

Poisoning in Forensic Medicine and Toxicological Analysis Methods

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In this report, recent literature on poisoning are reviewed and in addition to classical toxicological methods, new, specific, practical, rapid and reliable methods are discussed.

Poisoning is of interest to many and particularly to physicians. Furthermore, public awareness and the level of education about poisoning need be heightened and awareness campaigns need be conducted on this matter.

Key words: *Poisoning, analytic toxicological methods, forensic medicine.*

Adli tıp'da zehirlenmeler ve bazı toksikolojik analiz metodları

Bu derlemede; zehirlenmeler irdelenmekte ve bu konudaki klasik toksikolojik yöntemlere ek olarak, spesifik, hızlı, pratik ve güvenilir yeni yöntemlerden söz edilmektedir. Hekimler başta olmak üzere herkesin, toplum sağlığı yönünden önemli görülen bu potansiyel tehlikeye gereken önemi vermesi, toplumun zehirlenme konusundaki bilgilerinin geliştirilmesine ve eğitimine hassassiyet göstermesi gerekmektedir.

Anahtar kelimeler: *Zehirlenme, analitik toksikoloji metodları, adli tıp.*

Poisons induce physiological, biochemical and biological effects resulting in illness and even deaths in living organisms (1-5). These substances may be taken perorally, parenterally (intravenous, intramuscular, intradermal), mucosally (rectum, vagina, conjunctiva), dermally or by inhalation. The effects of poisons in living organisms are generally referred as "poisonings" (1,4,5).

From the Early Ages on, poison and poisonings have always been focus of interest. Paracelsus indicated that "All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy".

During the prehistoric ages, animal poisons or some plant extracts have been used by human beings for hunting, assassination and fighting purposes. Eber papyruses (BC 1500) mentioned hemlock, aconite poisons, opium, lead (Pb), copper (Cu) and antimony (Sb) and described some plants such as digital and belladonna alkaloids (6).

Today, many effective and new plant-derived or mineral substances are extracted or some of them are synthetically obtained for industrial use (4,7). Currently, there are about 80 000 chemical substance used and is believed that every year around 1 000 new substances are

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added to the already existing list (2). In addition, every day new drugs are introduced. Huge amount of chemical substances are offered to our daily lives. Thus, so many chemical substances and drugs are in use or in abuse by people (6,8). These drugs may be prescribed drugs (analgesics, anti-depressants, hypnotic, tranquilizers, anti-histaminic, anti-emetics), abused drugs (stimulants, hallucinogens, narcotics), commercial substances (anti-freeze, aerosols, insecticides, rodenticides, herbicides, detergents) and some gases (carbon monoxide, cyanide) (6,8-15). Furthermore, alcohol and narcotics like opium (morphine etc.), hashish (marihuana), cocaine and barbiturates should be added to the list (2,6,9,10,12,14). Additionally, it is already known that all human beings and other living organisms are, at least, partially under effects of pollution. For example in a World Health Report, it is indicated that an average Englishman has 2 ppm insecticides in his body. In Americans and Frenchmen, this value is 10 ppm and an Indian has an average 30 ppm insecticides in his body (16).

Poisonings have both medical and legal aspects; physicians should urgently treat these cases and inform relevant government offices. It is also necessary to obtain specimens for toxicological analyses. Thus, analytical, forensic toxicology is linked to poisonings (1,3,4,6,17). Toxicological analysis should always be performed whether specimens are taken from autopsy or from live subjects (6,18).

Most poisoning cases occur as accidents. The accidents are commonly caused by misuse of medical or poisonous substances by children and adults (2,3-5,10). In addition, the poisoning is one of the leading childhood health problems. Particularly 1-5 age group children are affected (1-3,5). For example, in a study performed in Elazığ, between 1990 and 1992, it was indicated that 30.7% of all poisoning cases occurred in children aging between 0 and 14 (5). Other poisoning cases are caused during transportation, stock and use of chemicals in industry (2-4). Similarly, during storage and use of agricultural pesticides and herbicides, poisonings may be induced.

Furthermore, medical or chemical poisons are frequently used to commit suicide and rarely for murderous purposes (2,3,5,8,14,19,20). However, insecticides usually have an intense odor and color, making them difficult to add into the food and drink without being noticed. Consequently, these substances are infrequently used for murderous purposes. Particularly in people over 10 years old, these substances are not usually used for murder. In one of our reports, it was indicated that fathers committing suicide had two children drink insecticides. The ages of the children were 1 and 5 (8).

While in developed countries, suicides are induced by psychotropic drugs such as acetaminophen, liquid agricultural chemicals are used for the same purpose in Turkey and other developing countries (2, 12, 21). For example, in İzmir, between 1980 and 1990, 473 suicide cases were autopsied and it was noticed that 215 case (45.4%) were self-poisoning cases. Among these, 154 (32.5%) had drunk agricultural chemicals (21).

Classification of poisonous substances

Poisonous substances are classified as air-environment polluters, industrial chemicals and acute/chronic poisons. Detailed classification could also be based upon (1,6);

A) Nature of the substance:

1. Organic materials:

a- Plant derived poisons: Food / mushroom poisons and some plant alkaloids (strychnine, ergo, barbiturates, glycosides, atropine, morphine, nicotine etc.) could be counted in this group (3-5,7).

b- Animal based poisons: Toxins from microorganism such as Botulism toxin, metabolic by products, snake, scorpion, bee poisons and Cantharides are derived from animal products. Cantharis known as plant parasite is picked up, dried and crushed. Cantharis are generally used for criminal abortion (1,3,4,10).

2. Inorganic materials: Metals; Mercury (Hg), Lead (Pb), Arsenic (As), Thallium (Tl), natural and synthetic chemicals are in this group (1,4,10).

B) Physical Properties of poisons:

1. Solid poisons: Every poisonous material with solid physical structure could be classified in this group.

2. Liquid poisons: Poisonous liquid materials are placed in this group. Liquids such as alcohol, chloroform, benzene, hydrocyanic acid and phosphor compounds are poisonous materials widely dispensed in medicine, laboratories and industry. These substances may induce chronic, acute or job related toxicosis (1,4).

Furthermore, abuse of solvent and volatile substance also pose a significant problem in large metropolitan areas (2,10,14,17,22). For this purpose, butane, freon, fluorocarbon, toluene, derivatives of petroleum, trichlorethylene, ethane are used. Symptoms of solvent abuse are very similar to alcohol toxicosis. These findings appear right after the inhalation of solvents and disappear shortly after the inhalation (2,10).

3. Gases; Poisonous gases include carbon monoxide (CO), carbon dioxide, hydrogen sulphur, sulphur dioxide, methane, ethane, buthane, propane, acetylene and war gases (tabun, sarin) (1,4,6,10). CO toxicosis is one of the most frequently encountered toxicosis cases. CO is a colorless and odorless gas and the density of CO is lighter (0.967) than air's. CO has approximately 20 time more affinity for hemoglobin than that of oxygen. In acute CO toxicosis, livor mortis appear in cherry-red color and it is disseminated. Also, bloody foamy secretion leaks out from oral and nasal openings. These findings are pathognomonic for CO toxicosis (1,2,10).

C) Effect of Poisons: In this type of classification, the primary concern is the affected organs and tissues.

1. Local irritants (corrosive materials) induce tissue damage at the site of exposure. Among these substances are hydrochloric, nitric and sulfuric acids, sodium hydroxide (caustic soda), potassium hydroxide, ammonia, organic acids (acetic, oxalic acid, phenol). Corrosive irritants: Mineral/metal compounds; Sb, Pb, Cu, Cl₂, Pb, Tl, As, Bromide, Iodine, Barium, Potassium permanganate (1,2,10).

2. Deep tissue irritants: These substances are able to penetrate into tissues from the first site of exposure and to disseminate into the body. Consequently, poisonous influences are noticed at both local exposure site and other parts of the body. Among these compounds are Hg, phenol, oxalic acid, Cantharis, carcinogen and mutagen agents (1,6).

3. Poisons effecting organs or system: These group substances influence a certain organ (liver, kidneys etc.) or systems (hemopoetic etc.) (1,6).

D) Utilization of poisonous substances:

1. Therapeutic materials: Substances used in medical or veterinary practice are classified in this group. These substances are utilized for diagnostic, therapeutic or prophylactic purposes (1,4).

2. Industrial and laboratory materials: Solvents (benzene, toluene, xylene etc.), formaldehyde, food/drink additives, conservative substances and agricultural chemicals (insecticides) are in this group (1,2,4,6,10).

Insecticides (pesticides) are used to eliminate microorganisms (pests) and insects which spoil and damage food during production, consumption and storage (7,10,19,20). In this country, between the years of 1977 and 1981, 1484 people died of toxicosis by insecticides (16). These chemicals are divided into 3 groups according to their chemical structures (1,4,16,19):

a- Organochlorides: (derivatives of chlorbenzen, hydrocarbons with chlorine), DDT (dichloro-diphenil-trichlorethane), dieldrin, heptachlorine are in this group.

b- Organophosphorous: (parathion, malathion, tabun, sarin): Other colin esterase inhibitors and parasymphathetic excitants could be placed in this group. Since most agricultural chemicals are considered as organophosphorous substances, most accidental poisoning cases and suicides are caused by these compounds. Poisonings with these substances induce muscarinic and nicotinic influences on nervous system.

c- Carbamates: Effects of dimeton and aminocarb, carbofuran etc. are similar to organophosphorous.

Steps of toxicological analysis

Toxicological analyses are performed in 3 general steps (6).

1. Case history and proper specimens:

When a physician encounters a known or suspected poisoning case, S/he should follow the course indicated below (1,2,6,23).

Duty Of A Physician On Poisoning Cases:

a-) Anemnesis should be taken carefully. Symptoms and their starting time should be noted in detail. Age, sex, and weight of case (or victim), his medical history (time covered between diagnosis and death, any medical treatment before death), his last job and autopsy findings should be examined and noted carefully.

b-) First aid and emergency treatment should be performed.

c-) Whether suspicious substances are taken or by any other person should be determined.

d-) Samples of vomit, gaita, urine and blood should be taken and sent for toxicological analysis.

e-) Government offices should be informed of the cases.

f-) If death is happened, autopsy should be done and all organ samples should be sent to forensic toxicology laboratories.

Turkish Forensic Laws (Ceza Muhakemeleri Usulü Kanunu madde 83) indicate that: "When an organ sample is taken from suspicious poisoning cases, it is necessary to describe this organ sample with its damaged shape. Suspicious substances found in dead or other places are analyzed by a chemist or an officer assigned. Judge has a right to say that: the analyses should be performed with a physician." (4).

Age of subject is an important factor in poisoning cases. Children and old people show extreme reaction to substances like; opium, emetin, and morphine (1,2). Digital/digitoxin and As are processed slowly. When these substances

are taken frequently in small amounts, they built up in the body (1,24,25). Consequently, it is very important to determine the identity of the substance and the way it is processed.

It is impossible to know exactly which substances induce hypersensitivity reactions in the body. If a substance has a capability to induce hypersensitivity, a person may develop allergy and idiosyncrasy after the substance is taken. Some people are very allergic to fish and sea foods, egg, fruits such as; banana and strawberry etc. drugs such as; sulfonamide, procaine, penicillin and bromide etc. (1,2). When these substances are taken, symptoms like runny nose and urticaria may begin. Anaphylactic reactions may cause sudden death (1). For these cases, physician should immediately perform first aid and emergency treatment. In this country a centrally managed "Poison Information Center" is designed to help patients and physicians over the phone around the clock. In Singapore, it is reported that a similar center is serving on a computerized network (26).

During the examination of the dead, physician may be suspicious of poisonings. For example; in cadavers where death is caused by CO, nitric acid and cyanide, livor mortis are light red color and liquidity of blood is increased (1,2).

During autopsy, specimens are filled into bottles and some fixative solutions are added. Then, case name, number and autopsy date are written by physician. Later these bottles are given to Public Prosecutor for toxicological analysis. Formaldehyde is known to be a good organ fixative solution for this purpose (27). In cases of TI, As, P, Hg and opiate poisonings, in addition to organs and body fluids (blood, urine and stomach content) fingernail, bone and hair samples should be taken (1,2,6,28,29).

Sending suspicious materials found in the place make laboratory analysis easy and speeds up poison identification. This saves time and money. In addition, suspicious substances could be compared with the ones obtained from death.

2. Toxicological Analysis:

In this stage many analytical procedures are followed. Poisonous substances are discarded

from the body by the way of kidneys (urine), liver, sweat, spit and breathing. It is possible that in toxicosis cases, no poison could be determined in the body at systemic toxicological analysis. Thus during the examination for a toxic substance in poisoning cases, one should consider the amount and the longevity of the time in which the victim is exposed to the poison previously. If a substance is taken in small amounts for a long time, a larger quantity of the material might be needed in order to induce a pathological effect compared to the case where the victim is not exposed to the substance previously. In toxicosis cases where a several days of hospital treatment is followed, it is possible that no poisonous material could be recovered during a systemic toxicological analysis. Because during the treatment period, poison may be discarded from the body.

In laboratory; amount of samples is measured and qualities of poison and its biotransformational products are studied. Chemical substances in the body are changed by metabolism. These products may be found in organ and body fluids either as free or bound to other cellular compounds. When main chemical substance cannot be separated from these compounds, metabolites of poisonous substance are analyzed and information on main chemical is gathered indirectly. Nowadays, many poisonous substances are found in toxicosis cases. However, limited amount of investigation material could be taken during the autopsies. Consequently, it is impossible to find all possible poisons in this limited samples. Thus it is advisable to start first toxicological analysis for the most suspected substance. When poisons taken by mouth, first investigation are performed on gastrointestinal tract. Because some amount of unabsorbed poison could still be found in gastrointestinal tract. Even a small amount of strong corrosives such as sulfuric acid, lye, phenol may induce death if taken through gastrointestinal tract. The amount of the material consumed is not important in these cases. Because right after the intake, hemorrhagic shock is formed and it is usually the cause of death in these cases (6).

After gastrointestinal tract investigation, samples of urine are examined and toxic

substance metabolites are analyzed. Non-specific tests are directly applied for this purpose. Typical example test (for drugs in phenothiazine group) is urine color test (ferric chloride, perchloric and nitric acid) (6).

Every poison present in the circulation should pass through the liver (6,18,30). Thus, during the investigation of various organs, the liver should first be examined. However, specific organ or body fluids are initially studied on special poisoning cases. For example, vitreous humor may be examined for measuring the level of postmortem digoxin / digitoxin (24,25). Toxicological analysis may also be performed on bone marrow. Even if dead body is decayed, it is possible to examine the maggots feeding on the dead body and consequently to isolate the poisonous material from the maggots (31,32).

Since postmortem chemical changes occur in decomposed dead bodies, their toxicological analyses are quite complicated. In these cases, chemical structure of poison is decomposed by natural enzymatic/non-enzymatic processes and by microbial metabolism or poisons are converted into other compounds. In addition, in deaths caused without poisonings, cadaveric alkaloids showing similar properties are frequently found as in these bodies. The compounds obtained from putrefied bodies may exhibit similar properties with morphine etc. during color tests. As noted by Evans in 1963, amino acids such as ornithin and lysine are converted into Putresin and Cadaverin by bacterial decarboxilation. Similarly, phenyl alanin is changed into phenyl ethyl amine that has similar chemical and physical characteristic with Amphetamine. As it has been found in 1969 by Kaempe; protein, nucleic acid and lipids undergo hydrolysis, oxidation and reduction processes. These compounds are converted into aliphatic and aromatic carboxylic acids derivatives of pyridine and piperidine and aromatic heterocyclic compounds. Depending on rate and amount of microbial action, concentrations of cyanide, ethyl alcohol and CO may be increased. But As, Hg, and strychnine show rather stable character and their presence could be determined years after from death (6).

Techniques of Toxicological Analysis

Many analytical methods have been applied for analysis and determination of drugs or poisons in bodies. With recent technological improvements new and more specific techniques are developed. These improvements are still continuing. Although sensitive and correct analytic methods are being applied, countless number of chemicals are still a handicap for forensic toxicologists (13). For the first time, alkaloid poisons have been isolated by Belgian chemist, J.S.Stas in 1850's. Later, this method has been modified by German chemist, F.Otto. This method is now called as "Stas-Otto Method" and commonly used for isolation of many alkaloid substance today (6). As a routine method the following tests are performed at Forensic Medicine İzmir Group Head Toxicology Laboratory: Schreening Test Analysis with Modified Stas-Otto Method prepared in watered phase extraction (for organ pieces with stomach, small intestine content); color tests; Thin Layer Chromatography (TLC), spectrophotometric analysis with Ultra Violet (UV) light and various quantitative toxicological investigations (19).

Some of toxicological techniques which are routinely utilized and continuously developed in Forensic Toxicology are listed below.

1) CHROMATOGRAPHY: Chromatographic methods are based upon the migration differences between substances. The substances are applied onto various porous medium where patterns of migrations are determined. There are several chromatographic methods which utilize different medium (1). There are some subgroups:

a-) Thin Layer Chromatography (TLC): It is used as a main method at Forensic Toxicology Laboratories (11,19,33).

b-) Adsorption Chromatography: It is based on partition and ion exchange properties of substances (6).

c-) Paper Chromatography: It is widely used for various substances. In this method, materials are forced to migrate onto paper medium.

d-) Colon Chromatography: This method is used both for research and routine analysis. Various colon chromatographic methods such as

exclusion chromatography, ion exchange chromatography, and affinity chromatography are utilized.

e-) High Performance Liquid Chromatography (HPLC): With these method, minute amount of substances could be separated and analyzed. This method represent an advanced analytical technology (20,30,34).

f-) Gas Chromatography: It is especially used for determination of gas or evaporating poisons (1,6,22). It is known that gases can change their conditions easily. Thus, specimen like liquid nitrogen should be stored at low temperatures (6).

g-) Gas Liquid Chromatog-raphy: Like evaporators, it is used for determination of amount and decomposition of substances with low boiling temperatures (6).

h-) Gas Chromatography/Mass Spectrometer (GC/MS): It has definite applications for drug identification. This technique is mostly used to determine the effective substance in a compound. (6,13,17,35)

2) COLORIMETRIC METHODS: Qualitative and quantitative investigation of metals and industrial and environmental pollutants are performed by these methods. Very small amount of metals can be detected (1,6). In this methods, after reaction develops, color change is observed and this change is directly proportional to the substances entering the reaction.

3) SPECTROGRAPHIC METHODS

It is based on obtaining different spectrums and graphics under the visible light, UV and Infra Red rays according to their wave length. Poisonous substances and their amount are determined by spectrometer/spectrophotometer. In these methods, the amount of material to be tested is deduced from optical density of the known standard used in the assay (1,13).

Flameless Atomic Absorption Spectrometer: This method is a new and advanced test system. Antimony in biologic cells is analyzed by this method (13).

4) POLAROGRAPHY: It is an electro-chemical technique based on electro-dialysis (1).

Corrosives composed from mineral acid and bases which have ion concentrations above are measured by this technique and ion concentrations are determined (6).

5) LASER: Laser, like in many fields, are being applied in toxicology and it is possible to perform micro spectral analysis by laser light (1).

6) IMMUNOASSAY: Immunological techniques have the advantage of being applicable for various substances. Thus, very specific analytical methods are developed. It is accepted as the most practical method for determination and measurement of substances with high protein content and difficult to isolate. Barbiturate, benzodiazepin or opiate derivatives may be studied by this method (6,13). In Japan, Immunohistochemical Techniques are used to reveal presence of paraquat in rat skins and eyes (36). In Immunoassay, it is necessary to use very specific monoclonal antibody. For example; antidiquat monoclonal antibody cannot give any reaction to paraquat and other analogs (36). So by using these antibody, serum of poisoned person can be investigated by ELISA (Enzyme Linked Immunosorbent Assay) (37). In addition to ELISA, radio immuno assays may also be used in searching various proteinous materials. In immunological methods, the sole requirement to develop an assay for a substance is that the substance should be able to elicit a specific antibody response in an animal. Afterwards, using these antibodies, assays for almost any substance could be devised.

7) NEUTRON ACTIVATION ANALYSIS TECHNIQUE:

The principle of this method is the fact that in some toxic substances, ions could be activated by neutron bombardment. Consequently, a radiation is formed. According to the structure of the substance, the radiation profile varies. For example, in Tl and As poisoning, it is possible to identify these substances from small amount of hair by this method (1).

3. Writing a forensic report:

Forensic report is written after examination of the reports of physician who is attending the case, and giving the permission for burial. People

who design the forensic report should also consider the statements or reports of coroner and pathologist and the findings of the toxicology laboratory related to the case. It should be born in mind that a complete and correct report may only be written as a result of team work of pathologist and toxicologist on the case. All data should be searched in detail. Each finding and piece of information should be taken into consideration (6). In addition, followings should always be kept in mind. If some drugs and toxic substances are taken continuously, they may cause addiction (physical/psychic dependence). If some drugs are taken for long periods of time, their effects may be lessened. Consequently to induce pathological changes in these cases, an extraordinarily high doses is needed. For example, if As or Sb is taken in small amounts for a long time, the body develops resistance to high doses (1).

In conclusion, everybody first and foremost the physicians should be aware of the fact that poisonings are potential public health problems. Public awareness on this subject should be heightened. People making, using and working with poisonous material should be very careful when handling this material. It should born in mind that poisonings has medical as well as legal aspects. A large part of Turkish population works in agriculture and people working in this field is poorly educated. Public education campaigns especially about pesticide poisoning should be conducted and the target population should be identified and reached in these campaigns.

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