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The Treatment of a Patient with Intravenous Lipid Emulsion Infusion after Amitryptiline Overdose which Caused in QRS Interval Prolongation: A Case Report

***Filiz İzci*[1],**
***Servet İzci*[2],**
***Emrah Acar*[3],**
***Vedat İzci*[4]**

[1]*Asist. Prof., İstanbul Bilim Üniversitesi Tıp Fakültesi, Ruh Sağlığı ve Hastalıkları Anabilim Dalı, İstanbul*

[2]*Specialist,*

[3]*M.D., Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kardiyoloji Bölümü, İstanbul*

[4]*M.D., Kartal Eğitim ve Araştırma Hastanesi, Acil Tıp Birimi, İstanbul*

***Corresponding Author:** Filiz İzci, İstanbul Bilim Üniversitesi Tıp Fakültesi, Ruh Sağlığı ve Hastalıkları Anabilim Dalı, İstanbul, Türkiye.*

***Phone:** +90 505 450 30 13*

***E-mail:** filizizci@yahoo.com*

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ABSTRACT

Amitriptyline is a member of the tricyclic antidepressant (TCA) drug group and can cause electrocardiographic (ECG) changes. Some of these changes include the prolongation of the QRS and QTc intervals, increment of R/s ratio on derivation aVR besides of arrhythmias such as supraventricular tachycardia (SVT) and ventricular tachycardia (VT) on overdose. Here, we present a case concerning a QRS interval prolongation caused by the intentional use of high doses of amitriptyline and treated with an intravenous lipid emulsion (ILE) infusion.

Key words: Amitriptyline, suicide, prolongation of QRS interval, intravenous lipid emulsion infusion

ÖZET

Amitriptilin İle İntihar Girişimi Sonrası QRS İntervalinde Genişleme Ortaya Çıkan Hastanın İntravenöz Lipit İnfüzyonu İle Tedavisi: Bir Olgu Bildirimi

Trisiklik antidepresanlardan olan amitriptilin yüksek dozlarda supraventriküler taşikardi ve ventriküler taşikardi gibi kardiyak aritmilerin yanısıra, QRS ve QTc süresinde uzama, aVR derivasyonunda R/S oranında artma gibi EKG değişikliklerine neden olabilmektedir. Bu yazıda, amitriptilin ile intihar girişiminde bulunan bir olguda QRS intervalindeki genişlemenin, intravenöz lipit infüzyonu ile tedavi edilmesi tartışılmıştır.

Anahtar kelimeler: Amitriptilin, intihar, QRS intervalinde genişleme, intravenöz lipit infüzyonu

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INTRODUCTION

Drug intoxication is common in psychiatric and general emergency departments and has a high mortality rate. The antidepressant drug class is one of the drug groups that causes drug intoxication. Most drug intoxications with antidepressants are seen after the suicidal use of the drug. Antidepressant intoxication is the third leading cause of suicidal drug use, intoxication with analgesics and sedational/hypnotic drugs are primary causes.[1] The most commonly used suicidal drug among the tricyclic antidepressants (TCAs) is amitriptyline.[2] Amitriptyline intoxication has several systemic effects but the most important and lifethreatening effect is on the cardiovascular system. TCAs block potassium channels and thus, prolong the QTc interval and induce torsades des pointes (TdP).[3] In literature, there are cases concerning the successful treatment of cardiotoxic side effects caused by drug intoxication with an intravenous lipid emulsion (ILE) infusion.[4,5] Haemodynamic deterioration after a TCA overdose has been treated well with an ILE infusion. Here we present a male patient who intentionally took 80 tablets (2,000 mg) of an amitriptyline-containing drug (25 mg/tablet). This dosage caused a prolongation of QRS interval and was treated successfully with an ILE infusion.

CASE REPORT

A 44-year-old male patient was admitted to the emergency services by his relatives who confirmed that the patient had taken 80 tablets of a drug containing 25 mg of amitriptyline with the intent of suicide. According to his relatives, for the last month, he complained about a lack of desire, restlessness, reluctance about working and he had self-administered a drug containing amitriptyline for sleep without a physician's consultation during the previous week. He was comatose and his Glasgow coma score (GCS) was 7. His blood pressure was 80/40 mmHg, his pulse was 140 beats/minute (bpm) and his temperature was 37.2 °C. On electrocardiogram (ECG), the QRS interval was 180 msn (normal < 120 msn). We inserted a central venous access line and administered 0.9% NaCl and 8.4% $NaHCO_3$ intravenously, and to decrease the respiratory effort, we intubated him oropharyngeally. We performed a gastric lavage and gave 50 mg of active charcoal by a gastric tube. In spite of these treatments, the haemodynamic deterioration persisted and we decided to add the ILE infusion to the treatment. We administered a 100 ml 20% ILE infusion in the first minute and following that bolus, we continued with 400 ml of ILE about following 30 minutes. The QRS interval then decreased to 85 msn and the heart rate decreased to 90 bpm. After six hours his spontaneous respiratory effort returned and he was successfully extubated. His vital signs were normal. After discharge, his psychiatric examination revealed a depressive mood, anxiety, insomnia, anorexia, anhedonia, impulsivity, passive death thoughts, feelings of guilt, and feelings of worthlessness. HAM-D and HAM-A scale scores were 24 and 18, respectively. His treatment is currently followed by a psychiatry clinic.

DISCUSSION

TCAs are drugs used in the treatment of psychiatric disorders that include depressive disorders, panic disorders, obsessive-compulsive disorders, other anxiety disorders, insomnia, nicotine addiction, attention deficient and hyperactivity disorders, neuropathic pain, enuresis nocturna, and bulimia nervosa. Furthermore, these drugs inhibit the re-uptake of noradrenaline and serotonin.[9] Mortality cases caused by TCA use is commonly related to the use of amitriptyline. Lethal doses of TCAs in adults are generally 10–30 mg/kg, and cardiotoxicity and mortality are typically seen at serum levels of > 1,000 ng/ml.[10] The most common side effects of TCAs are anticholinergic effects caused by muscarinic receptor blockage; orthostatic hypotension related to alpha-1 receptor inhibition, and possibly alpha-2 receptor inhibition; and the antihistaminic side effects like sedation, dizziness and weight gain.[11] The most important side effects of TCAs are the cardiotoxic effects. Cardiotoxic effects are caused by their anticholinergic mechanisms, noradrenaline re-uptake inhibition, membrane stabilizing effects and quinidine-like effects. These mechanisms decrease myocardial contraction, diminish coronary blood flow, induce rhythm disorders and promote pulmonary oedema. Moreover, they cause oxidative stress and this mechanism contributes to the cardiotoxicity.[9]

Severe amitriptyline toxicity may result in central nervous system depression, seizures, hypotension, and abnormalities to cardiac conduction characterised by QT and QRS prolongation of ECG, in addition to supraventricular and ventricular arrhythmias. The cardiotoxicity caused by TCAs is treated by gastric lavage, active charcoal, fluid replacement, lidocaine and diazepam administration, and sodium bicarbonate used as a specific antidote.[2] It is known that resistant cardiac collapse caused by local anaesthetics and intoxication from lipophilic drugs like TCAs have been treated with ILE infusions in recent studies and trials. The predominant theory for its mechanism of action is that, by creating an expanded, intravascular lipid phase, equilibria are established that drive the offending drug from the target tissues into the newly formed "lipid sink". Based on this hypothesis, lipid emulsion has been considered a candidate for generic reversal of toxicity caused by an overdose of any lipophilic drug. The lipid sink theory hypothesizes that the mechanism behind the lipid

treatment is the entrapment of toxic drugs in the plasma, preventing them from reaching target receptors. Lipid sink treatment has also been used as a last refuge treatment for severe tricyclic antidepressant intoxication with seemingly beneficial results.[12,13] Fourteen case reports were identified in which ILE was used to treat toxicities due to local anaesthetics and other medications (amitriptyline, diltiazem, bupropion, dosulepin, lamotrigine, quetiapine, and verapamil). Thirteen of these cases demonstrated a beneficial response in reversing systemic toxicity.[14] Also, three case reports support the use of lipid emulsion to reverse systemic toxicity, including seizures, ECG abnormalities, and cardiac arrest, resulting from the administration of levobupivacaine, ropivacaine, bupivacaine or mepivacaine.[15] In another case, drug-induced cardiotoxicity occurred similar to our case and was treated with an ILE infusion.[16]

A study using clomipramine, which is lipophilic and, in high doses, causes cardiovascular collapse, reported that cardiac side effects were treated more rapidly with ILE than with sodium bicarbonate.[6] In amitriptyline intoxicated patients who were infused with ILE treatment early, the brain crossing velocity of amitriptyline was slowing.[17] In four volunteers who were amitriptyline loaded, ILE treatment decreased the severity of intoxication.[18] In a similar case with an elderly male who had suicidal attempt with quetiapine and sertraline, an early ILE infusion was successful in decreasing the side effects.[19] In a patient who had taken high doses of lamotrigine and bupropion and had resistant cardiovascular collapse, ILE treatment resulted in dramatic changes that included an increased heart rate.[20] In another study with rats, after the cocaine intoxication, cardiovascular collapse occurred, and with an ILE infusion, haemodynamic stability was achieved.[21] An ILE infusion causes positive inotropic effects and increases both arterial blood flow and blood pressure.[22]

In our case, similar to those in the literature, after a high dose of amitriptyline, the QRS interval widened. ILE infusion treatment stabilized cardiac activity and dramatically returned haemodynamic parameters to normal levels. It should be remembered that drugs like amitriptyline, in high doses, can cause mortal effects, and ILE is a treatment option for amitriptyline intoxication.

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