

Case report

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Low-dose intravenous lipid emulsion for the treatment of severe quetiapine and citalopram poisoning

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The treatment of quetiapine and/or citalopram poisoning is mainly supportive and involves gastric lavage, activated charcoal, intubation, and mechanical ventilation. Recently, however, there were reports of successful treatment with intravenous lipid emulsion. Here we report a case of a 19-year-old Caucasian girl who ingested approximately 6000 mg of quetiapine, 400 mg of citalopram, and 45 mg of bromazepam in a suicide attempt. The patient developed ventricular tachycardia and epileptic seizures 12 h after admission to the hospital. As the patient's condition deteriorated, we combined standard therapy (intubation, mechanical ventilation, and vasopressors) with low-dose intravenous lipid emulsion (ILE) (a total of 300 mL of 20 % lipid emulsion) and normalised her heart rhythm and stopped the seizures. She was discharged to the psychiatric ward after 48 h and home after a prolonged (2-month) psychiatric rehabilitation. Intravenous lipid emulsion turned out to be effective even in the lower dose range than previously reported for quetiapine poisoning in patients presenting with seizure and ventricular arrhythmia. To our knowledge, there are no case reports describing the use of ILE in treating citalopram poisoning.

KEY WORDS: *cardiac arrhythmias; complementary therapies; emergency treatment; epilepsy; poisoning*

Severe poisoning with quetiapine or citalopram can lead to life-threatening dysrhythmias and epileptic seizures. Therapy is mainly supportive (1-2). In recent years, there have been reports of successful use of intravenous lipid emulsions (ILE) to counter poisoning with lipophilic drugs, mainly local anaesthetics, beta blockers, and calcium channel blockers (3), including quetiapine (4-6). Here we present a patient with severe poisoning with quetiapine and citalopram (yet another lipophilic substance), who was successfully treated with ILE in the lower dose range than reported in most cases.

CASE REPORT

A 19-year-old girl was admitted to the hospital after having ingested about 6000 mg of quetiapine (20 300-mg tablets), 400 mg of citalopram, and 45 mg of bromazepam in a suicide attempt. The doses of ingested drugs were determined from medical history and empty packaging. On admission the patient was aroused; her Glasgow coma scale was 11, blood pressure 128/60 mmHg (17.1/8 kPa), and peripheral oxygen saturation without supplemental oxygen was 95 %. The pupils were dilated, symmetrical, and poorly reactive to light. Electrocardiogram revealed sinus

tachycardia with the heart rate of 150 min⁻¹, incomplete right bundle branch block, and prolonged corrected QT interval of 510 ms. We performed gastric lavage, applied activated charcoal, and drew urine for toxicology testing, which turned positive for quetiapine and citalopram. The concentrations of quetiapine and citalopram were not determined.

Twelve hours after the admission, we registered monomorphic premature ventricular contractions (PVCs) and generalised epileptic seizures. During the hour that followed, PVCs became more frequent and progressed to ventricular tachycardia with pulse, whereas epileptic seizures progressed to generalised convulsive *status epilepticus*, which was unresponsive to multiple bolus doses of diazepam. Potassium was just below the normal range, and magnesium was normal (3.71 mmol L⁻¹, and 0.78 mmol L⁻¹, respectively). She was intubated and ventilated mechanically. The maximum prolongation of corrected QT interval was 570 ms. Because of the combination of life-threatening arrhythmia and epileptic seizures we decided to infuse 100 mL of 20 % lipids (1.5 mL kg⁻¹ of Lipofundin MCT/LCT 20 %, B. Braun Melsungen AG, Melsungen, Germany, composed of soya oil 100 g per 1000 mL of emulsion, medium-chain triglycerides 100 g per 1000 mL of emulsion, glycerol, egg-lecithin, α -tocopherol, and sodium oleate) over 10 min, followed by additional 200 mL over the following 2 h. As soon as the first 100 mL were infused, the corrected QT interval dropped to normal (370 ms), and ventricular

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tachycardia and epileptic seizures stopped entirely. Subsequent treatment in the ICU was uneventful. The patient was extubated 24 h later, and her level of consciousness returned to normal (Glasgow coma scale 15). She was transferred to the psychiatric ward on the following day and was discharged home after two months of psychiatric rehabilitation.

DISCUSSION

Quetiapine is an atypical antipsychotic used for the treatment of schizophrenia, bipolar disorders, depression, and sleeping disturbances. Its antipsychotic effects are mediated via serotonin 5HT₂ and dopamine D₁ and D₂ receptors. It also has affinity for serotonin 5HT_{1A}, muscarinic M₁, adrenergic α -1 and α -2, and histamine H₁ receptors. An overdose results in hypotension, sinus tachycardia, cardiac dysrhythmias, prolongation of the corrected QT interval, delirium, seizures, central nervous system depression, respiratory depression, coma, and death (1, 5, 7).

Citalopram is a selective serotonin reuptake inhibitor (SSRI). In overdosed patients it has shown higher toxicity than other SSRIs, manifesting in the prolongation of corrected QT interval, widening of the QRS complexes, tachycardia, generalised convulsions, acute respiratory distress syndrome, rhabdomyolysis with acute renal failure, and CNS depression (2, 8). To our knowledge, there are no case reports describing the use of ILE in treating citalopram poisoning.

ILE is a treatment strategy for lipophilic drug poisonings. At least two explanations exist regarding the mechanism of action: firstly, the lipid sink theory proposes a separate pharmacologic compartment into which the lipophilic drug may diffuse from the tissues, and secondly, the delivery of energy-rich substrate to energy depleted cells (e.g. myocardium) might improve their function. The lipid sink theory is the most widely accepted mechanism of action. A number of commercial products with different lipid formulations have been successfully used to treat lipophilic drug poisonings. However, not all effects of ILE can be explained solely by the lipid sink theory, especially rapid effects immediately after the start of the infusion (3, 4).

The decision to use ILE in our patient was based on the occurrence of sustained ventricular tachycardia and generalised epileptic seizures. Standard treatment (gastric lavage, activated charcoal, intubation, mechanical ventilation) did not succeed in preventing life-threatening complications. Immediately after the infusion of ILE our patient's condition improved, and we observed no complications attributable to ILE. Successful use of ILE in quetiapine poisoning has been described before. Finn et al. (6) described a patient who attempted suicide by ingestion of 4300 mg of quetiapine and 3100 mg of sertraline. The

patient presented with hypotension and hypothermia but had no epileptic seizures or arrhythmias. The patient received symptomatic treatment and infusion of 20 % ILE. Like in our case, the initial bolus dose was 1.5 mL kg⁻¹ (100 mL), followed by an infusion of 6 mL kg⁻¹ h⁻¹ for 1 h (in total 400 mL). His level of consciousness improved soon after the administration of ILE, which removed the need for intubation and mechanical ventilation. Eren Cevik et al. (9) reported on a patient who ingested 2400 mg of quetiapine. That patient presented with hypotension and sinus tachycardia. The patient received ILE consisting of 100 mL bolus, followed by 30 mL kg⁻¹ h⁻¹ infusion over 2 h (total dose of 3580 mL). Bartos and Knudsen (5) presented a female patient who ingested 24000 mg of quetiapine. Her cardiovascular collapse was refractory to all standard symptomatic treatment (intubation, mechanical ventilation, vasopressors). She was treated with 20 % ILE 170 mL bolus, followed by an infusion of 500 mL over 1 h. In all these cases treatment with ILE was reported efficient.

We used a similar initial bolus compared to other authors, but due to a clear clinical improvement, we continued the treatment at lower doses (cumulatively 300 mL). The treatment showed no adverse effects such as allergic reactions, fat overload syndrome with hepatosplenomegaly, jaundice, acute pancreatitis, seizures, fat embolism, coagulopathies or alteration of laboratory tests (10-11).

To conclude, treatment with ILE for severe poisoning with quetiapine and citalopram could be effective even in the lower dose range than previously reported.

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Zdravljenje hude zastrupitve s kvetiapiinom in citalopramom z nizkim odmerkom intravenske lipidne emulzije

Zastrupitve s kvetiapiinom in/ali citalopramom večinoma zdravimo podporno. Ob zdravljenju s spiranjem želodca, aktivnim ogljem, intubacijo in mehansko ventilacijo pa so opisani primeri uspešnega zdravljenja z intravensko lipidno emulzijo. Predstavljamo primer 19-letne ženske, ki je v samomorilne namene zaužila približno 6000 mg kvetiapina, 400 mg citaloprama in 45 mg bromazepama. Bolnica je imela 12 ur po sprejemu prekatno tahikardijo in epileptične napade. Ob kliničnem poslabšanju stanja smo jo zdravili s standardno terapijo (intubacija, mehanska ventilacija, vazopresorna podpora) in nizkim odmerkom intravenske lipidne emulzije (celokupno 300 mL 20 % lipidne emulzije). Srčni ritem se je po terapiji normaliziral, epileptični krči so prenehali. Po 48 urah zdravljenja v enoti intenzivne terapije je bila premeščena na oddelek za psihiatrijo in po 2-mesečnem zdravljenju domov. Zastrupitev s kvetiapiinom in citalopramom, ki se pri bolniku kaže z epileptičnimi krči in prekatnimi motnjami ritma, lahko uspešno zdravimo z nizkimi odmerki intravenske lipidne emulzije.

KLJUČNE BESEDE: *dopolnilna terapija; epilepsija; srčne aritmije; urgentno zdravljenje; zastrupitev*