

COMPARISON OF ATROPINE INTRAVENOUS INFUSION VERSUS INTERMITTENT ATROPINE IN THE MANAGEMENT OF ORGANOPHOSPHORUS POISONING IN ICU

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ABSTRACT

BACKGROUND

Comparison of atropine intravenous infusion with intermittent atropine in earlier recovery, atropinisation and complications of organophosphorus poisoning. It is very commonly seen in Indian population among patients admitted in hospital/ICU. Organophosphorus compounds bind irreversibly to the acetylcholinesterase in the plasma, red cells and cholinergic synapses in the CNS and the PNS.

MATERIALS AND METHODS

50 patients of organophosphorus poisoning from July 2016 - February 2017 were included in study.

RESULTS

Atropine infusion is better as compared to intermittent atropine in the management of organophosphorus poisoning.

CONCLUSION

All patients on intravenous atropine infusion responded earlier and with less amount of atropine. Their pupillary dilatation, which is an (important criteria) for atropinisation occurred earlier than on intermittent atropine.

KEYWORDS

Acetylcholine, Atropine, Organophosphorus, Effects.

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BACKGROUND

Organophosphorus poisoning is very commonly seen in Indian population among patients admitted in hospital/ICU.

Crop fungicide, pesticide, etc. are easily accessible to general population without any restriction on sale, India being an agricultural country.

- Accidental (uneducated class) suicidal (mouth-to-mouth) publicity and homicidal.
- Atropine ampoules are one millilitres in quantity and contain 0.6 milligrams and at times total dose needed maybe more than 50 ampoules to achieve optimal atropinisation and oximes are also used.¹
- Hence, to use an atropine drip through an accessible peripheral line was planned.

Aim- Comparison of atropine intravenous infusion with intermittent atropine in the management of organophosphorus poisoning in ICU.

Objectives- Comparison of atropine intravenous infusion with intermittent atropine in earlier recovery/ atropinisation/ complications of organophosphorus poisoning.

Large dosage of atropine can be given for early recovery and prevention of complications.

Study Centre- IMCHRC, Indore.

MATERIALS AND METHODS

50 patients of organophosphorus poisoning from July 2016-February 2017.

Inclusion Criteria- Organophosphorus poisoning suspected on clinical grounds or confirmed by container from which consumed. Age more than 18 years with both male and female.

Exclusion Criteria

- Critically-ill patients.
- Doubtful op ingestion.
- Consumed with other substances such as alcohol.
- Pregnant and lactating mothers.

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Receptor-specific Manifestations-

Organophosphorus compounds bind irreversibly to the acetylcholinesterase in the plasma, red cells and cholinergic synapses in the CNS and the PNS.²

Red cell cholinesterase activity is better correlated with the severity of exposure than plasma cholinesterase activity.

The cholinergic system- cholinergic synapses are present in sympathetic system.

Absorption-

It is absorbed by the inhalation through the skin, mucous membrane and the gastrointestinal tract. Solvent used are kerosene/water, which is responsible for smell from the body and breath and gastric contents.

Neurotransmitter, acetyl ester choline (Figure 1).

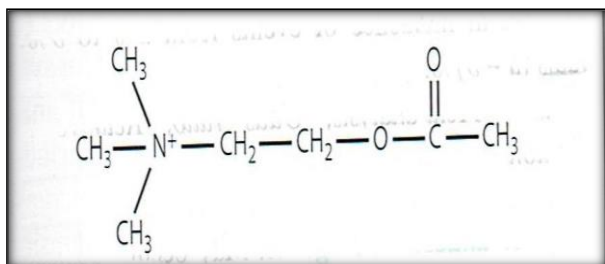


Figure 1. Structure of Acetylcholine

Synthesised from acetyl coenzyme A and choline in nerve ending cytoplasm, the reaction is catalysed by choline acetyltransferase.

Choline is actively transported into the nerve and the acetyl coenzyme A is formed in the mitochondria.

Acetyl choline is stored in the vesicle.

Acetylcholine is the Transmitter at-

- 1 Autonomic ganglia.
- 2 Parasympathetic postganglionic nerve endings.
- 3 Sympathetic postganglionic nerve endings at sweat glands.
- 4 Blood vessels supplying the skeletal, smooth muscle and cardiac muscles.
- 5 The neuromuscular junction many parts of the CNS.
 - Actions may be broadly divided into either muscarinic or nicotinic depending on the acetylcholine receptors involved.
 - Acetylcholine is hydrolysed to choline and acetate by acetylcholinesterase on the postsynaptic membrane.
 - Other esterases also exist, e.g. plasma cholinesterases.

Each receptor consist of five glycosylated protein subunits that projects into the synaptic cleft.

The adult receptors consists of 2 alpha, beta, delta and epsilon unit.

The subunits span the postsynaptic membrane forming a cylinder around central ion channel.

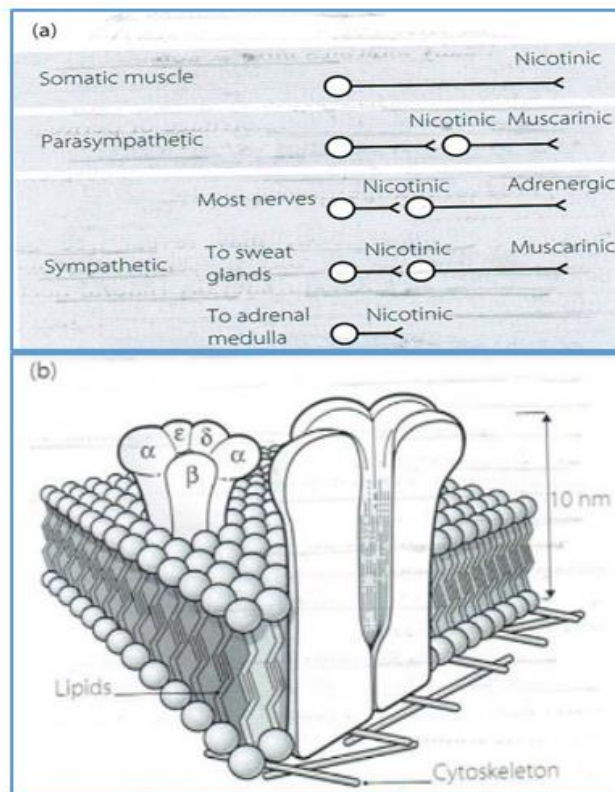


Figure 2(a) Types of Acetylcholine Receptors. (b) Structure of Nicotinic Acetylcholine Receptor.

The two alpha subunits of each receptor carry the binding site for acetylcholine.

- Beta and delta subunits, although present do not actively participate in the binding of acetylcholine.
- Occupation of these sites open the ion channel allowing cations (mainly sodium potassium and calcium) to flow into the cell down their concentration gradients, this produces an excitatory postsynaptic potential.

Muscarinic Receptor-

G protein coupled receptors, largely coupled to either adenylate cyclase or phospholipase C via Gi and Gq proteins, respectively.

Mediate postganglionic neurotransmission via parasympathetic neurons as well as sympathetic outflow to sweat glands.

Classified According to Structural Subtypes-

- M1- Gq coupled- Gastric secretion and memory.
- M2- Gi coupled- Heart, decreases heart rate, contractility and atrioventricular nodal conduction.
- M3- Gq coupled- Smooth muscle - increased tone, exocrine glands - stimulatory and in brain – Chemoreceptor trigger zone.
- M4/5- Brain and adrenal medulla.

Muscarinic activity is more than nicotinic activity.

Injection of acetylcholine or poisoning with acetylcholinesterases, thus causes parasympathetic stimulation and sweating at lower doses before having effects at autonomic ganglia and the NMJ at higher doses

(patient consume more quantity of organophosphorus poison).³

Acetylcholinesterases-

Enzyme present at the synaptic membrane of cholinergic synapses and neuromuscular junctions, RBC and placenta.

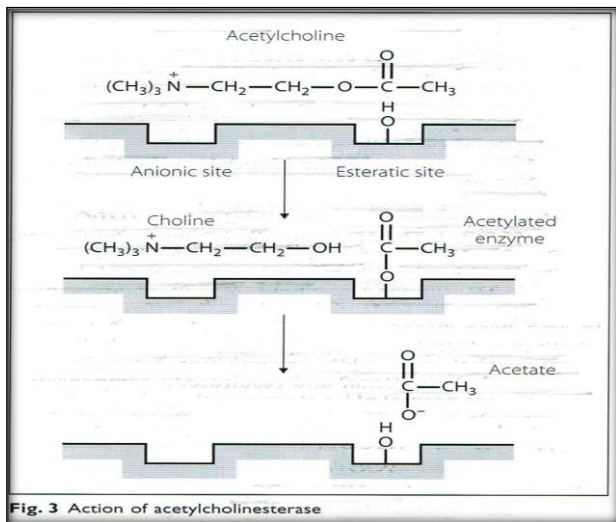


Figure 3. Action of Acetylcholinesterase

Choline is hydrolysed, and acetate released.

Acetylcholinesterases Inhibitors-

Acetylcholinesterases (AChE) inhibitors are used for the treatment of neuromuscular disorders such as myasthenia gravis.

Concurrent administration of an antimuscarinic agent, e.g. atropine reduces unwanted effects of increased acetylcholine concentration at muscarinic receptors and ganglia at low doses.⁴

Half-lives may vary from minutes to hours with metabolism by oxidation, ester hydrolysis and combination with glutathione and excretion by liver and kidney.

Toxic Effects-

Peripheral Enzyme Inhibition-

Phosphorylation of acetylcholinesterases.

Maybe irreversible depending on the compound involved.

Features are those of cholinergic crisis and include muscarinic effects (bronchospasm, sweating, increased secretions, abdominal cramps, bradycardia and miosis) and nicotinic effects at large doses (muscle twitching, weakness, hypertension and tachycardia), phosphorylation of enzymes, e.g. lipases, gastrointestinal enzymes and pancreatic hepatic enzymes.

Myopathic Effects-

Weakness may occur within 24 to 96 hours and can persist up to 3 weeks.

Mainly affecting proximal muscle, it is thought to involve postsynaptic dysfunction at the neuromuscular junction.

Delayed polyneuropathy- Usually follows poisoning with non-insecticide compounds with weakness and paraesthesia can develop in 3 weeks.

Pyramidal signs can occur during recovery.

CNS Effects-

Anxiety, tremor, confusion, coma and convulsions may occur with EEG abnormalities.

Respiratory failure may result from increased tracheobronchial secretions, proximal muscle weakness and action on central nervous system.

Diagnosis- Is based on history, clinical examination and response to therapy.

Treatment in ICU

After patient consent is taken and completion of medico-legal norms in casualty.

Airway, breathing and circulation should be ensured and monitored.

Further contamination is prevented by removal of clothings.

Skin is cleaned thoroughly with sponging with water.

The airway should be cleared and high flow oxygen is administered up to 5-10 litres/minutes as needed.

Drug Therapy-

Atropine Sulphate-

Anticholinergic drug (competitive antagonist at muscarinic acetylcholine receptor) an ester of tropic acid and tropine.

Atropine used to reduce muscarinic effects of acetylcholinesterase inhibitors and treatment of bradycardia due to vagal effect.

Atropine IV infusion 0.01-0.02 mg per kg is given with acetyl cholinesterase inhibitors to reduce tracheobronchial secretions and respiratory distress.⁵

If dysrhythmias occurred as sinus tachycardia is taken as effect of atropinisation and was not treated by beta blockers.

Effects of Atropine-

Cardiovascular System-

Low dose may cause bradycardia initially thought to be due to vagal stimulation and then tachycardia and cutaneous vasodilatation.

Central Nervous System-

Excitement, hallucination and hyperthermia.

Antiparkinsonian Effect-

Respiratory System-

Bronchodilatation and increased dead space and reduced secretions.

Gastrointestinal Tract-

Reduced salivation, lower oesophageal sphincter tone, motility and gastrointestinal secretions.

Others-

Reduced sweating and cause mydriasis and cycloplegia.

Reduced bladder and ureteric tone.

Atropine 2 mg intravenous infusion or each 5-10 minutes until dry flushed skin, dilated pupils and tachycardia (clinical parameters to be achieved).

For Nicotinic Effects-

Injection Pralidoxime 30 mg per kg diluted in 10-15 mL water, intravenous over 5-10 minutes.

Maybe repeated up to twice if no improvement is seen within 30 minutes up to usual maximum of 12 grams/24 hours.

Rarely, intravenous infusion of up to 500 mg/hour may be required.

For Seizures-

Diazepam or midazolam as needed.

Treatment of Intermediate Syndrome-

Early institution of ventilatory support, which may be required for a prolonged duration is essential for management.

After gastric lavage, if the patient in respiratory distress immediate intubation is done for removal of secretions and reducing respiratory distress.

If mixed acid base disturbance occurred was treated accordingly.

ABG shows metabolic alkalosis with compensatory respiratory acidosis treated by potassium and soda bicarbonate.

Dyselectrolytaemia and acid base balance corrected accordingly.

RESULTS

Treatment	Gone Home Early (P [^])	Gone Home Late (P)	Total Patients
Atropine infusion	27	23	50
Intermittent atropine	23	27	50

Z test is used for statistical purpose when two proportions compared is used.

When Z test is less than two and significant that at p value less than 0.05.

After calculation, Z test came out to be 1.80, which signifies p value less than 0.05.

Atropine infusion is better as compared to intermittent atropine in the management of organophosphorus poisoning.

DISCUSSION

Patient who were put on intravenous atropine infusion responded better and earlier at least 12-24 hours as

compared to atropine in interval and there was no error in medication in dose regulation.

They had less complication early and remote and less amount of atropine medication was needed.

Injection atropine at least 15 to 20 millilitres ampoules less as compared to intermittent for total dosage is used.⁶

CONCLUSION

All patients on intravenous atropine infusion responded earlier and with less amount of atropine. Their pupillary dilatation, which is an important criterion for atropinisation occurred earlier than on intermittent atropine.

The amount of atropine used was less (10-20 ampoules), recovery was fast as compared to intermittent injections of atropine symptomatically.

Signs of over atropinisation were lesser seen on our study. Hence, in our study, we found that intravenous infusion of atropine is better for management of organophosphorus poisoning and earlier discharge from intensive care earlier (48 to 72 hours).

In both cases, there were no deaths were reported in our study.

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