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CASUAL COMPARATIVE ANALYSIS OF SPEED OF INITIAL ATROPINIZATION AND RATE OF SYMPTOM RESOLUTION AMONG PATIENTS OF ACCIDENTAL ORGANOPHOSPHATE POISONING

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Abstract

Objective: *This study hopes to compare the rate of symptom resolution achieved with different recommended speeds of initial atropinization as part of treatment of patients presenting with accidental organophosphate insecticide poisoning.*

Methodology: *The casual-comparative analysis was conducted at the department of medicine, Liaquat university hospital, upon a total of 117 patients from October 2016 to July 2017. Informed consent was acquired from each patient before administering each of the recommended dosage regimens.*

Results*: The best performing regimen was administration of a beginning bolus of one to two milligrams of atropine, seconded shortly (five minutes) by a doubled dose of atropine. This practice of administering a doubled dose after 5 minutes is followed till complete atropinization is obtained. Among the many up sides of our most successful regimen, most notable were the facts that, administration of a mean dose (25 mg) required not more than twenty minutes, it worked well even for rare cases that required rather large quantities of atropine, allowing 75 mg of atropine to be administered in no more than 25–30 minutes, and finally, it even catered to the needs of patients that require small doses owing to the fact that the beginning bolus can be a mere 1 mg.*

Conclusion: *After careful consideration and deliberation on the obtained results, the use of a dosage regimen with the high pace of initial atropinization to halt the adverse effects seems to be the best choice. It shall help to considerably decrease the mortality owing to organophosphate poisoning. It addition to that, the use of a simple and easy to follow dosage regimen is more likely to be followed correctly.*

Keywords: *Atropinization, Organophosphate Poisoning, Accidental Poising, Symptom Resolution, Treatment Speed and Modality Speed Comparison.*

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INTRODUCTION:

Organophosphate (OP) poisoning continues to be a matter of great concern, particularly in the developing faction of the world. [1-3]. This is attributed to the easy access to insecticide/pesticides of organophosphate origin owing to the fact that many of the developing countries thrive off an agricultural economy and products such as insecticides and pesticides are readily available. The death toll, brought about by toxicity of such pesticides may climb up to 0.2 million deaths annually. [4-6]

The untimely demises occur due to failure of respiration, weakness of neuromuscular junction, central respiratory depression, bronchospasm and bronchorrhoea and due to cardiovascular collapse [7]. Atropine administration is urgently required in sufficient doses to counter the cholinergic signs. [8–10] This prime step of treatment is often called "atropinization". Following atropinization, airway and ventilator support too may be required in severe cases. [11]

Despite the fact that atropine is acknowledged by all as a cornerstone of initial treatment, [12] firm consensus regarding the atropine dosage regimen and the pace of initial administration is yet to be achieved. This is mainly due to scarcity of evidence pertaining to the matter, particularly, the lack of comparative analysis that may put all advised/recommended regimens to the test in control environments to assess the performance of each regimen against the other tests.

However, even though the precise dosage of atropine or its initial pace of administration is not agreed upon, there is consensus on the signs that manifest, once an adequate dosage of atropine has been administered. The signs and symptoms are namely, tachycardia, halted sweating and miosis reversal. [13-14] The clear signs thus ensure that the therapy is timely halted and overdose is not administered.

The aim of this study was thus, to compare all worthy atropine dosage regimens and their respected speed of initial administration to see how each of the regimens and their initial speed of atropinization, in particular, fairs when put to the test.

METHODOLOGY:

The casual-comparative analysis was conducted at the department of medicine, Liaquat university hospital, upon a total of 117 patients from October 2017 to July 2017. Patients with a history contact with organophosphorus insecticides/pesticides that exhibited cholinergic signs and required atropine administration were considered eligible for inclusion in the study.

Methods of identification of organophosphorus exposure included, history from patient or attendant; clinical features shown by patients were assessed for consistency with a diagnosis of OP poisoning. Each of the 29 separate dosage regimens, their quantity and the pace of atropine given to each patient was noted. Standard protocols were employed while managing the patient. Each dosage regimen was administered to three patients and their mean rate of symptom resolution was used to enhance accuracy and reliability and account for external biases.

	Target end-points for atropine therapy included:
1	Clear chest on auscultation.
2	Heart rate >80/min.
3	Systolic BP >80 mmHg.
4	Pupils no longer pin-point.
5	Dry axillae.

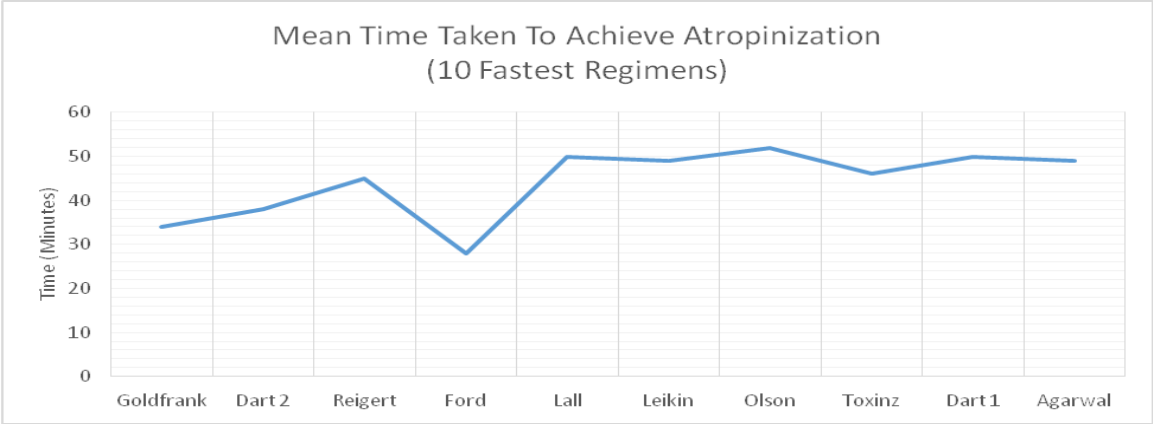
The symptoms, whose rate of resolution was investigated were the following: Depending on the time elapsed since exposure of the patient to organophosphorus.

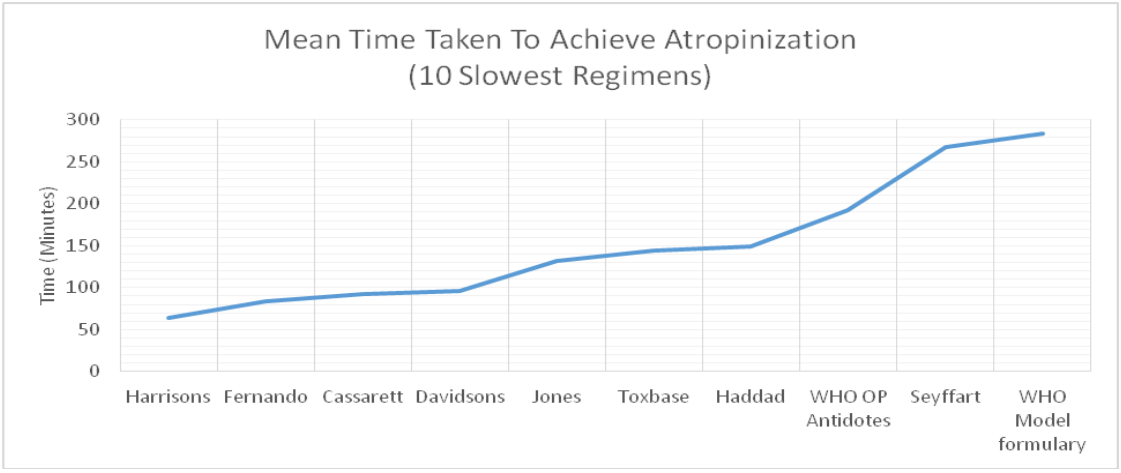
Time elapsed since exposure to organophosphorus	*Prominent Symptoms*
Minutes to Twenty-Four Hours	*1. Excessive salivation, lacrimation and urination.* *2. Gastric cramps and emesis.* *3. Bradycardia and Hypotension.* *4. Dyspnea*
24 hours and above	*1. Excessive salivation* *2. Bradycardia* *3. Miosis and Blurred vision*

RESULTS:

The best performing regimen was administration of a beginning bolus of one to two milligrams of atropine, seconded shortly (five minutes) by a doubled dose of atropine. This practice of administering a doubled dose after 5 minutes is followed till complete atropinization is obtained.

Among the many up sides of our most successful regimen, most notable were the facts that, administration of a mean dose (25 mg) required not more than twenty minutes, it worked well even for rare cases that required rather large quantities of atropine, allowing 75 mg of atropine to be administered in no more than 25–30 minutes, and finally, it even catered to the needs of patients that require small doses owing to the fact that the beginning bolus can be a mere 1 mg.

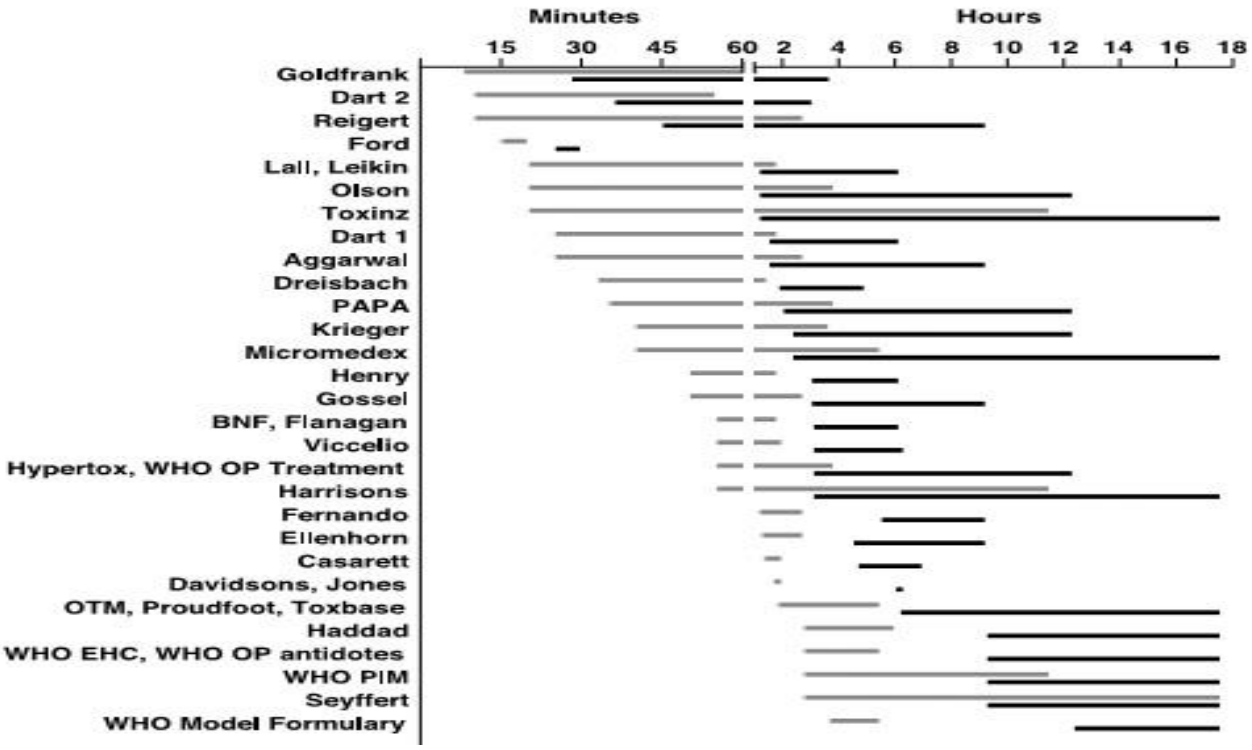




The complete list of recommended dosage regimens & their individual pace are tabulated below.

SOURCE	EDITION/YEAR	RECOMMENDED REGIMEN
Goldfrank	7th / 2002	1–5 mg, repeated every 2–3 min
Dart 2	3rd / 2003	2–4 mg, repeated every 2–5 mins, with increasing incremental doses
Reigert	5th / 1999	If GCS normal: 2–4 mg, repeated every 15 min. If GCS reduced: >4–8mg, repeated every 5–15 min
Ford	1st / 2001	1–2 mg; repeated every 5 min doubling the dose
Lall	1st / 1998	2–5 mg, repeated every 5–10 min
Leikin	3rd / 2001	2–5 mg, repeated every 5–10 min
Olson	3rd / 1999	1–5 mg, repeated every 5–10 min
Toxinz	2002	2mg, repeated every 10–30 min
Dart 1	1st / 2000	2–4 mg, repeated every 5–10 min
Aggarwal	1st / 1997	2–4 mg, repeated every 5–15 min
P.A.P.A	2nd / 1999	1–3 mg, repeated every 5–10 min
Krieger	2nd / 2001	2mg, repeated every 10 min
Henry	1st / 1997	2–4mg, repeated every 10 min
Gossel	3rd / 1994	2–4 mg, repeated every 10–15 min
British National Formulary	46th / 2003	2mg, repeated every 5–10 min (IM or IV according to severity)
Flanagan	1st / 2001	2mg, every 5–10 min
Vicellio	2nd / 1998	1–2 mg, then 2mg repeated every 5–10 min. Larger increments of atropine may be used.
Hypertox	3.7 / 2003	1–2 mg, repeated every 5–10 min
WHO Treatment Guide	1999	1–2 mg, repeated every 5–10 min
Harrisons	15th / 2001	0.5–2 mg, repeated every 5–15 min
Fernando	2nd / 1998	2–10 mg, then 2 mg repeated every 10–15 min
Cassarett	7th / 2003	2–10 mg, then 2 mg repeated every10–15min
Davidsons	19th / 2002	2 mg, repeated every 10 min
Jones	1st / 2001	2 mg, repeated every 10 min
Toxbase	2002	2 mg, repeated every 10-30 min
Haddad	3rd / 1998	1–2 mg, then 2 mg repeated every 15–30 min
WHO OP Antidotes	2002	2 mg, then same or increased dose every 15–30 min
Seyffart	4th / 1996	1-2mg, repeated or increased in increments every 15–60 min
WHO Model Formulary	1st / 2002	2 mg, repeated every 20–30 min

A pictorial depiction of the individual initial speed of atropinization is also provided below:



A break-up rate of the resolution rate of muscarinic symptoms is provided below

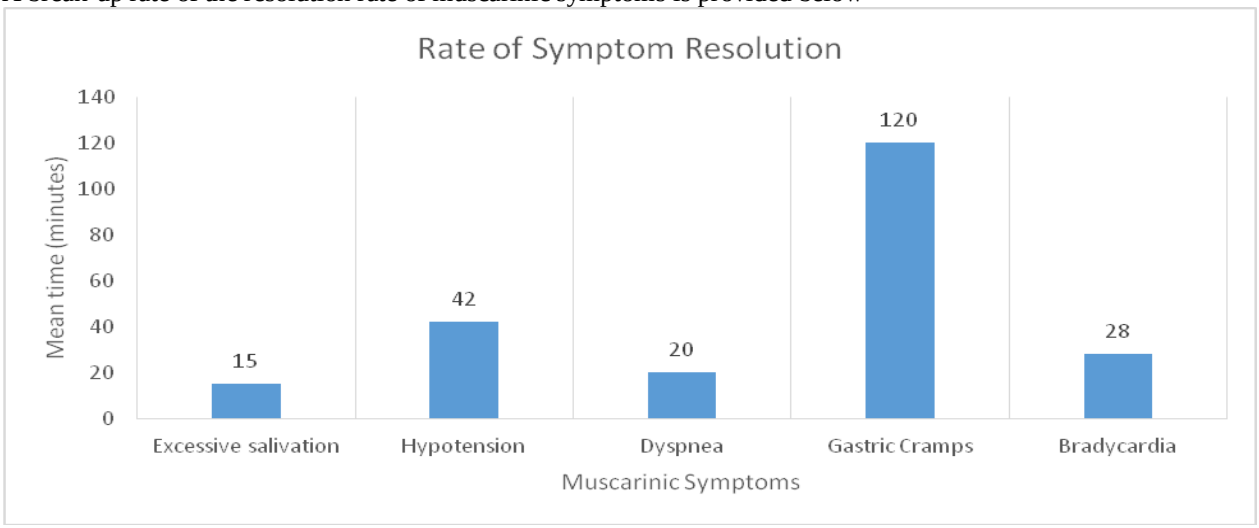


Fig 3: Gastric cramps went took the most time and were the last to be relieved.

DISCUSSION:

Severe organophosphate poisoning is a major clinical issue in our part of the world with death toll, rising up to 0.2 million deaths annually. [4-6] However, most deaths occur due to delayed and/or improper treatment a regimen which often leads to due to failure of respiration, weakness of neuromuscular junction, central respiratory depression, bronchospasm and bronchorrhoea and due to cardiovascular collapse. [7] Research conducted upon animals has revealed the primary cause of death to be central cholinergic stimulation. [14, 15]

Atropine is a competitive Ach antagonist at the post-synaptic muscarinic nerve membrane. It is ideal to administer it in an initial dose test dose of 1 to 2 mg intravenously (0.05 mg/kg). If no intravenous access is available, it can be given intramuscularly.

Atropine begins to resolve the symptoms of the poison and manifests signs of atropinization (if the poison is ingested in small amounts) in 1 to 4 minutes

after administration and peak effect is observed by 8 minutes; so, if there is no effect from the administered dose, than the administered dose can be doubled every 5 minutes until muscarinic findings subside. [16] Once the adequate atropine dose has been established, this dose should be adjusted to maintain a dry tracheobronchial tree for 24 hours.

The amount of atropine needed may be very large. In some cases, hundreds of milligrams of atropine may be quired. An atropine drip can be made by reconstituting into an infusion of dextrose 5 percent water (D5W) or normal saline. There is no specific concentration for the drip. Once atropinization has been achieved, atropine can be slowly withdrawn. [17]

Glycopyrolate (0.05 mg/kg I.V) may also be used to treat the peripheral muscarinic effects. It does not penetrate the CNS and will only treat peripheral findings. Scopolamine is useful where glycopyrolate falls short but it too has its short-comings. Other essential drugs that are part of mandatory treatment protocol and essential for resolution of nicotinic and central receptor symptoms, such as pralidoxime, are not discussed here, since it is outside the scope of this research.

CONCLUSION:

After careful consideration and deliberation on the obtained results, the use of a dosage regimen with the high pace of initial atropinization to halt the adverse effects seems to be the best choice. It shall help to considerably decrease the mortality owing to organophosphate poisoning. It addition to that, the use of a simple and easy to follow dosage regimen is more likely to be followed correctly.

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