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CASE REPORT

Cathine and alcohol involved fatality: A rare case report with a brief review of the literature

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Abstract Toxicology screening of unusual poisons is important. We report a case of death of a young female suspected to die due to drug overdose. Medico legal autopsy was indicative of cerebral hemorrhage. The deceased had no previous history of drug dependence. Toxicological analysis revealed the presence of cathine {(+)-norpseudoephedrine} and alcohol in the blood. The concentration of ethyl alcohol in blood was determined as 85.57 mg per dL.

An overview of toxicology of cathine and its side effects are presented. The reports due to fatal intoxication of cathine in combination with alcohol are rarely reported. The present case substantiates that an intake of low potent drug like cathine in combination with alcohol can cause fatal intoxication.

1. Introduction

Cathine {(+)-norpseudoephedrine, IUPAC Name: (1S,2S)-2-Amino-1-phenylpropan-1-ol} is a naturally occurring phenylalkylamine alkaloid obtained from the fresh or dried leaves of Khat (Catha edulis) of Celastraceae family. Khat plant is an evergreen shrub cultivated in East Africa and the Arabian Peninsula and used for recreational use. Khat contains a number of pharmacologically active components. In addition to Cathine it also contains another major phenylalkylamine alkaloid cathinone {S(−)-alpha-aminopropiophenone)}. Cathine and cathinone are central nervous system (CNS) stimulants.[1] These alkaloids are structurally closer to synthetic stimulants such as amphetamine.[2] Khat has been described as a natural amphetamine because its effects are similar to those produced by other known psychostimulants such as amphetamine and its congeners.[3] Khat chewing sessions are rampant in regions of north east Africa and the Arabian Peninsula, however its usage is now spreading in other areas of the world too.[4]

Adverse drug reactions due to the use of drug of abuse with ethanol are common and many cases of fatal poisoning are reported. Alcohol and drug combination is responsible for many deaths of both accidental and suicidal intents. Alcohol causes serious interactions with drugs like barbiturates, propoxyphene etc. It is commonly encountered with drugs like benzodiazepines during toxicological screening.[5] It is also most commonly encountered in combination with other drugs like sedatives and drug of abuse in drug facilitated sexual assault (DFSA) cases.

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This paper reports a case of a young female whose death was suspected to be drug overdose. Toxicological analysis revealed the presence of cathine and alcohol. The literature review suggests that few cases of fatal intoxication of khat alkaloids in combination of other drugs and alcohol are reported. The present case study is the first to report the fatality due to combination of cathine and alcohol.

2. Case report

An incident was reported from a metropolitan city of India during winter of 2014 in which a young female was reported missing. She was reported to be in her early twenties who was average built. During investigation her corpse was recovered from a forest area nearly 36 h after the victim was last seen alive by the family. No physical clues were found near the body and on the clothes of the victim. It was suspected that sexual assault was committed after the victim had booze and insufflated di-acetyl morphine for the recreational purpose. No previous history of the victim toward any kind of drug dependence or chronic illness was available. The victim's body was subjected to medico legal autopsy, next day after recovery of the dead body. The time of death was approximated to 36–48 h before autopsy. The external examination during autopsy revealed no external injury, needle marks or any kind of marks was observed except reddish blood tinged fine froth which was present over both nostrils. In the postmortem findings no signs of putrefaction were observed. The main autopsy findings were congestion in lungs, liver, spleen, gallbladder and brain. Stomach wall was also congested with hemorrhagic patches. Subdural hemorrhage was present over the right and left occipital and right high parietal lobes, diffuse subarachnoid hemorrhage was present over the occipital and parietal lobes of brain. During the autopsy, samples of blood and stomach along with its contents were collected for the toxicological analysis. In addition, to the above samples portions of liver, spleen, kidneys and small intestine were also preserved to rule out any poisoning and confirm the distribution of poison to different body organs, if required. Samples were also collected for histopathological examination and to confirm sexual assault. Toxicological analysis was carried out in our laboratory.

3. Methods and materials

Systematic toxicological analysis was carried out for analysis of general unknown poisoning on the post-mortem samples of the deceased for the detection of different poisons like pesticides, gaseous, metallic poisons, drugs and volatile poisons including alcohol. Samples of stomach and its contents, small intestine, liver, spleen, kidney and blood were analyzed separately for different groups of poisons.

The tissue samples were cut into small pieces and divided into two portions. The first portion of tissue samples were taken up for analysis of pesticides. The samples are soaked in sufficient quantity of n-hexane and kept for the period of 8 h. The samples are filtered through anhydrous sodium sulfate. The organic layer was collected and evaporated to dryness. The dried filtrate was reconstituted in acetone and initial screening for different group of pesticides was carried out with Thin Layer Chromatography (TLC).

Analysis of drugs of abuse and other drugs was performed in visceral samples as well as blood sample. The second portion of tissue samples are acidified with acetic acid following addition of solid ammonium sulfate to make it saturated solution. The sample was heated on water bath at the temperature of 60 °C till protein of tissue sample coagulates. After the completion of coagulation it was allowed to cool at room temperature and was filtered and aqueous layer was collected. The collected aqueous layer was subjected to extraction. To the postmortem blood sample saturated solution of sodium tungstate and 1 N sulfuric acid (2 mL each) was added and sample was heated on water bath at the temperature of 60 °C till deproteination of blood occurs. The sample was filtered to collect the aqueous layer. Two step liquid–liquid extractions were carried out with both the aqueous filtrates. The filtrate was extracted with diethyl ether (3 times) for extraction of acidic drugs. The organic phase was collected and evaporated to dryness. The samples were further reconstituted in methanol for analysis. The aqueous layer collected after this step was treated for extraction of basic drugs. Aqueous portion was made basic (pH 8–9) by addition of ammonia solution. This alkaline aqueous layer was extracted with chloroform (3 times). The organic phases were combined and evaporated to dryness. The samples were further reconstituted in methanol for analysis.

Initial screenings were carried out with TLC. Further investigation for the presence of poisons was carried out with Gas Chromatography–Mass Spectroscopy (GC–MS). A GC–MS System equipped with a Finnigan Trace GC Ultra interfaced with a Thermo DSQ Quadrupole MS with Thermo auto sampler AS 3000 was used for analysis. The column used was BP-5 (30 m × 0.33 mm i.d × 0.5 μ film thickness). Helium was used as carrier gas at a flow rate of 1 mL/min. The temperatures of injection port and MS transfer line were 250 and 310 °C respectively. Initial oven temperature was 120 °C with hold for 2 min with final temperature increased to 300 °C with final hold time of 5 min. The oven temperature was ramped at the rate of 15 °C per min. Sample injection volume was 1 μL. The mass spectrometer was operated in electron impact ionization (EI) positive mode. Full-scan spectra in the mass range of 50–550 amu were recorded. Data acquisition and processing was done on Xcalibur 1.4 software using mass spectral libraries for screening the results to confirm the presence of any kind of drugs and pesticides.

For estimation of blood alcohol concentration (BAC) Kozelka & Hine method[6] was followed. In brief 1 mL blood sample was added with 5 mL each of solution of sodium tungstate (10%) and sulfuric acid (1 N). Steam from steam generator was passed through the sample and the distillate was allowed to pass through the mixture of saturated solutions of sodium hydroxide and mercuric chloride. Finally the distillate was collected in solution containing 0.1 N potassium dichromate and concentrated sulfuric acid (5 mL each). Resulting distillate was titrated against 0.1 N sodium thio sulfate using starch as an indicator. BAC results were confirmed chromatographically.

4. Results

Toxicological analysis of stomach and its contents, liver, spleen, pieces of kidney and small intestine were tested negative for any kind of poisons. The TLC screening of basic drug extract of blood was positive for the presence of drug. Further

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