Severe childhood amitriptyline intoxication and plasmapheresis: a case report

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Tricyclic antidepressant intoxication is one of the most frequently encountered and life-threatening causes of intoxication among referrals to emergency departments due to drug intoxication. There is no known antidote against any of the tricyclic antidepressants. The American Society for Apheresis (ASFA) recommends plasmapheresis to support primary treatment in this type of drug poisoning, which does not respond to certain and traditional treatments. We present a 15-year-old girl who ingested amitriptyline with suicidal intent. On admission, she was in a comatose state (Glasgow Coma Scale score: 5), with no spontaneous respiration and presence of pathological reflexes. Due to the intake history of lethal doses and the severe clinical picture, plasmapheresis was performed. She was discharged on her fifth day of hospitalization.

Due to the high plasma protein binding property of amitriptyline, plasma exchange therapy should be considered in cases of severe amitriptyline intoxication as a life-saving therapeutic modality.

Key words: amitriptyline, childhood, intoxication, plasmapheresis.

Amitriptyline is a commonly prescribed antidepressant drug in Turkey; therefore, antidepressant drug poisoning due to amitriptyline is the most commonly encountered type of poisoning among the tricyclic antidepressants[1,2]. According to the report of the American Association of Poison Control Center published in 2006, the intoxication rate due to antidepressants was stated to be 4% among all drug poisonings. In that report, it was claimed that the overall death rate due to antidepressant-associated poisonings is 0.25%, and that it is the fifth most frequently encountered cause of death among drug poisonings[3]. In Turkey, however, the intoxication rate due to antidepressants is between 8% and 34%[4].

Tricyclic antidepressants are absorbed rapidly from the gastrointestinal tract and are bound to plasma proteins with high affinity. Plasma exchange can be a life-saving procedure in the most severe cases, where a dramatic improvement in the clinical condition can be achieved[5]. In this report, we aimed to present the effective utilization of plasma exchange in a 15-year-old female patient with severe amitriptyline intoxication.

Case Report

A 15-year-old female patient was referred from a local hospital to our pediatric emergency department. Gastric irrigation and activated charcoal had been administered via nasogastric tubing two hours after the suicide attempt. The patient had been intubated at the local hospital due to weak respiratory efforts and a decreased level of consciousness and hypoventilation. We estimated that she had taken 22 mg/kg amitriptyline with suicidal intent 4 hours (h) prior to admission. The patient was admitted to our pediatric intensive care unit. The initial physical examination revealed loss of consciousness with a Glasgow Coma Scale (GCS) score of 5 (E1 V-intubated M3). Pupil reflexes were weakly positive bilaterally and pupils were slightly dilated. Her deep tendon reflexes were increased with bilateral positive Babinski reflex. Her

body temperature was 36.6°C, blood pressure 121/66 mmHg and heart rate 102 bpm. Arterial blood gas analysis revealed pH: 7.42, PO_2: 57.4 mmHg, PCO_2: 38.4 mmHg, HCO_3^-: 25 mmol/L, and arterial oxygen concentration of 94.2% during mechanical ventilation. Complete blood count, serum chemistry profiles including electrolyte levels and liver and renal function, and hemostasis tests were within normal limits. Electrocardiographic (ECG) examination revealed a normal QRS (0.8 s) and QTc interval (0.45 s). Sodium bicarbonate infusion was initiated for alkalinization followed by mechanical ventilation. Because of the lethal dose of amitriptyline and respiratory depression, plasmapheresis was performed via femoral venous catheter. Plasmapheresis was performed for 4 h, using an intermittent apheresis device (Hemonetics® MCS (+) USA). A total of 2015 ml plasma volume was removed during the procedure. Fresh frozen plasma was used as a replacement fluid. No complications concerning the procedure were encountered. At the end of the fourth hour of the procedure, she became responsive to verbal stimuli, her GCS score improved to 13 (E4 M5 V4), and she was extubated. Plasma amitriptyline levels were 9.23 ng/ml after the procedure compared to 112.78 ng/ml before the plasmapheresis session. Thereafter, the patient was evaluated and treated by our pediatric psychiatry department. She was discharged on the fifth day of admission without any complications.

Discussion

Amitriptyline is the most commonly used agent among the antidepressants. Amitriptyline poisoning is seen frequently in accidental ingestions in children, while suicidal ingestions are seen in adolescents. High doses may result in death[1-3]. There is no specific antidote but precautions like gastric irrigation, activated charcoal administration, antiarrhythmic and anticonvulsant drugs, and sodium bicarbonate infusion can be taken with the support of mechanical ventilation[1]. Amitriptyline binds to proteins in the plasma with a high affinity of 95%. Therefore, plasma exchange is one of the reasonable treatment options for amitriptyline intoxication[5].

There is no defined exact toxic limit for the dose of amitriptyline in childhood. The lethal dose interval is usually considered to be 15-30 mg/kg[1,6]. The most common findings are life-threatening arrhythmia, hypotension, convulsions, respiratory depression, and coma. Generally, abnormal findings in amitriptyline overdosage occur at doses higher than 10 mg/kg. However, there is no correlation between the symptoms and the drug dose, and severe symptoms may be precipitated by the ingestion of a lesser amount[4,6]. We estimated the ingested amount of amitriptyline to be 22 mg/kg in our case. Respiratory depression and coma developed very rapidly in this case.

There were no specific laboratory abnormalities, including complete blood count, biochemistry profiles and hemostasis tests, in the previously published cases. In the present case, all laboratory tests were also within normal limits. Abnormalities of ECG parameters may be seen in severe amitriptyline intoxication. The most common electrocardiographic abnormalities are QT prolongation and QRS widening[6]. However, all these findings may not be seen in all patients. No abnormal ECG patterns were seen in our case on admission or during the follow-up period.

Plasmapheresis is a non-specific treatment method used for many immunological and toxic diseases[7]. In the literature, it has been reported that plasmapheresis resulted in dramatic improvements in the treatment of severe amitriptyline intoxication that did not respond to conventional therapies[7-10]. Furthermore, Kolsal et al.[9] and Belen et al.[8] reported a significant reduction in serum amitriptyline levels with a single plasma exchange session. In our case, plasma amitriptyline levels before and after the plasmapheresis session were 112.78 ng/ml and 9.23 ng/ml, respectively.

There is no clear relationship between plasma amitriptyline concentration and clinical response or toxicity. Thus, measurement of the plasma drug concentration following intoxication is not routinely recommended[6]. Our patient presented with a GCS score of 5 on admission, and after treatment, she was responsive to verbal stimuli and was extubated at the end of the session. All the vital signs had completely normalized at the 10th hour of arrival to the hospital.

Due to the high plasma protein-binding property of amitriptyline, plasma exchange

therapy should be considered in cases of severe amitriptyline intoxication as a life-saving therapeutic modality. Especially respiratory depression, seizure, coma, prolongation of the QRS duration and QTc interval, or ventricular tachycardia may be considered as presenting signs in determining this intoxication.

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