Diphenhydramine Overdose Related Delirium: A Case Report

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Diphenhydramine (DPHM) overdose is one of the most common causes of acute poisoning encountered in the emergency department. DPHM possesses both anticholinergic and sedative effects. Many authors have reported that topical and oral doses have led to hallucinatory psychosis, delirium, wide-complex tachycardia, hyperthermia, seizures and rhabdomyalysis, and the well-known anticholinergic syndrome has been well documented.

We report on a young female patient who presented with delirium after ingesting 24 pills (one pill contains 50 mg) of DPHM to attempt suicide. Although the patient was treated with early gastric emptying followed by activated charcoal and general supportive care, she developed mental confusion, disorientation and short-term memory loss three hours after ingestion of DPHM. These symptoms subsided about seven hours after ingestion without neuropsychiatric sequelae.

Key words: antihistamine, diphenhydramine (DPHM), delirium, overdose

Introduction

Diphenhydramine (DPHM) is one of many antihistamine agents and is a common component in many over-the-counter medications for allergies, the common cold and as a sleeping aid. The USA’s Food and Drug Administration (FDA) approved DPHM for use as a nonprescription antihistamine and hypnotic in doses up to 50 mg(1). Some authors have reported life-threatening problems with DPHM overdose(2-11). Tejera reported a case of delirium in an elderly patient that was associated with a high blood level of the anticholinergic drug(10). Sexton described a case of DPHM-induced psychosis after therapeutic doses(11). We report on a young woman who had delirium after ingesting 24 pills (one pill contains 50 mg) of DPHM to attempt suicide. We also discuss DPHM, its adverse effects and overdose management.

Case Report

A previously healthy young woman was sent to our emergency department (ED) after ingesting 24 tablets of DPHM to attempt suicide. Details of the patient’s drug ingestion history were obtained from her mother, who brought in four empty cards of DPHM that were found at the patient’s bedside. Ingestion of the drug was confirmed by the patient herself. She denied any history of psychiatric disorders, any underlying medical problems or previous trauma. The patient had taken 24 tablets of DPHM after an argument with her family, without coingestion of other drugs or alcohol.

On presentation, her vital signs and physical examination were unremarkable except for slight anxiety, mild fever, tachycardia and mildly dilated, reactive pupils bilaterally. Complete blood count, electrolyte levels, liver function test and renal
function test were within reference ranges. Pulse oximetry showed oxygen saturation of 98% at room air status. The patient received early gastric emptying followed by activated charcoal and general supportive care. During observation in the ED, she appeared anxious, mentally confused, disoriented in place and time and had short-term memory loss three hours after ingestion of the DPHM. She had forgotten about events that had occurred a few hours earlier. The patient’s mother told her that she had been wandering around other patients’ beds and talking to other patients using inappropriate language. The patient was awake but presented with mental confusion, disorientation and reduced clarity of awareness of her environment. These symptoms gradually improved about seven hours after ingestion of the DPHM. We collected the patient’s urine for toxin screening and it tested positive for DPHM. We gave a detailed explanation to the patient of the adverse effects of taking the drug and suggested close observation whilst she remained in the ED.

After consulting with a psychiatrist, it was suggested that the patient remain under close observation and be admitted for further psychiatric evaluation. However, the patient was discharged 12 hours after arrival at our ED, against our advice. She was followed up 12 days later and reported no further psychiatric or amnestic symptoms.

Discussion

Antihistamines of the ethanolamine class, such as DPHM, are potent histamine antagonists noted for sedative and anticholinergic properties. Many people use DPHM as a sleeping aid, and it is also taken when attempting suicide\(^1\). It is a first-generation H\(_1\)-antagonist and still one of the most frequently used antihistamines for allergies, the common cold and as a sleeping aid. Overdose may cause dilated pupils, CNS stimulation, tremor, hallucination, seizures and hyperpyrexia\(^{1-10,15}\). Topical and oral doses have led to hallucinatory psychosis, delirium, wide-complex tachycardia, hyperthermia, seizures and rhabdomyolysis, and the well-known anticholinergic syndrome has been well documented\(^{4-10}\). Early gastric emptying followed by activated charcoal may have contributed to our patient’s survival\(^1\).

Clinical features of DPHM overdose depend on the patient’s age. Children and young adults quite commonly present with fixed, dilated pupils and CNS stimulation including excitement, tremors, hyperactivity, hallucinations, hyperpyrexia and tonic clonic seizures. Adults usually present with CNS depression leading to coma, and only rarely suffer from seizures\(^2\). Some authors have reported death from massive overdoses of DPHM\(^{1,2,15}\). Although our patient received early gastric emptying followed by activated charcoal, she developed mental confusion, disorientation and memory loss three hours after ingestion of DPHM. Rapid absorption and tissue distribution may be responsible for such early presentation of symptoms following a DPHM overdose\(^1\). Besides its well-known anticholinergic activity, an increase in dopaminergic brain activity is proposed as the causal mechanism for hallucinations\(^{12}\). Another factor contributing to delirium in our case may be the anticholinergic effects of DPHM and its ability to cross the blood-brain barrier, making the clinical effects of a DPHM overdose different from nonsedating, second-generation H\(_1\)-receptor antagonists\(^{12}\).

We observed that our patient recovered about seven hours after ingestion of the drug. At that time, she was able to follow simple commands and communicate well. For several decades, DPHM has been known to cause various medical and psychiatric adverse effects\(^{11}\). Both drowsiness and impairment of some types of mental performance have developed after a single 50 mg oral
Delirium and diphenhydramine overdose

The adverse effects depend on the dose; more than 1.0 gm oral dose results in severe symptoms in patients without risk factors\(^{(13)}\). Therefore, the patient who develops severe symptoms should be hospitalized. A 27-year-old female patient developed anticholinergic syndrome after DPHM poisoning and recovered after administration of 2 mg physostigmine within 12 hours\(^{(4)}\).

In agreement with previous authors, our case presented with mental confusion, disorientation and memory loss after ingestion of 24 tablets of DPHM (total dose over 1.0 gm) and so required hospitalization. DPHM-induced delirium or psychosis may occur after a therapeutic dose or overdose, especially in elderly patients\(^{(6,10,11,14)}\).

We suggest that emergency physicians keep in mind the differential diagnosis of acute delirium or psychosis, especially for elderly patients taking over-the-counter medications at the time of presentation. Management of DPHM overdose comprises of early gastric emptying followed by activated charcoal and general supportive care.

References

抗組織胺過量引起譁妄：病例報告

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服用過量抗組織胺藥物(diphenhydramine)，而中毒個案是在急診常見的急性中毒之一。它有抗乙醯膽鹼(anticholinergic)及鎮靜安眠的作用。根據以往的文獻報告指出服用抗組織胺藥物包含局部的抗組織胺藥物引起妄想，錯覺，譁妄，寬波心搏過速，高體溫，抽搐，橫紋肌溶血症，抗乙醯膽鹼症候群等症狀。我們遇有一位年輕女性病患服用二十四顆抗組織胺藥物(diphenhydramine)過量自殺，而引起譁妄的病例。雖然病患曾接受早期治療包括臨床觀察及支持性療法，如洗胃，活性碳灌注及靜脈輸液等，但病患服用藥物後三小時出現混亂，迷失方向及短暫性記憶力喪失。這些症狀服用藥物後大約七小時時消失，且並無神經後遺症。

關鍵詞：抗組織胺，苯海拉明(diphenhydramine, DPHM)，譁妄，過量