Arch Argent Pediatr 2023;e202310095

Methemoglobinemia and acute ıntravascular hemolysis after naphthalene poisoning in a pediatric patient

Özhan Orhan[a], *Mehmet N. Talay*[a]

ABSTRACT

Poisoning by naphthalene is uncommon in children. It is a type of poisoning brought on by ingesting, inhaling, or coming into touch with naphthalene-containing substances on the skin. Patients typically present with an initial onset of dark brown urine, watery diarrhea, and bile vomit. The signs include fever, tachycardia, hypotension, and low pulse oximetry readings even with oxygen support. Hemolytic anemia, methemoglobinemia, renal failure, and hyperbilirubinemia are all detected in blood tests. Erythrocyte transfusion, ascorbic acid, methylene blue, and N-acetylcysteine (NAC) therapies are provided to inpatients in addition to symptomatic treatment.

We present a 23-month-old male patient who developed methemoglobinemia and acute ıntravascular hemolysis, who was followed up in the intensive care unit for five days due to naphthalene intoxication.

Although naphthalene poisoning is very rare, it should be known that it has fatal consequences, and more care should be taken in its use and sale.

Keywords: *naphthalenes; hemolysis; methemoglobinemia; ascorbic acid; poisoning.*

doi: http://dx.doi.org/10.5546/aap.2023-10095.eng

To cite: Orhan Ö, Talay MN. Methemoglobinemia and acute ıntravascular hemolysis after naphthalene poisoning in a pediatric patient. *Arch Argent Pediatr* 2023;e202310095. Online ahead of print 12-OCT-2023.

[a] *Mardin Artuklu University Faculty of Medicine, Turkey.*

Correspondence to *Özhan Orhan: ozhan.orhan@hotmail.com.tr*

Funding*: None.*

Conflict of interest*: None.*

Received: *5-18-2023*
Accepted: *8-1-2023*

INTRODUCTION

When a poisonous drug is consumed unintentionally or intentionally, it can endanger life and result in intoxication. Children experience it frequently all across the world.[1] Only a small number of deaths happen in children under 5 years old, despite the fact that this age group accounts for the majority of occurrences.[2]

Naphthalene known as mothballs contain a potent aromatic hydrocarbon. It is frequently used as a deodorizer and moth repellent in homes. If accidentally consumed even at low concentrations, naphthalene can be extremely poisonous. Naphthalene exposure can cause methemoglobinemia and hemolytic anemia.[3,4]

We present a patient who developed hemolysis and methemoglobinemia due to naphthalene ingestion.

CASE REPORT

A 23-month-old male patient took the mothball was located in his parents closet 16 hours ago, thinking it was a candy. The patient, who applied to the district state hospital 2 hours after taking it, was taken to the ward for follow-up.

At admission to the district hospital, the patient had a temperature of 37.4 °C, a heart rate of 128, and a normal blood pressure. Pulse oximetry was 74% in a 100% non-rebreathing mask. Venous blood gas pH was 7.36, partial carbon dioxide pressure (pCO_2) was 36.3 mmHg, and partial oxygen pressure (pO_2) was 27 mmHg. The patient had no respiratory distress. The patient's blood test results were as follows: hemoglobin 10.7 g/dL, white blood cell (WBC) 17 600/µl, blood urea nitrogen 17 mg/dL, creatinine 0.57 mg/dL, total bilirubin 0.2 mg/dL, metHb 18.5%, lactate dehydrogenase (LDH) 339 U/L (*Table 1*). Urine color was light yellow. The patient developed pale color, biliary vomiting and diarrhea and was referred to our hospital at the 12th hour of the follow-up.

The patient was evaluated in the emergency room after being referred, and his general health was described as moderate, conscious, and pale. The patient's temperature was 37.8 °C, heart rate was 164 and oxygen saturation was 75% despite oxygen support. Blood gas showed pH 7.42, pCO_2 31.6 mmHg, metHb 14.1%, hemoglobin 6.9 g/dL, WBC 30 900/µl, blood urea nitrogen 10 mg/dL, creatinine 0.38 mg/dL, total bilirubin 2.19 mg/dL, indirect bilirubin 1.74 mg/dL, and LDH 402 U/L. The patient who experienced methemoglobinemia due to hemolysis brought on by naphthalene consumption was given 300 mg of ascorbic acid intravenously. A blood sample was sent for glucose 6 phosphate dehydrogenase (G6PD) enzyme deficiency because the patient had a history of hospitalization due to jaundice on the postnatal 3rd day in the neonatal period. For this reason, methylene blue was not applied. Blood was prepared for the transfusion of erythrocytes, and the patient was brought to the pediatric intensive care unit. for close monitoring.

The 23-month, 12-kg, male patient admitted to the intensive care unit was tachypneic, cynotic, and his pulse oximetry was 74% in a 100% non-rebreathing mask. Ascorbic acid 4 x 300 mg,

Table 1. Blood tests

	Application time	12 hours	24 hours	Day 3	Day 4	Day 5	Discharge time
WBC (1000/µl)	17,64	30,9	31,1	29,26	18,2	16,6	17,8
Hemoglobin (g/dL)	10,7	6,9 (tx)	11,2	8,5	7,2	7.4	8.2
Creatinine (mg/dL)	0,57	0,38	0,3	0,3	0,2	0,2	0,26
pH	7,36	7,42	7,35	7,44	7,45	7,42	7,43
pCO_2 (mmHg)	36,3	31,6	26,6	35,7	33,2	36,2	36
MetHb (%)	18,5	10,1	4,4	3,6	2,1	2	1,6
Total bilirubin (mg/dL)	0,2	2,19	2,86	3,9	2,58	0,61	0,34
İndirect bilirubin (mg/dL)	0,17	1,74	2,19	3,75	2,06	0,43	0,25
CRP (mg/L)	0,9	54,3	65,2	79,5	82,2	64,2	32
Urea (mg/dL)	17	10	25	36,3	34,2	23,5	17,1
Platelet (1000/µl)	441	351	283	226	173	165	212
MCV (fL)	71,7	71,2	79,9	82,7	90,3	92	95
LDH (U/L)	339	402	537	1437	951	642	463

WBC: white blood cell, Methb: methemoglobin, CRP:C reactive protein, MCV: mean corpuscular volume, LDH: lactate dehydrogenase.

N-acetylcysteine (NAC) 3 x 200 mg and saline were started as treatment. During the 4-hour hemogram follow-up, the patient's hemoglobin level decreased and 15 cc/kg blood transfusion was given. The patient's temperature was 38.7 ºC after being admitted to the intensive care unit for two hours. Blood culture was taken and cefotaxime was indicated.

At the 24th hour of hospitalization, venous blood gas pH was 7.35, pCO_2 was 26 mmHg, metHb level was 4.4. After receiving blood transfusions, the hemoglobin level was 11.2 g/dL. The patient's WBC was 31 100/µl, platelet count was 283 10*3/uL, and creatinine level was 0.3 mg/dL. Total bilirubin increased to 2.86 mg/dL, indirect bilirubin increased to 2.19 mg/dL (normal range 0.2-1 mg/dL). Liver function tests were within the normal range.

The color of the urine darkened on the third day of hospitalization. The level of the G6PD enzyme was 13.22 U/g Hb (normal range: 5.5–20 U/gHb). the patient's oxygen saturation was 92% in room air, and his heart rate was 112. Hemoglobin was 8.5 g/dL, LDH was 1437 U/L, creatinine was 0.3 mg/dL, metHb: 3.6. Findings of hemolysis continued in the peripheral blood smear. Ascorbic acid and hydration were still administered.

The outcome was anticipated because methylene blue is contraindicated in G6PD enzyme impairment. The patient whose enzyme value was within the normal range improved clinically, and because methemoglobin levels tended to drop, methylene blue was not administered to the patient.

Dialysis or inotropic assistance were not required for the patient. The urine color of the patient, who was not oliguric during his hospitalization, turned light yellow on the 5th day. On the day he was discharged, his methemoglobin level dropped to 1.6%. WBC 17 800/µl, LDH 463 units/L, creatinine 0.26 mg/dL, total bilirubin 0.34 mg/dL, and indirect bilirubin decreased to 0.25 mg/dL The patient was dicharged with an outpatient control recommendation after undergoing control exams and clinic visits without any issues.

DISCUSSION

Volatile hydrocarbon naphthalene is a crystalline, colorless substance. This material is used as an insecticide, a moth repellent, a deodorant, and a surface cleaning both in industry and at home. Occupational naphthalene exposure has been recorded in industrial employees. If naphthalene is consumed, comes into touch with the skin, or is inhaled, it can cause major health concerns.[5,6]

Many negative effects have been recorded following the accidental or intentional ingestion of moth repellents containing mothballs. The most common side effects are acute hemolytic anemia with decreased hemoglobin and hematocrit levels, decreased reticulocyte count, presence of Heinz bodies and increased serum bilirubin levels.[7] People who lack the G6PD enzyme may develop hemolytic anemia after being exposed to naphthalene. Naphthalene has been linked to gastrointestinal symptoms like nausea, vomiting, and diarrhea as well as renal effects like hematuria, increased urea, elevated creatinine levels, and renal failure. There have also been reports of neurological symptoms like convulsions, dizziness, cerebral edema, and coma, as well as hepatitis effects like hepatomegaly and jaundice. Hemolytic anemia and methemoglobinemia are characteristic of naphthalene poisoning.

Naphthalene promotes oxidative stress by increasing free oxygen radical generation. Naphthalene's oxidative stress causes methemoglobinemia, which is the oxidized form of hemoglobin. Methemoglobin, the iron (Fe) portion of unoxygenated hemoglobin is in the ferric (Fe^{+3}) state and does not bind oxygen. Thus, the affinity of oxygen for the partially oxidized portion of hemoglobin increases. The patient gets cyanotic if the methemoglobin level exceeds 1.5 g/dL. In patients with this kind of methemoglobinemia, pulse oximetry is unreliable. When methemoglobinemia is present, conventional pulse oximeters use two wavelengths of light that cannot detect methemoglobin and accurately calculate oxygen saturation. These patients' pulse oximetry readings are low, despite the fact that their blood gas levels are normal.[8]

Ascorbic acid acts as a free radical scavenger and can be used to reduce the oxidative stress of naphthalene.[9] Doses of 300 mg per day gave good results in naphthalene poisoning. Methylene blue is used in the treatment of methemoglobin. Methylene blue, on the other hand, can produce hemolysis and paradoxical methemoglobinemia in people with G6PD deficiency. Before use, a G6PD test should be performed.[10] NAC therapy can also be utilized to treat methemoglobinemia as a lowering agent, particularly in patients with G6PD deficiency. In these cases, exchange transfusion

is an alternative option.[11]

The therapy of naphthalene poisoning is not well defined, and overall treatment approaches may differ depending on the severity of the clinical presentation. In the treatment of naphthalene poisoning, red blood cell transfusion, intravenous infusion of methylene blue, NAC, and ascorbic acid have all proved successful.[3]

Hydration, ascorbic acid, NAC and a blood transfusion were administered to our patient. He improved four days after ingesting naphthalene and was discharged on the sixth day.

As a result, naphthalene poisoning cases, which are extremely rare in our nation, necessitate a high level of suspicion if the source of the exposure is unclear. It is important to remember that naphthalene, which is widely available in markets and is used in homes and industries, can cause severe problems. It should be examined in the differential diagnosis of individuals with acute onset of dark urine, vomiting, diarrhea, methemoglobinemia, hemolysis, and kidney injury, particularly in the pediatric age group.

In the event of naphthalene poisoning, seek medical attention immediately. When using naphthalene-containing products at home, it is critical to follow the instructions, store the products properly and keep them away from children. ■

REFERENCES

1. Napodano S, Rigante D, Pulitanò S, Covino M, et al. Acute intoxication and poisoning in children: the experience of a tertiary-care hospital from 2001-2012. *Signa Vitae*. 2015;10(2):33-53.
2. Citak A, Soysal DD, Yildirim A, Karaböcüoğlu M, et al. Cocukluk yas grubu zehirlenmelerinde tehlikeli degisim. *Cocuk Dergisi.* 2002;2:116-20.
3. Rahman MM, Mogni Mowla SG, Rahim A, Chowdhury FR, et al. Severe haemolytic anaemia due to ingestion of naphthalene (mothball) containing coconut oil. *J Coll Physicians Surg Pak*. 2012;22(11):740-1.
4. Sillery JJ, Lichenstein R, Barrueto F Jr, Teshome G. Hemolytic anemia induced by ingestion of paradichlorobenzene mothballs. *Pediatr Emerg Care*. 2009;25(4):252-4.
5. Willems BAT, Melnick RL, Kohn MC, Portier CJ. A physiologically based pharmacokinetic model for inhalation and intravenous administration of naphthalene in rats and mice. *Toxicol Appl Pharmacol.* 2001;176(2):81-91.
6. Cho M, Jedrychowski R, Hammock B, Buckpitt A. Reactive naphthalene metabolite binding to hemoglobin and albumin. *Fundam Appl Toxicol*. 1994;22(1):26-33.
7. Warren DL, Brown DL Jr, Buckpitt AR. Evidence for cytochrome P-450 mediated metabolism in the bronchiolar damage by naphthalene. *Chem Biol Interact.* 1982;40(3):287-303.
8. Annabi EH, Barker SJ. Severe methemoglobinemia detected by pulse oximetry. *Anesth Analg*. 2009;108(3):898-9.
9. Niki E. Action of ascorbic acid as a scavenger of active and stable oxygen radicals. *Am J Clin Nutr*. 1991;54(6 Suppl):1119S-24.
10. Kundra TS, Bhutatani V, Gupta R, Kaur P. Naphthalene Poisoning following Ingestion of Mothballs: A Case Report. *J Clin Diagn Res*. 2015;9(8):UD01-2.
11. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: etiology, pharmacology, and clinical management. *Ann Emerg Med*. 1999;34(5):646-56.