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Case report: Management of an unknown TCA diagnosis: The importance of rapid diagnosis and the use of CVVHDF in toxin elimination

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ABSTRACT

This case report highlights the effective medical management of a 27-year-old woman in critical condition due to an unknown medication overdose. The patient's initial condition at the emergency department (ED) indicated TCA (Tricyclic antidepressant) toxicity, which implied a poor prognosis based on clinical presentation and measurable criteria. The patient's systemic collapse was managed emergently in accordance with the TOXBASE guidelines. Additional supportive measures, including Continuous Venovenous Hemodiafiltration (CVVHDF), were employed in this severe case. Swift therapeutic interventions administered in the Emergency Department (ED) and Intensive Care Unit (ICU) resulted in enhanced clinical outcomes and improved haemodynamic status within five days. The patient successfully achieved complete clinical recovery without any neurological sequelae. She was discharged home within a week. This case underscores the importance of early recognition and highlights the utilisation of CVVHDF as an adjunct therapy in the advent of a lethal TCA overdose.

1. Background

Tricyclic antidepressants (TCAs) were among the first classes of commonly prescribed antidepressants. However, due to its potentially fatal side effect profile, it has predominantly been substituted by novel and safer medications such as Selective Serotonin Reuptake Inhibitors (SSRIs). TCAs continue to be frequently prescribed to patients who have not responded to alternative treatment for depression and to those whose chronic pain has not been alleviated by other therapeutic methods [1]. If abused, clinical signs of an overdose include cardiac dysrhythmia, depression of the central nervous system (CNS), seizures, and in severe cases, progression to a comatose state. The manifestation of an overdose of TCA often presents as a critical emergency, with significant mortality rates of 70% if patients fail to promptly access a healthcare facility [2]. The current mainstay of management includes airway protection, vasopressors for hypotension, and intravenous sodium bicarbonate for metabolic acidosis.

Continuous venovenous hemodiafiltration (CVVHDF) is a form of renal replacement employed to correct electrolyte imbalance through the principles of haemodialysis and hemofiltration. During this procedure, the blood undergoes a high degree of ultrafiltration, resulting in an increased transfer of water and solutes from the blood to the dialysate. The loss of water often necessitates regular infusions to replenish the lost volume. The principle of diffusion in correcting electrolyte imbalance is also exercised, with a counter-current flow of blood against the dialysate fluid ensuring the movement of solute from areas of high concentration to low concentration. The utilisation of both processes leads to favourable outcomes by efficiently removing solutes with varied molecular weights and sizes [3].

Here, we present the case of a 27-year-old female with an unknown severe amitriptyline overdose who was effectively treated in accordance with the TOXBASE guidelines with the addition of CVVHDF.

2. Case presentation

A 27-year-old female presented to the emergency department in peri-arrest with a Glasgow Coma Scale (GCS) score of 3 following a witnessed collapse in public. There were no signs of trauma nor any evident drug paraphernalia. On arrival, the patient had dilated pupils, an unrecordable blood pressure signifying systemic shock. Her ECG demonstrated sinus tachycardia (presence of p waves and a heart rate > 100) with a regular rhythm, alongside a widened QRS interval of 0.142 s (normal range: 0.08–0.1 s), indicating ventricular tachycardia. The patient was intubated without the need for sedatives and underwent a CT scan which

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Table 1
A table detailing the change in pH and lactate over time. The acidic pH from the TCA overdose stabilised upon administration of a bicarbonate infusion and CVVHDF. The target pH, according to TOXBASE guidelines, is 7.45–7.55. The lactate also reduced significantly and was thus appropriately controlled (normal range <1 mmol/L).

Date	25/04/23 09:53	01/05/23 04:45	01/05/23 09:00	01/05/23 16:00	02/05/23 04:04
pH (7.35–7.45)	7.08	7.39	7.37	7.37	7.41
PCO2 (4.7–6.0)	8.1	4.6	4.7	4.4	4.8
Lactate	5.7	0.4	0.7	0.4	0.4

uncovered no remarkable changes. A bedside echocardiogram, however, displayed global hypokinesia with a poor left ventricular function, operating at an ejection fraction of ~15%.

Upon ITU admission, the patient was started on mechanical ventilation to ensure adequate airflow and high doses of vasopressors to remediate the systemic shock. Though unconfirmed, the idea of a TCA overdose was suspected, resulting in an immediate bicarbonate infusion as per TOXBASE guidelines with a target pH set for 7.45–7.55. The patient additionally received Continuous Venovenous Hemodiafiltration (CVVHDF) to eliminate excess TCA, and she achieved a high filtration rate of 60 ml/kg/hr.

Despite no previous history, the patient suffered from multiple seizures during her stay in ITU and was consequently commenced on Keppra during her stay. Her treatment plan continued in the aforementioned manner until she was extubated on day five and removed from the filter on day six. At this point, the patient's observations were all within normal ranges, target blood pH was achieved, and she could maintain her airway, manage oral intake, produce an adequate volume of urine, and was saturated on room air (Table 1).

A collateral history from the patient's husband was obtained after the patient had been stabilised and treated for a suspected TCA overdose. The history revealed that the patient had recently migrated from Ukraine and received a batch of antidepressants from her mother. It was suspected that she had ingested 119 Amitriptyline tablets, each dosed at 50 mg. The patient confirmed the overdose was unintentional and claimed no thoughts of self-harm or suicidal ideation but had recently been feeling depressed and isolated since her move to the UK. She declined support from liaison psychiatry.

3. Discussion

The pathophysiology of TCA overdose involves various mechanisms, including inhibition of noradrenaline reuptake, serotonin reuptake, and blockade of GABA receptors. These actions lead to metabolic acidosis through increased carbon dioxide production and impaired mitochondrial function. Additionally, TCAs block alpha-adrenergic, histaminic, muscarinic, and central serotonin receptors, resulting in hypotension, altered mental status, dry mouth, and arrhythmias [2].

As per current TOXBASE guidelines, treatment for TCA overdose starts with ensuring the patient's airway is clear and maintaining proper ventilation. Close monitoring of vital signs and cardiac rhythms is crucial. If the patient presents within an hour of ingestion, activated charcoal may be considered to help remove the drug from the stomach. However, the primary approach involves administering sodium bicarbonate infusions. Sodium bicarbonate works by competitively inhibiting the binding of TCAs to cardiac sodium channels. This reduces the blockade of sodium channels caused by TCAs and helps restore normal electrical conduction in the heart. This intervention is the cornerstone of managing the cardiovascular effects of TCA overdose [2].

A lack of available diagnostic markers for a TCA overdose emphasises the importance of a bedside ECG. This is reinforced by its accuracy in reflecting changes associated with TCA overdose, i.e., Ventricular Tachycardia and prolonged QT, and therefore should be assessed with priority in situations of an unknown overdose.

TCA's have a large volume of distribution, rendering its removal complicated. Typically, respiratory, or metabolic acidosis increases the unbound fraction of TCA, potentiating its harmful effects [4]. The use of CVVHDF as a means of therapy is not suggested in the current TOXBASE guidelines due to its ineffectiveness in eliminating the toxin. CVVHDF is primarily used in acute kidney injury, septic shock, metabolic and lactic acidosis. Numerous studies account for its benefit [5,6]; however, there is also the increased risk of side effects, notably hypotension and infection. There is also a divergence in the current literature on the practicalities of its use as an early intervention. The ELAIN randomised clinical trial found that early renal replacement therapy reduced mortality for patients with acute AKI over the first 90 days [7]. However, a systematic review regarding patient mortality and early employment of renal replacement therapy indicated otherwise [8]. Regardless, its administration's advantage lies in reversing metabolic acidosis and modulation of high lactate levels [5]. This is evident in this case study, where the patient's pH and lactate were significantly stabilised with the assistance of CVVHDF. The overall rationale behind choosing CVVHDF was to correct the severe metabolic acidosis and hyperlactaemia which was due to the significant hypotension and hypoperfusion. Ameliorating the metabolic acidosis in a swift and promptly manner ultimately improved the inotropic effect which in turn, aided in the patients recovery. The large volume of TCA taken consequently led the patient into a state of cardiogenic shock, the anticholinergic effects of TCA causes blockade of sodium channel receptors thus resulting in arrythmias and heart failure. To rectify this, CVVDHF was used to reduce the toxicokinetic effects by keeping the pH towards the alkalotic side (7.45–7.55).

It is thought that the ingestion of 10–20 mg/kg of Amitriptyline is potentially life-threatening. Our patient consumed over 5 g, which far exceeds that threshold. We argue that the swift diagnosis - aided by the patient's clinical signs and ECG, management suggested by TOXBASE guidelines, and the addition of CVVHDF all assisted in the full recovery of a patient with a life-threatening TCA overdose.

The patient presented with no evidence of brain perfusion and minimal cardiac contractility. The overarching challenge here were to treat her in an acute manner and carry out the life-saving interventions within an increasingly narrow time-frame. Making endeavours to overcome the metabolic failure and the critical haemodynamic compromise in approximately 48 h proved to be extremely difficult. There was also the worrying concern of possible neurological deficits due to the prolonged hypoperfusion which was causing her seizures. As part of her recovery, when the patient was coming in and out of consciousness, she was progressively getting more agitated and became combative. To manage this we utilised analgesia for intermittent sedation.

4. Conclusion

In conclusion, this case report highlights the successful management of a severe amitriptyline intoxication using a combination of standard TOXBASE guidelines and the adjunctive use of Continuous Venovenous Hemodiafiltration (CVVHDF). The report also emphasises interpreting the ECG when patients present with an unknown overdose, as an early diagnosis is associated with better patient outcomes.

Author contribution

T.M. and M.S.Z conceived the idea of writing the manuscript. T.M and N.Q contributed to the design and revised it critically. S.R, N.Q.and T.M collected the patient information. T.M and N.Q prepared the draft of this manuscript. T.M., M.S.Z. and N.Q reviewed and approved the final manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

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