The İmportance of Hemodialysis in Intoxications with 3 Case Reports

Veysel Garani SOYLU¹, Ayşe YILMAZ¹, Öztürk TAŞKIN², Ufuk DEMİR², Bülent UYAR¹ Kastamonu Training and Research Hospital ² Kastamonu University, Faculty of Medicine

Abstract

Introduction: While many intoxication cases are cured with medical treatment, antidote therapy and symptomatic treatment; some cases may need hemodialysis treatment or even invasive mechanical ventilation support. We aimed to examine the place of hemodialysis in three rare intoxication cases seen in our hospital.

Case Reports: 43-year-old male patient was admitted to the emergency service with metformin intoxication. The patient with type B lactic acidosis was treated with urgent hemodialysis After a session of hemodialysis, the clinical and laboratory data returned to normal. 19-year-old female patient admitted to the emergency service with theophylline intoxication. The blood theophylline level was toxic. The patient with symptoms of intoxication (tachycardia, hypokalemia, severe nausea and vomiting, etc.) regressed after a session of hemodialysis. 22-year-old mental retarded male patient was admitted to the emergency service with loss of consciousness. The patient with metabolic acidosis was taken to the intensive care unit with coma of unknown cause. 4 sessions of hemodialysis was applied to the patient who developed acute renal failure. It was learned that the patient drank ethylene glycol (antifreeze).

Result: All our patients could be discharged with full recovery. Hemodialysis treatment has an important place in the treatment of intoxication cases.

Keywords: Intoxication, Hemodialysis, Intensive Care Unit

Introduction

Intoxication could be very dangerous for life. Sometimes patients may be unconscious so that anamnesis cannot be taken from the patients, or they may be conscious enough to convey these complaints themselves. In our country, intoxication cases are quite common. Some of these cases may be in the form of drug-substance use for suicidal purposes, as well as drug-drug reactions or involuntary overdose of drugs. 0.91% of the patients admitted to the emergency service while intensive care unit (ICU) patients % 5.11 were intoxication cases in Turkey¹. In addition to emergency medical treatment, reduce the absorption or increase the excretion of toxic substances from the gastrointestinal system, using specific antidotes, and to apply urgent hemodialysis treatment under certain conditions is required.

In intoxication cases; If the substance taken develops acute kidney damage, causes severe clinical symptoms and natural renal clearance is insufficient, hemodialysis is required. Continuous renal replacement therapy can be performed in the intensive care unit, as well as short-term renal replacement therapy when hemodynamic parameters are appropriate.

We aimed to present a case of ethylene glycol intoxication, which caused acute kidney damage as a result of involuntary use and was successfully treated as a result of sequential hemodialysis treatments, with two cases who received single-session hemodialysis due to severe symptoms resulting from suicidal metformin and theophylline intoxication.

Case report

Case Report 1: A 43-year-old male patient, who had no known illness, applied to the emergency service of Kastamonu Training and Research Hospital, after taking 50 tablets of the preparation containing 1 gram of metformin for suicide. The patient's consciousness was confused, Glaskow Coma Scale (GCS): 10, Pulse: 100 / min, respiratory rate: 26 / min, arterial blood pressure: 126/66 mmhg. Laboratory data: glucose: 126 mg / dl, ph: 7.25, pCO2: 29.4 mmhg, p02: 90 mmhg, HCO3: 20.3 mmol / L, lactate: 13.8 mmol / l, creatine: 1.93 mg / dl, aspartate transaminase (AST): 32 u / l, alanine transaminase (ALT): 45 u / l, potassium: 6.83 mEg / l. The patient was consulted poison counseling; He was administered activated charcoal and intravenous fluid therapy. The patient was admitted to the intensive care unit due to the severe type of lactic acidosis and GCS: 10. A hemodialysis catheter was placed in the intensive care unit, and she was taken for 4 hours without ultrafiltration After 2 hours following hemodialysis treatment,

Corresponding Author: Veysel Garani SOYLU e-mail: vgsoylu@hotmail.com

Received: 14.09.2020 • **Accepted:** 20.11.2020

DOI: 10.33706/jemcr.794850

©Copyright 2020 by Emergency Physicians Association of Turkey - Available online at www.jemcr.com

Sovlu

her consciousness was cooperative and her blood lactate level was between 1.1 and 2.1 mmol / 1 in the follow-up of the patient with GCS 14. After two days of follow-up, the patient was discharged with full recovery without organ damage.

Case Report 2: A 19-year-old female patient, who had no known illness, applied to the emergency service of Kastamonu Training and Research Hospital with oral intake of 30 tablets of 100 mg theophylline for suicide. The patient was planned to apply activated charcoal in the emergency room, but could not be administered effectively due to severe nausea and vomiting, and intravenous fluid therapy was started. When the patient had severe symptoms and laboratory findings due to theophylline intoxication, he was admitted to the intensive care unit. Conscious, cooperative, oriented GKS: 15. Vital signs were: pulse: 148 /min, arterial blood pressure: 136/68 mmHg Spo2: 96, respiratory rate: 28/min. Patient's white blood cell (WBC): 22000 / ul, glucose: 310 mg / dl, lactate: 6 mmol / l, potassium: It was 2.9 mmol / l, creatine: 0.9 mg / dl, b-hcg: 0.2 mIU / ml. The patient had severe nausea, vomiting and abdominal pain. Theophylline level was sent from the patient to the laboratory. In addition to reducing tachycardia with diltiazam, a calcium channel blocker, intravenous fluid therapy was initiated. In the follow-up of the patient, the complaints of nausea and vomiting increased, clinical symptoms did not improve despite medical treatment and theophylline level was 106 ug/ml, so the patient was taken to 4-hour ultrafiltration-free hemodialysis. After hemodialysis treatment, the patient's complaints of nausea and abdominal pain resolved, his tachycardia, blood lactate and glucose blood levels returned to normal. Hypokalemia was treated with potassium replacement. After hemodialysis, blood sample was taken from the patient again for theophylline blood level and sent to the laboratory and the theophylline blood level was 4 ug / ml. The patient was transferred to the internal disease service after two days of intensive care. The patient was discharged with full recovery, without organ damage, after two days of follow-up in the internal disease service.

Case Report 3: 22 years old male patient with mental retardation, he applied to the emergency service of Kastamonu Training and Research Hospital by his relatives with complaints of nausea, vomiting, sleepiness. There was substance use. The patient with GCS: 6 was intubated orotracheally and taken to the support of invasive mechanical ventilation. Arterial blood pressure: 96/45 mmhg, pulse: 124 / min, respiratory rate: 38. In blood tests performed in the emergency department, ph: 7.27, lac: 27 mmol / l, pco2: 23mmhg, sodium: 141 mEg / l, potassium: 5.55 mEg / l, AST: 11 u / l, ALT: 14u / l creatine: 2.12 mg / dl. A toxic blood panel was sent from the patient and the results were negative. Intracranial pathology was not detected in the imaging. The patient was admitted to the general intensive care unit with the diagnosis of coma and metabolic acidosis of unknown cause. We had a pre-diagnosis of intoxication in the patient. Since etiology could not be determined exactly due to the fact that ethylene glycol blood level could not be studied in the laboratory of our hospital,

no antidote treatment was initiated and mechanical ventilator support and anti-poatassium treatment was applied.

When the patient became anuric during the first 12 hours of his admission to the intensive care unit and his creatinine levels increased to 5.08 mg / dl, he was placed on hemodialysis catheter with 2000 cc UF. In the following four days, when the patient was anuric and his creatinine levels were high, 3 cycles of hemodialysis were performed. The patient started to communicate on the 5th day of the ICU follow-up and on the 6th day his GCS was 14 and was extubated. After communicating with the patient, it was learned that he drank 1.5 liters of antifreeze (ethylene glycol). Since ethylene glycol blood level could not be studied in our institution, the level could not be monitored. The patient was transferred to the nephrology service on the 9th day of the intensive care follow-up. The patient, who had 1500-2500cc diuresis daily and whose kidney function tests returned to normal levels, was discharged with recovery without organ damage.

Discussion

Traditional hemodialysis is a frequently preferred treatment due to its widespread availability and proven efficacy for certain drugs and toxins. The primary determinants of the ability of a substance to be removed from blood by hemodialysis are the weight of the molecule, the volume of distribution (VD), the hydrophilicity or lipophilicity state of the substance, the protein or tissue binding capacity, and endogenous clearance. Substances with low molecular weight can be easily dialyzed. High efficiency high flow dialysers with diffusive modalities can remove medium molecular weight (<15,000 Da) materials. Convective modalities such as Hemofiltration and Hemodiofiltration allow removal of solutes approaching 25,000 Da².

Metformin is a biguanide antidiabetic agent commonly used in the treatment of type-2 diabetes mellitus. The plasma half-life of metformin is about six hours. Lactic acidosis may be seen in acute and chronic use of biguanides. There are few case reports associated with high doses of metformin, and it is generally fatal. Metformin is thought to reduce lactate metabolism by suppressing pyruvate carboxylase and increase lactate production by reducing pH in the liver. It also reduces glucose utilization and increases lactic acid release from hepatocytes. Lactic acidosis is defined as blood pH below 7.35 and serum lactic acid level above 2 mmol / l. It is divided into two subtypes, of which type A is the form associated with tissue hypoxia and mostly occurs in sepsis is the form associated with an external agent (metformin poisoning) as a result of a decrease in lactate clearance without hypoxia^{3,4}. Metformin poisoning may present with nonspecific symptoms such as nausea, vomiting, abdominal pain, hypoglycemia, hypothermia, tachypnea, tachycardia / bradycardia, hypotension / hypertension, agitation, drowsiness, and coma. Therefore, anamnesis is important in differential diagnosis⁵. The classic

triad of metformin toxicity can be listed as acute renal failure, high plasma metformin concentration, and severe lactic acidosis. Hemodialysis or continuous renal replacement therapies; It is preferred to eliminate overdose of drug, normalize serum potassium level and eliminate lactate, which is the cause of metabolic acidosis. Our patient had hyperlactataemia, hyperkalaemia and metabolic acidosis and was successfully treated with hemodialysis.

Theophylline is an effective bronchodilator used in the treatment of diseases like asthma, chronic obstructive pulmonary disease (COPD), neonatal apnea and bradycardia syndrome. A level of theophylline in the blood above 15 µg / mL carries the risk of intoxication. Therefore, when steady state is reached, 5-15 µg / mL blood level is considered as an effective and safe dose range⁶. When the toxic dose is reached, metabolic abnormalities such as nausea, vomiting, agitation, palpitations, hyperglycemia, hypokalaemia, acid-base imbalance and leukocytosis. traceable. In addition, life-threatening conditions such as convulsions and ventricular arrhythmias can be seen depending on the dose⁷. Our patient had nausea, vomiting, palpitations, hyperglycemia, hypokalaemia, acid-base disorder and leukocytosis, which are signs of severe theophylline intoxication. Our patient did not only have convulsions and agitation findings

Theophylline is well adsorbed by charcoal and therefore activated charcoal should be used even in poisoning with IV theophylline overdose. Hemoperfusion or high-throughput hemodialysis is indicated if vomiting prevents the use of activated charcoal, or it can be used as an adjunct therapy in patients with seizures, hypotension or arrhythmia. Hemodialysis / hemoperfusion should be considered in acute intoxications above 100 mg / L and chronic toxicity above 60 mg / $\rm L^2$. In our patient, active charcoal treatment could not be successfully applied due to nausea and vomiting, and hemodialysis treatment was performed due to the toxic doses of blood theophylline and severe intoxication findings. After hemodialysis treatment, the patient's blood theophylline level came as 4 $\rm \mu g$ / ml and intoxication symptoms disappeared.

Intoxications should be considered in the foreground in cases of coma of unknown cause and acute renal failure. Ethylene glycol poisoning is one of the rare types of poisoning in our country with high mortality. In the first 12 hours after ingestion of ethylene glycol, it can cause central nervous system depression, confusion, ataxia, hallucination, ambiguous speech and coma. A cardiorespiratory phase (12 to 24 hours) then occurs with the onset of tachypnea, hypotension, and congestive heart failure. Finally, 24 hours after ingestion, oliguria and acute kidney injury often follow this process⁸. In our patient, we encountered a picture of acute renal failure following central nervous system depression, but we did not see a cardiorespiratory phase in our patient.

Intravenous ethanol, fomepizole and hemodialysis are the most important treatments in patients with ethylene glycol poisoning. The American Academy of Clinical Toxicology primarily recommends fomepizole as the treatment of choice in such situations. Fomepizole is a relatively new agent with a specific indication for ethylene glycol poisoning⁹. In a case report by Buchanan et al., A patient consuming high doses of ethylene glycol was treated with fomepizole alone without hemodialysis. They suggested that treatment with fomepizole may be feasible even with high-dose ethylene glycol consumption, provided that renal function is maintained¹⁰. Although fomepizole treatment could not be applied to our patient due to diagnostic difficulty, hemodialysis treatment was applied due to being anuric and impaired renal functions. In the ongoing process, three more hemodialysis sessions were applied, depending on the indication, and the patient was successfully treated.

Conclusion

Intoxication cases are medical emergencies, and severe cases may require urgent extracorporeal treatments to prevent or reverse major toxicity. Hemodialysis is the leading extracorporeal treatment. It can also be applied as short-term high-flow hemodialysis in suitable patients.

References

- Goktas, U., Isık, Y., Cegin, M. B., Soyoral, L., Kati, I. A. Retrospective analysis of the poisoning cases who were followed in our intensive care unit. Journal of Anesthesia 2011; 19 (2): 114 – 116
- 2. Jha VK, Padmaprakash KV. Extracorporeal Treatment in the Management of Acute Poisoning: What an Intensivist Should Know?. Indian J Crit Care Med. 2018;22(12):862-869. doi:10.4103/ijccm.IJCCM_425_18
- **3.** Biradar V, Moran JL, Peake SL, Peter JV. Metformin-associated lactic acidosis (MALA): clinical profile and outcomes in patients admitted to the intensive care unit. Crit Care Resusc. 2010;12(3):191-195.
- **4.** Nguyen HL, Concepcion L. Metformin intoxication requiring dialysis. Hemodial Int. 2011;15 Suppl 1:S68-S71. doi:10.1111/j.1542-4758.2011.00605.x
- Friesecke S, Abel P, Roser M, Felix SB, Runge S. Outcome of severe lactic acidosis associated with metformin accumulation. Crit Care. 2010;14(6):R226. doi:10.1186/cc9376
- Çevik Y, Kavalcı C, Daş M, İzdeş S. Severe theophylline intoxication, rhabdomyolysis, disseminated intravascular coagulopathy and death: Case report. AKATOS 2010;1:24-27.
- **7.** Açıkalın A, Gülen M, Kösenli Ö, Topal M. Teofilin zehirlenmesi: Hemodiyaliz mi? Hemoperfüzyon mu? AKATOS 2011;2(3):39-41. doi: 10.5505/jaemcr.2011.87587
- **8.** Latus J, Kimmel M, Alscher MD, Braun N. Ethylene glycol poisoning: a rare but life-threatening cause of metabolic acidosis-a single-centre experience. Clin Kidney J. 2012;5(2):120-123. doi:10.1093/ckj/sfs009.
- **9.** Lister, D., Tierney, M., Dickinson, G. Effectiveness of IV ethanol therapy combined with hemodialysis in the treatment of methanol and ethylene glycol poisoning. The Canadian Journal of Hospital Pharmacy, 2005;58(3):142-147
- 10. Buchanan JA, Alhelail M, Cetaruk EW, Schaeffer TH, Palmer RB, Kulig K, et al. Massive ethylene glycol ingestion treated with fomepizole alone-a viable therapeutic option. J Med Toxicol. 2010;6(2):131-134. doi: 10.1007/s13181-010-0061-2.