Case Report

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Plasmapheresis as Rescue Therapy in Severe Pediatric Amitriptyline Intoxication

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ABSTRACT

Drug intoxications remain a major challenge in pediatrics, particularly when involving uncommon medications such as tricyclic antidepressants, whose cardiotoxic and neurotoxic potential carries a high risk of mortality. We report the case of a 13-year-old girl with severe amitriptyline intoxication who was admitted to the Pediatric Intensive Care Unit with deep coma, ventricular arrhythmias and seizures. Despite initial treatment with bicarbonate, activated charcoal, vasoactive support and lipid emulsion therapy, hemodynamic and neurological instability persisted. Plasmapheresis was initiated as rescue therapy, leading to a progressive reduction in plasma amitriptyline levels and progressive clinical and neurological recovery, including normalization of the electroencephalogram and cardiovascular stabilization, which allowed extubation and withdrawal of hemodynamic support.

This case highlights the potential role of plasmapheresis in severe tricyclic antidepressant intoxications when conventional measures are insufficient.

Keywords

Drug overdose, Amitriptyline, Arrhythmias, Plasmapheresis, Child.

Case Report

A 13-year-old previously healthy adolescent girl was admitted to the Emergency Department after a suicidal ingestion of amitriptyline. During transport she developed a generalized tonic–clonic seizure and episodes of ventricular tachycardia. On arrival she was in deep coma (Glasgow Coma Scale 3) with bilateral fixed and dilated pupils, requiring endotracheal intubation and mechanical ventilation.

Initial toxicology screening was positive for tricyclic antidepressants, with plasma amitriptyline levels of 992 ng/ml (toxic dose >500 ng/ml) and concomitant detection of nortriptyline. Intravenous bicarbonate, activated charcoal, and lipid emulsion therapy were administered. Because of hemodynamic instability with persistent hypotension, low-dose norepinephrine infusion was initiated.

Electroencephalography performed within the first hours of admission showed alpha coma and bilateral frontal irritative activity, findings that persisted unchanged at 24 hours. Given the lack of clinical improvement and ongoing neurological and hemodynamic instability, plasmapheresis was started as rescue therapy. Five sessions were performed, one every 24 hours, with a progressive reduction in plasma amitriptyline and nortriptyline levels (Figure 1).

The patient showed progressive neurological and hemodynamic recovery, allowing discontinuation of vasopressor support within 48 hours. Elective extubation was carried out on the fifth day, after documented neurological improvement on EEG and sustained hemodynamic stability. She subsequently developed withdrawal symptoms and delirium, which resolved with specific treatment.

She was finally discharged without neurological or cardiac sequelae.

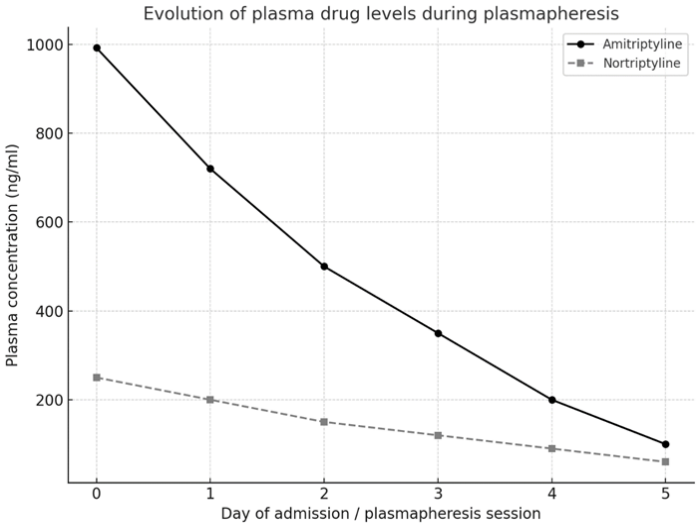

Figure 1: Evolution of plasma amitriptyline and nortriptyline concentrations during plasmapheresis. Baseline levels were 992 ng/ml for amitriptyline and 250 ng/ml for nortriptyline, decreasing to 100 ng/ml and 60 ng/ml respectively after the fifth session.

Discussion

Drug intoxications in children remain a challenging emergency for pediatricians and intensivists, not only due to their variable clinical presentation but also because of the risk of life-threatening complications. Among these, tricyclic antidepressant (TCA) overdoses are relatively uncommon in pediatrics but carry high morbidity and mortality because of their narrow therapeutic index and complex pharmacologic profile. Amitriptyline exerts anticholinergic, antihistaminic, and sodium channel–blocking effects, which explain the combination of severe neurological and cardiovascular compromise observed in severe intoxications [3].

The clinical course can be unpredictable. Patients may initially appear stable after ingestion, followed by rapid deterioration characterized by coma, seizures, ventricular arrhythmias, or refractory hypotension. This fulminant evolution underscores the importance of maintaining a high index of suspicion and instituting prompt supportive therapy in all suspected cases.

Conventional management focuses on advanced life support measures, including airway protection, mechanical ventilation, and vasoactive support for shock. Sodium bicarbonate remains the cornerstone of pharmacologic treatment, as it mitigates both acidosis and cardiotoxicity by widening the sodium gradient and alkalinizing serum. Activated charcoal can be used in selected patients if airway protection is assured. Lipid emulsion therapy has also been employed as rescue therapy in severe poisonings with lipophilic agents, although evidence in children is limited and its efficacy in TCA intoxication remains debated. Despite these measures, outcomes may be poor in massive ingestions or in cases refractory to conventional therapy.

In recent years, extracorporeal therapies have been considered for the management of severe intoxications. A structured review has shown that plasmapheresis can significantly influence drug pharmacokinetics in children, particularly for drugs that are highly protein-bound, such as amitriptyline [1]. Clinical series also support its safety profile in pediatric poisonings, with no major adverse events reported [2].

Case reports remain scarce but provide valuable insights. In pediatrics, plasmapheresis has been successfully used in isolated cases of severe amitriptyline intoxication [3], and similar favorable outcomes have been described in adults [4]. In our patient, plasmapheresis was initiated after failure of conventional therapies and was associated with a progressive reduction in plasma amitriptyline and nortriptyline levels (Figure 1), paralleled by neurological and hemodynamic recovery. While causality cannot be definitively established, the temporal association strongly suggests that plasmapheresis contributed to the improvement.

Furthermore, unusual and severe complications of amitriptyline intoxication, such as compartment syndrome, irreversible neurological injury, or refractory arrhythmias, have recently been reported [5]. These findings highlight the potential for unpredictable and devastating outcomes, reinforcing the rationale for considering early extracorporeal interventions in selected life-threatening cases.

In conclusion, severe pediatric TCA intoxication represents a medical emergency with limited therapeutic options once conventional measures fail. Our case adds to the growing but still limited evidence supporting plasmapheresis as a potential rescue therapy in refractory situations. Further experience and systematic studies are needed to define its precise role, but our findings suggest that plasmapheresis should be considered when faced with life-threatening amitriptyline intoxication unresponsive to standard treatment.

Summary

What is new?

Plasmapheresis may serve as a novel rescue therapy in severe pediatric amitriptyline intoxication, providing clinical improvement when conventional management proves insufficient.

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