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Lipid Emulsion Therapy in Tricyclic Anti-depressants Poisoning: Does Early Initiation Improve Outcomes?

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ABSTRACT

Tricyclic anti-depressants are commonly implicated drugs in self-poisoning ,second only to analgesics as the commonest drugs involved in a fatal drug overdose. Severe toxicity involves central nervous system and cardiovascular system and may present as seizures, coma, hypotension, or arrhythmias. The role of lipid emulsion therapy (LET) has been reported in severe toxicity, when patient's symptoms are refractory to standard therapy including sodium bicarbonate. In the present case, we used early LET in a patient with symptoms of severe toxicity which might have prevented complications and optimised outcome.

KEYWORDS

Tricyclic anti-depressants; Drug overdose; Lipid emulsion therapy

INTRODUCTION

Tricyclic anti-depressants (TCAs) have been in use for decades [1]. Recently, use of selective serotonin reuptake inhibitors (SSRIs) have increased and they are preferred over TCAs because of their better safety profile. In spite of their reduced usage, the rate of hospitalization continues to be higher with TCA overdose because of their narrower therapeutic index [2]. Even though, mortality is generally secondary to cardiac complications, studies have suggested that in cases of fatal overdose, central nervous system (CNS) symptoms like altered mental state, seizures, coma, and respiratory distress precede cardiovascular system (CVS) signs like arrhythmias, widened QRS and sudden cardiac arrest [3]. Death generally occurs within the first few hours of consumption and many patients die even before they reach the hospital [3].

Sodium bicarbonate is indicated in the treatment of TCA toxicity and it may be effective in resolving hypotension and QRS prolongation in majority of patients. Lipid emulsion therapy (LET) has been advocated as an adjuvant therapy in severe TCA toxicity, not responding to standard therapy [4]. It may be contemplated that with this short window of intervention, early LET initiated at the development of severe CNS symptoms, may be useful in preventing life-threatening complications.

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CASE REPORT

An 18-year-old female, a known case of fibromyalgia, on TCA, SSRI, benzodiazepine and beta-blocker presented to our hospital with an alleged history of consumption of multiple drugs tofisopam 50 mg (80 tablets), amitriptyline 10 mg (60 tablets), escitalopram 5 mg (10 tablets), and etizolam 0.25 mg (24 tablets). She was brought to the hospital in an altered mental state. On presentation, she was hypotensive and hence, aggressive fluid resuscitation was done.

On arrival to the hospital, her Glasgow coma score (GCS) was E2V2M5, pupils were bilaterally 2 mm with sluggish reaction to light with vitals of HR 84/min, BP 80/50 mmHg, RR 16-18/min spo2 97% on room air. Ryle's tube was inserted and gastric lavage was done. Urine output was adequate. Arterial blood gases revealed pH - 7.35, PO2 - 72.9, PCO2 - 48.9, HCO3 - 24.9, base deficit 0.6 and lactate - 0.3. Over the next few hours, her GCS deteriorated to E1V1M5, and she was intubated for airway protection. Supportive treatment was initiated including ventilatory and hemodynamic support. Her urine drug analysis was positive only for TCA.

LET was considered because of rapid decline in her neurological status and hypotension. Bolus dose of 1.5 ml/kg of 20% lipid emulsion was given intravenously over 1 minute and maintenance infusion was initiated at a rate of 0.25 ml/kg - 1/min and continued for 2 hours duration, till she became hemodynamically stable. She showed gradual improvement over the next three days and was extubated after 36 hours of invasive mechanical ventilation. She was discharged after 4 days of hospitalisation.

DISCUSSION

Patients with TCA overdose generally present with initial CNS symptoms, followed by life-threating cardiac symptoms [3]. A great majority of these patients have symptoms like coma, seizure, or respiratory distress on presentation to the hospital [2,3]. Cardiac complications have been shown to be present in only around 11.7% of patients, up to 3 hours or more after hospital arrival [3]. However, patients may show rapid deterioration, with a meantime from arrival to death being only 5.43 hours [3]. Death is generally secondary to cardiac complications like AV conduction disturbances, wide complex arrhythmias, and myocardial depression.

Use of LET has been validated and being recommended in the management of local anaesthetic systemic toxicity (LAST) [4,5]. When large volumes of lipids are infused intravenously, they act as a “lipid sink”. This removes large quantities lipophilic drugs from their target sites and hence reducing their harmful effects and development of complications [5,6]. Recently, its role has expanded to managing other severe toxicities like beta-blockers, calcium channel blockers and several others [6]. LET has also been shown to be beneficial as an adjuvant therapy in management of severe TCA toxicity. However, it is generally initiated later in the treatment course when life-threatening cardiac complications are already present [3]. There is emerging evidence suggesting role of early initiation of LET for improving patient outcomes in LAST [5,7]. Extrapolating the same rationale, we initiated LET in our patient immediately with the development of severe neurological signs and hypotension, which may have proved beneficial and prevented the development of further life-threatening cardiac complications.

The recommended dose for LET is a 1.5 ml/kg of 20% lipid emulsion intravenously over 1 minute as bolus followed by a maintenance infusion of 0.25 ml/kg - 1/minute for at least 60 minutes [8]. Bolus dose can repeat up to two times after 5 min interval and the infusion rate can be doubled (up to 0.50 ml/kg - 1/min) if there is no hemodynamic improvement after five minutes

of initiation of therapy [8]. Longer regimens of up to 6.5 hours have also been tried, without any significant side effects [9]. We continued the infusion for 2 hours, till hemodynamic stability was achieved. LET has been shown to be a safe therapy with rare side effects like interference with lab values, pancreatitis ,acute respiratory distress syndrome [10]. It should be kept in mind that the total dose of 20% lipids should not exceed 10 ml/kg - 1 over 30 minutes, as the rate of complications may increase beyond this dose [8].

CONCLUSION

Role of LET in clinical poisoning is evolving. Our case illustrates early use of LET in TCA poisoning in the presence of severe neurological symptoms. Early LET might have prevented the development of life-threatening cardiac complications and metabolic acidosis and enabled us to achieve a positive clinical outcome. Further reports may strengthen our view of early initiation of LET, as it is a safe and easily available treatment modality.

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