CASE REPORT

Treatment of Quetiapine Overdose with Intravenous Lipid Emulsion

Engin Deniz Arslan, Ali Demir, Fevzi Yilmaz, Cemil Kavalci, Evvah Karakilic and Elif Çelikel

Emergency Department, Ankara Numune Training and Research Hospital, Samanpazarı, Ankara, Turkey

We report the case of a 29-year-old woman who attempted suicide by oral ingestion of potentially fatal doses of multiple drugs including quetiapine. Intravenous lipid emulsion (ILE) was administered at a dose higher than that used in the standard management of toxicity. Rapid improvement was observed in the patient's status, and no additional treatment was required during the period of observation. No adverse effect of lipid administration was observed. ILE treatment seems to have great potential in the management of lipophilic drug toxicity in the future. (doi: 10.2302/kjm.2012-0010-CR) ; Keio J Med 62 (2) : 53–57, June 2013)

Key words: intravenous lipid emulsion, quetiapine, toxicity

Introduction

Quetiapine is an atypical antipsychotic drug that, in toxic doses, has severe adverse effects such as coma, respiratory depression, and hypotension. Toxic ingestions of quetiapine primarily are managed with gastric lavage and active charcoal administration to prevent or reduce absorption; the management of toxic effects is achieved by supportive therapy.

Intravenous lipid emulsions (ILEs) are used as a source of calories and essential fatty acids in patients who require parenteral nutrition. In addition, ILEs have reportedly been successful in the treatment of local anesthetic systemic toxicity; their successful use in case reports and animal studies of drug toxicity other than local anesthetics has been reported.

Case

A 29-year-old woman presented to our emergency department because she was suspected of having ingested toxic levels of multiple drugs. She had been found comatose at home by family members. Empty blister packs of quetiapine, escitalopram, ibuprofen, and amoxicillin were found at the scene, and the estimated ingested amounts of the drugs were 9 g quetiapine, 4 g ibuprofen, 280 mg escitalopram, and 5 g amoxicillin. On arrival, the patient's blood pressure (BP) was 90/55 mmHg, her heart rate (HR) was 110 /min, and her oxygen saturation was 91%. She was non-cooperative and disorientated, and on painful stimulation she flexed her arms, opened her eyes, and moaned [$E_2M_4V_2$ on the Glasgow Coma Scale (GCS)]. The patient's pupils were midpoint and reactive, and her blood glucose level was 114 mg/dl according to a strip test. She was intubated to ensure airway patency and ventilation. Gastric decompression was performed and 50 g of active charcoal was administered via a gastric tube. An electrocardiogram (ECG) revealed sinus tachycardia with a QRS duration of 110 ms (**Fig. 1**). The patient's symptoms attributed to quetiapine toxicity were depressed consciousness, tachycardia, and hypotension. Two liters of isotonic fluid was administered intravenously within 1 h of the patient's admission without any clinical improvement. Because of the lipophilic nature of quetiapine, ILE therapy was considered to prevent further complications. One hour after admission, when the

Fig. 1 ECG of the patient before ILE administration.

patient's vital signs were BP 95/55 mmHg, HR 120 /min, GCS $E_1M_1V_T$, a 20% lipid emulsion bolus dose was administered intravenously at 1.5 mL/kg. Fifteen minutes later, an additional bolus dose of 1.5 mL/kg was given to give a total dose of 3 mg/kg. Thirty minutes after the second dose, the patient's vital signs improved to BP 115/70 mmHg and HR 95/min and she opened her eyes and began to move her upper extremities to painful stimuli ($E_2M_4V_{Intubated}$). An ECG was obtained 30 minutes after ILE administration illustrating QRS duration had fallen to 99 ms (**Fig. 2**). The patient was extubated 3 h after the second dose and her vital signs improved to BP 125/81 mmHg and HR 93 /min. At this time, the QRS duration was 85 ms, and the patient was localizing pains, opening her eyes to pain, and was speaking in a disoriented manner ($E_2M_5V_4$). The patient's vital signs and GCS score are illustrated in **Figure 3-4**. Her physical and mental status progressively improved to a normal state and was sustained, so she did not need any other medication or intervention during the observation period. The patient confirmed that she had taken large amounts of quetiapine pills. The patient was discharged the next day and underwent psychiatric follow up.

Discussion

Quetiapine is an atypical antipsychotic drug that provides efficacy with a lower risk of extrapyramidal symptoms compared to typical antipsychotics. Quetiapine affects multiple neurotransmitter receptors, including serotonergic, dopaminergic, alpha adrenergic, and histaminergic receptors. Its antipsychotic efficacy is attributed to antagonistic effects on D_2-receptors and 5-HT$_2$A-receptors. However; atypical antipsychotics are associated with a variety of metabolic and cardiovascular adverse effects. Sedation and somnolence are explained by antagonism of histamine H1-receptors, whereas hypotension is associated with an antagonistic effect on α1-adrenergic receptors. Quetiapine also reportedly has an antagonistic effect on M1-muscarinic receptors, resulting in tachycardia. Currently, there are no specific therapeutic recommendations for quetiapine overdose, and highly supportive conventional therapeutic measures are applied according to the patient's clinical status.

Escitalopram is a selective serotonin reuptake inhibitor antidepressant that has the advantage of low toxicity in overdose. In a review of escitalopram overdoses, hyperreflexia and clonus were the most common features and central depression was rare. ECG changes involved both bradycardia and tachycardia, and observed QT prolonga-
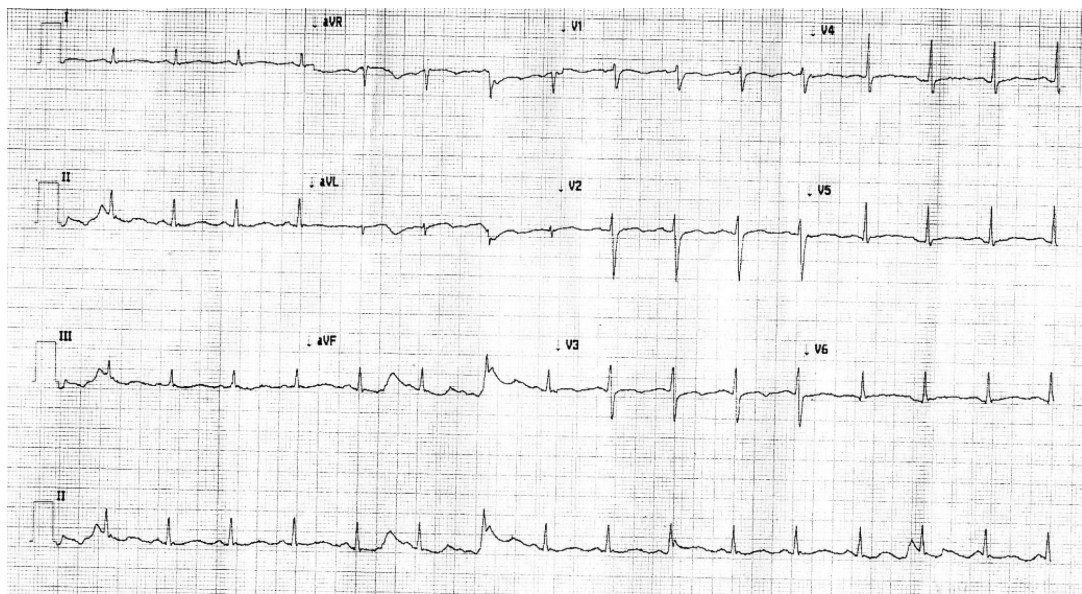
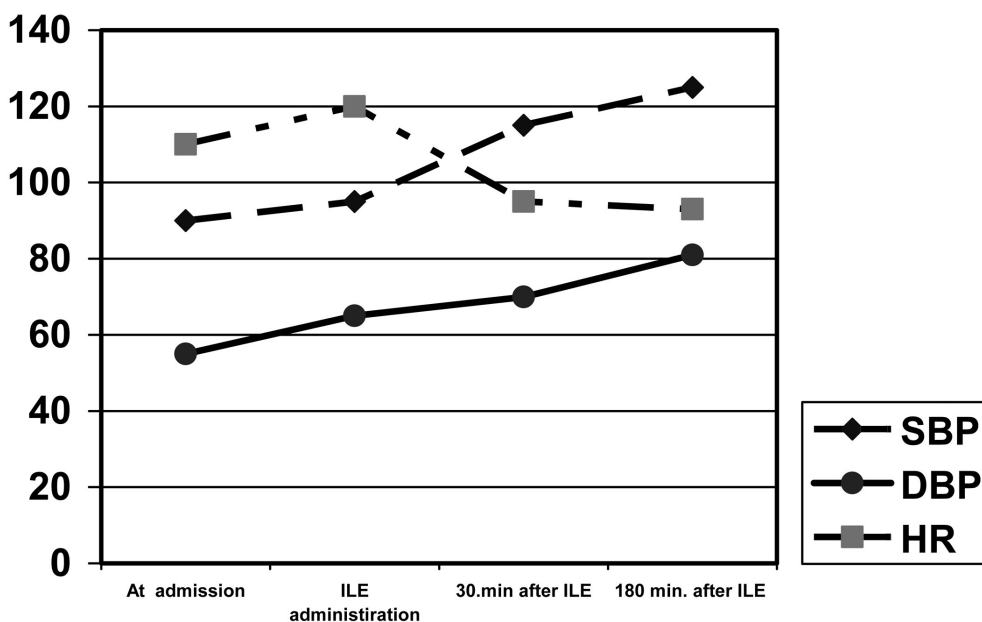**Fig. 2** ECG of the patient 30 min after ILE administration.

Fig. 3 Patient's blood pressure and HR over the course of treatment.
SBP, systolic blood pressure; DBP, diastolic blood pressure.

tion was associated with bradycardia.[1] In our patient, the observed hypotension tachycardia and depressed consciousness can be attributed to the antagonistic effects of quetiapine on H1, α1-adrenergic, and muscarinic receptors.

Weinberg and colleagues demonstrated that lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats[2]. This observation leads to the suggestion of ILE use in patients with highly lipophilic drug toxicity, including that caused by bupropion/lamotrigine, sertraline/quetiapine, verapamil, and atenolol.[3–6] Animal studies have also indicated the efficacy of ILE in drug toxicity.[7] Highly lipid soluble agents demonstrably respond to lipid infusion, and this fact supports the theory of the lipid sink, with lipid infusions resulting in an expanded plasma lipid phase that reduces tissue drug levels.
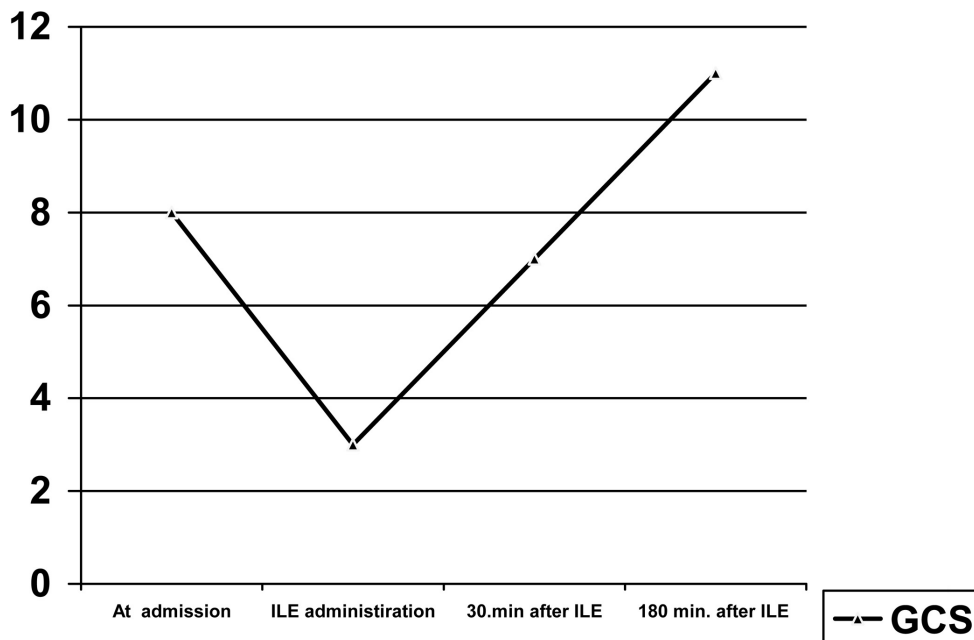
Fig. 4 Patient's Glasgow coma scale over the course of treatment.

Harmon and colleagues reported a patient who ingested more than 10 g quetiapine who became comatose and recovered 16 h later with supportive therapy.[8] In a 5-year case series, the largest amount of ingested quetiapine was 24 grams, and the patient deteriorated into a coma and required intubation; the patient was extubated 4 days later with supportive therapy.[9] Although the ingested amount of quetiapine was not known exactly in our case, the patient regained consciousness earlier than might be expected with supportive management of quetiapine toxicity. ILE also improved the cardiovascular side effects of quetiapine overdose. Finn and colleagues reported that a patient treated with ILE for a quetiapine plus sertraline overdose underwent rapid recovery consistent with our patient.[4]

Early reports on ILE treatment considered its use as a rescue therapy, whereas Finn and colleagues recommend the earlier use of ILE to prevent adverse events.[4] The recommended dose as a rescue treatment in arrest patients is 1.5 mL/kg 20% lipid followed by 0.25–0.5 mL/kg/min to a total dose 8 mL/kg, with the bolus dose applied a maximum of twice to restore circulation. However, there is no dose recommendation for critically ill patients who have not arrested. We applied two 1.5-mL/kg bolus doses 15 min apart with no infusion drip and the patient did not need any additional treatment during the observation period. No adverse effect of lipid administration was observed. Although no adverse effects have been reported

in trials and case reports, the theoretical adverse effects of ILE treatment are pancreatitis, acute lung injury, allergy, hypercoagulability, and fat embolism.

Conclusion

ILE treatment has the potential to play an important role in the management of lipid-soluble-drug toxicity in the future. Its use should be considered earlier in patients who have a potential risk of a poor outcome due to lipophilic drug toxidrome. Trials are needed to evaluate the efficacy and potential side effects of ILE therapy.

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