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Postmortem Toxicology: An Overview

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Abstract: Postmortem toxicology is one of the important disciplines among toxicology, analytical chemistry, clinical chemistry and pharmacology and is an important tool to know about any death caused by poisoning, its causes, and the type of poisonous substance that led to the death of a person. In this review postmortem toxicology has been discussed in detail. It is focused on different types of poisons and poisoning, causes of poising and forensic investigations involved to find out the reason behind the poisoning and deaths including criminal procedures.

Keywords: Postmortem, Toxicology, Poisoning, Poisonous substances, Forensic investigations

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Introduction

Postmortem toxicology is one of the important disciplines among toxicology, analytical chemistry, clinical chemistry and pharmacology. All these disciplines are used to assist in obtaining legal and medical verifications of death and its possible causes. Postmortem toxicology is an important tool to know about any death caused by poisoning, its causes, and the type of poisonous substance that led to the death of a person (Poklis, 1979). Poison is defined as a harmful substance that may cause adverse effects on human health and lead to death in extreme poisoning. Once the poison enters the body, it changes the functioning of biological systems and may cause death (Ivar *et al*., 2010).

Two types of poisoning may occur, one is unintentional poisoning from food, spoiled food and contaminated food, and second is intentional poisoning which is a criminal activity of person, when someone tries to kill someone using toxic substances (Cantrell, 2015). The primary objective of postmortem toxicology is to investigate the possible causes and explanations for cause of death. Post-mortem toxin testing can be performed on different types of specimens. The postmortem toxicologist collects all evidences at the scene of crime, any physical symptoms of the deceased and other information that may be useful to reaching any conclusion (Rohrig, 2019).

The process of investigating toxins in the body of dead person is one of the complex process and difficult to analyze the toxic substances as they are

rarely remaining in the body after death. Another difficulty is that these substances may change their form from when they are consumed. For example, death due to heroin poisoning may immediately change and seems to be the death caused by morphine, which will need more investigations to find out the actual substance which caused death. In further investigations any injection marks on the body and others will be recorded to reach the final conclusion (Ferner, 2008).

Several studies indicated that the investigations by the doctor during postmortem of a poisoning case are correlated with the circumstantial evidences of death of the person such as symptoms, signs, results of laboratory tests, and the testimony of witnesses. In addition, fundamental anatomical examination is conducted and organ samples and bodily fluids are sent for the toxicological examination and then only a forensic medical death certificate is issued and fill the anatomical report questionnaire based on the observations. The toxicological investigations for the cause of death are based upon blood sample, urine sample and hair samples.

1. *Blood sample*: A blood sample (10 ml) from the deceased person is used to determine alcohol poisoning and for the presence of any toxic substances.

2. *Urine sample*: The urine sample is considered best to detect toxins in deceased body, as it gives more accurate results but the samples should not be exposed to any viruses (hepatitis and HIV) or drugs and narcotic substances remain in the body that may spoil the whole analysis. Urine should be in its true actual and not kept for a long time. After death, the urine samples are usually, obtained from the urinary bladder in an easy and non-surgical way.

3. *Hair sample*: A hair sample is used to check the type of toxins present in the deceased's body because the hairs are capable of recording a high to moderate doses of a substance abuse. The chemicals in the bloodstream may turn into ingrown hairs and can be stored in the hair follicles, that may give an idea that when these drugs have been taken. The hair sampling method has not been considered much reliable, but it may give better results whenever the hair is coarse and dark and reveals narcotic substances quickly. For example, if two different people use toxic substances, the person with darker and coarser hair will show the results of the drug more accurately than the person with lighter and smoother hair (Butt, 2020).

In this review important information has been gathered to explore the methods and mechanisms of postmortem toxicology through different resources such as websites, articles, journals, text and reference books. The review may be helpful in obtaining answers and solutions of many problems and questions come to our mind regarding the postmortem toxicology, that may improve the quality of results in poisoning investigations.

After detecting toxins in the body after death, it was observed that the death was of suffocating nature. The observations on the apparent examination were the bluish lips and fingernails along with the colored regressive blood spots, facial congestion, the appearance of bloody foam at the nostrils and mouth, and the emission of a kerosene-like smell. Internal examination showed congestion of intestines and stomach lining, that also contains an emulsion solution with a kerosene-like smell, hemorrhagic drops under the pleura and various membranes. Severe congestion and edema was also observed in the lungs, brain and rest of the body organs.

In some other cases of thallium poisoning, which is a heavy metal toxin and has a cumulative action which is characterized by its resistance and impediment to disintegration and its ability to disrupt cellular enzymes. It can be detected after death by hair loss and signs of severe anemia, either internally or externally a fatty degeneration is noted in the liver and kidneys. The chemical examination can verify the presence of thallium compounds in the tissue samples taken from

organs and body fluids which can be examined even after several years of death (Jaishankar *et al.*, 2014).

Sarkar *et al.* (1994) revealed that there are many cases reported of poisoning due to white oil or kerosene, which are volatile toxins. These toxins are transparent, flammable liquids with a distinctive smell and a widely used as organic solvents. The smell of kerosene can be detected at the time of dissection of abdomen and chest cavity. Severe congestion with hemorrhagic points in the lining of the stomach and the surface of the lungs and severe pulmonary edema with degeneration of the kidney tissues can also be noted. The chemical examination is enough to diagnose cases of poisoning (Sarkar et al., 1994). Runde and Nappe (2017) indicated that some poisoning cases are reported due to salicylates (aspirin), which is one of the widely used drugs for many reasons. In most cases of aspirin poisoning it was an accidental consumption and mostly the victims are children. As there are no diagnostic observations of poisoning due to aspirin, reason observed in most of the death are due to suffocation. However, rashes and hemorrhagic points under the skin may be seen, especially in cases of hypersensitivity. Internal anatomy shows severe congestion and hemorrhagic spots, ulcers of the lining of the stomach and intestines, swelling, congestion and hemorrhagic spots in the rest of the viscera and membranes (Runde and Nappe, 2021).The main objective of this review is to see the postmortem toxicology in terms of the concept, the mechanism of detecting toxins after death and the difficulties in this process.

Methodology:

A survey was carried out at the Municipal Public Health Service's Forensic Medicine Department in Amsterdam, the Netherlands. Unnatural death in Amsterdam and the surrounding regions (1.25 million residents) were investigated by the forensic physician from this department. Approximately 1100 decedents were examined in a year. The external examination's main purpose was to determine the reason and manner of deaths due to any toxicity. The causes of death were recorded. In most of the cases sickness, injury, or defect that triggered physical and biological events were the causes of death. The mode of dying ((natural or unnatural) and cause of deaths were recorded. The data was based upon postmortem urine screening of adult decedents and this investigation was done from April 2008 to April 2009.

In this analysis violent fatalities (n 1424), euthanasia and physician-assisted suicide (n 14188), deaths in hospitals or nursing homes (n 14198), and deaths with a postmortem interval of seven days or more (n 1466) were excluded. The cases where patient died outside the hospital or if death was verified in a hospital's emergency room before admission were only included in this study. The primary researcher briefed the forensic physicians on the study protocols.

Data Collection:

Based on external examination, the forensic physician evaluated the decedent, the scene of death, and the medical history in accordance with the Dutch Forensic Medical Society's guidelines in order to discover symptoms and the causes that may have contributed to the death. Physical evidence of recent intoxication, such as the presence of drugs/medications and marks of injection on the body or drug paraphernalia were scrutinized. The manner and cause of death were determined based on all of these observations and results. Following that, a postmortem urine sample from the dead body was acquired by urethral catheterization or suprapubic puncture for on-site toxicological screening. The urine samples were screened out for the presence of the following commonly used drug classes: barbiturates, amphetamine benzodiazepines, morphine, 3,4-Methylenedioxymethamphetamine, cannabis, cocaine, methadone, methamphetamine, and tricyclic antidepressants (TCA)(Ceelen *et al*., 2010).

This test includes a unique set of lateral flow chromatographic immunoassays that use drug-

protein conjugates and mouse monoclonal antibody-coupled particles. The systems of control line make use of goat antibodies. If both the test and control lines were visible, the multidrug test considered positive and if only the control line was visible, it was considered negative. The tint of red in the test line looked to fluctuate, but the test was deemed negative if even a slight pink line was present. Finally, the urine samples were delivered to ATAL Medical Diagnostic Center in Amsterdam in a polypropylene test tube with no preservative for immunoassay validation. The Cedia test of the Thermo Fisher/Microgenics type was employed on an Olympus 2700 analyzer to detect amphetamines, cocaine, methadone, and benzodiazepines (Ceelen *et al*., 2010).

The enzyme of DRI-ethyl alcohol homogenic process was employed to produce ethanol. The European Laboratory Guidelines Testing cut-off values for screening were used-- Benzodiazepines (after glucuronidase treatment, calibrated on nitrazepam): 300 ng/ml, cannabis (delta-9-THC-carboxylic acid): 100 ng/ml, 200 ng/ml, cocaine (benzoylecgonine), 50 ng/ml, methadone (EDDP): and opiates (morphine): 300 ng/ml Furthermore, all test findings were evaluated in the context of the case (PZ).

Cocaine, methamphetamine, amphetamine, MDMA, cannabis and opiates were also deemed misuse drugs used for pain management (e.g., tramadol, oxycodone and paracetamol combined and mixed to codeine). Drugs of abuse were divided into two categories based on their toxicity: 'low-risk drugs of abuse' (cannabis) and 'high-risk drugs of abuse'. Medicinal opiates were categorized as pharmaceuticals such as benzodiazepines, barbiturates, and TCA. The electronic register utilized by forensic physicians for documentation of findings of the external examination was used to collect the information concerning the presence of drugs or paraphernalia at the scene of death, usage of drugs soon before death, or history of drug misuse. In addition, the forensic physician completed a questionnaire to collect specific information for the on-site examination of postmortem toxicological screening, including drug screening results and collection of urine sample. Indicators which show that the drug was recently used (based on heteroanamnesis or the presence of drugs or paraphernalia) were separated from indicators of a history of addiction or drug use from the following sources (based on heteroanamnesis or medical records). An interview with family members, bystanders, and/or physicians such as the family doctor was defined as heteroanamnesis. All drug indications were categorized as recent usage (Ceelen *et al*., 2010).

Urine collection and drugs screen on-site:

Supra-pubic puncture (n 1457), catheterisation (n 1446), and other general methods/method unknown (n 1410) methods were used to obtain urine samples from the 113 decedents selected for this study. One out of every 113 multidrug tests was found invalid. Thirty instances (27%) of urine samples were found positive for one of the tested compounds, whereas 26 cases (23%) had positive urine samples for two or three compounds, and three cases (3%) were positive for four or more compounds. Benzodiazepines (n 1437), cannabis (n 1418), morphine (n 1416), cocaine (n 1413), and methadone (n 1412) are the most commonly discovered drugs found in urine samples. Although the statistical comparison was difficult in few cases, but the decedents who tested positive for cocaine or cannabis in their urine were considerably younger at the time of death.

Some Case Studies on Postmortem Toxicology:

Toxicology research has shown that the effects of toxins vary from organ to organ, even when multiple organs are affected at the same time. Further the effect may be more severe in one individual than other and may results into serious health condition and possibly death of the person. Many mechanisms of toxicological action of different poisons have been reported and some are still unknown. For example, cyanur salts, which cause rapid mortality by inactivating the yeast cytochrome oxidase in all of the body's cells

(Flanagan, 2017). Followings are some important case studies on postmortem toxicology:

1. A case study by Leikin and Watson (2003): This study indicates that the postmortem toxicology is a work to analyze the information collected through the evidences of a criminal nature such as a breach of procedure or investigation of a homicide by a random or pre-working examination to detect whether the drug has been used. For more accurate results, forensic toxicologists may interact with other professionals working in this field such as pathologists, medical examiners, or law enforcement organizations. Expertise in forensic toxicology needs experience in pharmaceuticals, chemical, phytochemical and bioanalytical techniques. Ability and productivity of a postmortem toxicologist is enhanced by familiarity with crime scene investigation. Processing, sample collection, knowledge of criminal law and procedures and expertise in fingerprint examination is also an advantage. Test sensitivity errors or sample handling, postmortem procedures, and postmortem drug redistribution may also affect the results of the investigation. Also if the investigation is delayed it becomes almost impossible to obtain the blood and urine samples and stomach contents from a victim's body, but it is possible to work on larvae developed on the dead body at the crime scene, in order to verify the presence of any drug in the body at the time of death (Leikin and Watson, 2003). The limited sample size, number of tests and its duplication is also considered as a critical and stressful factor for the forensic toxicologist investigating the crime. The fingerprint may also help in establishing the presence of someone (suspect) at the crime scene. To perform all the necessary investigations, only a little amount of victim's blood and drug is required to reach any conclusion (Leikin and Watson, 2003).

2. A case study by Ahmed et al (2015): This study revealed that except for single substance categories like fentanyl and its analogues, there are no specific updated recommendations on forensic toxicological investigations for drug related deaths (DRDs). However, international accreditation criteria have been applied to the general forensic toxicological recommendations. While they are applicable to postmortems, which follow the same fundamental quality assurance guidelines, some aspects of drug poisoning are not covered, such as the collection of samples other than urine and blood. The statements on minimal standards in the recommendations are likewise often limited. It's also worth noting that screening for novel psychoactive substances (NPS) in postmortem tissues requires a cutting-edge technical equipment, therefore it's usually limited to specialized laboratories. Current international recommendations include non-targeted comprehensive/'general unknown' screening (GUS) approaches, however, they are not considered as a minimum requirement in postmortem investigations. Targeted screening with second-step confirmation is still a viable option. The guidelines revealed some disparities in techniques of toxicological examinations. This has a great impact on the comparability of the available data and should be taken into account when analyzing and presenting data on DRDs.

3. A case study by Milroy and Forrest (2000): This study showed that the advanced technical equipment allows laboratories to detect a wider range of chemical groupings such as cocaine, opiates, amphetamine, 3,4-methylenedioxy-N-ethylamphetamine (MDEA), 3,4-methylenedi-oxymethamphetamine (MDMA), methamphet-amine and 3,4-methylenedioxyamphetamine (MDA), which are the substances of abuse that may be detected in all the forensic laboratories. Only approx 75% of laboratories can perform the tests for buprenorphine, fentanyl, and the antiepileptic drugs. Synthetic cathinones (82%) and phenethylamines (71%) were the most often tested drugs among the NPS, followed by piperazines and synthetic cannabinoids. According to the forensic toxicology testing, the proper interpretation of findings requires the exchange of case-related information among institutions, laboratories, hospitals, police and forensic pathologists (Milroy and Forrest, 2000).

4. A case study by Kennedy (2015): The study revealed that the quantity and identification of poisons and drugs found in postmortem specimens are correlated with the circumstantial evidences surrounding a person's death and help in postmortem toxicology to reach any conclusion. Due to the decomposition of human tissues and remains, microbial activity may impair the evaluation of quality and volume of biological specimens and it can also modify the drug, toxins, and metabolite concentrations in the dead body (Kennedy, 2015).

5. A case study of Junior *et al.* (2021): In this study it was observed that the toxicological analysis results are utilized in the process of death investigations to determine whether any foreign chemical substance was the reason of death. But the possibility of postmortem alterations of drugs must also be noticed. Autolysis and putrefaction can cause the formation of new entities as well as the deterioration of medications, especially in putrefied corpses. In addition to that, autolysis and putrefaction can adversely harm human fluids and tissues. Specimens for the study should be selected depending on the case history of the individual and its available records. Analytical processes should be quality assured for toxicological studies. Identification and isolation of a drug is also a difficult task. The insufficient information presented in a particular case typically limits the interpretation of analytical results (Junior *et al*., 2021)

6. A case study by Ferner (2008): The study revealed that there are three important samples viz. urine, blood and hair that are used by specialists to detect the reason of poisoning in the postmortem toxicology. Urine samples are usually taken from the bladder after death. It is unlikely that the viruses such as hepatitis B or HIV might be transmitted from blood samples to the urine. The drugs can be found concentrated in the urine for a longer time than the blood, and it is possible to collect a set of urine samples in a non-surgical manner that does not require a specialist. The evidence of medication in the urine indicates that it has been previously exposed and employed for qualitative examination. A blood sample of 10 ml is sufficient for the confirmation of a toxicant in the blood. The blood sample gives the toxicologist an insight into the subject, for example the testing of blood alcohol content in drunk driving instances. The third sample commonly used is the hair sample, which indicates the moderate to long-term or high-dose substance consumption. Chemicals in the bloodstream can be transported and preserved in the follicles of growing hair, providing a general timeline of drug misuse occurrences. Cross-sections from different portions of the follicles can also give an idea to estimates the time of ingestion of the chemical because head hair grows at a pace of roughly 1 to 1.5 cm per month. Hair drug testing is not a general practice. Hairs may accumulate more drug if they are darker and coarser. If two different persons ingest the same amount of drugs, the person with coarser and darker hair will have more drugs in their hair during the test than the one with lighter hair. This could raise concerns about racial bias in hair sample subject tests (Ferner, 2008).

Conclusion

The postmortem toxicology is one of the important disciplines related to analytical chemistry, clinical chemistry and pharmacology. In postmortem toxicological technologies evidences of criminal nature are analyzed to reach any conclusion whether there is a breach of procedure or investigation of a homicide. It can also be concluded that there are large number of laboratory methods to detect toxins in the body of a dead person to find out the possible causes of death using blood, urine or hair samples or tissues from liver and other organs. Blood is always a preferred specimen to detect, measure and interpret the relation of drug and other toxicant concentrations with the death of a person. A wide range of chemical groups which may affect the dead body such as opiates, amphetamine, cocaine and 3, 4- methylenedioxy-N-ethylamphetamine (MDEA) can be detected through advanced

technical equipment.

Some other professionals such as pathologists, medical examiners and law enforcement agencies should also collaborate with the forensic toxicologists for more authentic and accurate results.

In absence of any clues at the scene of death the postmortem toxicology helps in reaching any conclusion. The forensic physician can take urine samples to do an on-site multidrug test to verify the consumption of any drugs. We strongly recommend for more researches in postmortem toxicology in order to gather information on the investigations carried out on deaths caused by some toxins or poisons.

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