



Case Report

Hyperglycemia and late onset seizures associated with quetiapine overdose

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ABSTRACT

Quetiapine is an atypical antipsychotic agent which is being increasingly prescribed for psychotic disorders because it has fewer side effects than other antipsychotics. Consequently, overdoses of quetiapine have gained attention, given its widespread use. We report a 31-year-old man with schizophrenia who allegedly ingested 4 g of immediate-release quetiapine. He presented with common manifestations of quetiapine overdose such as sinus tachycardia, dry mouth and mucosa, hypotension, and coma. He also had hyperglycemia and late onset seizures (>24 hours post ingestion) which are not frequently reported. The patient was given activated charcoal while hypotension was managed with fluid resuscitation and intravenous noradrenaline. Intravenous diazepam and phenytoin were given for the seizure. The patient recovered without residual complications. Although a quetiapine overdose can result in serious medical complications, it can be managed by early intervention, mainly supportive care and close monitoring. Copyright © 2012, Buddhist Compassion Relief Tzu Chi Foundation. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

Quetiapine is a dibenzothiazepine atypical antipsychotic agent which has a higher affinity for 5-hydroxytryptamine (HT)₂ receptors than dopamine (D)₂ receptors [1,2]. Thus, it has fewer extrapyramidal side effects than typical antipsychotics and has become widely prescribed for schizophrenia and bipolar disorders. Nevertheless, an overdose of quetiapine has serious medical consequences although the fatality rate is low [2]. Previous case series and case reports revealed that central nervous system depression and tachycardia are more common clinical manifestations of quetiapine overdose while hypotension, respiratory depression, prolonged QT and QRS intervals and seizures are infrequent [1–5]. Hyperglycemia and late-onset seizures are even less documented and can only be found in a very few case reports [4,5]. Here we describe a case of quetiapine overdose manifesting with hyperglycemia and late-onset seizures.

2. Case report

A 31-year-old, approximately 60 kg man with schizophrenia allegedly ingested 40 tablets of 100-mg immediate-release

quetiapine (total dose 4 g). He was found unresponsive at home and was subsequently admitted to the casualty unit. He had been prescribed quetiapine 300 mg per day for schizophrenia and had no other medical diseases.

The patient presented with a Glasgow Coma Scale score of 3, dry mouth and mucosa, hyperglycemia (random blood glucose level of 17.0 mmol/L) and a respiratory rate of 16 breaths per minute. He was hemodynamically unstable with a blood pressure of 97/42 mmHg which later decreased to 73/30 mmHg. The patient was given 50 g of activated charcoal and fluid resuscitation. He was then transferred to the general intensive care unit (GICU) for respiratory support and close observation. Later that day, he developed sinus tachycardia at 121 beats per minute. A complete blood count showed a slightly low hematocrit of 37.9%, normal white blood count of $9.4 \times 10^3/\mu\text{L}$ and normal platelet count of $222 \times 10^3/\mu\text{L}$. The renal profile showed a calculated creatinine clearance of 113.54 mL/min, while serum electrolyte analysis revealed a borderline low sodium level of 132 mmol/L, potassium of 3.6 mmol/L, and magnesium of 0.8 mmol/L. The patient's coagulation values were normal with a prothrombin time of 11.0 seconds, activated partial thromboplastin time of 25.0 seconds, and international normalized ratio of 1.0. Liver function tests showed normal values for alanine aminotransferase (17 U/L) and alkaline phosphatase (47 U/L). Levels of creatine kinase (171 U/L), lactate dehydrogenase (214 U/L), and aspartate aminotransferase (24 U/L) were elevated. His arterial blood gas profile showed slight metabolic acidosis (pH 7.31, pCO₂ 44 mmHg and HCO₃⁻ 22.2 mmol/L), which normalized on Day 2. His blood

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Table 1
Random blood glucose level throughout hospital admission.

Day of admission	Random blood glucose level (mmol/L)
On admission	17.0
1	5.4
2	6.4
3	7.6
4	6.4
5	7.7
6	7.2

glucose level normalized within one day of GICU admission (Table 1).

On Day 2, sinus tachycardia was resolved and no QT interval prolongation was seen. However, his chest radiograph showed collapse of the right upper lung and he had a generalized tonic clonic seizure (27 hours after hospitalization) which lasted for 45 seconds. The seizure was treated with 5 mg of intravenous diazepam immediately, followed by 5 mg three times daily and 1 g of intravenous phenytoin immediately, and then 100 mg three times daily. The seizure responded to the treatment and the patient remained seizure free thereafter. The next day, his blood pressure was persistently low (99/50–100/60 mmHg) despite fluid challenge, and 0.1 µg/kg/minute of intravenous noradrenaline was subsequently given. On Day 4, his right upper lung was successfully re-expanded with chest physiotherapy. His blood pressure normalized and the noradrenaline was discontinued. On Day 6, the intravenous phenytoin was discontinued and he was transferred to the general ward.

3. Discussion

Quetiapine is an atypical antipsychotic which is increasingly prescribed to a population prone to overdose [6]. Overdoses have been reported to be less lethal than those from typical antipsychotic agents [6,7]. Quetiapine has a high inhibitory affinity for serotonergic 5-HT_{2A} receptors and a moderate affinity for dopamine D₂-receptors, which mediate its antipsychotic actions with minimal or no extrapyramidal effects at clinical doses. An appreciable affinity for α₁-adrenergic, α₂-adrenergic, and histamine H₁-receptors has been observed but it has no significant affinity for antimuscarinic receptors, except at higher doses [1,2]. Central nervous system depression including somnolence and drowsiness which are the most common manifestations of quetiapine poisoning may be related to histamine H₁-receptor inhibition. Hypotension is attributed to antagonism at α₁-adrenergic receptors which leads to vasodilation [1,2]. Tachycardia may be caused by a reflex to vasodilation and interaction at antimuscarinic receptors which cause vagal blockade to the heart.

A retrospective case series of quetiapine poisoning revealed that seizures occurred in only 2% of cases but the onset was not reported [2]. Balit et al reported two cases of seizures in 18 cases of quetiapine poisoning, but the onset was only documented in one case, which was 4 hours post ingestion [1]. A late-onset seizure as in our case is rarely reported. We found only a case report by Young et al in which a patient experienced seizures 24 hours after ingesting 30 g of quetiapine [5]. The form of quetiapine ingested (immediate release or extended release) was not reported in any of the above-mentioned case reports [1,2,5]. The immediate release form has a more rapid rate of absorption and reaches a peak concentration in about 2 hours compared with 5 hours for the extended-release

tablet [8]. The two formulations have similar clearance profiles with a terminal half-life of approximately 6 hours for the immediate-release formulation and 7 hours for the sustained-release formulation [9]. Clinicians should recognize that seizures can occur with a late onset and at low doses, such as 4 g of immediate-release quetiapine, as in this case.

Hyperglycemia, as in our case with a random blood glucose of 17.0 mmol/L, is another rarely reported manifestation of quetiapine overdose. According to the International Diabetes Federation and American Diabetes Association, a random blood glucose >7.8 mmol/L [10] or a fasting blood glucose >5.6 mmol/L [11] is considered hyperglycemia. This symptom was documented in two case reports. One patient who ingested 36 g of quetiapine presented with a fasting blood glucose level of 8.96 mmol/L 26 hours after ingestion [4], whereas the other patient who ingested 9.6 g of quetiapine presented with a fasting blood glucose level of 7.61 mmol/L approximately 22 hours after ingestion [3]. This symptom can be explained by quetiapine interaction at serotonergic 5-HT_{2A} receptors (reducing muscle glucose uptake), serotonergic 5-HT_{2C} receptors (mediating insulin resistance) and muscarinic M₃ receptors, which results in dysregulation of insulin secretion [4].

The range of toxicity of quetiapine overdoses is highly variable [12]. One patient who ingested 36 g survived with early intervention [4]. Nevertheless, fatalities have been reported and some were associated with co-ingestion and underlying medical illnesses such as cardiac dysrhythmias [2]. To date, there is no antidote for quetiapine overdose and the cornerstones of management are supportive care and continuous monitoring [12]. Initially, quetiapine overdose can be treated with activated charcoal, as was done in 82% of cases in one case series [2]. Hypotension can be managed by fluid resuscitation with normal saline and vasoconstrictors, which have a high affinity for α receptors, such as noradrenaline and phenylephrine [12]. Tachycardia and hyperglycemia usually require no management but warrant continuous monitoring. Quetiapine-induced seizures can be treated the same as status epilepticus with prompt administration of first-line benzodiazepines (lorazepam, midazolam, or diazepam) [13]. If seizures recur, additional administration of a second-line treatment (phenytoin or barbiturate) should be considered [13]. However, the only seizure in our case was promptly terminated by a combination of benzodiazepine and phenytoin and the patient remained seizure free with this regimen.

In conclusion, hyperglycemia and late-onset seizures may occur after overdoses of 4 g of quetiapine, although there is limited documentation of this clinical presentation. Clinicians should be aware of these potential clinical manifestations in quetiapine poisoning.

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