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Carbamate Poisoning with Benzodiazepines Overdose and Alcohol Dependence Syndrome - A Clinical Case Report

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Abstract

Globally, self-poisoning with various substances like pesticides, and chemical substances with suicidal intention is a major cause of death and disability. It appears that the variety of drugs that induce poisoning is influenced by several obscure factors, including ease of access to poisons, sociodemographic characteristics, and geographic location. The most often used toxins in India reportedly include chemicals, pharmaceutical substances, and pesticides. Poisoning management by the healthcare team is made more difficult by various aspects like the difficulty in identifying the allegedly consumed poison, co-ingestion of alcohol, and overdosing of other medications, the variety of clinical symptoms, and the requirement for prompt access to precise information for treatment. Furthermore, due to a lack of reliable diagnostic tools and criteria, conditions like poison-induced seizures, respiratory paralysis, and neuropsychiatric disorders are frequently misdiagnosed. Inappropriate treatment resulting from a misdiagnosis may raise the risk of morbidity or suicidality. This case report aims to present the conservative measures taken, the consequences seen, and the clinical results of carbamate poisoning in a chronic liver disease-diagnosed adult man. Adhering to the evidence-based guidelines for the ultimate management of poisoning may reduce poison-related morbidity and mortality while also improving patient outcomes.

Keywords: *Alcohol Dependence Syndrome, Benzodiazepines, Carbamate Poisoning, Neuropsychiatric Disorder.*

Introduction

In many of the low-income countries, poisoning with various chemicals, insecticides, and medications to kill oneself is not unusual. In Asian countries like India, Sri Lanka, Nepal, and China, it is one of the most important public health concerns. Pesticides, such as those containing organophosphates, carbamates, chlorinated hydrocarbons, pyrethroids, and aluminium or zinc phosphide, are the most frequent cause of poisoning in developing countries. The financial implications of agriculture, poverty, lethal practices, illiteracy, ignorance, and ready access to highly hazardous pesticides are the causes of this surge. In addition, most of the poisoning victims belong to lower socioeconomic backgrounds [1, 2]. An estimated 3,55,000 persons worldwide die away from accidental poisonings each year. According to WHO estimates, there are up to 2,20,000 pesticide-related fatalities annually, mostly in developing nations, and 30,00,000 cases of pesticide poisoning [3]. India has one of the highest rates of self-poisoning worldwide. The National Poisons Information Centre, New Delhi estimates that over 50,000 individuals die annually as a result of toxic chemical exposure, with agricultural pesticides

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alone accounting for 12.8% of these deaths. The majority of poisonings with the intention of self-harm are carbamate poisonings. An estimated 200,000 individuals die annually from OP self-poisoning, mostly in the Asia Pacific region, with a fatality rate of 10–20 per cent [4].

Due to the high lipid solubility, Organo-Phosphate and carbamate (OPC) chemicals can easily pass through the gastric and skin mucosa, quickly distributing throughout tissues and passing across the blood-brain barrier to affect the central nervous system. The phosphorylation of acetylcholinesterase inhibits its action, making it inactive in the case of OPC poisoning. This leads to a buildup of acetylcholine at the synapse, which results in the cholinergic toxidrome. Due to increased muscarinic and nicotinic stimulation, the most common symptoms of pesticide poisoning are SLUDGE (salivation, lacrimation, urination, defecation, gastric cramps, and emesis), other symptoms include miosis, bronchospasm, increased secretions, arrhythmia, fasciculation, and respiratory failure. Acetylcholinesterase and pseudocholinesterase levels are usually examined to confirm these poisonings [5].

Suicidal behaviour is often linked to alcohol usage and alcohol use disorders (AUD, including dependency). Self-poisoning with pesticides sometimes involves the ingestion of ethanol, which is a significant risk factor for pesticide poisoning. In 2016, 12.2% and 3.8% of deaths among 15–49-year-old men and women, respectively, were alcohol-related, and it is also a factor for one in five deaths worldwide due to self-harm. The increase in alcohol use in areas where the burden of pesticide suicide and self-harm is high indicates the need for further attention. Co-absorption of alcohol increases the difficulty of management because it is linked with the ingestion of larger amounts of pesticide, which increases the effects and results in more adverse outcomes. Also, individuals who consumed alcohol concurrently had a higher risk of intubation and were more likely to die from self-poisoning. Higher suicidality, underlying medical issues, or higher pesticide consumption may all be associated with an increased chance of mortality [6, 7, 8].

OP poisoning is classified as acute (occurs within minutes to 24 hours), delayed (occurs between 24 hours and 2 weeks), and late (occurs after 2 weeks) depending on the onset of signs and symptoms. In cases of pesticide intoxication, two outcomes can be observed which are Intermediate syndrome (IMS) and neuropsychiatric problems. The intermediate syndrome is the delayed onset of nicotinic symptoms. The development of Intermediate Syndrome (IMS) often occurs 2-4 days following oral pesticide ingestion. It is a highly common consequence of OP poisoning and includes paralysis of the respiratory muscles and peripheral limbs. It happens in about 20% of cases of OP poisoning. A patient bears a significant risk of mortality if they experience respiratory failure. For seven to fifteen days, mechanical ventilation is the only treatment used for IMS [9, 10, 11].

In addition, agricultural pesticide exposure over an extended period at low levels is also positively correlated with the development of chronic neurotoxic and cognitive effects. Long-term exposure to OP pesticides (with or without acute cholinergic episodes) can lead to the emergence of a variety of neuropsychiatric symptoms like anxiety, mood swings, emotional lability, depression, fatigue, irritability, drowsiness, confusion, and lethargy were the hallmarks of chronic OP-induced neuropsychiatric disorder (COPIND) [12]. Given these repercussions, proper evaluation and diagnosis must be done as soon as possible after pesticide exposure. This will help develop the best management plans for these cases within the constraints of available resources. Maintaining close observation of these conditions lowers associated morbidity and mortality as well as treatment costs. Carbamate and organophosphate poisoning are

mostly treated with supportive measures. The severity of the condition can be minimized by early, aggressive gastrointestinal decontamination, appropriate atropine and oxime therapy, and timely ventilator support [13].

Case Description

A 48-year-old male agricultural worker was brought to the emergency department in an unresponsive state with symptoms of frothing at the mouth, profuse sweating, hypersalivation, pinpoint pupils and miosis present with an alleged history of consumption of Furadan, a carbamate insecticide along with tablet diazepam 0.5 mg around 15 tablets (7.5 mg), tablet Nexito plus 0.5 mg around 15 tablets (7.5 mg) and consumption of alprazolam 0.5 mg around 45 tablets (22.5 mg) with suicidal intention. The quantity of Furadan consumed was unknown. History from the patient attender reveals the patient developed these symptoms within 30 minutes after consuming Furudan and other drugs. He was a chronic alcohol abuser and has consumed about 200 ml - 500 ml of liquor daily for the past 15 years with the last binge on the day of admission (quantity unknown). Patient history did portray patterns of alcohol dependency. He was diagnosed with Chronic Liver Disease (CLD) with alcohol withdrawal syndrome 2 weeks prior in another hospital, and prescribed tablet Udliliv, tablet Nexito Plus, and tablet Diazepam, however the patient was not on regular medication. On arrival at the emergency department, initial investigations revealed that the Glasgow Coma Scale (GCS) interpretation was severe (3/15) with tachycardia (135 per min), SPO_2 level of 89%, Respiratory Rate at 13 per min, high blood pressure of 180/110 mmHg. The patient was immediately intubated, and emergency care was given in the emergency department. The patient underwent gastric lavage and was admitted to the intensive care unit. He was started with activated charcoal 70g every 6 hours x 24 hours and was on continuous atropine infusion @ 4 ml/hr with tablet Nicardia 10 mg.

Anthropometric data reveals that the patient is obese with a BMI of 30.2 kg/m^2. Laboratory Investigations revealed that certain renal parameters like serum Bicarbonate levels (11 mmol/L), and serum potassium (3.0 mmol/L) were low, and elevated liver function tests, which showed total bilirubin levels of 1.5 mg/dL, aspartate transaminase (AST) of 85 U/L and alanine transaminase (ALT) of 58 U/L. Pseudocholinesterase levels have shown 3, 346 IU/L with positive Benzodiazepines qualitative analysis. The patient was given supportive pharmacotherapy with an injection of Xone 1g twice daily, an injection of Thiamine 200 mg in IV twice daily, a tablet of Pan 40 mg twice daily, a tablet of Ativan, and haloperidol 5 mg injection. As part of the patient's treatment, he was advised to the psychiatric department, however, the patient denied psychotherapy. Patient improvement was noticed following the prescribed treatment and atropine infusion was discontinued after 30 hours. On the third day of admission, the patient reported severe signs of tremors, mental confusion, irritability, drowsiness, anxiety, restlessness, nonsensical talking, and nightmares. Despite the presence of abnormal psychological symptoms, the patient denied psychotherapy and requested immediate hospital discharge. Supportive treatment was given, and the patient was discharged with the same medication and advised to return after 7 days for follow-up. However, the patient did not appear for the follow-up care.

Results

Patient follow-up care is vital in treating any medical complication, however, in this case, the patient lost to follow-up care and couldn't be tracked. Furthermore, despite the presence of neuropsychiatric symptoms, the patient was not willing to take psychotherapy. Even after multiple trials of insisting on the

importance of psychotherapy to the patient and the patient's family, the denial of psychotherapy was a major drawback. However, psychotherapy if given in this case, patient positive outcome would have been seen.

Discussion

Throughout the world, self-poisoning is thought to be one of the main causes of death in rural and agricultural communities. According to WHO 99% of fatal poisonings out of annual 251,881 occur in developing nations, especially among agricultural workers which is supported by the present study [14]. In the majority of investigations conducted in rural Asia, including the present study, carbamate insecticidal toxins are the most often identified cause of toxicity in poisoning cases. Carbofuran with the trade name Furadan is a highly toxic carbamate pesticide to both animals and humans, is an endocrine disrupter known to be fatal at even a small quantity of 1ml and has killed many human lives globally [15]. Previous research evidence has revealed that a male-to-female ratio of 2.2:1 supports male preponderance in poisoning, which is corroborated by the current study [5]. In the present study, the patient was obese and there was the presence of neuropsychiatric symptoms which is supported by the results of Lee et al., study which highlights the negative effects of organophosphate or any other carbamate toxins effect in obese people. The concentration of these toxins in the vascular compartment will be for a longer duration with a longer toxic effect in obese patients. Further, the need for both mechanical ventilation and the ICU stay was longer in obese patients than in nonobese patients [16].

A toxicology review by Eddleston et al., revealed that acute alcohol intoxication can lead to issues from alcohol cardiomyopathy and alcohol withdrawal, which can worsen tachycardia complications in organophosphate (OP) poisoning and impacts patient care which was evident with the presence of tachycardia in the present study [17]. Agriculture workers exposed to organophosphate chemicals were shown to have experienced neuropsychiatric disorders, including anxiety, depression, and memory and concentration issues. Furthermore, there have been reports of schizophrenia-related symptoms like psychosis, mood labiality, delirium, violence, and recurring suicidal thoughts. These reports corresponded with the findings of our investigation since the patient had abnormal psychological symptoms. These symptoms are frequently observed during the recovery process from cholinergic syndrome, while the processes behind their development are yet known [18, 19]. In addition, it was observed that there was a positive association between the length of hospital stays and the severity of poisoning. The potential of liver enzyme analysis as a severity predictor is demonstrated by the link found between transaminases and patient outcome. Depending on how severe the poisoning is, liver measures like AST and ALT levels are markedly elevated which is positively evident in the present study [20].

Furthermore, cholinergic symptoms like miosis, excessive sweating, poor air entry into the lungs due to bronchorrhea and bronchospasm, and bradycardia suggest potential consumption of carbamate and indicate the requirement of atropine for treatment. Atropine (ATR) remains the cornerstone for treating organophosphate toxicity due to its anticholinergic properties. It inhibits additional stimulation by aggressively blocking muscarinic acetylcholine receptors. Guidelines suggest that, for an unconscious patient, atropine 1.8–3 mg rapidly as intravenous therapy into a fast-flowing IV drip should be given regardless of the availability of oxygen therapy. Atropine dosages are typically different for each patient. The patient in this case study had a better prognosis after receiving a continuous IV infusion of 4 ml of atropine per hour. The course of treatment is

continued until the indicative end-points of atropinization such as dry axillae, Systolic blood pressure >80 mmHg, a clean chest on auscultations, Heart rate >80 beats/min, and pupil dilation are met. Based on the patient's state, antidotes such as glycopyrrolate (GPR) and oximes were taken into consideration in addition to atropine [5, 21].

According to research conducted by Davies et al, suicidal thoughts in people with OP poisoning typically start rapidly and end fast. Under these kinds of circumstances, hospitalization and strict observation are essential. In OP or carbamate poisoning, patients with chronic or degenerative neurological diseases, psychotherapy and cognitive therapy are the most suitable options because they primarily focus on problem resolution and accepting one's limitations. In contrast, the patient from the current study did not opt for psychological support which was a major drawback for a positive patient outcome [22].

Conclusion

Poisoning management is a difficult task for medical professionals around the world. The management of poisoning is complicated by factors such as uncertainty in identifying the poison that has allegedly been taken, varied clinical features, and the requirement for prompt access to precise information for treatment. However, careful resuscitation with an appropriate choice of antidotes, followed by good patient care and observation, should minimize the consequences faced post-hospital admission. Conservative actions taken on time can surely help avoid complications and mortality risks.

Conflict of Interest

Nil.

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