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Case Report

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Calcium Dramatically Reverse the Hypocalcemic-Induced QT Prolongation in a Multiple Drug Toxicities Post-Suicidal Attempt

Yasser Mohammed Hassanain Elsayed

Critical Care Unit, Fraskour Central Hospital, Damietta Health Affairs, Egyptian Ministry of Health (MOH), Damietta, Egypt

ABSTRACT

Rationale: Multiple drug toxicities are usually associated with unexpected future adverse effects and drug interaction. QT prolongation may be drug-induced. Hypocalcemia also is a trigger for QT prolongation.

Patient concerns: A young-aged married female patient presented to the emergency department with marked irritability and tachypnea after swallowing multiple oral drug strips.

Diagnosis: Hypocalcemic-induced QT prolongation in a multiple-complex drug toxicities post-suicidal attempt.

Interventions: Gastric lavage, electrocardiography, and arterial blood gases.

Outcomes: The dramatic response to calcium intravenous injection with subsequent reversal the hypocalcemic-induced QT prolongation in a multiple drug toxicities post-suicidal attempt.

Lessons: This is the first case that reports these adverse drug reactions with multiple oral drug toxicities. QT prolongation may be drug-induced. Hypocalcemia also is a trigger for QT prolongation. The identification of drug-induced complications is a pivotal step in the diagnosis decision making of any medical problems. The effects of multiple drug toxicities may be balanced end results.

***Corresponding author**

Yasser Mohammed Hassanain Elsayed, Critical Care Unit, Fraskour Central Hospital, Damietta Health Affairs, Egyptian Ministry of Health (MOH), Damietta, Egypt. E-mail: dryaser24@yahoo.com

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Introduction

Specific and several changes due to electrolyte imbalance may be seen on an electrocardiogram (ECG) [1]. The electrocardiogram may be normal during critical hypocalcemia and a normal ECG cannot, therefore, be relied upon to exclude this condition [2]. The prolongation of the QTc interval is an old ECG sign for hypocalcemia. This is because of lengthening of the ST segment which is directly related to the degree of hypocalcemia and inversely related to the serum calcium level [3]. However, QTc prolongation will be predisposing to serious ventricular arrhythmias [4]. Hyperventilation-induced alkalosis may aggravate the symptoms of hypocalcemia [4].

Propranolol is a beta-blocker drug, commonly used as antihypertensive, antianginal, antiarrhythmic, and heart failure. Typical dosage: 80–320 mg. Don't use medications used to increase heart rate and blood pressure with propranolol. Trouble breathing, bradycardia, and heart block are the serious side effects. It might have decreased liver, renal, and cardiac function [5]. Propranolol clearance increases linearly with liver blood flow [6]. The elimination half-life of propranolol is about 8 hours. The plasma half-life of propranolol is 3-6 hours [6]. Propranolol has a moderate risk of QTc prolongation [6]. Amitriptyline hydrochloride is a tricyclic antidepressant (TCA). The drug is indicated for the major depressive disorder, neuropathic pain, chronic tension-type headache, migraine, and nocturnal enuresis in children. Amitriptyline may increase the risk of arrhythmia. Confusion, hypothermia, hypotension, and tachycardia are frequent side effects. Amitriptyline and its metabolites are mainly excreted in the urine. The elimination half-life (t1⁄2 β) after oral administration is nearly 25 hours. Ingestion of 750 mg or more by an adult may result in severe toxicity. Amitriptyline has a moderate risk of QTc prolongation [7]. Paracetamol is a widely used nonprescription analgesic and antipyretic medication. It has direct hepatotoxic potential when taken as an overdose and can cause acute liver injury and death from acute liver failure [8]. In adults, hepatic toxicity rarely has occurred with acute overdoses of less than 10 g, although hepatotoxicity has been reported in fasting patients ingesting 4-10 g of acetaminophen. Fatalities are rare with less than 15 g [9]. Pseudoephedrine is a sympathomimetic amine used for its decongestant activity. The sympathomimetic effects of pseudoephedrine include an increase in mean arterial pressure and tachycardia. The majority of pseudoephedrine is eliminated unmetabolized in the urine. The mean elimination half-life of pseudoephedrine is 6.0 hours.

The oral LD_{50} of pseudoephedrine is 2206 mg/kg in rats and 726mg/kg in mice. An overdose of pseudoephedrine may present with headache, irritability, circulatory collapse, coma, respiratory failure, and arrhythmias [10]. Caffeine anhydrous is a processed, dehydrated form of caffeine. This dehydration process means caffeine anhydrous is more concentrated and, therefore, more potent than regular caffeine. It is alleviating tension headaches in combination with pain relievers. Headaches, irritability, anxiety, and tachycardia are common side effects of heavy caffeine anhydrous. Toxicity is more likely with anhydrous caffeine though, particularly when it is in a pure powdered form as this is difficult to measure accurately [11]. Chlorpheniramine maleate is one of the most widely used traditional antihistaminics (a histamine H1 antagonist). It is commonly used in allergic reactions, hay fever, rhinitis, urticaria, and asthma. Half-life is 21-27 hours. Maximal dose not to exceed 24 mg/day. It has a risk for QTc prolongation. The risk or severity of QTc prolongation can be increased when propranolol is combined with chlorpheniramine [12]. The adverse effects include dizziness, confusion, anxiety, tachycardia, hypotension hypertension, shallow breathing, irritability, and trouble urinating [13].

Aim of this study

In this manuscript, I reported the development of QTc prolongation within 3 hours after of suicidal attempt using a mixture of propranolol, amitriptyline, caffeine anhydrous, paracetamol, and chlorpheniramine maleate in a young-aged female patient.

Case presentation

A 25-year-old married, housewife, Syrian female patient presented to the emergency department with marked irritability, rapid breathing, and dizziness. Her mother gave a recent history of suicidal attempts using many oral drug strips. The patient tried the suicide attempt after exposure to socio-familial troubles. She present within 2 hours of swallowed; Inderal; 40 mg, 10 tablets (propranolol), tryptizol; 25 mg, 10 tablets (amitriptyline HCL), Cetal Sinus; 10 tablets (combination of paracetamol 500 mg with pseudoephedrine HCL; 30 mg), and Power Cold & Flu; 10 tablets (combination of paracetamol; 500 mg, Caffeine Anhydrous; 30 mg, pseudoephedrine HCL; 30 mg, and chlorpheniramine maleate; 3 mg) (Figure 1).The patient denied a history of psychiatric or other relevant diseases. Upon examination, the patient appeared irritable, distressed, and tachypneic. Her vital signs were as follows: blood pressure of 100/60 mmHg, the pulse rate of 54/bpm; and regular, the respiratory rate of 38/min, the temperature of 36.1°C, and the pulse oximeter of oxygen (O_2) saturation of 98%. No more relevant clinical data were noted during the clinical examination. Gastric lavage with active charcoal was done in the emergency department. The patient was admitted to the ICU. Ringer solution 500 ml solution and normal saline 0.9% was given. The initial emergency electrocardiogram (ECG) was taken on ICU admission which showed sinus bradycardia at VR; 55 beats/min with QT prolongation best seen at lead II (QT;495 ms, QTc;481 ms on using Fridericia's formula), Wavy triple an electrocardiographic sign of hypocalcemia (Yasser sign) is seen at V6. (Figure 2). The immediate ABG showed compensated respiratory alkalosis (PH;7.41 mmHg, PCO2;31 mmHg, HCO3;19.6 mmHg, and PaO2; 96 mmHg). Measured random blood sugar was 112 mg/dl. Full blood count (FBC); Hb was 10.2 g/dl, RBCs; $4.29*10^3/mm^3$, WBCs; $8.0*10^3/mm^3$ (Neutrophils; 66.7 %, Lymphocytes: 28.2%, Monocytes; 5.1%), Platelets; $274*10^3/mm^3$. SGPT;23 U/L, SGOT;28 U/L, serum creatinine;0.7 mg/dl, blood urea;14 mg/dl. Plasma sodium was normal (144 mmol/L). Serum potassium was normal (5.5 mmol/L). Calcium showing hypocalcemia with ionized Calcium; 0.33 mmol/L. Two calcium gluconate ampoules (10 ml 10% over IV over 20 minutes) were given as an emergency dose. Maintenance therapy with calcium gluconate ampoules (10% with the rate; 0.5 mg/kg/hour over IV over 6 hours) was the infused. The second ECG was taken on 6 hours of admission which showed normal sinus rhythm at VR; 60 beats/min with QT interval normalization best seen at lead II (QT;460 ms, QTc; 460 ms on using Bazett's formula). Wavy triple an electrocardiographic sign of hypocalcemia is still seen at V6 (Figure 3). Later follow up with serial liver function and kidney function tests was done. There were no detected abnormalities. The patient as discharged within 24 hours of clinical, electrocardiographic, and laboratory improvement. Oral calcium and vitamin-D preparation were prescribed on discharge. Future serial liver function tests and ionized calcium were advised. Complete clinical characteristic of the patient on presentation and after treatment was summarized (Table 1).

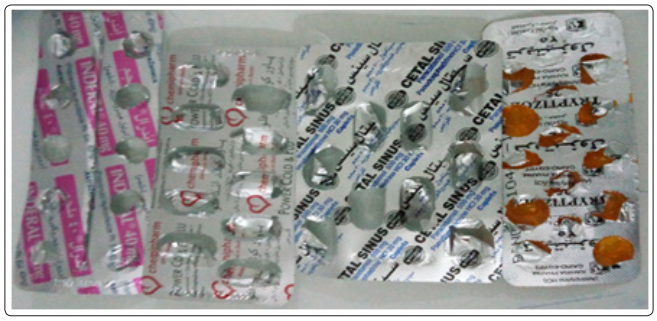

Figure 1: showing swallowed 4 strips (from left to right) of Inderal; 40 mg, Power Cold & Flu, Cetal Sinus, and Tryptizol; 25 mg

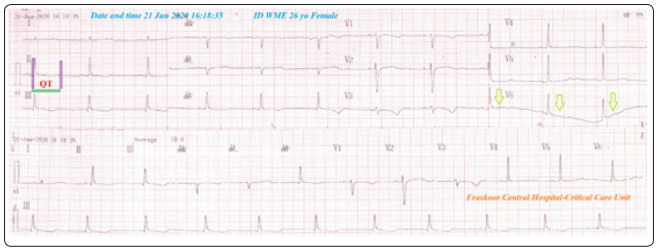

Figure 2: An initial ECG tracing was done 3.30 hours of presentation on ICU admission which showed sinus bradycardia at VR; 55 beats/min with QT prolongation best seen at lead II (QT;495 ms, QTc;481 ms on using Fridericia's formula; pink and green rods). Wavy triple an electrocardiographic sign of hypocalcemia (Yasser sign) is still seen at V6 (lime color).

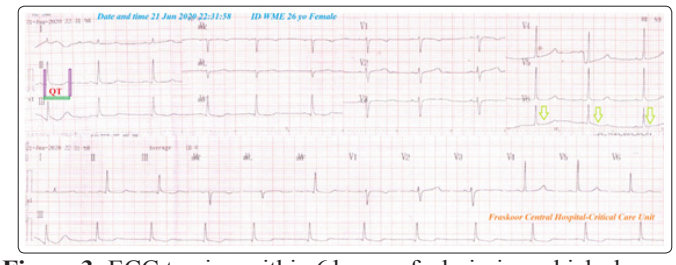

Figure 3: ECG tracing within 6 hours of admission which showed normal sinus rhythm at VR; 60 beats/min with QT interval normalization best seen at lead II (QT;460 ms, QTc;460 ms on using Bazett's formula; pink and green rods), Wavy triple an electrocardiographic sign of hypocalcemia is still seen at V6 (lime color).

Table 1: Summary of the clinical characteristic of the patient on presentation and after treatmeant

Issue	On presentation	After treatment
• Complaint	Dizziness and tachypnea	Disappear
• Generally	irritable	Calm
• Vital signs		
• Blood pressure (mmHg)	100/60	100/70
• Pulse rate (bpm)	55	60
• Respiratory rate (bpm)	38	16
• Temperature (°C)	36.1	36.6
• O_2 saturation (%)	98	99
• ECG	Sinus bradycardia QT prolongation Wavy triple electrocardiographic sign of hypocalcemia (Yasser sign)	Normal sinus hythm QT interval normalization Wavy triple electrocardiographic sign of hypocalcemia (Yasser sign)
• ABG	Compensated respiratory alkalosis	Normal
• Ionized Calcium;	0.33 mmol/L.	1.0 mmol/L.

Discussion

Overview

The current case is a young-aged married female patient presented to the ICU department with tachypnea, marked irritability, and dizziness. This was happened after suicidal attempts using oral 40 tables of 6 drug combinations due to socio-familial troubles.

The generic ingested drug sum doses were Propranolol (400mg), Amitriptyline HCL(250mg), Paracetamol (1000mg), Caffeine Anhydrous HCL (300mg), Pseudoephidine (600mg), and Chlorpheniramine maleate (30mg).

- The primary objective for the current case study was the presence of tachypnea and marked irritability after the ingested drugs. There was latent tetany with low very ionized calcium synchronized with electrocardiographic QTc prolongation and bradycardia.
- The secondary objective for the case study was; How would you manage the case?
- Indeed, the mechanism of tachypnea, hypocalcemia, bradycardia, and QTc prolongation in the current case was unknown. The author thinks that;
- According to the above literature, there is no direct relationship among all ingested drugs and the current hypocalcemia.
- But breathing disorders which are adverse effects for Propranolol, Amitriptyline, Caffeine Anhydrous, Paracetamol, and Chlorpheniramine Maleate maybe interpret the present tachypnea. This adverse effect was mostly summing for the potentiation of these four dugs.
- The author thinks that patient anxiety was a trigger factor for tachypnea.
- Tachypnea is a risk factor for respiratory alkalosis which is an inducible factor for hypocalcemia.
- Irritability mostly had happened with Pseudoephedrine, Caffeine Anhydrous, and Chlorpheniramine Maleate.
- Regards the borderline bradycardia in ECG, Indeed, there were contradictory effects for the four drugs; propranolol, amitriptyline, caffeine anhydrous, pseudoephedrine, and chlorpheniramine maleate on the heart rate.
- Propranolol is a well-known negative chronotropic drug. On the other side, pseudoephedrine, caffeine anhydrous, and chlorpheniramine maleate are positive chronotropic drugs.
- The author thinks that the negative chronotropic effect of propranolol was slightly stronger than the sum positive chronotropic of pseudoephedrine, caffeine anhydrous, and chlorpheniramine maleate.
- So, the sum net effect of these drugs on the heart rate was borderline or slight bradycardia.
- Regards the QTc prolongation in ECG, propranolol, amitriptyline, and chlorpheniramine maleate are known inducing for QTc prolongation. The severity of QTc prolongation mostly was interpreted with a sum for potentiation these three dugs.
- This is the first case that reports these adverse drug effects with the above 5 drugs. So, I can't compare this case with another case because there was no similar publicized case report.
- The drug-drug interactions (DDIs) have a strong impact on inducing various serious drug adverse effects in my case report.

Limitations of the study

- There are no known limitations in the study.
- Finally, I reported the development of tachypnea, hypocalcemia, bradycardia, and QTc prolongation within 3 hours after suicidal using oral propranolol, amitriptyline, pseudoephedrine, caffeine anhydrous, paracetamol, and chlorpheniramine maleate in a 25-year old. female.

Conclusions

Drug-induced diseases is a pivotal step in the diagnosis decision making of any medical problems.

- Drug side effects are a sometimes strong way for the diagnostic challenge in clinical medicine.
- So, attention must be taken on using the sum of these drugs to reduce the risk of the development of these adverse drug reactions.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

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