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Case Report

Can agricultural drugs be used against lice? accident, suicide or truth? case presentations

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Abstract. Agriculture is an important source of living in our country. Therefore, poisoning with agricultural drugs is quite common. 4,6 dinitro-ocresol nitrophenol ($C_7H_6N_2O_5$) is a pesticide, which belongs to the nitrophenol group, is used on fruit trees in winter and is known as the "yellow" drug among the public. In our country, intoxication with nitrophenols has not been reported previously in the literature. However, they may be lethal even by dermal route. This rare type of intoxication should be recognized and kept in mind by physicians. A careful and detailed history should be taken in all cases of intoxication and the treatment should be based on the type of intoxication. The aim of the present study is to evaluate 5 cases of serious toxicity that occurred accidentally and/or because the drug was applied on hair for anti-louse purposes in our region, where agriculture and breeding animals are important sources of life.

Key words: Agricultural drugs, pesticides, nitrophenol, suicide, accident

1. Introduction

Agriculture is an important source of living in our country especially in rural areas. Growing fruits and vegetables is dominant in our region. Therefore we frequently encounter agricultural accidents. The most frequent one among these accidents is poisoning by agricultural drugs. 4,6 dinitro-ocresol nitrophenol ($C_7H_6N_2O_5$, DNOC) is a pesticide, which belongs to the nitrophenol group, is used on fruit trees in the winter and is known as the "yellow "drug among the public (1-3). This substance is also a selective herbicide used in growing fruits, vegetables, grains and seeds. It also possesses insecticide, acaricide and secondary fungicide effects. It is used as a winter drug in trees, which shed their leaves in the pollination period of plants.

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The substance is produced synthetically. As it readily dissolves in water, some certain formulations may be prepared such as DNOC-ammonium and DNOC-sodium (4). Nitrophenolic compounds have toxic effects when they are taken orally and subcutaneously. Doses over 25-50 mg/kg are toxic (5).

The aim of the present study is to evaluate 5 cases of serious toxicity that occurred accidentally and/or because the drug was applied on hair for anti-louse purposes in our region, where agriculture and breeding animals are important sources of life.

2. Case reports

The first four patients were from the same family. Two females aged 53 (Case 1) and 35 (Case 2) and two females aged 9 and 12 (Case 3-4) were brought to our hospital by ambulance from another hospital with the suggested diagnosis of drug intoxication. One to two hours after they washed their hair with an agricultural drug, they began to suffer from nausea, vomiting, dizziness, headache, abdominal pain, fatigue, numbness and imbalance. They had presented to the nearest hospital with these complaints. The

patients were examined and treated at the primary healthcare facility, after which they were transferred to our hospital for further investigation and treatment.

According to the history obtained from the patients and their relatives, they had severe pruritus on the scalp; they detected lice, washed their hair with an anti-louse drug, but had accidentally mistaken the anti-louse drug with an agricultural drug, because the boxes of two drugs were very similar. The drug was an agricultural agent named ABC® (DNOC-Ammonium), used in gardens and fields.

The fifth patient (Case 5) was a previously healthy 70-year-old female who had was dispatched from a secondary healthcare facility to our hospital, with the complaint of altered state of consciousness, with the suggested diagnosis of cerebrovascular accident (CVA). It was deduced from the patient's history that she lived alone, and was found unconscious by her relatives at home. She had vomited, and had froth on her mouth, in addition to suffering from dyspnea. The patient had been taken to the nearest hospital by her relatives who used their own facilities for transportation. Following initial examination, treatment was begun for the diagnosis of CVA. However, the clinical status of the patient did not improve with treatment. She was then transferred to our hospital for further investigation and follow-up treatment. The initial history and examination findings in our clinic were consistent with CVA. However, clinical and laboratory findings did not match. After having eliminated the CVA diagnosis by a neurology consultation, work-up for other etiologies was begun.

The history was reviewed once more in detail. Detailed history revealed that the patient had borrowed an antilouse drug from her neighbour the same day. The house of the patient was investigated once more. A box of an agricultural drug named Gebütox® (DNOC-ammonium) was found.

The patients were admitted to the emergency unit. They were put on non-invasive cardiac monitorization. 2/min O_2 was administered by a nasal canula. 16-gauge granules placed in the antecubital regions of both upper extremities provided intravascular access. Physiological serum infusion was begun according to their clinical status. Their bodies were entirely cleaned with soap water 4-5 times every day during their hospitalization. Their hair was cut and washed with soap water.

Toxicological screening for benzodiazepines, barbiturates, metamphetamine, cocaine, opioids, phencyclidine, tetrahydrocannabion and tricyclic antidepressants from the urine samples were found to be negative in all patients.

Case 1

The patient was dyspneic, sleepy, orientated, cooperative responded to verbal stimuli and with a Glascow coma score (GCS) of 12. On physical examination, blood pressure was 145/70 mm Hg, pulse was 108 beats per minute, respiratory rate was 36 inspirations per minute, body temperature was 38 ºC and her oxygen saturation (during nasal oxygen intake) was 93%. Conjunctivae were hyperaemic. On neurological examination, pupils were light reflexes were positive bilaterally, and there were no pathological reflexes. On cardiovascular examination, she had tachycardia. On respiratory examination, she was tachypneic, had rhonchi in the bases of the lungs and hoarse respiratory sounds. On electrocardiography, she had sinus tachycardia. Blood glucose was 431 mg/dl and other biochemical findings were normal. Complete blood count was normal except for leukocytosis of 15.340/µl. In urinanalysis, ketones were negative and glucose was (++).

Case 2

She was dyspneic, conscious, responded to verbal stimuli, orientated, cooperative and with a GCS of 14. Blood pressure was 130/70 mm Hg, pulse was 100 beats per minute, respiratory rate was 30 per minute, her body temperature was 38.2ºC, and Oxygen saturation was 95%. On neurological examination, pupils were light reflexes were positive bilaterally, and she had no pathological reflexes. On cardiovascular examination, she was tachycardic. On respiratory examination she was tachypneic and had rough respiratory sounds in the bases of the lungs. She had sinus tachycardia on ECG. White blood cell count (WBC) was 14000/ µl, with all other parameters being normal.

Cases 3-4

The patients were conscious, responded to verbal stimuli, they were orientated cooperative and their GCSs were 14. Their blood pressures were 150/70 mm Hg and 140/65 mm Hg, their pulses were 118 beats per minute and 105 beats per minute, respiratory rates were 40 and 43 inspirations per minute, body temperatures were 38.7 and 38.1 ºC, Oxygen saturations were 94% and 92% by pulse oximetry while receiving 2 liters/min nasal oxygen, respectively. On neurological examination, their pupils light reflexes were bilaterally positive, and they had no pathological reflexes. On cardiovascular examination, they were tachycardic.. On respiratory examination, they were tachypneic

and had rough respiratory sounds. On ECG, they had sinus tachycardia. On complete blood count, WBC count was 15.4 /µl and other parameters were normal.

3. Treatment and follow-up

In the first 12 hours, 0.5 mg atropine was perfused intravenously every 30 minutes.The atropine dose was lowered to 0.25 mg intravenous perfusion every hour after the secretions decreased, respiratory sounds improved and miosis resolved. On the second day of hospitalization, findings of atropinization (agitation, mydriazis, decreased secretions, flushing, etc.) occurred and the atropine was ceased.

Pralidoxim (PAM) was introduced together with atropine as IV bolus of 800 mg in 100 ml saline. For two days, 200 mg PAM in 100 ml saline was infused 4 times a day. The patients were supported with fluids according to their clinical requirements.

In the case of the 53-year-old female patient, blood glucose test was performed every 4 hours due to hyperglycemia. On the third control, her blood glucose was 190 mg/dl. The patient underwent a psychiatric consultation and discharged with relief on the 4th day of her hospitalization.

Case 5

On the first evaluation, her general status was poor; she did not reasonably respond to verbal stimuli, was agitated, uncooperative, disorientated, restless and pale. On physical examination, she was confused, pupils were isocoric and miotic, light reflexes were bilaterally positive and her GCS was 11 (E3M4V3). Blood pressure was 155/88 mm Hg, pulse was 115 beats per minute, body temperature was 35ºC, respiratory rate was 38 inspirations per minute, and Oxygen saturation was 91% by pulseoxymetry (with respiration of room air). Blood glucose, performed at bedside was 256 mg/dl. On cardiovascular examination, she was tachycardic. On respiratory examination, she was tachypneic, had rough respiratory sounds on the basal portions of her lungs, and had widespread rhonchi.

A urine sample was obtained for routine and toxicology screening tests. Initial laboratory findings were as follows: WBC:17860/µL, blood glucose:236 mg/dL, urea:62mg/dL, creatinin: 1.36 mg/dL, Na:149 mmol/L, K:3.8mmol/L, Cl:101mmol/L, CK: 548 U/L, CK-MB: 86 U/L, LDH: 943 U/L, AST: 46U/L, ALT: 26U/L, myoglobin: 74 ng/ml, Troponin-T: negative. Blood gase and coagulation profile were normal. Chest X-ray and computed tomography of the brain revealed no pathology. There was a right bundle branch block on the ECG.

As the patient was old and her enzyme levels were elevated, she was monitored for coronary artery disease by measurement of cardiac enzymes and ECG. No changes were found on control ECGs. The elevated cardiac enzyme levels showed a tendency to decrease and troponin values were negative during the entire follow-up.

The patient was under follow-up at the intensive care unit with the suggested diagnosis of organophosphate intoxication. Nasogastric and foley catheters were inserted, peripheral vascular access was obtained, and crystalloid solutions were administered after her initial stabilization was provided.

In the first 1-2 hours, 0.5 mg atropine was perfused intravenously every 15 minutes. During the following 12 hours, 0.5 mg of atropine was perfused intravenously every 30 hours. The atropine dose was lowered to 0.5 mg IV perfusion every hour after the secretions decreased, respiratory sounds improved and miosis regressed. On the second day of hospitalization, findings of atropinization (agitation, mydriazis, decreased secretions, flushing, etc.) appeared and the atropine was ceased.

PAM was introduced together with atropine as an IV bolus of 800 mg in 100 ml saline. For two days, 200 mg PAM in 100 ml saline was infused 4 times a day. During the time the patient spent in the intensive care unit, sulbactam-ampicillin (Ampisid®) was administered intravenously at a dose of 4X1 g/d. She was supported with fluids according to her clinical status. Midozolam (Dormicum®) and Haloperidol (Nörodol®) were administered for agitation. She was taken to the emergency unit observation room from the intensive care unit on her first day of hospitalization. She was discharged on the eighth day of hospitalization, after having undergone a psychiatric consultation. No additional pathologies were seen during the follow up.

4. Discussion

Agriculture is an important source of living in our country. A significant portion of the population lives in rural areas and makes money through agriculture and breeding animals. Therefore, poisoning with agricultural drugs is quite common. Intoxication occurs via oral route

or via inhalation. However, it is not common to use the drug for hygienic purposes and to apply it on hair.

Poisoning with organophosphates and similar pesticides is the most commonly seen form of intoxication. In our country, intoxication with nitrophenols has not been reported previously in the literature. These drugs are either taken accidentally or for suicidal purposes, and intoxications occur mostly via the oral route or inhalation. However, intoxication via dermal route is rare (6,7). There are some striking points in our study: First of all, all cases of intoxication should be questioned well and the entire history should be obtained in detail. In our patients, the reason for intoxication, which seemed to be covert at first, was enlightened by the accidental use of agricultural drugs in the history. The second point is that the clinical situation was similar to organophosphate intoxication and the case was treated accordingly at the beginning. The clinical picture on admission was in favor of organophosphate intoxication. After the boxes of drugs were found, it was understood that intoxication was due to DNOC, which belonged to nitrophenol group, and the treatment was regulated again.

Another point is that, the type and route of intoxication was unusual. Four of our cases were from the same family and intoxication was moderate. The fifth patient was admitted at another time and she had the clinical picture of a serious intoxication.

Nitrophenolic components are sticky fluids, which are used as insecticides, herbicides, tree protectors, preventing tree decay. Recently, there has been an increase in human and animal intoxications with the increasing use of nitrophenolic compounds. Therefore, their use is limited. DNOC was developed as a herbicide, in addition to its use as an insecticide like all other dinitrophenol compounds (Dinoseb (DNBP), 2,4 dinitrophenol (DNP)), and it was used in a large number of foods and food products (8). These chemicals are quite potent in toxicity. They are used as herbicides (which eliminates harmful weeds and causes shedding of leaves), acaricides, nematocides, ovicides and fungicides all around the world (4,9). Spray forms, which are prepared as non-water soluble emulsions are available. They are dissolved in organic solvents. Soluble formulations in powder form are available as well. In our cases, the patients confused the agricultural drug with anti-louse agent, because of its yellow color. Nitroaromatic compounds are extremely toxic for humans and animals in doses of 25-50 mg/kg (10). The detection of the received dose was quite difficult in our patients. Nitrophenols and nitrocresols can be inhaled in the form of small droplets. They may be absorbed through the skin and gastrointestinal tract as well (5). They may be lethal even by dermal route. However, there is a moderate irritation on the skin and mucosa. In our cases, the drug, which was received by dermal route, caused hyperemia of the skin.

Nitrophenols and nitrocresols are sometimes degraded to amino and a nitro group by biotransformation. Although its metabolites are found in urine, the main route of elimination is through the liver. Its elimination rate is slow (half life 5-14 days). Repetitive exposure causes progressive increases in blood and tissue concentrations. DNOC blocks oxidative phosphorylation, like other dinitrophenols, by inhibiting adenosine triphosphate. The basic mechanism of intoxication is stimulation of the oxidative metabolism by oxidative phosphorylation and the increase in heat production by direct cellular effect. It causes hyperemia, tachycardia and fatigue, and it consumes the reserves of carbonhydrates and lipids (1,8,10).

The major systems prone to toxicity are neurological, hepatic and renal systems. Intoxication causes hyperthermia and direct toxicity on the brain, restlessness and headache (10,11). All of the patients had mild hyperthermia. Degenerative changes are observed in renal tubules and liver parenchyme. Albuminuria, pyuria, hematuria and azotemia are the findings of renal damage. In animal models, long term DNOC exposure resulted in cataract and glaucoma (2,3). However our patients had no persistent problems. Excessive sweating, thirst, fever, headache, confusion, fatigue and restlessness were the most commonly observed signs and symptoms. These symptoms occurred within a few hours after exposure.

The symptoms were consistent with those in the literature (12,13). There is not the definition of “moderate” and “serious (severe)” dinitrophenol poisoning in the literature. Hovewer; in serious cases of intoxication may result in death, renal failure, seizures, coma and cerebral edema (5,10,11). In cases of survival of severe poisoning, complete resolution of symptoms may be slow due to the toxicant’s long half-life (1,5).

The toxic material is yellow in color. Therefore, a bright yellow color on the hair and skin of suspected patients may be a clue for topical exposure. No yellow discoloration was

observed in our patients, because they had bathed after the use of the drug. Yellow discoloration of the sclera and urine is an indication of absorption of a toxic dose. Weight loss occurs in patients who are exposed to low doses of nitrocresols for a long period of time (2,10,11). It is useful to keep the blood and urine samples at -20ºC, in order to avoid further confusion.

Nitrophenol and nitrocresols, which are not metabolized, may be detected by spectrophotometric methods or gas-liquid chromatography. Systemic toxicity occurs at blood concentrations above 10 mcg/dL. In the literature, death was reported in one patient whose blood level was 75 mcg/dL (5,10). Treatment is usually supportive (oxygen and fluid replacement) and hyperthermia should be controlled. No specific antidote is available for intoxication with nitrophenolic or nitrocresolic herbicides. Salicylates are contraindicated for antipyresis, since they increase oxidative phosphorylation. Other anti-pyretics are considered in cases where hyperthermia cannot be controlled by peripheral cooling. If intoxication occurs via shampooing, bathing, swimming or contamination of body surfaces, the contaminated skin and hair must immediately be cleansed (5).

As pointed out in our study, since the patient's relatives did not know what medication the patient had been on, the patient was initially treated as a case of organophosphate poisoning. However, when they brought the medication to us, it became certain that organophosphate poisoning was not the case. We were not able to make a precise diagnosis whether the case was one of organophosphate poisoning in our first examination, because neither we nor other hospitals in the neighborhood have the necessary facilities to measure pesticide levels in urine and blood, to calculate RBC indices or to test for plasma cholinesterase levels.

Moreover, organophosphate and nitrophenol poisoning have many clinical features in common such as fever, tachycardia, hyperthermia, sweating, headache, anxiety, emesis, and agitation (3,5,14). In order for a correct diagnosis to be made, it is crucial that patients' relatives be cognizant of the medication/substance the patient has been taking and bring a sample of it to the physician (14). Management of nitrophenol toxicity is limited as there is no specific antidote. Therefore, the mainstays of therapy for DNP poisoning remain supportive (3,5). As for treatment, both organophosphate and nitrophenol poisoning require supportive care as well as skin decontamination, especially if the patient was exposed to poison through skin contact (3,14). On the basis of clinical features and anamnesis on the patients' first visit, it was speculated that they might have organophosphate poisoning and thus were administered atropine and pralidoxime. In the meantime, there were no complications related to PAM or atropine use. There is no indication in the literature that PAM and atropine are contraindicated in DNOC intoxication.

In conclusion, intoxications with agricultural drugs may be various in our country, the economy of which is largely dependent on agriculture, and treatment may vary according to the received agent. This rare type of intoxication should be recognized and kept in mind by physicians. A careful and detailed history should be taken in all cases of intoxication and the treatment should be based on the type of intoxication.

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