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CASE REPORT

Silent Danger of Quetiapine Overdose Leading to Rhabdomyolysis: A Case Report

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ABSTRAK

Quetiapine merupakan sejenis antipsikotik atipikal yang mempunyai pelbagai jenis kesan sampingan, termasuk komplikasi yang jarang tetapi serius seperti rhabdomiolisis. Laporan ini membincangkan seorang wanita berusia 32 tahun yang mempunyai masalah kemurungan dan telah mendapatkan rawatan di Jabatan Kecemasan selepas cubaan membunuh diri dengan pengambilan dos ubat berlebihan iaitu 8 mg clonazepam dan 4800 mg quetiapine. Beliau mengalami simptom pening, mual, pengsan, denyutan jantung laju serta peningkatan tahap urea dan kreatinin berbanding bacaan asalnya. Semasa di hospital, beliau mengadu sakit seluruh badan, terutamanya pada anggota bawah dan aras kreatin kinase (CK) beliau meningkat kepada 10,691 IU/L. Terapi cecair intravena berjaya menurunkan tahap CK dan fungsi ginjal kembali turun ke bacaan asal. Beliau dibenarkan keluar dari hospital dalam keadaan yang stabil dan disarankan untuk mengikuti temujanji susulan di klinik psikiatri. Antagonisma quetiapine pada reseptor serotonin, terutamanya 5-HT_{2A}, boleh mengubah kebolehtelapan membran sel otot, menyumbang kepada peningkatan tahap CK. Walaupun pada dos terapeutik iaitu 800 mg/hari, quetiapine boleh meningkatkan tahap CK, namun disebabkan ujian CK tidak dibuat secara rutin untuk semua pesakit yang datang ke Jabatan Kecemasan, diagnosis rhabdomiolisis menjadi lewat. Kes ini menekankan keperluan untuk pemantauan yang teliti dan mengesyorkan penggabungan ujian CK dalam penilaian rutin dos berlebihan quetiapine, walaupun tanpa gejala yang ketara untuk mencegah komplikasi serius rhabdomiolisis.

***Kata kunci**: Kreatinin kinase; quetiapine; rhabdomiolisis; terlebih dos*

ABSTRACT

Quetiapine, an atypical antipsychotic, has various side effects, including the rare but severe complication of rhabdomyolysis. This report detailed a 32-year-old female with persistent depressive disorder (PDD) and major depressive episodes (MDE), who presented to the Emergency Department after a parasuicidal attempt involving an overdose of 8 mg of clonazepam and 4800 mg of quetiapine. She exhibited symptoms of dizziness, nausea and transient loss of consciousness, along with mild tachycardia, elevated urea and creatinine levels from her baseline. During

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hospitalisation, she complained of generalised body aches, especially in the lower limbs, and her creatine kinase (CK) level peaked at 10,691 IU/L. Intravenous fluid therapy led to a reduction in CK levels and normalisation of renal function, allowing for a stable discharge and psychiatric clinic follow-up. Quetiapine's antagonism of serotonin receptors, particularly 5-HT_{2A}, may alter muscle cell membrane permeability, contributing to elevated CK levels. Even at therapeutic doses up to 800 mg/day, quetiapine can elevate CK levels, yet routine CK testing is not standard, which can delay the diagnosis of quetiapine-induced rhabdomyolysis. This case underscores the necessity for vigilant monitoring and advocates for incorporating CK testing in the routine evaluation of quetiapine overdose, even without significant symptoms, to prevent severe complications of rhabdomyolysis.
Keywords: Creatinine kinase; overdose; quetiapine; rhabdomyolysis

INTRODUCTION

Quetiapine, an atypical antipsychotic, is widely prescribed for the treatment of schizophrenia, mania, and as an adjunct therapy in managing depression (Maan et al. 2024). This medication is available in both extended-release (ER) and immediate-release (IR) formulations, allowing for flexible dosing based on patient needs (Maan et al. 2024). Optimal therapeutic outcomes with quetiapine are typically observed at dosages ranging from 300 mg to 800 mg/day, with the maximum recommended dose of 800 mg/day for the IR formulation, administered in two or three divided doses (Maan et al. 2024). Despite its effectiveness, quetiapine is associated with a range of adverse effects. Common side effects include neuroleptic malignant syndrome, somnolence, orthostatic hypotension, dizziness, and prolonged QT intervals, which can lead to Torsades de Pointes, a potentially life-threatening arrhythmia (Maan et al. 2024). Although rhabdomyolysis is not a widely recognised adverse effect of quetiapine, a study conducted in the United States highlighted that out of 673 cases of rhabdomyolysis, 71 (10.5%) involved patients on antipsychotics, with quetiapine being the most frequently implicated drug (Packard et al. 2014). In this case report, we documented a rare instance of rhabdomyolysis induced by a quetiapine overdose, underscoring the need for heightened awareness of this potential complication among clinicians.

CASE REPORT

A 32-year-old female presented to the Emergency Department (ED) following a suicide attempt via drug overdose. She had a known history of persistent depressive disorder (PDD) with a major depressive episode (MDE) and was on treatment and care of a psychiatric clinic. On the day of the incident, she ingested 8 mg of clonazepam and 4800 mg of quetiapine IR tablets, an amount six times the recommended maximum daily dosage. Shortly after ingestion, she experienced dizziness, nausea and eventually fainted.

Upon arrival at the ED, the patient was conscious with a heart rate ranging from 100 to 110 beats/minute. Her blood pressure, respiratory rate and pulse oximetry readings were within normal limits, and she was afebrile. A physical examination did not reveal any significant abnormalities. Initial blood investigations, including a full blood count (FBC) and electrolytes were within normal ranges. However, her renal profile (RP) showed a mild elevation from her baseline, with a urea

level of 7.1 mmol/L and a creatinine level of 96.9 µmol/L, compared to her previous baseline of urea 1.9 mmol/L and creatinine 65.4 µmol/L. Blood gas analysis did not indicate acidosis, and her serum lactate levels were not elevated. Electrocardiography revealed a sinus rhythm with no QT prolongation.

The patient received thorough evaluations from both the medical and psychiatry teams. Her antidepressant medications (clonazepam and quetiapine) were temporarily discontinued. She was administered 2 litres of intravenous normal saline over 24 hours for hydration and subsequently admitted to a general medical ward. On the second day of hospitalisation, the patient reported generalised body aches, particularly in her bilateral lower limbs, although she remained ambulatory and neurological examinations were unremarkable. Further investigations revealed a significantly elevated creatine kinase (CK) level, peaking at 10,691 IU/L, indicative of possible rhabdomyolysis. Urine myoglobin was not tested due to the unavailability of the test. The intravenous fluid regime was subsequently increased to 3 litres of intravenous normal saline 0.9% per day for fluid therapy (125 mL/h). Over the next four days of her hospital stay, her CK levels gradually decreased (from 10,691 IU/L to 6,360 IU/L, 3,974 IU/L and 2,373 IU/L prior to discharge), and her renal function returned to baseline (urea 2.5 mmol/L and creatinine 55.5 mol/L). The patient was eventually discharged in stable condition and given a follow-up outpatient appointment at the psychiatric clinic, ensuring continued care and monitoring.

DISCUSSION

Quetiapine reaches its peak plasma concentration within 1 to 2 hours after oral administration and has a half-life of approximately 7 hours, primarily metabolised and excreted via hepatic pathways (Maan et al. 2024). Its pharmacological effects are largely mediated through the antagonism of serotonergic 5-HT_2 and dopaminergic D2 receptors, with additional antidepressant activity linked to its 5-HT_{2A} and 5-HT_7 antagonistic properties (Maan et al. 2024). The antagonism of serotonin receptors, particularly 5-HT_{2A}, has been implicated in altering muscle cell membrane permeability, potentially contributing to elevated serum CK levels, a marker for muscle damage (Meltzer 2000).

Rhabdomyolysis is a serious condition characterised by the breakdown of muscle tissue, leading to the release of intracellular contents into the bloodstream. Clinical manifestations include myalgia, muscle weakness, swelling, and myoglobinuria, which presents as dark-coloured urine (Khan 2009). Laboratory diagnosis primarily relies on measuring serum CK levels and, where available, urine myoglobin. Serum CK levels begin to rise to 2-12 hours post-injury, peak within 3-5 days and typically normalise over 6-10 days (Khan 2009). In the absence of myoglobin testing, serum CK serves as the main diagnostic tool for rhabdomyolysis in many clinical settings.

In the case presented, the initial ED assessment did not suggest neuroleptic malignant syndrome (NMS), as the patient lacked fever, arrhythmia, altered mental status, muscle rigidity or other hallmark symptoms. Consequently, serum CK levels were not tested initially, as the patient did not report muscle-related complaints or dark-coloured urine at that time. It was only after the patient later reported myalgia that rhabdomyolysis was suspected, leading to the discovery of significantly elevated CK levels. Other potential risk factors for rhabdomyolysis, such as prolonged immobilisation, intramuscular

injections, use of restraints, or strenuous exercise were ruled out, strongly suggesting that the rhabdomyolysis was induced by the quetiapine overdose.

The management of rhabdomyolysis is consistent across both traumatic and non-traumatic causes. Patients with CK levels exceeding 5,000 IU/L are at high risk for acute renal failure and require aggressive intravenous fluid hydration to maintain adequate intravascular volume and urine output (Yang et al. 2020). In the current case, although the patient presented with high CK levels, vigilant daily monitoring of renal function, combined with intravenous fluid hydration and adequate oral intake resulted in the gradual normalisation of CK levels and renal function. This underscores the importance of early detection and proactive management in preventing serious complications associated with rhabdomyolysis.

Despite the absence of direct studies linking quetiapine to rhabdomyolysis, case reports suggest that quetiapine can induce this condition at both therapeutic and overdose levels. The onset of symptoms and timing of presentation varies widely, from days to months (Heng et al. 2024; Packard et al. 2014), complicating the correlation between dosage and CK levels. In this case, our patient ingested six times the maximum daily quetiapine dose and developed rhabdomyolysis the following day, with a CK level of 10,691 IU/L. Nonetheless, this case highlights the need for cautious CK monitoring, particularly in overdose scenarios, as even moderate CK elevations can lead to adverse outcomes if undetected. The variability in symptom onset and presentation further emphasises the importance of individualised monitoring for patients on quetiapine, especially when overdose is involved.

CONCLUSION

This case adds to the growing body of evidence highlighting the risk of rhabdomyolysis associated with quetiapine, particularly in overdose situations. Early detection and intervention are essential to prevent the progression of rhabdomyolysis and related severe complications, thereby improving patient outcomes. Although there is no standardised guideline for CK testing in quetiapine use or overdose, and not all patients will develop rhabdomyolysis, this case underscores the importance of vigilance in recognising this potentially life-threatening complication associated with quetiapine.

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