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Pyridostigmine Suicidal Attempt in a Myasthenia Gravis Patient

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 47
Final Diagnosis: Pyridostigmine overdose
Symptoms: Bronchorrhea • sweating • vomiting
Medication: Pyridostigmine
Clinical Procedure: —
Specialty: Toxicology

Objective: Adverse events of drug therapy
Background: Pyridostigmine is a quaternary amine parasympathomimetic which inhibits acetylcholinesterase for the treatment of various conditions such as myasthenia gravis. Previously, no cases of pyridostigmine toxicity in human beings have been reported except the cases reported among the troops of Persian Gulf War.
Case Report: A 47-year-old female intentionally ingested a high dose of pyridostigmine (Mestinon) and developed its toxic symptoms within 1 hour of ingestion. She was treated with injections of atropine and pralidoxime. The patient made an excellent recovery and responded to the classical treatment using atropine and pralidoxime. She was discharged on the second day of admission.
Conclusions: The authors demonstrated that pyridostigmine poisoning is self-limiting and well tolerated by young adults; however, unwanted effects of pyridostigmine on the heart has still to be considered which may become profound to the point of generating heart failure, syncope, or stress particularly in elderly patients. As the literature on human toxicity with pyridostigmine is scarce, not much data is available on its toxicity. However, prompt and specific management of pyridostigmine toxicity promises safety.

MeSH Keywords: Drug Overdose • Myasthenia Gravis • Pyridostigmine Bromide • Suicide, Attempted

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/917308>

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Background

Pyridostigmine is a quaternary amine parasympathomimetic which inhibits acetylcholinesterase for the treatment of various conditions such as myasthenia gravis, post-operative ileus, Alzheimer's disease, glaucoma, and the effects of curariform drug toxicity [1,2]. Pyridostigmine has been used for myasthenia gravis for many years and is generally considered safe [2]. However, reports showed that 64% of myasthenia gravis patients on daily dose of 150 to 900 mg/day of pyridostigmine experience cholinergic and muscarinic side effects including electrophysiological signs particularly among elderly patients, abdominal cramps, fasciculations, diaphoresis, urinary incontinence, blurred vision, bradycardia, cardio spasm, confusion, coma, and many more side effects [1,3]. Maximum tolerated dose of pyridostigmine is 180 to 540 mg per day [4]. Toxicity of pyridostigmine was well documented during the Persian Gulf War when the troops took pyridostigmine in order to protect themselves from the effects of nerve gas agents [5]. The troops developed a multi-symptom condition named "Gulf War Illness" with predominant symptoms of fatigue, muscle aches, gastrointestinal complaints, and memory problems.

Previously, no cases of pyridostigmine toxicity in human beings have been reported except the cases reported among the troops of the Persian Gulf War. We present a case of a suicidal attempt with a high dose of pyridostigmine by a patient with myasthenia gravis. In its own, it is a unique and first case report on pyridostigmine toxicity after a suicidal attempt by a patient with myasthenia gravis. Thus, it will be a valuable addition to the literature.

Case Report

A 47-year-old Syrian female, known to have myasthenia gravis, on pyridostigmine (Mestinon) 60 mg orally 3 times per day

was brought to the Emergency Department by her husband and son after an attempted suicide. She took 120 tablets containing 60 mg of pyridostigmine (a total of 7200 mg), an hour prior to arrival to the hospital after she received news of the death of all her family members in a misfortunate accident resulting from the Syrian War. She had 6 episodes of vomiting in the car. She was immediately transferred from the private car to the resuscitation bay. Her vitals were: blood pressure at 121/76 mmHg, heart rate at 50 beats per minute, respiratory rate at 16 breathes per minute, temperature at 36.7°C, oxygen saturation at 98% at room air, and random blood sugar at 7.5 mmol/L. On examination, she was conscious, but disoriented, distressed, ataxic, sweating (her clothes were drenched in sweat), covered in her own vomitus, with increased salivation, frothy mouth discharge, excessive lacrimation and bronchorrhea. She also had fasciculation of all muscles, most apparent on her face. She was unable to talk. Her pupils were equally reactive bilaterally and were not constricted. She had blurred vision. Drooling and excessive salivation was apparent. There was equal bilateral air entry with mild crackles and no wheezing. Cardiovascular examination was normal except with weak thready non-constant pulses ranging from 25 bpm to 140 bpm. Abdomen was neither distended nor sunken, but was tender mainly in the epigastric area with guarding and no rigidity. Urinary incontinence was present with no diarrhea or stool incontinence. On central nervous system examination, weakness, flaccidity, fasciculations all over her body (mainly on the face) were identified.

Electrocardiogram was done initially which turned out to be normal (Figure 1). Venous blood gas test showed metabolic alkalosis with the following results: pH was 7.43, CO_2 was 30, HCO_3 was 21, and base excess was -4.0 (Figure 2). Chest radiograph was normal. Complete blood count showed elevated white blood cells (14 400 cells/ μL) with hemoglobin at 9.8 g/dL and platelets at 416 000 cells/ μL . Blood chemistry showed normal serum urea and serum creatinine levels but

Figure 1. Electrocardiogram of the patient with myasthenia gravis who attempted suicide with pyridostigmine.

Figure 2. Chest x-ray of the patient with myasthenia gravis (AP view) who attempted suicide with pyridostigmine.

with hypokalemia (serum potassium was 3.1 meq/L), hyperglycemia (serum blood sugar was 7.5 mmol/L), and lactic acid was 3.2 mmol/L. Blood cholinesterase level was not performed due to non-availability. Toxicological screening was negative for co-ingestion of paracetamol, aspirin, ethanol, barbiturates, opiates, cocaine, benzodiazepines, amphetamines, and cannabis. Liver function tests were normal. Amylase and lipase were normal. Coagulation profile was normal.

No activated charcoal was given as she was vomiting and unable to control secretions. No lavage was done. She was given 1 mg of intravenous atropine every 5 minutes until symptoms resolved with a total of 3 mg given then she relapsed with vomiting and mild diaphoresis and 0.5 mg atropine was added and 2 g pralidoxime was given intravenously over 30 minutes. One liter of intravenous sodium chloride 0.9% bolus was given in the Emergency Department. One gram of intravenous paracetamol and one gram of intravenous pantoprazole were also given. The patient was admitted under medical care for 2 days for observation. On the first day, she was having on/off symptoms and 0.5 mg of intravenous atropine was given. On the second day, symptoms improved, and the patient was discharged free of symptoms and a psychiatric consultation was done. She was discharged with follow up.

Discussion

Intentionally taken high dose of pyridostigmine (7200 mg) led to toxicity in the form of disorientation, distress, ataxia,

diaphoresis, vomiting, salivation, excessive lacrimation, bronchorrhea, blurred vision, weakness, fasciculations, thread pulses, and urinary incontinence. The patient was symptom-free after having been given 3.5 mg of atropine and 2 g of pralidoxime. In other words, in spite of a heavy dose of pyridostigmine, the patient did not develop a life-threatening condition, and she recovered and discharged. This excellent outcome may be due to immediate initiation of vomiting, prompt treatment with atropine and pralidoxime, and reversible inhibition of acetyl cholinesterase. Additionally, the patient was in need of pyridostigmine as a treatment of her myasthenia gravis which might have hampered the effects of the drug. However, no lethal effects or mortalities by pyridostigmine toxicity have yet been reported in the literature.

The published literature on the toxicity of pyridostigmine is scarce. In 1991, Almos et al. [6] reported 9 cases of self-poisoning with pyridostigmine during the Persian Gulf War, with cases who developed symptoms of vomiting, diarrhea, abdominal cramps, increased salivation, fasciculations, muscle weakness urinary incontinence, and blurred vision at several minutes after the drug ingestion. In these cases, the dose ingested ranged from 300 mg to 900 mg and the symptoms remained for 24 hours. All the patients underwent gastric lavage with activated charcoal and only 3 patients required atropine. Contrary to the present case, the patients developed no neurological symptoms.

Conclusions

In our case report we demonstrated that in a pyridostigmine poisoning, our patient made an excellent recovery and responded to classical treatment using atropine and pralidoxime. However, despite our patient showing no immediate and unwanted impact of pyridostigmine ingestion on heart function, several unwanted effects of pyridostigmine on the heart still need to be considered including sinus bradycardia due to stimulation of the muscarinic receptors in the sino-atrial node, a problem particularly in children, sino-atrial block and atrio-ventricular block which may become profound to generate a heart failure, syncope or stress, a problem particularly in elderly patients [7]. In cases of large dose ingestion and organophosphate poisoning, atropine sulfate has been shown to counteract the severe cholinergic reactions which thus minimizes the gastrointestinal side effects and aids in resolution of arrhythmias, but extra attention should be given since atropine sulfate can mask signs of overdosage and can lead to inadvertent induction of cholinergic crisis [8]. As the literature on human toxicity with pyridostigmine is scarce, not much data is available on its toxicity. However, prompt and specific management of pyridostigmine toxicity promises safety.

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Conflict of interest

None.

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