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Research Article

ATROPINE INDUCED PSYCHOSIS DURING THE TREATMENT OF ORGANOPHOSPHATE INTOXICATION: A CASE REPORT

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ABSTRACT

The use of antipsychotic medications necessitate a hard indulgence between the benefit of alleviating psychotic symptoms and likelihood of concern, sometimes life shortening adverse effects. Psychotic symptoms such as restlessness and excitement, hallucinations, delirium might occur following the atropine administration. Moreover atropine induced psychosis has been reported rarely in literature. A 26year old male patient manifested with visual and auditory disturbances, hallucinations, fatigue and anxiety following the atropine administration during the treatment of organophosphate intoxication. The adverse drug reaction was classified as probable with a score of 6 according to Naranjo's casualty assessment scale and on the Hartwig's sale it is at level 5 (severe). The WHO-UMC casualty assessment system is indicated as probable with atropine. Initially the patient was managed by gastric lavage. Further management was done by tapering the dose of atropine and by supportive therapy along with antipsychotic medications. However the patient was not rechallenged with atropine owing to severity of reaction. Since atropine is one of the highly potent drug used in the treatment of organophosphate intoxication, due care is essential while prescribing doses especially with IV administration and early withdrawal of the offending drug is crucial to avoid further complications.

Keywords: Organophosphate intoxication, Atropine, psychosis, adverse drug reaction.

INTRODUCTION

Atropine is a naturally occurring alkaloid extracted from the deadly nightshade (Atropa belladonna) and other plants of the nightshade family (Solanaceae), which antagonises the muscarinic like actions of acetylcholine in the central and peripheral nervous system.[1]Competitive or surmountable antagonism is one of the major action of atropine. Atropine is most widely used to treat conditions such as excessive saliva or mucous production, colitis, diverticulitis, inflammatory bowel disease, spasms of gastrointestine, bladder and urinary tract, pepetic ulcers, infant, renal and biliary colic, Parkinson's disease and poisoning caused by organophosphate insecticides and nerve gases. It works by blocking the neurotransmitter (acetylcholine) actions on the structures innervated by post ganglionic nerves and on smooth muscles.[2,3]

Common side effects due to atropine such as xerostomia, photophobia , blurred vision and tachycardia usually appear at or below the therapeutic dose. Serious adverse effects such as dilated pupil marked palpitations, restlessness, tremor, delirium, hallucinations and fatigue occur at toxic doses. In addition psychotic symptoms such as restlessness and excitement, hallucinations, delirium might occur following the atropine administration.[2,3]Atropine administration for treatment of intoxication to a large population carries a risk of allergic or toxic reactions only in small number of patients. Moreover, atropine induced psychosis has been reported rarely in the literature.

Here we describe a case of atropine induced psychosis which developed during the treatment of organophosphate intoxication and it's management.

CASE REPORT

A 26 year old male patient presented to the emergency department with an alleged history of ingestion of organophosphorous compound along with alcohol which was followed by shortness of breath and multiple episodes of vomitings. The patient was initially taken to the local hospital where gastric lavage was done using normal saline. There was no history of seizures, lacrimation, salivation, fasiculation or paralysis. On examination the patient was conscious and oriented but restless with no focal deficits and no neck muscle weakness. His vitals at the time of admission were:

B. P: 110/80 mm of Hg
Pulse rate: 89 beats/min
Respiratory rate:20 cycles /min
SpO2: 98%
GRBS: 125 mg%

On further examining the patient, pupil was mildly dilated and reactive to light while the plantar reflex were decreased. Rest of the physical examination was normal except for sluggish breath sounds. Features were consistent with organophosphate poisoning and the patient was managed conservatively.

Haematologic analysis revealed relative neutropenia, while the other parameters were normal. Serum electrolyte levels , alkaline phosphate and random blood sugar levels were elevated, whereas the serology report and other liver function parameters were normal. Coagulation profile was altered and the ultrasound of abdomen and pelvis suggested no obvious sonological abnormality. Table 1

Table 1: Laboratory reports

Laboratory parameters (units)	Reports		reference values
	On Admission	At Discharge	
Complete Blood Picture			
Haemoglobin (gm/dL)	14.9	15.1	11.5 - 17.0
Mean Corpuscular Haemoglobin concentration (g/dL)	31.8	32.4	32.0- 36.0
Total Leukocytic count (x 10^3/mm^3)	5.1	9.8	4.0 - 10.0
Differential leukocytic count (%)			
Neutrophil	86.5	60.7	50.0 – 80.0
Lymphocyte	11.7	30.8	25.0 – 50.0
Eosinophil	0.6	1.4	0.00 – 0.50
Basophil	0.3	0.3	0.00 – 0.20
Platelet count (x 10^3 mm^3)	220	410	150 – 500
Liver function test			
Bilirubin (mg/dL)			
Total	0.5	0.9	0.2-0.8
Direct	0.1	0.2	Upto 0.2
ALT (U/L)	11	21	5 – 45
AST (U/L)	19	20	5 – 45
Alkaline phosphatase (IU/L)	98	86	28-88
Protein, total (g/dL)	6.2	6.3	6.0-7.5
Albumin (g/dL)	3.7	3.5	3.5- 5.0
Globulin (g/dL)	0.8	0.6	0.2- 0.8
Coagulation Profile			
Prothrombin time (s)	18	13	13-15
INR	1.5	1.4	1.3
Renal Profile			
Serum Creatinine (mg/dL)	0.9	0.7	0.6-1.5
Blood urea (mg/Dl)	28	32	10-45
Sodium (meq/L)	149	146	135-145
Potassium (meq/L)	4.1	3.1	3.5-5.0
Chloride (meq/L)	108	104	95-105
Random Blood Sugar (mg/dl)	200	145	79-160
Urine Analysis		Not done	
Colour and appearance	Light red & clear	Pale yellow Clear	
Specific gravity	1.005	1.005	
Albumin	Traces	NIL	
Sugar	NIL	NIL	
Pus Cells (/HPF)	2-3	2-3	1-2
RBCs (/ HPF)	NIL	1-2	NIL
Epithelial Cells (/ HPF)	2-3	1-2	1-2

Initially the patient was started with supportive care using IV fluids and oxygen therapy. Pulse oximetry, Blood Glucose levels, Cardiac parameters and symptoms of SLUDGE (salivation, lacrimation, urination, defecation, GI cramping, Emesis) were constantly monitored. Repeated bolus doses of atropine was administered at a rate of 10 ml/hour to maintain pulse rate>80beats/min Complete atropinisation was achieved, which required upto 10mg of atropine. IV Pralidoxime (PAM) 1 gm in 100ml of normal saline was administered every 8 hourly as an antidote.

On the next day, the patient started experiencing severe agitation, disorientation and delusions, dilated pupil(size>8mm) with decreased response to light. Based on these symptoms developing following the atropine administration, a diagnosis of atropine induced psychosis was made. Severity assessment was done using Hartwigs Severity assessment scale and Casualty assessment of atropine induced psychosis was done using Noranjo Casualty assessment scale and WHO-UMC scale.

Using Naranjo's scale of casualty assessment the adverse effect is classified as probable with a score of 6(Table 2) and on Hartwigs severity assessment scale the adverse effect was classified as moderate at level 3 (Table-3). The WHO -UMC casualty assessment system is indicated as probable associated with atropine.

Table 2: Naranjo Adverse Drug Reaction Probability Scale[4]

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	0
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0

8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	1
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	0
	Total Score:6			

Table 3: Hartwig's Severity Assessment Scale[5]

LEVEL 1	An ADR occurred but required no change in treatment with the suspected drug.
LEVEL 2	An ADR required that the treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
LEVEL 3	The ADR required that the treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR An antidote or other treatment was required. No increase in length of stay (LOS).
LEVEL 4	Any level 3 ADR which increases length of stay by at least 1 day. OR The ADR was reason for the admission.
LEVEL 5	Any level 4 ADR which requires intensive medical care.
LEVEL 6	The adverse reaction caused permanent harm to the patient.
LEVEL 7	The adverse reaction either directly or indirectly led to the death of the patient.

Mild = Level 1,2; Moderate = Level 3,4; Severe = Level 5,6,7.

Table 4. WHO-UMC Causality Categories[6]

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable / likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional / Unclassified	Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination176
Unassessable / Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

* All points should be reasonably complied with

The patient was appropriately managed by tapering the dose of atropine to about 0.5ml/hr and discontinued after the appearance of signs of complete atropinisation. Midazolam 5ml/hr IV was administered to relieve agitation and anxiety. Tablet Halodol(haloperidol) 10mg BD was given for managing the psychiatric effects. Antiulcerants (pantoprazole-40mg IV BD) and Injection Piptaz(piperacillin/ tazobactum) 4.5gm IV BD was administered as prophylactic. Atropine was stopped completely on the fifth day and the patient was discharged in a much stable condition.

DISCUSSION

Atropine is a highly potent drug indicated for treatment of organophosphate nerve agent and insecticide poisoning for several decades. Most of the adverse effects are due to its antimuscarinic action and usually are reversible on discontinuation of therapy. Frequency and severity of adverse effects are dose related. Serious adverse effects are usually a result of excessive dosage arising from single or repeated injection of atropine.

Drug induced psychosis can de determined based on the four defining criteria:(DSM-IV TR criteria)

1-proximal delusions,

2- evidence from history, physical examination or laboratory findings either (a) or (b) (a- symptom in criteria 1 developing during or within a month of substance intoxication or withdrawal, b- medication use is etiologically related to the disturbance),

3- the disturbance is not better accounted for by a psychotic disorder that is not substance induced,

4-the disturbance occur during the course of delirium.[7]

In our case 3 out of 4 criteria are satisfied simulating drug induced psychosis. Based on drug induced psychosis criteria and a history of Atropine administration, proceeding the development of psychosis, a diagnosis of atropine induced psychosis in organophosphate poisoning was apparent.

Management

Atropine induced psychosis can be managed either by terminating the offending drug or continue the suspected drug with some alterations. Cessation of atropine and the use of alternative muscarinic drugs such as physostigmine, glycopyrollate and scopolamine would reduce the psychotic symptoms. In addition antipsychotics such as haloperidol (0.5-2mg orally 1-4 times daily) and antidepressants such as benzodiazepines (diazepam 5-

10 mg four times daily, Lorazepam 1mg OD/TID) are also used as a treatment of choice for atropine induced psychosis.[8]Symptomatic treatment would be more appropriate since long term treatment is not required and atropine toxicity is likely to resolve with in a few days after the discontinuation of suspected drug.

CONCLUSION

Since atropine is one of the highly potent drug used in the treatment of organophosphate intoxication, due care is essential while prescribing doses especially with IV administration and early withdrawal of the offending drug is crucial to avoid further complications.

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