Case Report

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# Simultaneous Use of Intravenous Lipid Emulsion and Plasma Exchange Therapies in Multiple Drug Toxicity

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**Key Words**
Lipid emulsion · Plasma exchange · Multiple drug toxicity

**Abstract**
***Objective:*** The aim of this study was to highlight the use of combined intravenous lipid emulsion (ILE) and plasma exchange (PE) therapies in multidrug toxicity. ***Clinical Presentation and Intervention:*** A 45-year-old woman who attempted suicide by ingesting large quantities of amisulpride (28 g), diazepam (250 mg), valsartan (2,240 mg), aripiprazole (45 mg) and paliperidone (21 mg) was taken to the hospital of Adnan Menderes University School of Medicine. Upon arrival, she exhibited signs of cardiotoxicity and severe depression of the central nervous and respiratory systems. She was treated successfully with ILE for 4 h and PE therapy for 36 h, consecutively. She was discharged on the fourth day of hospitalization having fully recovered. ***Conclusion:*** The patient was successfully treated with the combination of ILE and PE.

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## Introduction

The management of multiple medication toxicity among patients admitted to emergency departments remains a challenge [1]. Each drug has its characteristics in effect and metabolism. Multiple treatment modalities including antidotes of medication, charcoal, lipid emulsion therapy, specific anticore to the drug and plasma exchange (PE) have been used based on the mechanism of drug intoxication. Here, we present a case of multiple medication toxicity and successful patient management.

## Case Report

A 45-year-old woman who attempted suicide by ingesting large quantities of antipsychotic, benzodiazepine and antihypertensive drugs was taken to the hospital of Adnan Menderes University School of Medicine in a critical condition. Based on information from the patient's family, the ingested drugs were amisulpride (28 g), diazepam (250 mg), valsartan (2,240 mg), aripiprazole (45 mg) and paliperidone (21 mg). She arrived at the emergency department in a critical condition approximately 2 h after the ingestion. Upon arrival, she exhibited signs of cardiotoxicity, including QT interval prolongation and atrial fibrillation (fig. 1a), in addition to profound hypotension and severe depression of the central nervous and respiratory systems. Her oxygen saturation was 79% using pulse oximetry and her pulse was 110 beats/min. The patient was monitored and fluid replacement was commenced. Flumazenil (0.1 mg i.v.) was administered because diazepam was the likely cause of her respiratory depression. The patient became agitated and her respiratory condition deteriorated, hence she was sedated and intubated 10 min following her arrival. An infusion of dopamine and norepinephrine was started because of persistent hypotension despite the rapid infusion of normal saline. Gastric irrigation was per-

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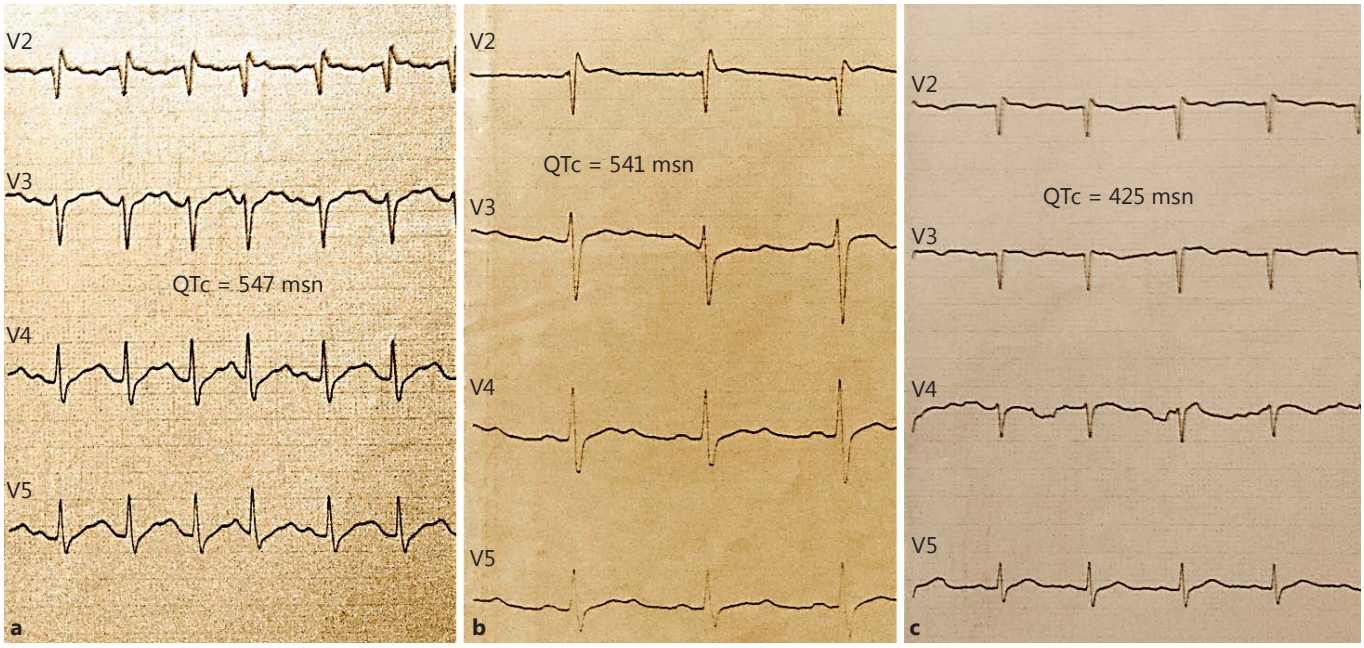


**Fig. 1.** Corrected QT interval on electrocardiography: on admission (**a**), after the ILE and PE therapy (**b**), and before discharge (**c**).

formed and activated charcoal (1 g/kg) was administered. The patient was then taken urgently to the emergency critical care unit. Initial laboratory data revealed a sodium level of 133 mmol/l, potassium level of 2.8 mmol/l, and an arterial blood gas analysis revealed a pH of 7.22. Her partial pressure of carbon dioxide was 30.7 mm Hg, partial pressure of oxygen was 70.3 mm Hg, bicarbonate was 12.9 mmol/l and lactate was 7.0 mmol/l. All other electrolytes, creatinine, blood urea nitrogen, glucose, hepatic transaminases, troponin and coagulation study results were within normal ranges. An infusion of sodium bicarbonate (20 mEq/h) was initiated due to acidosis in the blood gas report and potassium replacement was also started. Because the patient exhibited persistent hypotension despite vasoconstrictor therapy and her metabolic condition did not improve, intravenous lipid emulsion (ILE) therapy (Smoflipid; Fresenius Kabi, Bad Homburg, Germany) was started at a rate of 100 ml/h via the central venous catheter. One hour later PE therapy (1 plasma volume) was carried out. Following this procedure, the ECG returned to sinus rhythm and the QT interval shortened to 541 ms (fig. 1b). The patient's blood pressure started to improve. The ILE infusion was continued (100 ml/h) for an additional 4 h after the PE therapy. The PE procedure was repeated 18 and 36 h following arrival, and the patient was extubated after 40 h. Her general condition progressed well after extubation. The patient did not develop any additional problems and was discharged from the hospital in good condition 4 days following her admission. Her QTc was 425 ms on discharge (fig. 1c). During a follow-up appointment 20 days later, the patient's only complaint was mild hoarseness that was thought to be a complication of intubation.

## Discussion

The present case demonstrated the successfully management of a life-threatening multiple medication toxicity using ILE and PE therapies. The patient ingested large doses of amisulpride, diazepam, valsartan, aripiprazole and paliperidone. Amisulpride is an atypical antipsychotic drug that is used for the treatment of schizophrenia. Since it is highly bound to tissues in toxic dose ingestions, hemodialysis and hemofiltration are ineffective [2]. Diazepam is metabolized in the liver and eliminated by the kidneys. It is highly bound to plasma proteins and hemodialysis offers limited benefit in the case of an overdose [3]. Valsartan is an angiotensin receptor blocker used for the treatment of hypertension. Although its toxic dose is not known, hemodialysis does not provide much benefit in the case of an overdose [4]. Aripiprazole is highly bound to plasma proteins and it is metabolized in the liver. It is also not cleared with hemodialysis [5]. Paliperidone is another antipsychotic drug used for the treatment of schizophrenia. It is bound to plasma proteins at a rate of 74% and its volume of distribution is high.

Severe intoxication caused by antipsychotic medications causes marked hypotension in addition to prolongation of the QT interval and QRS complex. It can also lead to coma, seizures and respiratory arrest [2]. Similarly, in-

toxication due to benzodiazepines causes lethargy, speech apraxia, ataxia, coma and respiratory arrest. Unlike antipsychotic drugs, coma caused by benzodiazepines can be treated with flumazenil. In the case of intoxication due to angiotensin receptor blockers, hypotension, hyperkalemia and bradykinin-mediated effects can occur. The therapeutic dose range of amisulpride is 400–1,200 mg/day. Our patient arrived at the hospital after ingesting 28 g of amisulpride. The presentation included prolongation of the QT interval, bradycardia and hypotension, giving the impression of effects of antipsychotic drugs (amisulpride, aripiprazole, paliperidone), and in particular of amisulpride. The initial ECG showed prolongation of the QTc (547 ms) without tachycardia or prolongation of the QRS complex, although the patient did have bradycardia and hypotension. The diazepam, however, could have contributed to the patient's shallow respirations and central nervous system depression. The marked hypotension may have been partly related to the valsartan. Atrial fibrillation is not specifically stated in cases of intoxication from the abovementioned drugs. However, we can speculate that atrial fibrillation was the combined effect of multiple drug toxicity and recovered spontaneously.

In the management of the present case, ILE and PE therapies were deemed appropriate, in addition to conventional treatments that included charcoal and flumazenil, due to the patient's critical condition that had a risk of rapidly progressing to death. This was supported by the exposure to toxic doses of multiple drugs with different characteristics in terms of metabolism. ILE therapy was first reported in the literature for its quick and effective management of fatal intoxications of local anesthetics [6]. The efficacy of ILE is believed to result from its capacity to bind lipid soluble agents in blood and tissues [7]. In our case, all of the medications taken by our patient have lipophilic characteristics and ILE therapy continued determinedly. The patient then became hemodynamically stable. Therefore, considering the evidence in the literature, it was determined that ILE treatment would be useful and efforts should continue determinedly. In recent years, PE has been studied as a nonspecific treatment method in emergencies such as toxic ingestions [8]. In general, drugs with high lipoprotein binding rates and low volumes of distribution are effectively eliminated from the blood using PE [9]. Among the drugs taken by the patient, valsartan is the only one with high plasma protein binding and a low volume of distribution. Therefore, it is the only one that would have been eliminated with PE. This is in contrast with the general characteristics of antipsychotics, and in particular amisulpride, which include a very low rate of binding to lipoproteins [10].

## Conclusion

In this case, the patient was successfully treated with the combination of ILE and PE. The clinical condition and ECG findings of the patient improved dramatically immediately after the sequential use of ILE and PE therapies in addition to conservative therapy. Therefore, the combination of these treatment modalities has a promising future in the management of multiple drug intoxication and the treatment strategy should be individualized according to patients' clinical conditions.

## Disclosure Statement

The authors have no conflicts of interest to report.

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