CASE REPORT / OLGU SUNUMU

A Case of Fatal Poisoning: Use of 2-4 Dinitrophenol for Weight Loss

Ölümcül Zehirlenme Olgusu: Zayıflama Amaçlı 2-4 Dinitrofenol (DNP) Kullanımı

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ABSTRACT

Aim: 2,4-dinitrophenol (DNP®) causes rapid weight loss. Therefore, this drug is used for weight loss, is mostly sold on internet sites, and is banned for sale owing to its deadly side effects. In this case report, we aimed to report a patient who was admitted to our hospital with DNP poisoning.

Case: In the present study, we present a 29-year-old patient who took 200-mg DNP® once a day for 5 days and who applied to our emergency department approximately 6 hours after taking two tablets on the last day. He developed cardiopulmonary arrest 8 hours after admission despite all supportive treatments and died despite effective and adequate cardiopulmonary resuscitation.

Conclusion: DNP poisoning can be fatal even in small doses. It is difficult to control because the drug is freely available on the internet, and urgent diagnosis and treatment is critical. In recent times, where sedentary life and obesity are on the rise, people should be better informed about healthy living and the risks associated with weight loss drugs that can be obtained illegally. Preventing the unauthorized sale of these products, which have a limited response to treatment and a high mortality rate, over the internet and early recognition of poisoning by emergency room physicians is the most important preventive measure in DNP poisonings and the most important step in treatment.

Keywords: DNP, 2,4-dinitrophenol, poisoning, weight loss, malignant hyperthermia, emergency medicine

ÖZ

Amaç: 2,4 Dinitrofenol (DNP®)'nin çok hızlı kilo kaybına neden olduğu bildirilmiş bu nedenle zayıflamak amacıyla kullanılan, daha çok internet siteleri üzerinden satışı yapılan, ölümcül yan etkileri nedeniyle satışı yasaklanmış olan bir ilaçtır. Bu olgu sunumunda, 2,4-dinitrofenol ile ilgili deneyimimizi literatürle paylaşmak amaçlanmıştır.

Olgu: Çalışmamızda beş gündür günde bir adet 200 mg DNP® alan ve son gün iki tablet aldıktan yaklaşık altı saat sonra acil servisimize başvuran 29 yaşındaki hastada tüm destek tedavilerine rağmen başvurudan sekiz saat sonra kardiyopulmoner arrest gelişen, etkili ve yeterli kardiyopulmoner resüsitasyona rağmen eksitus olan olgumuz sunulmuştur.

Sonuç: DNP, küçük dozlarda bile ölümcül olabilen bir maddedir. İlacın internette serbestçe satın alınabilmesi nedeniyle kontrolü zordur ve acilde tanı ve tedavisi kritik öneme sahiptir. Hareketsiz yaşamın ve obezitenin arttığı günümüzde, insanların sağlıklı yaşam ve yasa dışı olarak elde edilebilen zayıflama ilaçlarının riskleri konusunda daha iyi bilgilendirilmesi gerekiyor. Tedaviye yanıtı sınırlı ve ölüm oranı yüksek olan bu ürünlerin internet üzerinden izinsiz satışının engellenmesi ve acil servis hekimleri tarafından zehirlenmelerin erken tanınması DNP zehirlenmelerinde en önemli önleyici tedbir ve tedavide en önemli adımdır.

Anahtar Kelimeler: DNP, 2,4-dinitrofenol, zehirlenme, kilo kaybı, malign hipertermi, acil tıp

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Introduction

2,4-dinitrophenol (DNP) is a weight loss drug that is banned owing to its serious side effects. However, it can still be obtained illegally via internet sites (1). DNP inhibits ATP (Adenosine triphosphate) production by affecting the phase 0 step of the electron transport chain (ETC) during oxidative phosphorylation in the mitochondria (2). The energy generated is released as heat because the chain is broken in phase 0. Therefore, the body temperature rises, resulting in life-threatening hyperthermia (3). DNP also increases glycolysis by stimulating muscle contraction. Even in small doses, carbohydrate consumption in the body begins to increase significantly, resulting in weight loss. As a result of carbohydrate consumption, pyruvic acid and lactic acid accumulate. Animal studies show potassium and phosphate accumulation in the kidney after DNP administration, which explains the hyperkalemia seen in patients with DNP poisoning. DNP is also a teratogen, mutagen, and carcinogen.

Poisoning usually develops after oral ingestion, but it can also occur via inhalation as well as skin and eye contact. Yellow spots and corrosive burns may occur after skin contact, whereas yellow sclera and conjunctival irritation may occur after eye contact. Systemic findings may also be seen in exposures other than oral route (4).

Even a single tablet can be considered poisonous because the drug itself is poisonous. Fatal cases have generally been reported after ingestion of 20–40-mg/kg DNP, but cases of death have been reported after ingestion of doses as low as 5 mg/kg (4,5). According to websites selling DNP tablets, the treatment should begin with one tablet of 100–200 mg DNP per day, with a maximum dose of 200–00 mg/day (6).

In these cases, controlling body temperature is the main treatment strategy (7). Findings related to DNP toxicity include malaise, agitation, rash, headache, seizure, sweating, thirst, and shortness of breath. Serious toxic effects include hyperpyresia, hepatotoxicity, agranulocytosis, respiratory failure, coma, and death.

In this report, we present the medical history, physical examination findings, and clinical course of a patient who had ordered DNP over the internet, who used a 200-mg DNP tablet once a day for 5 days, who applied to the emergency room after taking two tablets on the 6th day, and whose clinical condition deteriorated dramatically.

Case Presentation

A 29-year-old male patient applied to the emergency department with complaints of shortness of breath, restlessness, fever, and palpitation. The patient was admitted to the emergency department 6 hours after the onset of symptoms, which began half an hour after taking two DNP tablets on the 6th day, after taking one tablet per day for 5 days. The patient obtained DNP via the internet. The patient had no any disease in history other than Barrett esophagus (height: 176 cm, weight: 88 kg, BMI: 28.47). The vital signs of the patient measured at the time of admission revealed tachycardia (124 beats/min), tachypnea (32/min), and fever (39.5ºC). Blood pressure (120/80 mmHg) and saturation (96%) were found to be normal. Detailed physical examination showed that the general condition was moderate; the patient was agitated; the Glasgow Coma Score was 15 (E4V5M6); the skin was sweaty; and there were purpuric lesions on the lower extremities for the last 2 months. The patient was cordoned off in the emergency critical care unit; broad vascular access was established; and the body temperature was monitored. Blood samples were collected for laboratory evaluation. Electrocardiography revealed sinus tachycardia, and chest X-ray results were normal. Treatment was primarily aimed at reducing fever and agitation. Efforts were made to control these symptoms with intravenous (IV) fluid replacement and cold lavage via nasogastric and urinary catheters. Benzodiazepine (Diazepam 5 mg IV slow administration) was used for agitation. Initially, the body temperature decreased to 38.2ºC but rapidly increased to 41ºC. Dantrolene could not be administered because it was not available in our hospital. The command center was contacted to obtain dantrolene from other institutions, but it was not available in the province. Blood sample results of the patient are shown in Table 1. The patient's blood gas results are shown in Table 2.

	Presentation	1. Control	2. Control
White Blood Cell (x10^3/mcL)	11.07	8.42	14.68
Hemoglobin (g/dL)	15.1	13.7	13.8
Platelet Count (x10^3/mcL)	59000	49000	50000
INR	Very high	0.9	1.19
Glucose (mg/dL)	120	171	152
Na^+ (mEq/L)	140	135	137
K^+ (mEq/L)	3.1	4.2	4.6
Alanine Transaminase (U/L)	22	25	25
Aspartate Transaminase (U/L)	27	43	61
Creatinine (mg/dL)	0.5	1.43	1.22
Blood Urea Nitrogen (mg/dL)	21	19.7	15.6
CK-MB (ng/mL)	13	13	27,4
Troponin (ng/mL)	0	0.1	0.1
Creatine Kinase (U/L)	1016	2179	4379

Table 1. Biochemical values of the case
CK-MB; Creatine kinase-MB, INR; International normalized ratio.

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Time	pH	PO_2 (mmHg)	PCO_2 (mmHg)	HCO_3 (mmol/L)
Presentation	7.46	34.9	25.1	17.5
16.35	7.42	51.4	24.3	19.2
18.45	7.17	45.4	32.0	15.7
21.00	7.07	36.8	47.5	11.1

Table 2. Blood gas results at presentation and during follow-up

The patient's INR value was significantly beyond the reference range, and 10 mg of IV vitamin K and 3 units of fresh frozen plasma IV were administered to the patient. The INR value returned to normal upon this treatment. Because of the low platelet count, 1 unit of thrombocyte suspension was administered. During follow-up, agitation, respiratory rate (48/min), and body temperature (42.3°C) increased. The patient was intubated and placed in SIMV mode on a mechanical ventilator. The patient developed deep metabolic acidosis during the last blood gas procedure and suffered cardiopulmonary arrest 8 hours after admission to the emergency room. Cardiopulmonary resuscitation was applied for about an hour, but the patient could not be rescued. Written informed consent was obtained from the patient's relatives.

Discussion

2,4 DNP is a banned drug that is used to burn fat and lose weight. The aim of this case report was to draw attention to DNP poisoning, which can be fatal even in small amounts and cannot be controlled or regulated because it is freely available on the internet, and to emphasize the importance of prompt diagnosis and treatment.

Since the 1930s, when the weight loss and fat-burning effects of DNP were discovered in humans, 62 people have died because of DNP (8). Although it was blacklisted in the United States and the United Kingdom in the mid-2000s for being unfit for human consumption, it is still used, especially by bodybuilders and those looking to lose weight quickly. Although the sale of DNP is banned, it can be obtained illegally, especially on the internet.

Most of the evidence on the effects of DNP on humans comes from case reports of emergency patients. In most patients, the total dose of DNP taken is unknown. The lowest lethal dose after oral administration has been reported to be 4.3 mg/kg. The doses received by mortal cases are 2.8–5 g. The highest dose received by surviving patients is 2.4-g DNP, and this patient recovered without sequelae (4). No cases of DNP poisoning have been reported in Türkiye.

The most serious acute problem in patients using DNP is malignant hyperthermia, which occurs as a result of decoupling in oxidative phosphorylation (3). The main causes of death are malignant hyperthermia and metabolic changes that occur after tissue hypoxia due to the disruption of ATP production at the cellular level. There is no effective antidote for DNP poisoning. The most important step in the treatment is the inclusion of poisoning in the differential diagnosis and early diagnosis (9). Because no asymptomatic cases have been reported, each patient should be followed up on for at least 12 hours (9). During the follow-up period, the vital signs of the patients should be checked regularly, and any change of this vital signs should be addressed as soon as possible. Although there is no such case report in the literature, gastric lavage and activated charcoal administration are recommended in patients who apply within the 1st hour of intake. Because the patient in this case report was admitted to our emergency department 6 hours after taking DNP, activated charcoal and gastric lavage were not used. Furthermore, there is insufficient evidence to support the effectiveness of repeated administration of activated charcoal and whole bowel irrigation. In exposures other than the oral route, decontamination procedures, such as skin washing, are recommended (9,10).

Aggressive fluid therapy is the primary symptomatic treatment. If available, dantrolene can be used to treat hyperthermia (11). Supportive treatments are applied in centers similar to our hospital, where dantrolene is not available or cannot be obtained. Active and passive cooling methods, such as IV chilled fluids and gastric and bowel irrigation with chilled liquids, can be used to control body temperature (7).

Benzodiazepines can be used to treat agitation and seizures that may develop in patients. Intubation with paralyzing drugs can be considered in patients whose agitation and seizures cannot be controlled with benzodiazepine administration.

Patients should be examined for methemoglobinemia because the ETC is involved. In the case of methemoglobinemia, IV methylene blue should be added to the treatment. Continuous veno-venous hemofiltration can be applied in cases of hyperkalemia and hyperthermia (12).

Despite all treatments, our patient developed cardiopulmonary arrest due to malignant hyperthermia and multiorgan failure due to tissue hypoxia after 8 hours in the emergency department. Despite appropriate and adequate CPR, spontaneous recovery could not be achieved.

Conclusion

DNP poisoning can be fatal even in small doses. It is difficult to control because the drug is freely available on the internet, and urgent diagnosis and treatment is critical. In recent times, where sedentary life and obesity are on the rise, people should be better informed about healthy living and the risks associated with weight loss drugs that can be obtained illegally. Preventing the unauthorized sale of these products, which have a limited response to treatment and a high mortality rate, over the internet and early recognition of poisoning by emergency room physicians is the most

important preventive measure in DNP poisonings and the most important step in treatment.

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