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General Approach to Cases of Drug Intoxication

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Abstract

Emergency departments are the first places where patients with drug intoxication are evaluated, and all physicians working in the emergency department should know the approach to intoxication very well. The diversity of treatment includes supportive care, decontamination, antidote therapy and the use of elimination techniques. The management of the follow-up and treatment of the cases of intoxication, the creation of algorithms and the determination of strategies are important and the correct application of these algorithms will be life-saving.

Keywords: Drug; Intoxication; Emergency Medicine

Introduction

The substances that cause damage or death in biological systems by entering the body in various ways are called toxins (poisons), and the branch of science that studies toxins is called toxicology (1). The history of intoxication is as old as the history of mankind. Information on many toxins (hemlock, aconite, opium, lead, copper) is available in the Ebers papyrus, that are believed to have been written around 400 BC. Hippocrates also mentions the number and treatment of toxins in his professional book (2). Paracelsus (1493-1541) indicated that "Everything that exists is toxin, and there is nothing that does not contain toxin. Only the dose determines whether something is toxin or not". In case of high exposure to a substance, every substance is likely to turn into toxin. These substances may enter the body through various routes (oral, parenteral, inhalation, skin and mucous membranes) and cause unwanted side effects in the body. A toxin may affect the normal functioning of the organism in many ways. It may impair or alter cellular or organ functions and may lead to undesired results by affecting the uptake, excretion or transport of other substances into the organism (3). Cases of intoxication are very common all around the world. In most of the intoxications, acute intake of the drug causes that cases of intoxication have an important place in emergency department admissions. Cases of intoxication constitute 5-10% of all patients admitted to the emergency department, and only 5% of these cases of intoxication require hospitalization. Death occurs in only 0.03% of all cases of intoxication (4).

Cases of intoxication may present with various clinical findings depending on the affected system or systems. The extent of the symptoms may vary from gastrointestinal system complaints to CNS findings. It is not known what kind of drug causes intoxication in many cases at the beginning of emergency treatment. Due to the wide range of substances that may cause intoxication, it is important to find the primary agent or agents causing the event (5).

History is crucial in patients presenting to the emergency department with intoxication. However, the relatives of the patient (family, bringers, roommates or workmates) should be questioned in detail by the emergency physician due to both the psychology of the patient and the patient's inability provide medical history (5, 6).

Although the clinical examination findings of the patients were of diagnostic value, the determination of the substance taken is based on history and physical examination. Known diseases, currently or previously used drugs, empty drug boxes around, medical diseases and treatments of the relatives, or chemicals/drugs that can be accessed in the workplace should be included in the history (5, 6).

Some physical examination findings may be specific to some substances, however, they are not clinically associated with blood level for many substances (7).

Specific antidote therapy is available for very few substances. Thus, although it is important to identify the toxic agent, the initiation of symptomatic treatment should not be delayed for the stabilization of the patient. It is necessary

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to carry out physical examination, antidote treatment and history together after the stabilization of the critical patient.

The treatment of patients presenting with suspected intoxication is not different from other patients. The aim of treatment is to evaluate and stabilize the functions of neurological, nephrological, gastroenterological and other body systems, especially cardiopulmonary functions (airway, respiratory and circulation). During the initial assessment, it is necessary to prioritize ensuring the patency of the airway, breathing and circulation. In order to ensure airway patency, if there is a foreign body in the mouth, it should be removed, and intubation should be considered in patients without protective reflexes and with a GCS below 8 (3, 8)

While performing these procedures, necessary circulatory support should be provided, oxygen should be given, the patient should be monitored, and the rhythm should be evaluated by taking an ECG (6). The patient's vital signs should be corrected with appropriate interventions.

Although the use of antidotes may be required in the treatment of intoxicated patients, administration of antidotes only in certain circumstances may come before the end of stabilization. Patients may have altered consciousness that can be easily treated with specific antidotes such as opiate intoxication, hypoglycemia, and Wernicke's encephalopathy. With medical history, vital signs and anamnesis, empirical administration of oxygen, naloxone, thiamine and glucose, which is also called "coma cocktail", may be considered (3).

After ensuring the stabilization of the patient after the first examination, a more comprehensive assessment is made with a detailed history, physical examination and laboratory tests (8).

It is usually difficult to take an accurate history in patients with intoxication. Both the psychological state of the patient and impairment of the consciousness can make it even more difficult to take history. Nevertheless, taking the patient's history has an important role in guiding the treatment (3, 4, 9). In cases where adequate information cannot be obtained from the patient, patient relatives, colleagues, crime scene witnesses and, if any, the healthcare team bringing the patient should be investigated in detail (9). The drugs that can be accessed by the patient, currently or previously used drugs, and the diseases and treatments of the household or relatives should be investigated in detail. While accurate and reliable history may directly lead the physician to the diagnosis, the physician must consider the physical examination and laboratory findings while guiding the treatment (9).

Physical examination is highly important in the management of the diagnosis and treatment of the patients with intoxication (10). The assessment of patients with potential for toxic exposure requires a systematic approach (3). The patient should be completely undressed. The clothes of the patient should be checked for substances hidden in the body (marijuana, heroin and empty drug boxes), and if there is any odor from the clothes, it should be noted (3, 11). During the physical examination, vital signs, including pulse oximetry, should be accurately measured and repeated. The respiratory rate should be counted exactly instead of estimating, and it should be noted. Cardiac monitoring should be performed, a 12-lead ECG should be taken to evaluate QT, QRS and rhythm (12). It is extremely important to take ECG in intoxicated patients for the demonstration of complications and patient follow-up. Regular and continuous ECG monitoring should be performed on all patients, and it is necessary to focus on cardiac effects (13). While the drugs that block myocardial Na channels lead to prolongation in the QRS interval, the agents that block K channels may lead to ventricular arrhythmias such as Torsades de Pointes by prolonging the QT interval (11).

The general condition and consciousness of the patient should be evaluated, and attention should be paid to agitation, confusion, and drowsiness. The skin should be examined in detail for sweating or dryness, redness, bruising, trauma or injection scars. Bruising may be a clue for trauma and may also indicate a coagulation disorder. It should not be forgotten that physical scars may be observed in unexpected region in patients with intravenous drug use (3, 11). The eyes should be evaluated for pupil diameter and reactivity, nystagmus, unconjugated eye movements, and increased or dryness of tears (3). The oropharynx should be evaluated for increased secretion or dryness. The lungs should be auscultated for bronchorrhea and non-cardiogenic pulmonary edema, and the heart should be auscultated for rhythm, rate, and pattern (3). Abdominal examination should be performed for the presence of bowel sounds, globe vesical, abdominal tenderness or rigidity, and bowel sounds should be counted. Bowel sounds may increase or decrease depending on the effect of the toxic agent on the cholinergic system (3). The extremities should be evaluated for muscle tone and fasciculation, and detailed neurological examination including cranial nerves, muscle tone, DTRs and muscle strength should be performed (3).

After the physical examination, whether the patient's current examination findings are compatible with any toxic syndrome should be compared. The term toxidrome can be defined as the symptoms and physical examination findings caused by drug groups with the same pharmacological effect (10, 14). The most common toxidromes are anticholinergic syndrome, sympathomimetic syndrome, opiate/sedative/ethanol syndrome, cholinergic syndrome and serotonin syndrome (12). Some specific toxins can be identified by the patient's current vital signs, neurological examination, skin examination and odor (6).

Classification of symptomatic drugs based on vital signs (12):

1. Drugs causing bradycardia: Beta blockers, opiates, calcium channel blockers, anticholinesterase drugs, digoxin, clonidine and ethanol.

2. Drugs causing tachycardia: Anticholinergic drugs, amphetamine, sympathomimetics, theophylline, antihistamine drugs and cocaine.
3. Drugs causing hypothermia: Carbon monoxide, opiates, sedative hypnotics, oral antidiabetics and insulin.
4. Drugs causing hyperthermia: Nicotine, anticholinergic agents, antiepileptics, antihistamines, salicylates, sympathomimetics, and antidepressants.
5. Drugs causing hypotension: Alpha-1 adrenergic antagonists, alpha-2 adrenergic agonists, beta adrenergic antagonists, ACE inhibitors, antiarrhythmics, calcium channel blockers, cyanide, cyclic antidepressants, ethanol and other alcohols, iron, methylxanthines, nitrates and nitrites, nitroprusside, opiate, phenothiazine, phosphodiesterase-5 inhibitors, sedative hypnotics.
6. Drugs causing hypertension: Ergot alkaloids, lead (chronic), monoaminoxidase inhibitors, nicotine (in the early stage), phencyclidine, sympathomimetics, yohimbine.
7. Drugs causing hypoventilation: Alpha-2 adrenergic agonists, botulinum toxin, ethanol and other alcohols, gamma hydroxybutyric acid, neuromuscular blockers, opiates, organic phosphate insecticides, sedative hypnotics.
8. Drugs causing hyperventilation: Cyanide, dinitrophenol and the like, epinephrine, ethylene glycol, hydrogen sulfide, methanol, methemoglobin sources, methylxanthines, nicotine (in the early stage), salicylates, sympathomimetics.

Classification of symptomatic drugs based on neurological findings (12):

1. Drugs causing miosis: Cholinergics, clonidine, opiates, organophosphates, phenothiazines, pilocarpine, and sedative hypnotics.
2. Drugs causing mydriasis: Anticholinergics, antihistamines, antidepressants and sympathomimetics.
3. Drugs causing convulsions: Organophosphates, tricyclic antidepressants, isoniazid, insulin, sympathomimetics, cocaine,methylxanthines,phencyclidine,methylxanthines, phencyclidine, benzodiazepines, ethanol, lead, lithium, lidocaine and lindane; and moreover, lithium may lead to tremors, organophosphates may lead to fasciculations, and neuroleptics may lead to dystonic reactions.

Classification of symptomatic drugs based on dermal findings (12):

1. Drugs causing diaphoretic skin manifestations: Sympathomimetics, organophosphates, acetylsalicylic acid, phencyclidine
2. Drugs that give the appearance of red skin: Anticholinergics, boric acid, carbon monoxide
3. Drugs that give the appearance of blue skin: Nitrates and nitrites, dapsone, phenazopyridine
4. Drugs causing bulla on the skin: Barbiturates, carbon monoxide, sedative hypnotics

Laboratory and Imaging in Cases of Drug Intoxication

In patients with intoxication, laboratory tests such as general hemogram, biochemistry, and drug-specific tests (such as drug level) are studied as blood tests (12, 15). General laboratory tests should include comprehensive biochemistry analysis involving complete blood count, blood electrolytes, kidney function tests, liver function tests and glucose, coagulation values, cardiac markers, blood gas analysis, complete urinalysis, B-HCG value for each pregnant woman, and drug level if possible (15). General laboratory tests may help to know the initial blood values of the patient, to recognize the metabolic disorders caused by intoxication, and to guide the treatment.

Although radiological imaging is rarely useful in diagnosis, it may have an important role in the clinical management and follow-up of some intoxications (16, 17).

In cases of intoxication, the main goal is to first plan the supportive treatment of the patient, to reduce the concentration of the toxin in the target organ or tissue, and then to combat its pharmacological and toxicological effects (18). The inhibition of the absorption of toxic substance, the elimination of the toxic substance from the body, and the elimination of toxic effect with symptomatic supportive treatment and antidote constitute the stages of the intervention for intoxication (19). In line with these aims, decontamination methods are applied to prevent the absorption of the toxic substance, and it is ensured that the patient is removed from the substance and the substance is excreted from the patient and the drug is excreted from the body. The choice of the decontamination and excretion methods (gastric lavage, vomiting, administration of activated charcoal, cathartics, whole bowel irrigation, diuresis, body washing, excreting, hemodialysis, hemoperfusion etc.) depends on the toxin, time, and the patient's clinical picture.

Vomiting / Causing to vomit

In the past, regurgitation was performed to excrete the toxic substance taken orally in cases of drug intoxication. Nowadays, regurgitation is not recommended in cases of drug intoxication.

Gastric lavage

Gastric lavage is the process of washing the stomach by inserting a special catheter into the stomach through the mouth (orogastric) or the nose (nasogastric) to empty the stomach contents or to wash the stomach (3). An appropriately sized orogastric/nasogastric tube is sent to the stomach in gastric lavage. After checking the location of the tube, gastric lavage is maintained until the waste fluid is cleaned with appropriate amounts of fluid in adults (3).

Administration of Activated Charcoal

Activated charcoal binds to the drug irreversibly in the intestine and reduces the adsorption and enterohepatic circulation of the drug, and it is also considered to reduce the blood concentration of the drug in two ways, by creating a negative diffusion gradient between the intestinal lumen and the blood, and by allowing the drug called "gastrointestinal dialysis" to pass from the blood to the intestinal lumen (20). The earlier the administration of activated charcoal, the more effective it is considered to be.

Whole bowel irrigation

Whole bowel irrigation is a fast and usable method that allows the bowel to be emptied in 4-6 hours (12). In this way, absorption of the toxic substance can be prevented by giving a high volume of electrolyte solution enterally and increasing the rectal excretion of the ingested chemical.

Forced Diuresis

In cases of intoxication with substances excreted through the kidneys, the excretion of the toxin from the body can be accelerated by increasing the urination of the patients. This process is called forced diuresis. Kidney functions, cardiac and respiratory system must be intact to perform this treatment (18).

Hemodialysis

Hemodialysis is based on the principle of taking toxic substances from the blood into the dialysis fluid in the device through dialysis apparatus. The benefits of hemodialysis are removal of toxins absorbed from the intestinal lumen, removal of substances that do not bind to activated charcoal, and elimination of active toxic metabolites along with the parent compound (18). It can be applied in methanol, ethylene glycol, high-dose salicylate, theophylline, as well as acetaminophen, arsenic, bromide, chloralhydrate, ethanol and lithium intoxication (21).

Intravenous Lipid Emulsion (ILE) Therapy

Intravenous lipid emulsion (ILE) therapy describes the use of lipid emulsions by intravenous infusion to reduce the bioavailability and toxicity of the circulating toxic substances. Significant clinical improvement in the treatment of intoxication with lipophilic drugs, relatively easy application, and low cost led to an increased use of these lipid emulsions and paved the way for their use in the treatment of intoxication (22)

Antidote Treatment

The use of antidotes refers to reducing the effect of the toxin, and reversing or neutralizing its effects. They are chemical or physiological antagonists. The mechanisms of action of antidotes are the inhibition of toxin formation, activation of toxin-destroying enzyme systems, antibody properties against toxins, interaction with toxic agents at the receptor level, and binding of heavy metals. Common cases of intoxication in the emergency department and the antidotes to be administered are presented in Table 1 (23, 24).

Table 1: Toxin and Antidotes Causing Intoxication

Toxin Causing Intoxication	Antidote
Gold	Dimercaprol
Anticoagulants	Vitamin K, Fresh Frozen Plasma
Anticholinergic drugs	Physostigmine
Antimony compounds	Dimercaprol
Arsenic	Dimercaprol, Penicillamine
Copper	Dimercaprol, Penicillamine
Benzodiazepines	Flumazenil
Betablockers	Glucagon
Bismuth	Dimercaprol
Mercury	Dimercaprol, Penicillamine
Zinc	Dimercaprol
Iron	Desferrioxamine
Digoxin	Digoxin Binding Antibody
Ethylene Glycol	Ethanol
Heparin	Protamine
Hydrochloric Acid	Calcium
Hydrogen Sulfide	Sodium Nitrite
Isoniazid	Pyridoxine
Calcium Antagonist	Calcium
Carbamate	Atropine
Carbon Monoxide	Oxygen
Lead	Dimercaprol, Penicillamine
Metoclopramide	Procyclidine
Methanol	Ethanol
Methemoglobinemia	Methylene Blue
Methotrexate	Folic Acid
Nickel	Dimercaprol
Opioid Analgesics	Naloxone
Organophosphate	Atropine, Pralidoxime
Paracetamol	N-Acetylcysteine
Sympathomimetics	B Blocker
Thyroxine	Propranolol

National Poison Information Center (UZEM - 114)

As physicians, we usually know the medical approach to cases of intoxication that we face frequently. However, when we face cases of intoxication due to a drug whose content we do not know, herbal product that we do not know what it is, or an insect bite whose poison we do not know what effects it may have, we need support for the management of these cases. Call center 114 of the National Poison Information Center (UZEM) provides medical support by answering calls from all over Turkey 7/24. UZEM has an essential

role in case management and treatment in the hospital in cases of intoxication, with the medical support it provides via 114 phone line and the support for antidote supply to the hospitals. To get information about toxins and treatment recommendations by contacting poison counseling centers established in order to help the physician quickly and reliably will increase the success of treatment of the cases of intoxication.

Conclusion

Emergency departments are the first places where patients with drug intoxication are evaluated, and all physicians working in the emergency department should know the approach to intoxication very well. The diversity of treatment includes supportive care, decontamination, antidote therapy and the use of elimination techniques. The management of the follow-up and treatment of the cases of intoxication, the creation of algorithms and the determination of strategies are important and the correct application of these algorithms will be life-saving.

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