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ATROPINE INDUCED PSYCHOSIS: A CONSEQUENCE DURING THE ORGANOPHOSPHATE POISONING TREATMENT

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ABSTRACT:
Atropine is a known and an established antidote in organophosphorus poisonings and it also helps to improve the extrapyramidal symptoms as it can cross the blood brain barrier. In the literature, the reports of atropine intoxication is not rare. Nevertheless, the reports of atropine abuse leading to psychosis are infrequent. Here, we present the case of 39 year old male patient who received atropine as part of antidote therapy for Organophosphorus poisoning and the drug was within the recommended dose. After the drug was administered, the patient developed restlessness, delirium, hallucinations, irrelevant talk along with tachycardia and dilated pupils not reacting to light suggesting possible 'anti-cholinergic abuse'. The patient was managed by titrating down the atropine's dose and administration of haloperidol and promethazine.

INTRODUCTION:

The crucial step in case of organophosphorus intoxications' management is the early identification of the symptoms and prompt diagnosis. The management includes resuscitation of the patient, fluids administration, muscarinic antagonist (atropine) and an oxime, which helps in the reactivation of the acetylcholine esterase. The patient needs to be closely monitored for intermediate syndrome and recurrent cholinergic symptoms.

Atropine acts by inhibiting the muscarinic receptors of acetylcholine at postganglionic parasympathetic neuroeffector junction.[1,2] In case of poisoning, atropine help to manage the muscarinic symptoms and Central nervous system manifestations. Atropinization demands close monitoring of the patients, as it can cause toxic reactions. The authors present a unique case where the atropine was administered as a part of antidote therapy in the OP which led to development of "Atropine Induced Psychosis".

CASE REPORT:

A 39 year old male with no history of psychiatric illness was brought to the tertiary care hospital after he has allegedly consumed pesticide. At the time of admission, the patient had breathlessness, altered sensorium, non-coherent and delirium. The amount consumed was unknown.

On physical examination revealed that the subject was conscious and non-coherent with the blood pressure of 130/90 mmHg, heart rate of 130 beats/minute with no cardiac murmur and respiratory rate of 18 breaths/minute with symmetrical breath sounds, and bibasilar inspiratory rales but occasional crepts. His abdomen had normal bowel sounds. Pupils were non-reactive to light and constricted.

Initial laboratory investigations reported were as follows: serum sodium, potassium and chloride levels were 141, 3.6 and 105 meq/L respectively, urinalysis showed the presence of pus cells (1-2 HPF), RBC (5-6 HPF), amorphous urates and trace amount of albumin. Complete blood picture revealed lymphopenia with $5.6 \times 10^3/mm^3$ of WBCs and normal RBC and platelet count. 2D echocardiography recorded an ejection fraction of 60%, fractional shortening of 30%, normal valves and chambers along with the absence of RWMA, good left and right ventricular function, lack of - mitral valve regurgitation, trivial valve regurgitation, pulmonary arterial hypertension, pulmonary embolism, clotting or vegetation. The prothrombin time of test was reported as 14 seconds whereas that of control was 13 seconds with prothrombin ratio of 1.07 and an INR of 1. Activated partial thromboplastin time of test was revealed as 34 seconds and that of control was 33 seconds. Liver function test reports were normal.

TABLE 1: VITALS DURING HIS STAY IN HOSPITAL

VITALS	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	UNITS
BP	130/90	110/80	110/80	120/80	120/70	120/80	mmHg
HR	130	88	106	84	64	84	beats/minute
RR	18	16	15	20	14	20	breaths/minute
CVS	S1, S2+	S1, S2+	S1, S2+	S1, S2+	S1, S2+	S1, S2+	-
GRBS	113	147	138	110	110	107	mg/dl
SpO2	95% on room air	97% on room air	96% on room air	97% on room air	98% on room air	98% on room air	-

P/A	Soft, tender	Soft, tender	Soft, tender	Soft, tender	Soft, tender	Soft, tender	-
PUPILS	Constricted .Non-reactive to light	Mild dilated. Sluggish reacting to light	Mild Pupils dilated. Sluggish reacting to light	Mild Pupils dilated. Sluggish reacting to light	Pupils dilated. Reacting to light	Pupils dilated. Reacting to light	-

*BP= Blood pressure, HR=Heart rate, RR=Respiratory rate, CVD=cardiovascular system, GRBS=General random blood sugar, P/A=pelvis and abdomen.

Table 2: DOSE OF ATROPINE ADMINISTERED:

TIME FROM OP INGESTION	RANGE OF ATROPINE DOSAGE
Day 1	10.8 mg (given stat in ER)
Day 2	5 mg
Day 3	3 mg

On day 1, the subject was given atropine and Inj. PAM (pralidoxime) 2gm IV stat (loading dose) then the dose was reduced to 500 mg along with intravenous fluids like normal saline, dextrose and ringer's lactate at the rate of 100 ml/hour, Inj. Augmentin (containing amoxicillin and clavulanic acid) 1.2 gm TID, Inj zofer (ondansetron) 4 mg IV thrice a day and Inj. pan (pantoprazole) 40 mg IV OD. **On day 2**, Inj. Augmentin was stopped and Inj clinzucia (containing clindamycin) 600 mg IV TID was started along with other drugs like Doxycycline capsule 100 mg BD, nebulizers duolin (combination of sulbactam and ipratropium bromide) and budecort (containing budesonide). After the patient received atropine, the case got further complicated as he developed signs of anti-cholinergic abuse such as psychosis and tachycardia. **On day 3,** considering the need for atropinization, the drug could not be withdrawn but it's dose was reduced and the patient was managed by administering haloperidol 5 mg IV stat and phenergan (promethazine). The patient was also given Inj optineuron as neuroprotective agent and potassium binder to maintain serum electrolyte balance. After about 5 days, as the signs of atropinization such as dry mouth, no secretions and pupils mildly dilated and reacting to light, became apparent atropine and pralidoxime was stopped and glycopyrrolate was started to improve the muscarinic symptoms.

DISCUSSION:

The administration of atropine, remains the mainstay for the pharmacological management of OP poisoning. The dose is tailored for the individual patient so as to maintain the heart rate at about 80 beats/min, systolic BP >80mmHg and to help prevent the bronchospasm or bronchorrhea..[3]

Toxic reactions have been reported to be related to individual's susceptibility as they can occur even at the therapeutic doses.[4] The interpersonal variability have been suggested by certain cases which have recovered from doses as high as 1000 mg while others could not recover from doses that are well under the therapeutic range.[5]

In the present case, the patient developed psychosis after the anti-muscarinic agent, atropine was administered. A causal relationship between the drug reaction-central symptoms and the suspected agent, atropine was evaluated using Naranjo's causality assessment scale and WHO Uppsala monitoring probability scale and it was found to be probable/likely.

Usually the ADRs to drugs are managed by either withdrawing the suspected agent or reducing the dose. If the toxicity to atropine has been established, then the infusion should be terminated and the drug should be started only after the symptoms have been resolved but at the rate of 70-80% of the earlier rate. Another approach is to replace the drug with more safer one such as physostigmine, glycopyrrolate or scopolamine. The psychosis due to atropine can be managed by antidepressants and anti psychotics.[6] In this case, the patient was atropinized completely, atropine induced psychosis was managed symptomatically and did not require prophylactic therapy.

Beta adrenergic agonist such as salbutamol, budesonide, and ipratropium, given in combination with atropine helps to maintain the patency of airways for treating bronchospasm and bronchorrhea. Atropine only ceases the production of secretions in the lungs but not removes it. Salbutamol helps to remove the secretions from lungs, thus rapidly restoring the normal oxygen exchange.

The patient experienced anti-cholinergic abuse with atropine. Psychosis was managed with haloperidol and promethazine. The patient was taken off atropine until the symptoms subsided, nevertheless the patient was completely atropinized once his condition was stable enough to receive the drug. It's worth mentioning that atropine's dose was reduced after an abuse was established which was subsequently resolved.

CONCLUSION:

Centrally acting acting anti-cholinergics that are used to treat extrapyramidal symptoms have been reported in the medical literature to be prone to abuse. This can be partly attributed to their ability to cross blood brain barrier apart from genetic inter variability as some patients may be abused even at the recommended doses as seen in the present case. Such patients are managed either by drug withdrawal or by reducing the dose. In both the scenarios, an antipsychotic or anti depressant is bound to be administered as part of the ADR management until the symptoms subsides.

REFERENCES:

1. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet.2008;371(9612):597-607.
2. Sungur M, Güven M. Intensive care management of organophosphate insecticide poisoning. Crit Care. 2001;5(4):211-15.
3. Balali-Mood M, Saber H. Recent advances in the treatment of organophosphorus poisonings. Iranian journal of medical sciences. 2012 Jun 1;37(2):74-91.
4. Economacos G, Kanakis J: A case of hypersensitivity to atropine. Anesth Analg Reanim 1981; 38: 748.
5. O'Connor PS, Mumma J: Atropine toxicity. Am J Ophthalmol 1985; 99: 613-14
6. Dickson EW, Bird SB, Gaspari RJ, Boyer EW, Ferris CF. Diazepam inhibits organophosphate-induced central respiratory depression. Acad Emerg Med. 2003;10:1303–1306