, Electrolyte-imbalance, ICU (Intensive care unit), Osmolarity.

Introduction

Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) is a clinical disorder characterized by the excessive release of antidiuretic hormone (ADH), leading to impaired water excretion, resulting in hyponatremia, fluid retention, and electrolyte imbalances. The condition is frequently associated with various underlying causes such as malignancies, central nervous system disorders, pulmonary diseases, and certain medications. Ketamine, a dissociative anaesthetic and analgesic, has increasingly been utilized for its anaesthetic properties, for pain management, and in more recent years, in the treatment of depression.[1] Ketamine's interaction with the central nervous system may also play a role in triggering SIADH, though ketamine-induced SIADH remains a rare and underreported phenomenon in the literature.[2]

This case report presents a rare instance of ketamine induced SIADH in a young, otherwise healthy male, which highlights the importance of recognising this potentially serious adverse effect in clinical practice. The case aims to improve awareness of this condition among clinicians, especially with the growing recreational use of ketamine and its increasing use in medical treatments.

Case Presentation

A 30-year-old male, with no significant past medical history or previous psychiatric disorders, presented to the emergency department with confusion, generalised weakness, and a witnessed seizure episode following the recreational use of ketamine. The patient was a regular user of recreational drugs but had no history of chronic substance abuse. His symptoms began approximately 12 hours after taking a high dose of ketamine at a social gathering.

On examination, the patient was disoriented and lethargic. Neurological assessment revealed no focal deficits, but signs of generalized weakness were noted. Initial

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laboratory results revealed severe hyponatremia, with a serum sodium concentration of 104 mmol/L (normal range: 135-145 mmol/L). Further investigations revealed a low serum osmolality of 245 mOsm/kg (normal range: 275-295 mOsm/kg), and elevated urine osmolality of 630 mOsm/kg, consistent with SIADH. His urine sodium concentration was also elevated at 78 mmol/L (normal range: 20-40 mmol/L). These findings were consistent with SIADH induced by the ketamine use.

The patient was promptly admitted to the intensive care unit (ICU) for close monitoring and management of severe hyponatremia. Treatment included fluid restriction and administration of hypertonic saline (3% NaCl) to gradually correct the sodium imbalance. Over the course of several days, the patient's serum sodium level normalised, and his clinical symptoms improved. Repeat neurological assessment revealed resolution of confusion and weakness, and the patient was discharged in stable condition after 5 days in the ICU. Follow-up after discharge showed no recurrence of symptoms.

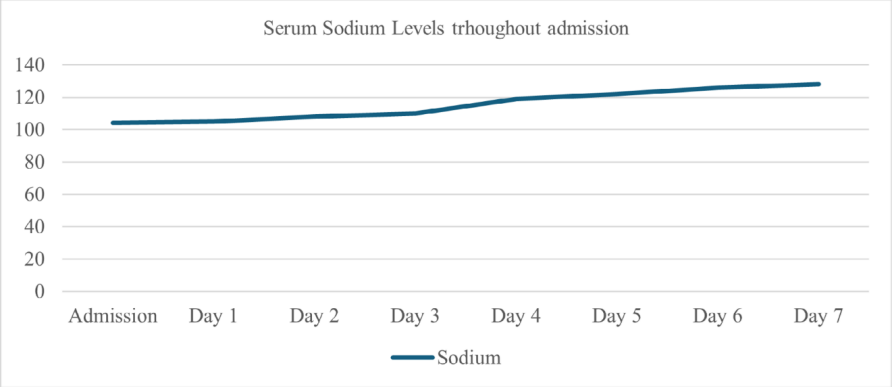

Figure 1: Sodium Trend Chart.

Discussion

SIADH is a well-recognized cause of hyponatremia, and its clinical presentation is often subtle, initially manifesting as nonspecific symptoms such as nausea, headache, and confusion. In severe cases, it can lead to seizures, coma, and death. Common aetiologies of SIADH include malignancy (such as small-cell lung cancer), CNS disorders (such as stroke, meningitis, and head trauma), and medications, including selective serotonin reuptake inhibitors (SSRIs), anticonvulsants, and antipsychotics.[3] However, ketamine-induced SIADH is rarely reported in the literature, making this case particularly interesting. The pathophysiological mechanisms by which ketamine induces SIADH are still not fully understood. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, and its central effects are believed to occur via interaction with the glutamatergic system. One proposed mechanism for ketamine-induced SIADH is that ketamine disrupts normal hypothalamic-pituitary function, leading to inappropriate secretion of ADH.[4] The NMDA receptor antagonism may interfere with the regulation of water balance through its effects on vasopressin release from the posterior pituitary.[5] Furthermore, ketamine may also activate the sympathetic nervous system, which may indirectly affect water retention by increasing renin angiotensin-aldosterone system (RAAS) activity, which in turn promotes water reabsorption in the kidneys.[2] Another possible explanation is that ketamine induces a state of relative hypoxia in the brain, potentially triggering the release of ADH as a response to hypovolemia or low blood pressure, even in the absence of genuine dehydration.[5] This is supported by the finding of low serum osmolality and high urine osmolality in our patient, consistent with SIADH.

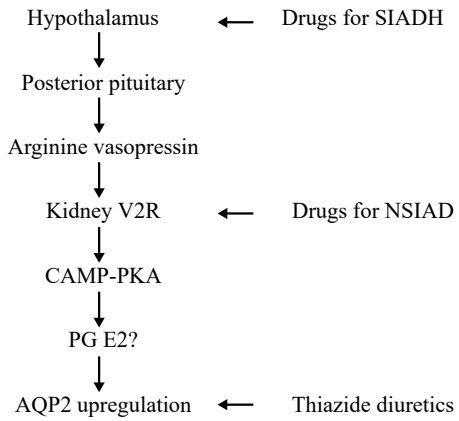

Figure 2: Pathophysiology of Drug-induced Hyponatremia.

Several studies have documented the association between ketamine and hyponatremia. van Bockxmeer *et al*.[2] reported a case of ketamine-induced SIADH in a patient with persistent lumbar pain who was receiving ketamine infusion therapy for pain management. Similarly, Kumar *et al*.[4] described a case of ketamine-induced hyponatremia and SIADH in a patient undergoing treatment for depression. These reports suggest that both recreational and therapeutic ketamine use can precipitate SIADH in vulnerable individuals.[6] Furthermore, it is important to note that recreational users of ketamine, who may take large doses intermittently, could be at higher risk for developing acute electrolyte disturbances.[4] In addition to

ketamine's direct effects, it is important to consider other factors that may predispose individuals to SIADH. For example, concurrent use of other drugs or pre-existing medical conditions may increase the likelihood of SIADH. However, our case involved a patient with no significant comorbidities or polypharmacy, which makes ketamine the most likely trigger for his hyponatremia.

Conclusion

This case illustrates a rare but significant adverse effect of ketamine-induced SIADH resulting in life-threatening hyponatremia. It serves as an important reminder for clinicians to consider drug-induced SIADH in patients who present with unexplained electrolyte abnormalities e.g. hyponatremia, especially in those with a history of ketamine use. Given the growing use of ketamine, both medically and recreationally, clinicians should be vigilant for this rare but potentially life-threatening complication. Prompt recognition and appropriate management of SIADH are crucial to avoid severe neurological complications, including seizures and coma. It is imperative that further research is conducted to elucidate the precise mechanisms behind ketamine-induced SIADH and to better understand which patient populations are most at risk.[1] Clinicians should be particularly aware of this adverse effect in patients using ketamine for chronic pain management or as part of psychiatric treatments. As the clinical use of ketamine continues to expand, it is essential that healthcare providers are aware of the potential for SIADH and are prepared to manage it effectively.

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