The Role of Plasmapheresis in Organophosphate Poisoning with Two Pediatric Patients Who Do Not Respond to Standard Treatment

Ufuk Yükselmis*, Dincer Yildizdas*, Hayri Levent Yılmaz**, Yusuf Sarı*

* Cukurova University Faculty of Medicine, Department of Pediatric Intensive Care, Adana/Turkey
** Cukurova University Faculty of Medicine, Department of Pediatric Emergency, Adana/Turkey

Close

SUMMARY

Aim: To assess the impact of plasmapheresis used in the management of two pediatric cases with organophosphate poisoning.

Patients : Two patients with severe organophosphate poisoning who do not respond to standard treatment.

Treatments: The treatment of signs and symptoms, supportive treatment, Atropine, Pralidoksim, Plasmapheresis.

Case Presentation: Two sisters aged five and seven who had signs of miosis, abdominal pain, vomiting, confusion, respiratory failure after their mother washed their hair with organophosphates and then the girls became sick and they were brought to the pediatric emergency department. They were taken to pediatric intensive care unit after the detection of Pseudocholinesterase levels 398 U / L and 428 U / L. The patients were given atropine infusion (0.08 mg / kg / hr) and five-minute intervals atropine 0.05 mg / kg / dose. For three times, pralidoksim loading and pralidoksim infusion were applied. Because of the worsening of clinical signs, patients were intubated and connected to mechanical ventilation. However, despite standard treatment, clinical symptoms did not improve and there was no change in plasma pseudocholinesterase levels. Therefore, plasmapheresis was done on three consecutive days. Consequently, the clinical signs improved, and there was no need for mechanical ventilation. Patients were discharged on the sixteenth day after their admission to the hospital.

Conclusion: In organophosphate poisoning, plasmapheresis can be considered as an option for the patients who do not respond to atropine and pralidoksim treatment.

INTRODUCTION

Organophosphates (OF) are poisons that are found in most of the pesticides. Therefore, OF poisoning is quite common in developing countries (1). Organophosphates inhibit the enzyme acetylcholinesterase (AChE) and cause the accumulation of acetylcholine (ACh) in the synapses. Since diethyl organophosphates are inactivated more slowly than dimethyl organophosphates, the reactivation of the enzyme AChE is slower (2). Traditionally, for the treatment of OF poisoning, atropine and oximes are used. Some studies have shown that it is not sufficient to prevent morbidity and mortality (2,3,4).

Plasmapheresis is used for curatory purposes in most medical cases. The purpose of plasmapheresis is to separate antibodies, immuncomplex, endogenous and exogenous toxins from the plasma and replace them with some plasma proteins and coagulation factors. During plasmapheresis, colloids, fresh frozen plasma and albumin are used. In the course of plasmapheresis, plasma, and thus serum cholinesterase are removed. In the studies done with albumin or colloids, it has been showed that the levels of normal or high cholinesterase decrease. Yet, the role of plasma or plasmapheresis on the treatment of OF poisoning is not known clearly (5,6).

Here, we have presented two cases whose clinical and laboratory findings developed in a better way with the application of plasmapheresis.

CASE-1

A 7-year-old female patient, who had the signs of vomiting, abdominal pain and decreasing conscious level, was brought to our pediatric emergency clinic 3 days after her hair was washed with an agricultural pesticide containing organophosphate to fight head lice. When she first came to the emergency department, her temperature was 37°C, respiratory rate 25/mn, blood pressure 120/80, heart rate 161/mn , and SpO_2 95%.

In terms of physical examination, general condition was poor , intubated, and there were miotic and pinpoint pupils, rough lung sounds , widespread crepitane rales. There were tachycardia and intense secretion in oropharynx and hypopharynx, GCS: 10, PRISM score: 18 (25%).

Hemogram and biochemical test results: WBC: 17.000/mm^3, platelet: 487.000/mm^3, hemoglobin: 13,7 g/dl, glucose: 140 mg/dl, BUN: 14 mg/dl, Cr: 0,36 mg/dl, Na: 141 meq/L, K: 3,3 mEq/L, AST: 25 U/L, ALT: 14 U/L, LDH: 288 U/L, CK: 1651 U/L, CK-MB: 12,5 ng/ml, Troponin I: 0,04 ng/ml Miyoglobin: 210 ng/ml. Blood gas: pH: 7,30, PaO_2: 145 mmHg, $PaCO_2$: 31 mmHg, HCO_3^-: 15 mmol/L, BE: -10. The level of plasma pseudocholinesterase was 428 U/L (the normal value: 3530-10800).

The level of plasma pseudocholinesterase was 428 U/L (the normal value: 3530-10800). The patient was diagnosed with organophosphate poisoning based on clinical and laboratory findings. Because her mother washed the patient's hair with an agricultural drug containing organophosphate, the body and hair of the patient were washed with soap and water, and her hair was cut. Monitoring clinical signs every 5 minutes, the patient was given atropine of 0.05 mg / kg / dose. In spite of intermittent application of atropine, atropine infusion was regulated as 0,08 mg/kg/hour because of the continuation of heavy bronkore ve secrations; additionally PAM (pralidoksim) 40 mg/kg/dose was applied, and PAM infusion (8 mg/kg/ hour) continued for two days. Following this, PAM 30 mg/kg/dose was given two more times.

In spite of sixty hours of intensive therapy, the clinical findings did not improve and the patient was received plasmapheresis in three consecutive days. On the fourth day, the clinical findings did improve and the pseudocholinesterase level of 3922 U/L reached up to 4868 U/L the next day (Figure 1).

The atropine need of the patient was supplied every 20 minutes after the first plasmapheresis, 30 minutes after the second plasmapheresis, and 1 hour after the third plasmapheresis. On the seventh day, it was every 3 hours; on the ninth it was every 6 hours; and it was decreased gradually and terminated on the twelfth day.

The patient was separated from mechanical ventilation and her consciousness became activated. The pseudocholinesterase level increased to 7566 U/L. The patient was discharged on the sixteenth day

CASE-2

A 5-year-old female patient, who had the signs of vomiting, abdominal pain and decreasing conscious level, was brought to our pediatric emergency clinic 3 days after her hair was washed with an agricultural pesticide containing organophosphate to fight head lice. When she first came to the emergency department, her temparature was 36,5°C, respiratory rate: 28/mn, blood pressure: 110/60, heart rate : 156/mn, SpO2: %97.

In terms of physical examination, general condition was poor , intubated, and there were miotic and pinpoint pupils, rough lung sounds , widespread crepitane rales. There was tachycardia and intense secretion in oropharynx, GCS: 11, PRISM score: 19 (30%).

Hemogram and biochemical test results: WBC: 14.880/mm^3, platelet: 257.000/mm^3, hemoglobin: 11,3 g/dl, glucose: 140 mg/dl, BUN: 7 mg/dl, Cr: 0,21 mg/dl, Na: 132 meq/L, K: 2,8 meq/L, AST: 29 U/L, ALT: 24 U/L, LDH: 178 U/L, CK: 193 U/L, CK-MB: 6,4 ng/ml, Troponin I: 0,35 ng/ml Miyoglobin: 26,3 ng/ml. Blood gas: pH: 7,24, PaO_2: 115 mmHg, $PaCO_2$: 24 mmHg, HCO_3^-: 17 mmol/L, BE: -8. The level of plasma pseudocholinesterase was 398 U/L.

The patient was diagnosed with organophosphate poisoning based on existing clinical and laboratory findings. Monitoring clinical signs every 5 minutes, the patient was given atropine of 0.05 mg / kg / dose. In spite of intermittent application of atropine, atropine infusion was regulated as 0,08 mg/kg/hour because of the continuation of heavy bronkore ve secrations; additionally PAM (pralidoksim) 40 mg/kg/dose was applied, and PAM infusion (8 mg/kg/ hour) continued for two days. Following this, PAM 30 mg/kg/dose was given two more times.

In spite of sixty hours of intensive therapy, the clinical findings did not improve and the patient was received plasmapheresis. Consequently, the clinical signs did improve, plasmapheresis was given in three consecutive days, and the pseudocholinesterase level reached 4073 U/L (Figure 11).

The atropine need of the patient was supplied every 20 minutes after the first plasmapheresis, 30 minutes after the second plasmapheresis, and 1 hour after the third plasmapheresis. On the seventh day, it was every 3 hours; on the ninth day it was every 6 hours; and it was decreased gradually and terminated on the twelfth day.

The patient was separated from mechanical ventilation and her consciousness became activated. The pseudocholinesterase level increased to 5682 U/L. The patient was discharged on the sixteenth day.

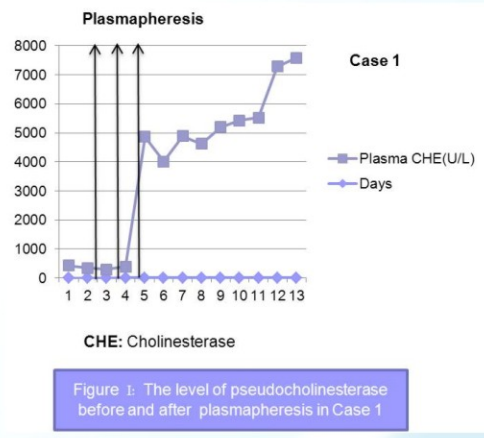

Figure I: The level of pseudocholinesterase before and after plasmapheresis in Case 1

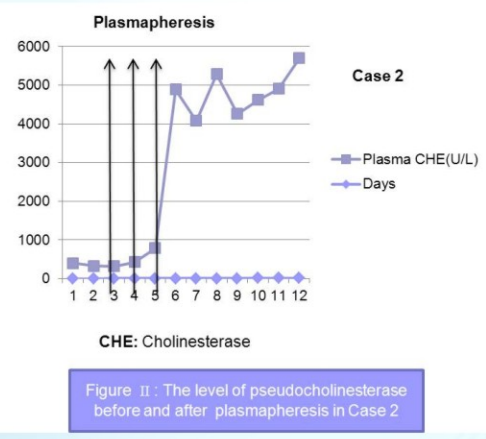

Figure II : The level of pseudocholinesterase before and after plasmapheresis in Case 2

DISCUSSION

Since OF poisoning is associated with morbidity and mortality, it is a major health problem in developing countries (1,7) OF compounds are attached to the enzyme AchE and lead to the inactivation serine hydroxyl group of the enzyme by phosphorylating it. Increasing Ach triggers off the clinical effects on the cholinergic synapses such as central nervous system, neuromuscular junction and autonomic ganglion. The first cholinergic crisis requires immediate treatment and the patient needs to be admitted into the in intensive care unit (8,9).

For the cure of OF poisoning, supportive therapy and antidotal treatment are being used. Antidote treatment atropine (anticholinergics) and oximes (cholinesterase reactivator) such as pralidoksim and obidoksim are used. In some cases, however, these treatments are not sufficient to prevent morbidity and mortality (5). In a case series study carried out for the treatment of OF poisoning, the atropine and pralidoksim in treatment was not found advantageous over the atropine-only treatment (4).

The reasons for the inadequacy of oxime therapy are as follows: 1) It might have been given in inadequate doses 2) Even though the oximes are eliminated from the body quickly, half-life of OF is too long 3) Oxime therapy might have started too late or terminated too early. Besides, the people with BuChe D70G mutation may also be resistant to the reactivation of the enzyme. In addition, cholinesterase inhibition and hepatotoxicity can be seen as a result of oxime therapy. Because of these reasons, new strategies should be developed for OF poisoning (7).

Fresh-frozen plasma contains many plasma proteins including cholinesterase. Plasma or fresh-frozen plasma products may influence cholinesterase levels since they are not attached to organophosphate. Epstein and his colleagues have showed that there is adequate cholinesterase activity in blood and fresh frozen plasma (10). Therefore, the authors recommend blood transfusion in case of prolonged plasma cholinesterase deficiency.

Plasmapheresis is a nonselective method used to dispose of hazardous and toxic products from the circulation. In preventing morbidity and mortality, atropine and / or PAM therapy added to the plasma treatment has been found more efficient than merely atropine and / or PAM therapy (11). Especially in the cases in which PAM therapy cannot be applied, plasmapheresis may be considered as an alternative or additional treatment (11,12). Güven and his colleagues showed that an adult patient with organophosphate poisoning could not respond to atropine and PAM treatment; however, the clinical signs and cholinesterase levels were increased after plasmapheresis. (13). We have found the plasmapheresis application successful in two cases resistant to the treatment. Our study is the first work of medical literature that examines the use of plasmapheresis in the treatment of organophosphate poisoning seen in children.

In conclusion, plasmapheresis can be used in organophosphate poisoning for the patients who do not respond to the treatment. However, randomized controlled studies are necessary to have a clearer idea on this issue.

REFERENCES

1) Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. Q J Med 2002; 93: 715-731
2) Eddleston M, Szinicz L, Eyer P, Buckley N. Oximes in acute organophosphorus pesticide poisoning: a systematic review of clinical trials. Q J Med 2002; 95: 275-283.
3) Sivagnanam S. Potential therapeutic agents in the management of organophosphorus poisoning. Crit Care 2002; 6: 260-261.
4) De Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome of management in acute organophosphorus poisoning? Lancet 1992; 339: 1136-1138.
5) Naik B, Hirshhorn S, Dharnidharka VR. Prolonged neuromuscular block due to cholinesterase depletion by plasmapheresis. J Clin Anesth 2002; 14: 381-84.
6) Busund R, Koukline V, Utrobin U, Nedashkovsky E. Plasmapheresis in severe sepsis and septic shock: a prospective, randomised, controlled trial. Intensive Care Med 2002; 28: 1434- 39.
7) Guven M, Sungur M, Tanrıverdi M, Eser B, Kekec Z. Evaluation of the patients with acute intoxication. Turk J Med Sci 2002; 32:169-172
8) Khan S, Hemalatha R, Jeyaseelan L, Oommen A, Zachariah A. Neuroparalysis and oxime efficacy in organophosphate poisoning: A study of butyrylcholinesterase. Hum Exp Toxicol 2001; 20(4):169-174.
9) De Bleecker JL. The intermediate syndrome in organophosphate poisoning: an overview of experimental and clinical observations. J Toxicol Clin Toxicol 1995; 33(6):683-686
10) Epstein HM, Jarzemsky D, Zuckerman L, Vagher P. Plasma cholinesterase activity in bank blood. Anesth Analg 1980; 59: 211-14.
11) Güven M, Sungur M, Eser B, Sarı I, Altuntaş F. The effects of fresh frozen plasma on cholinesterase levels and outcomes in patients with organophosphate poisoning. J Toxicol Clin Toxicol. 2004;42(5):617-23.
12) Pazooki S, Solhi H, Vishteh HR, Shadnia S, Beigi MJ. Effectiveness of fresh frozen plasma as supplementary treatment in organophosphate poisoning. Med J Malaysia. 2011 Oct;66(4):342-5.
13) Güven M, Sungur M, Eser B. The effect of plasmapheresis on plasma cholinesterase levels in a patient with organophosphate poisoning. Hum Exp Toxicol. 2004 Jul;23(7):365-8.