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CASE REPORT

Promethazine Poisoning in a 14 Months Old Girl: A Rare Case Report

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ABSTRACT

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Promethazine or 'Phenergan' is a phenothiazine derivative and a commonly prescribed first-generation antihistamine for various conditions. However, it is also one of the commonly misused drugs especially owing to its sedating properties. Reports of serious adverse effects caused by promethazine use have been described and it is currently not recommended for children under 2 years of age. Promethazine poisoning is difficult to diagnose and the clinicians are highly dependent on parents or caretakers' history for diagnosis. We report a 14 months old child who presented with repeated episodes of apnea and fits. She was initially diagnosed and prescribed accordingly as a case of idiopathic epilepsy as investigations were inconclusive. However, it was later discovered that she had repeatedly been given promethazine syrup for sedation by a household maid. Separation from the maid eventually led to improvement in symptoms. Currently, she is on follow-up with no neurological or developmental sequelae.

Key Words: *Promethazine, Phenergan, Poisoning, Anti-histamine*

INTRODUCTION

Promethazine, commonly branded as 'Phenergan', is a very commonly prescribed first-generation antihistamine worldwide. It is a phenothiazine derivative which has potent H1-receptor antagonistic properties. However, its actions on muscarinic, dopamine, serotonin and N-methyl-D-aspartate (NMDA) and alpha-adrenergic receptors are also well-documented.¹ It is widely used in the management of allergic reactions, motion sickness and as a sedating adjunct during various procedures.² However, despite its therapeutic significance, adverse effects of the drug like hallucinations and delirium have been reported as early as 1967.³ Moreover, in a study in 1982, phenothiazines were associated to be a cause of sudden infant death syndrome in 23 % of studied infants.⁴ Since then, various cases of intentional as well as accidental poisoning of the drug have been reported.^{5,6}

Common clinical features of promethazine poisoning are increased thirst, visual disturbances, restlessness and anxiety, disturbed sensorium, sinus tachycardia, urinary retention and opisthotonos.⁵ Due to these side effects, a boxed warning has been added to promethazine since 2004 by United States Food and Drug Regulatory Authority (US-FDA) contraindicating its use in children below 2 years of age.⁷ Promethazine has also been included in the Key Potentially Inappropriate Drugs in Pediatrics (KIDs) list by Pediatric Pharmacy Association (PPA) stating that it should be avoided in infants and used otherwise with caution in children.⁸ We hereby report a rare case of a 14 months old girl who presented with signs and symptoms of promethazine poisoning initially misdiagnosed as a case of epilepsy for two months.

CASE REPORT

A 14-month-old female child presented in August 2020 in emergency department with sudden onset history of apnea followed by generalized tonic-clonic fits for 20 minutes. She was a developmentally normal child with no significant past history and unremarkable birth events. The parents did not report any preceding trauma, fever, deterioration in consciousness or fits. Both her parents were working doctors and she used to be under the care of a household maid in their absence. The maid was herself 16 years old and had been at their home since the birth of the child, away from her own parents. On examination, the child was drowsy with hypertonia and normally reactive pupils. Her vitals showed BP 90/45, heart rate 94/minute, respiratory rate 34/minute and temperature of 98 °F. Her blood sugar level was 108 mg/dL. In the emergency department, she was managed supportively with intravenous fluids and oxygen inhalation. Her labs were normal with hemoglobin of 10 g/dL, TLC of 6500/ μ L and platelet count of 260,000/ μ L. Her serum calcium, magnesium and electrolyte panel, liver and renal function tests were all normal. A CT-Brain was done which was normal. The child responded to the supportive management and became fully conscious within a period of one hour and was subsequently discharged. There was no focal neurological deficit at discharge or at follow-up after one month. She also had an electroencephalogram which was reported to be normal.

After a period of about 6 weeks after the initial event, the child had another episode of similar presentation. She was managed with supportive treatment and showed improvement as before. She was now advised levetiracetam with a dose of 20 mg/kg/day after an initial loading dose, on the clinical suspicion of idiopathic epilepsy. The child responded after starting anti-epileptics and remained fit-free thereafter. However, after about 4 weeks following these episodes, mother noticed an empty bottle of syrup 'Phenergan' in her home. She had brought this many weeks before the first episode of apnea and had only given it once to the child for mild cough. This raised suspicion and when inquired from the maid, the actual history was revealed. The maid had been giving the syrup to the infant for irritability/sedation. She also

admitted the association of timing of the apneic episodes with the syrup ingestion of 2.5-5 mL (2.5-5 mg) doses and had stopped giving the drug since the last apneic episode as they had only one bottle available at home. The case was again reviewed and anti-epileptics were gradually weaned off. On follow-up after 3 months, the child is developmentally and intellectually normal. The child's parents refused any legal action against the maid. Neither did the maid's parents allow her psychiatric evaluation.

DISCUSSION

To the best of our knowledge, this is the first case report of acute poisoning by promethazine published in Pakistani literature to date. A case report in 2018 by Sarwar et al. described promethazine as a causative factor in intellectual disability in an 8 years old girl. However, it highlighted only the chronic effects associated with promethazine misuse and the intellectual disability of that patient was also confounded by other social factors.⁶ A national survey demonstrated that 70-80% of Pakistani pediatricians prescribed cough syrups containing anti-histamines for acute respiratory tract infections.⁹ Since there is no available database, institute or regulatory body at national level on poisoning in children, it is very difficult to ascertain the true incidence or level of morbidity associated with overuse or misuse of these drugs in the pediatric age group.

One possible reason to explain the low reported prevalence of promethazine poisoning in our society is the corresponding low mortality and morbidity associated with the drug. Recently, in a study conducted by Tsay et al. it was reported that 79.9% of patients had either no or mild side effects and no mortality associated with non-medical use of promethazine.² Another study done in Denmark revealed that 91% of all admissions related to 1st generation anti-histamine poisoning had only 1 day stay in the hospital with very low mortality.¹⁰ Hence, majority of these cases go un-noticed in our setup with a weak reporting system. The authors therefore propose that effective screening programs be designed and healthcare providers be educated about the possible side effects of the drug at basic healthcare levels.

Another important point highlighted by our case is the role of household maids/helpers in such cases. This problem is especially worth mentioning due to increasing proportion of working mothers and dependence on these domestic helpers for childcare in our society. Recently, a household maid was sentenced to prison in Singapore on account of physical abuse to an intellectually challenged child.¹¹ Jafree et al. in their report concerning children with special needs also mentioned incidents of physical abuse to these children by school maids.¹²

Medical child abuse (MCA) is a term coined in literature for children who receive unwarranted and harmful or potentially detrimental medical care, deliberately instigated by a care-provider, inducing illness in the child.¹³ A review study reflected an interesting finding that 2.6% of MCA perpetrators were caretakers other than the parents.¹⁴ Whether or not our case comes under the definition of MCA is arguable, as the intentions of the house-maid were unclear.

Currently there is no testing facility for blood levels of promethazine in most of the institutions around, therefore clinicians have to rely on history and examination findings for such a diagnosis. The diagnosis in our patient was further consolidated by the fact that the child has been asymptomatic since the change of the said care-taker. Promethazine has a half-life of only 6 hours and hence, a high index of suspicion is required at initial presentation for confirmation of diagnosis.¹⁵ As it has been declared as contraindicated in children under 2 years of age by US-FDA, no safe therapeutic or toxic dose of promethazine has been defined in this particular age group. However, oral doses given to children in the range of 0.45 to 6.4 mg/kg have been associated with respiratory depression and other adverse effects in literature.⁷ Although the exact dose given to our index patient on both occasions is not clear, the amounts given to the child as narrated by the care-taker maid are lower than 1 mg/kg and hence, the possibility of an idiosyncratic reaction to the drug cannot be ruled out. Treatment in cases of acute poisoning is generally supportive depending upon the level of consciousness and delirium. Oral activated charcoal given within two hours of ingestion has benefit and should be given in conscious patients. If the patient has moderate

anti-cholinergic symptoms, repeated doses of benzodiazepines are recommended as needed. However, patients with severe irritation, hallucinations and/or opisthotonos need to be given physostigmine slow infusion at dose of 0.02-0.04 mg/kg under strict cardiac monitoring.⁵

The authors hypothesize that anti-histamine poisoning, accidental or intentional, is highly under-reported in Pakistan and studies need to be conducted at national level to estimate the exact prevalence and burden of disease caused by it. Moreover, diagnostic facilities need to be established at least at tertiary healthcare level to confirm and manage these cases.

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