“Effect of Magnesium Sulphate in Acute Organophosphorus Poisoning – a comparative interventional study”

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DISSERTATION SUBMITTED TO THE

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Under the Guidance Of

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LIST OF ABBREVIATIONS

Ach - acetylcholine

AchE - acetylcholinesterase

ANS - autonomic nervous system

BP – blood pressure

Ca+2 - calcium

CNS – central nervous system

DAMA – discharge against medical advice

DBP – diastolic blood pressure

DDT - dichlorodiphenyltrichloroethane

DFP -Diisopropyl fluorophosphate

ECG – electro cardio gram

e.g - example

g - grams

FFP – fresh frozen plasma

GI - gastrointestinal

HETP - Hexaethyl tetra phosphate

HDU – high dependency unit

HR – heart rate

Hrs - hours

ICU – intensive care unit

IV - intravenous

kg - kilogram

L1 – lumbar 1

MgSo4 - magnesium sulphate

Mg - magnesium

Min - minute

mL – milli litre

mm – milli meter

Na+ - sodium

NAC – N acetyl cysteine

NMDA - N-methyl-D-aspartate

NMJ – neuro muscular junction

NS – normal saline

NTE - neuropathic target esterase

OP - Organophosphorus

OPC - organophosphorus compound

OPCP – organophosphorus compound poisoning

OPIDP organophosphate- induced delayed polyneuropathy

OPWs - organophosphorus chemical weapons

PAM - pralidoxime

POP - Paradeniya Organophosphorus Poisoning

RBC – red blood cell

RBS – random blood sugar

RCT – randomized control trial

RFT – renal function test

S2, S3 and S4 – Sacral 2,3 and 4

SBP – systolic blood pressure

T1 – thoracic 1

TEPP - tetraethyl pyrophosphate

WHO – world health organization

^{o}C – centigrade

ABSTRACT

"Effect of Magnesium Sulphate in Acute Organophosphorus Poisoning – a comparative interventional study"

Introduction

Organophosphorus poisoning (OP) is the most common poisoning in India because of agriculture being the predominant occupation in rural India and also due to its easy availability. With an estimated 3 lakhs death each year, the incidence of poisoning is on a raise especially in rural southern India.

OPC binds irreversibly to acetylcholinesterase resulting in classical cholinergic symptoms. Standard management involves reducing the OPCs absorption by decontamination of skin and gastric lavage, and administration of atropine and oximes. Oximes are relatively expensive and ineffective once acetylcholinesterase has aged. In spite of this standard treatment the mortality remains high.

Hence there was a need to look in to the newer treatment modalities that would have an impact on the course of OP poisoning. One such agent being magnesium sulphate. Magnesium inhibits acetylcholine release through blocking ligand-gated calcium channels, resulting in reduced Ach release from the presynaptic nerve terminal. Thus improving function at NMJ and reduced activation3.

It decreases the arrhythmias associated with OPCP and atropine, in the central nervous system decreases overstimulation by OPCP, acting on the N-methyl-D-aspartate receptor, and reverses neuromuscular weakness in the peripheral nervous system. Thus an alternative or an adjunctive treatment that may alter acetylcholine release or protect the neuromuscular junction needs to be explored.

Objectives

- To establish the severity of acute organophosphorus poisoning.
- To Administer MgSO4 in intermittent bolus given according to clinical severity when presented within 24hrs of consumption.
- To look at morbidity and mortality pattern in patients receiving MgSO4.

- To compare the morbidity and mortality with patients not receiving MgSO4.

Material And Methods:

The study included 80 patients with alleged history of Organophosphorus compound consumption who presented to RLJ Hospital, Kolar attached to SDUAHER during February 2018 - June 2019 who satisfied the inclusion criteria & exclusion criteria.

Sampling procedure - Consecutive recruitment (total enumerative sampling) of study participants was used. Investigator attended casualty and ICU on respective days targeting to recruit sampled OP poisoning patients.

Patients were divided into two groups based on severity of poisoning using PoP scale.

Group 1 (Moderate poisoning were allotted to this group) (52 patients) – 26 cases received 4g of MgSO4 & 26 controls did not receive MgSO4.

Group 2 (Severe poisoning were allotted to this group) (28 patients) – 14 cases received 8g of MgSO4 & 14 controls did not receive MgSO4.

Primary outcomes measures which will be observed are atropine requirement per day, number of patients requiring intubation and mechanical ventilation, day of intubation, duration of mechanical ventilation, ICU stay, and mortality.

Results

In the study 26 (32.5%) of the study subjects received 4mg of MgSo4 and 14(17.5%) of them received 8mg of MgSo4. Controls were equally matched.

In moderate poisoning, Atropine requirement was lower in MgSo4 treated patients on all the days compared to those who didn't receive it. Where as the in severe poisoning the initial days atropine requirement only reduced and other days decrease was not significant. There was no reduction in the need of intubation and mechanical ventilation. In moderate poisoning the duration of hospital stay and HDU stay was less in patients receiving magnesium, as atropine requirement was less. There was no difference in ICU stay. However there was no difference in hospital stay and ICU stay in severe poisoning. There was no significant difference in mortality between groups.

Conclusions

Addition of MgSO4 to standard therapy has shown significant clinical improvement of moderate OPC poisoning by reducing the atropine & oxime requirement and its

side effects. Duration of hospital stay was reduced after MgSo4 administration. It does not however influence the need for intubation, duration of ICU stay, mechanical ventilation and mortality. The adverse side effects of MgSo4 were not noted with single dose of 4g of MgSo4.

However in severe poisoning, there is no influence of MgSo4 on primary outcomes like atropine & oxime requirement, hospital stay, need for intubation and mechanical ventilation, ICU stay and mortality.

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INTRODUCTION

INTRODUCTION:

Organophosphorus (OP) poisoning is the most common poisoning in rural southern India. India being a major agrarian country and OP is routinely used in farming. Acute OP pesticides poisoning is the most common and important cause of severe toxicity and death in the world despite treatment. More than 3 million people worldwide are exposed to organophosphates each year, with an estimate of 3 lakh deaths.(1) The organophosphate accounts for > 80% of pesticide-related hospitalizations.

According to WHO estimate, each year 8,49,000 people die globally from self-harm (Parasuicide). And the commonest form of fatal self-harm is poisoning in rural Asia, which accounts for over 60% of all deaths. This is of greater importance than hanging and other physical forms of self-harm. Around, 90% of the poisoning is suicidal, 8-10% accidental and <1% homicidal. The fatality rate of suicidal poisoning is >10% and accidental poisoning is < 1%. (2)

Unintentional and intentional OP poisoning is a significant cause of mortality & morbidity in India**.**

OP compounds are used as commercial insecticides, chemical warfare as nerve gas and are also applied as aerosols or dusts. Toxicity occurs due to household or occupational exposure, military or terrorist action, or iatrogenic mishap. They are rapidly absorbed by skin or mucous membrane or by inhalation.

OP compound irreversibly binds to acetylcholinesterase (AchE) which results in classical cholinergic symptoms. (3) Symptoms include increased salivation, lacrimation, diarrhea, nausea, vomiting, constricted pupils, sweating, fasiculations and confusion. The onset of symptoms is often within minutes, and it can take weeks to disappear.

The standard management is to reduce the OP compounds absorption by gastric lavage & decontamination of skin along with administration of atropine and oximes.(4)

Atropine competitively binds to muscarinic and nicotinic receptors and inhibits acetylcholine (Ach) accumulation. Oximes remove the phosphoryl group on

acetylcholinesterase and regenerates AchE activity that was inhibited by an organophosphate compound previously.

Early intervention with oximes before chemical "aging" between the organophosphate & cholinesterase enzyme has occurred decreases the incidence of the intermediate syndrome that is characterized by early or late neuromuscular weakness and altered consciousness with an incidence of 15–30%. (5)

The role of oximes is not well defined, as efficacy as well as safety of oximes in these settings is not established. (6,7) Oximes are relatively expensive and ineffective once acetylcholinesterase has aged.

Increased mortality in OPC poisoning may be due to the high toxicity of the compound, time gap to transfer the patient, paucity of health care personnel and lack of antidote.

Despite the standard treatment the mortality is high, being 33.3% especially among the patients on mechanical ventilation. This requires further research to look into other modalities of treatment with morbidity and mortality benefit.

Other then the conventional therapies, various treatments like clonidine, Vitamin E, Na+ bicarbonate, Fresh frozen plasma, Gacyclidine and magnesium sulfate ($MgSO_4$) are tried in combination with oximes and atropine.(8)

The mortality rate and hospitalization days of patients who received MgSO4 treatment were significantly lower than those who had not received MgSO4.(9)

Magnesium blocks the ligand-gated Ca+2 channels, which results in reduced Ach release from the presynaptic nerve terminal which reduces the activation and improves function at NMJ. (3)

It also reduces arrhythmias seen in OPCP & atropine administration and it decreases overstimulation by OPCP in the CNS, it also acts on the N-methyl-D-aspartate receptor, which reverses neuromuscular weakness in the peripheral nervous system. (6,10,11)

It has several additional therapeutic properties including muscle relaxation, which could control spasms and cardiovascular effects (e.g. vasodilatation, lowering of heart rate and a reduction of systemic catecholamine release).

Many studies have taken 4 g MgSo4, administered within the first 24 hours after admission. (9)

Only one study, a phase 2 trial used 4g, 8g, 12g, and 16g and showed benefit as the dose of mgso4 increased. (12) As it was a phase 2 study the results could not be generalized. Future studies to assess the efficacy and safety of mgso4 with increasing dose are needed.

Some studies have shown no mortality benefit of Mgso4 in OP poisoning, but they have reported decreased use of atropine and need for intubation.

Thus an alternative or an adjunctive treatment that may alter acetylcholine release or protect the neuromuscular junction needs to be explored.

Both increasing the dose of MgSO4 and frequent dose administration is required.

Hence their was a neccesicity to assess the beneficial role of mgso4 at doses 4 grams and 8 grams in Acute OP poisoning based on severity of OP poisoning.

AIMS & OBJECTIVES

AIM AND OBJECTIVES

2.1. Aim

To study the Effect of Magnesium Sulphate in Acute Organophosphorus Poisoning.

2.2. Objectives

- To establish the severity of acute organophosphorus poisoning.
- To Administer MgSO4 in intermittent bolus given according to clinical severity when presented within 24hrs of consumption.
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REVIEW OF LITERATURE

REVIEW OF LITERATURE

The history of OP poisoning and its toxic effect is known for more than a century. Despite treatment, mortality due to acute OP poisoning is high,(13) with no new standard therapies. There are 150 different types of OPs, even though their generalized structure is the same. Each OP compound has a unique presentation of toxicity and behavior.

For instance, death due to dichlorvos poisoning occurs very rapidly, while dimethoate toxicity takes several hours to develop,(14) even though both belong to the same OP class.

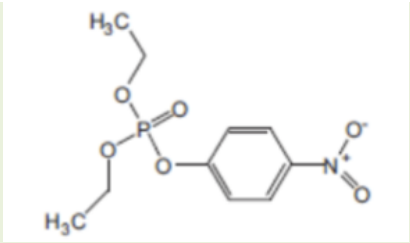
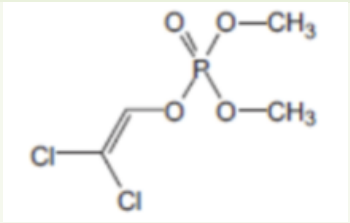
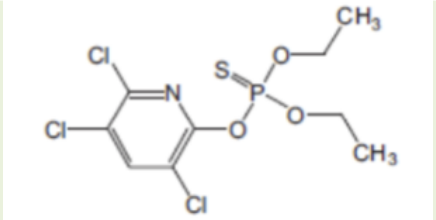
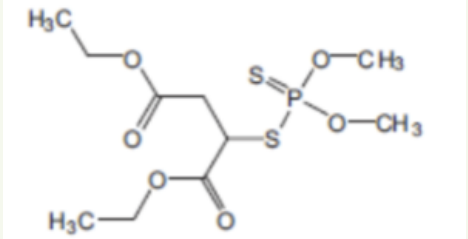
From the standpoint of chemistry, OP compounds comprise organophosphates, organophosphonates and organophosphinates, each of which is further divided into sub-groups.

- Insecticides– Dichlorvos, chlorpyrifos, Malathion, parathion, fenthion, diazinon, ethion.
- Nerve gases – Sarin, Soman, VX, tabun.
- Ophthalmic agents – Echothiophate.
- Antihelmintics – Trichlorfon
- Herbicides – Merphos, Tribufos (DEF).
- Industrial chemical (plasticizer) – Tricresyl phosphate.

Other classifications of OPs are based on the lethality of a compound.

According to the classification of the World Health Organisation (WHO),(15) Class Ia belongs to extremely toxic OPs, Ib is highly toxic, Class II comprises moderately toxic, whereas Class III consists of mildly toxic OP compounds. Besides, there are also deadly organophosphorus chemical weapons(OPWs), called nerve agents.

Table 1: Structure of OP compounds belonging to a different class

Organophosphorus compounds (WHO's hazardous level)	Structures
Paraoxon - ethyl **(Extremely hazardous; Class Ia)**	
Dichlorvos **(Highly hazardous; Class Ib)**	
Chlorpyrifos **(Moderately hazardous; Class II)**	
Malathion **(Slightly hazardous; Class III)**	

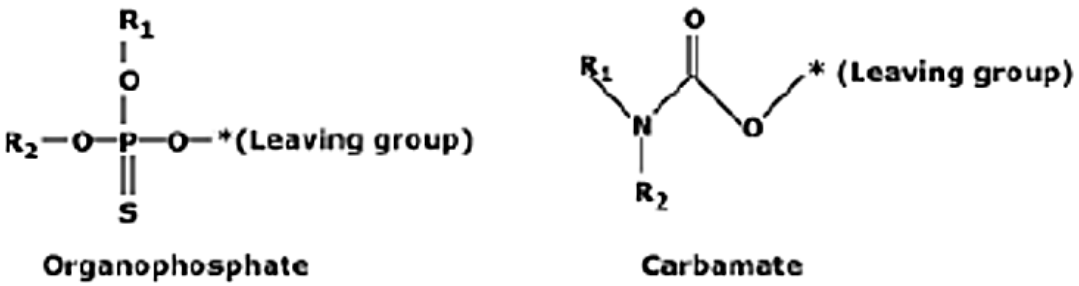
General structures of organophosphate (left) and carbamate (right) agents

The variable R1 and R2 groups are composed of either methyl (CH3) or ethyl (CH3CH2) moieties. The leaving group is generally an oxime or an aromatic group.

Figure 1 - Structure of organophosphate and carbamate:

The basic structure consists of phosphorus, which is bound to oxygen (O) by a double bond, R1and R2 may be alkyl, alkoxy, aryloxy, amido, mercaptan or other groups. “X” represents a conjugate base of a weak acid. This is found in cyanide, halide, phenoxy, thiocholine, thiocyanate or carboxylate group. (16)

Organophosphorus compounds inhibit enzyme acetylcholinesterase. The mechanism of inhibition of the enzyme is by reacting with the esteretic site on the acetylcholinesterase molecule. The bond formed between phosphorus atom and the esteratic site of the enzyme is stable and requires hours to weeks to reverse depending on the type of organophophorus compounds. The Phosphorylated enzyme is inhibited because of the occupation of its active site. It is not capable of carrying out its normal function of hydrolyzing acetylcholine. (17)

The effect of OP compound poisoning is therefore the result of continuing increased production of acetylcholine at the neuromuscular junctions resulting in a depolarization block.(18)

The phosphorylated enzyme undergoes either spontaneous hydrolysis or dealkylation. Due to spontaneous hydrolysis active enzyme cholinesterase is released and this is reactivation. Once dealkylation of phosphorylated enzyme occurs, reactivation is impossible. This process is called “ageing”.(19)

Once ageing occurs recovery of cholinesterase activity depends on the synthesis of a new enzyme by the liver which may take days or weeks.

Hence the three independent reactions determine the speed of onset and severity of poisoning –

1. Phosphorylation of cholinesterase by organophosphorus compounds.
2. Reactivation.
3. Ageing.

OP compounds are divided into two series of compounds, alkyl phosphates (direct inhibitors) like malathion, and arylphosphates (indirect inhibitors) like parathion. Direct inhibitors of acetylcholinesterase poisoning present in acute cholinergic crisis, they usually do not develop late type muscular weakness and response to atropine is rapid.

Table 2 - Broad classification of insecticide: (20)

Organochlorine compounds	Oranophosphorous compounds	Carbamates
Methoxychlor	Malathion	Carbaryl
DDT	Chlorthion	Propoxur
Lindane	Ronnel	Dimetilan
Chloride	Trichlorfos	Pyrolan
Heptochlor	Fenthion	
Dieldrin	Dichlorvos	
Aldrin	Dimethoate	
	Chlorpyrifos	**Synthetic**
	Parathion, methyl parathion	Pyrethroids
	Diazinon, Dioxathion	

Organophosphorous compound classification: (21)

- Older but most commonly used classification:
    - Alkyl phospates - TEPP, HETP, Malathion, systox ,DFP etc.
    - Aryl phosphates - Parathion, Chlorothios,Diazinon, Demeton etc.

- The Classification proposed by Holmstedt which is of pharmacological and toxicological interest where compounds are divided into 5 depending on different X in the structure of the OP compound.(22)

    - Group A
        - X-halogen, cyanide and thiocyanate
        - SOMAN, SARIN, DFP

    - Group B
        - X-Alkyl, alkoxy, aryloxy
        - Forstenon,Pyrazoxon

    - Group C
        - X-Thiol or Thiophosphorous compound
        - Parathion, Malathion, Azethion, Diazinon, Systox and
        - Demeton

    - Group D
        - Pyrophosphates and related compounds
        - TEPP

    - Group E
        - Quaternary Ammonium Compound
        - Phospholin

Based on grades of toxicity and use: (23,24)

Table 3 - Highly toxic- Used as agricultural pesticides

Insecticide	LD_{50} (mg/kg)	
	Oral	Dermal
1) TEPP	1.1	2.4
2) Mevinphos	3.7	
3) Chlorpyrifos	8	
4) Ethyl parathion	13	21
5) Methyl parathion	14	67
6) Fenthion	15	

Table 4 -Moderately toxic- Used as animal insecticides

Insecticide	LD_{50} (mg/kg)	
	Oral	Dermal
1) Leptophos	53	
2) Diohtorvos	80	107
3) Trichlorfon	630	>2,000
4) Ronnel	1,250	>4,000
5) Malathion	1.375	>4,444
6) Temophos	2000	>4,000

Table 5 - Low toxicity- Used for field sprays

Insecticide
1) Diazinon
2) Malathion
3) Dichlorvos

ROUTES OF OPC:

1. Inhalation: Airborne inhalation of pesticides while applying to plants as well as pets or household surfaces,carpets in less ventilated areas.
2. Ingestion: Eating of fruits and vegetables without washing that has treated with pesticides.
3. Drinking water from containers contaminated with discarded poison.
4. Absorption: unwashed hands after handling pesticides.

PHARMACOKINETICS:

Most organophosphorus compounds highly lipid soluble and are rapidly and well absorbed from the skin, mucous membrane, conjunctiva, gastrointestinal tract and lungs. They are rapidly distributed to all body tissues. The highest concentrations are found in the liver and kidney. These chemicals are detoxified by cytochromeP450 mediated mono-oxygenases in liver. But some metabolites are more toxic than parent compounds as conversion of parathion, diazinon & malathion to oxons.

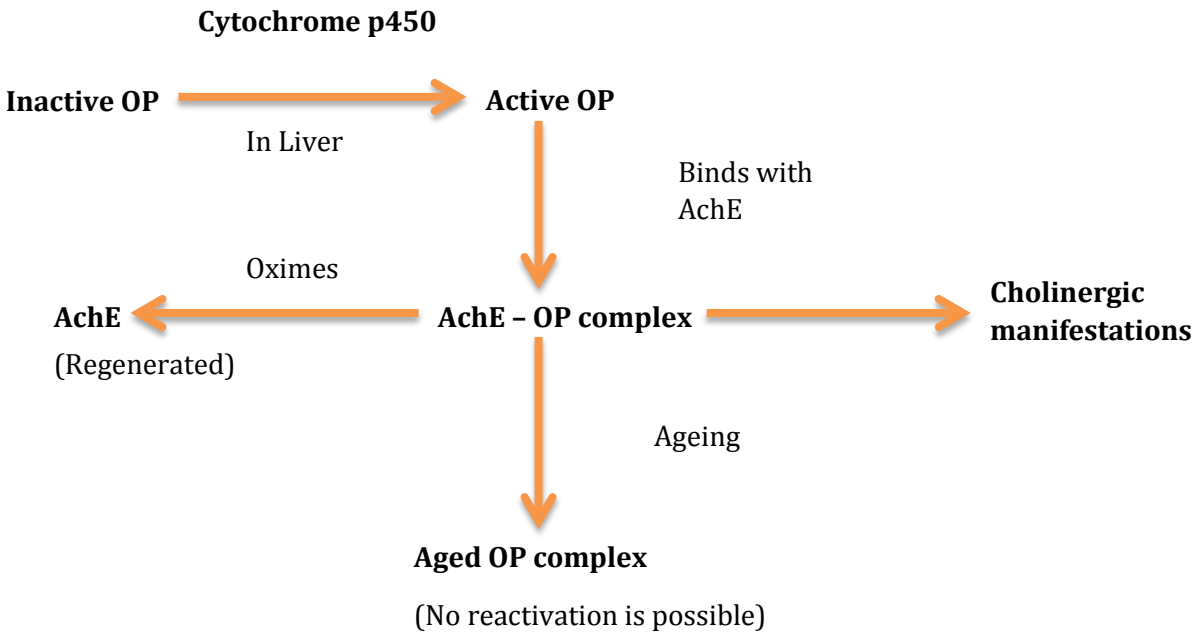


Figure 2 : Mechanism of OPC (25)

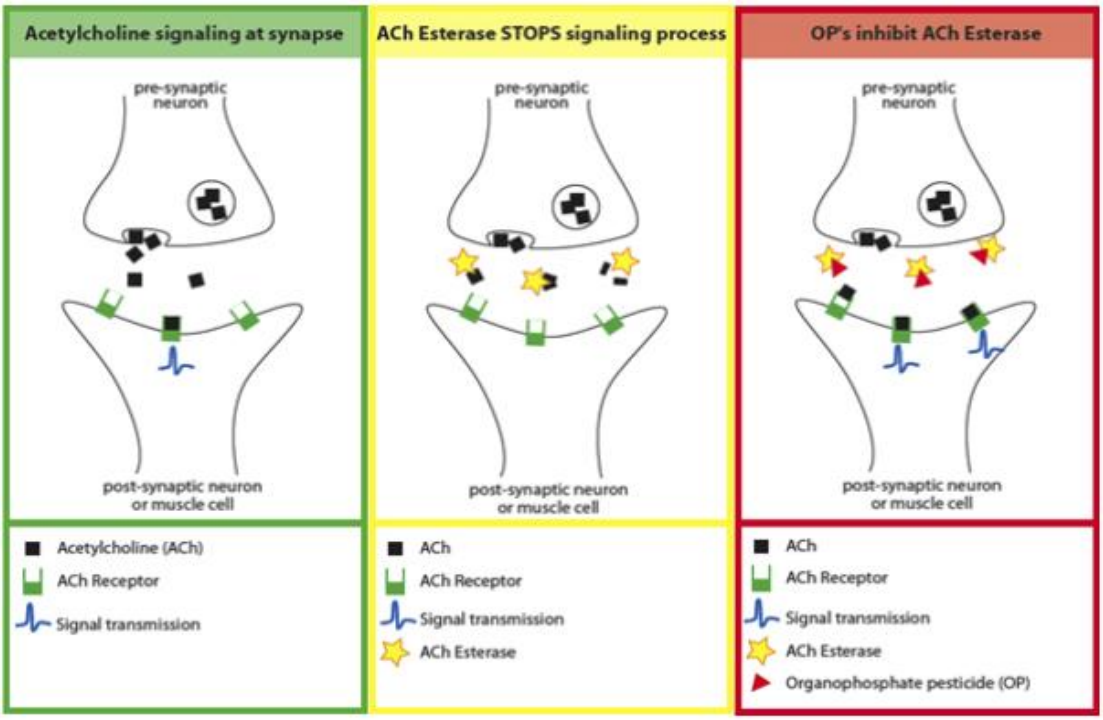


Figure 3 – mechanism of OP poisoning (25)

Anatomy of the autonomic nervous system

The **autonomic nervous system** (**ANS**) controls and regulates bodily functions unconsciously.

It also supplies the glands and smooth muscles that influence the function of internal organs.

The ANS has two main divisions:

1. Sympathetic (thoracolumbar)
    - Spinal cord - T1 – L1
    - Pre - vertebral ganglia - coeliac and hypogastric
2. Parasympathetic (cranio-sacral)
    - From the central nervous system – III, VII, IX, X cranial nerves.
    - Spinal cord – S2, S3 and S4 nerves

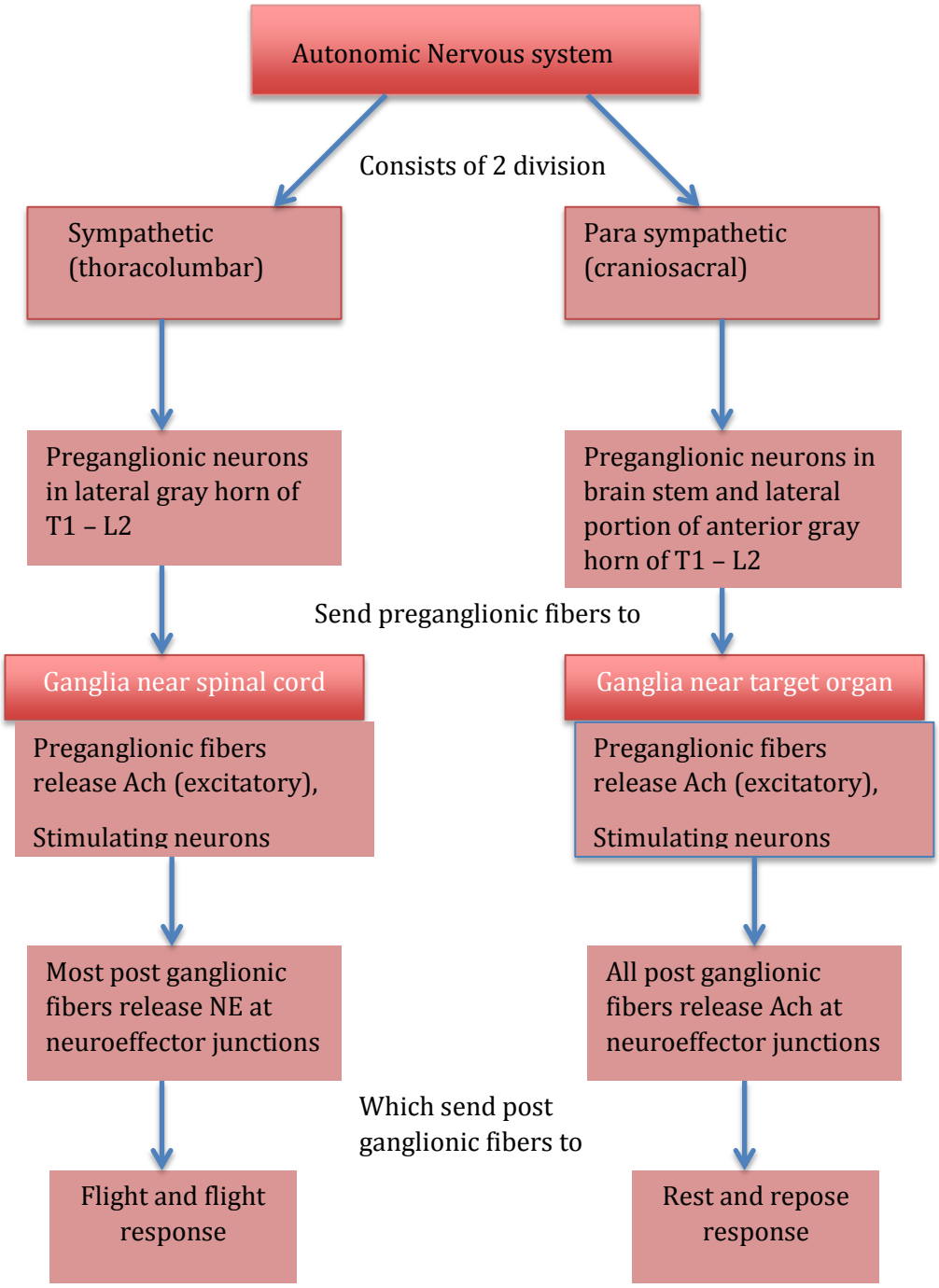


Figure 4 - Components and Anatomic Subdivisions of the ANS (26)

When the autonomic nervous system receives information about the body, it responds by

- Stimulating body processes → sympathetic division
- Inhibiting body processes → parasympathetic division.

An autonomic nerve pathway has two nerve cells. One cell is in either the brain stem or spinal cord. And another one is in the autonomic ganglion. Nerve fibers from these ganglia supply the internal organs. Sympathetic ganglia are just outside the spinal cord on either side. And parasympathetic ganglia are located near or in the effector organ.

The ANS controls:

- Blood pressure.
- Heart rate and respiratory rate.
- Body temperature.
- Digestion.
- Metabolism →affecting body weight.
- Electrolyte and water balance (sodium and calcium)
- Body fluids production (saliva, sweat, and tears)
- Urination
- Defecation
- Sexual response

Primarily control of an organ is either by the sympathetic or the parasympathetic division. The two divisions sometimes the have opposite effect. Example - the sympathetic division increases blood pressure, and the parasympathetic division decreases it. In short, the two divisions coordinate and work together to ensure that the body responds appropriately in different situations.

Generally, the **sympathetic division** does the following:

- Prepares the body for stressful or emergencies —fight or flight

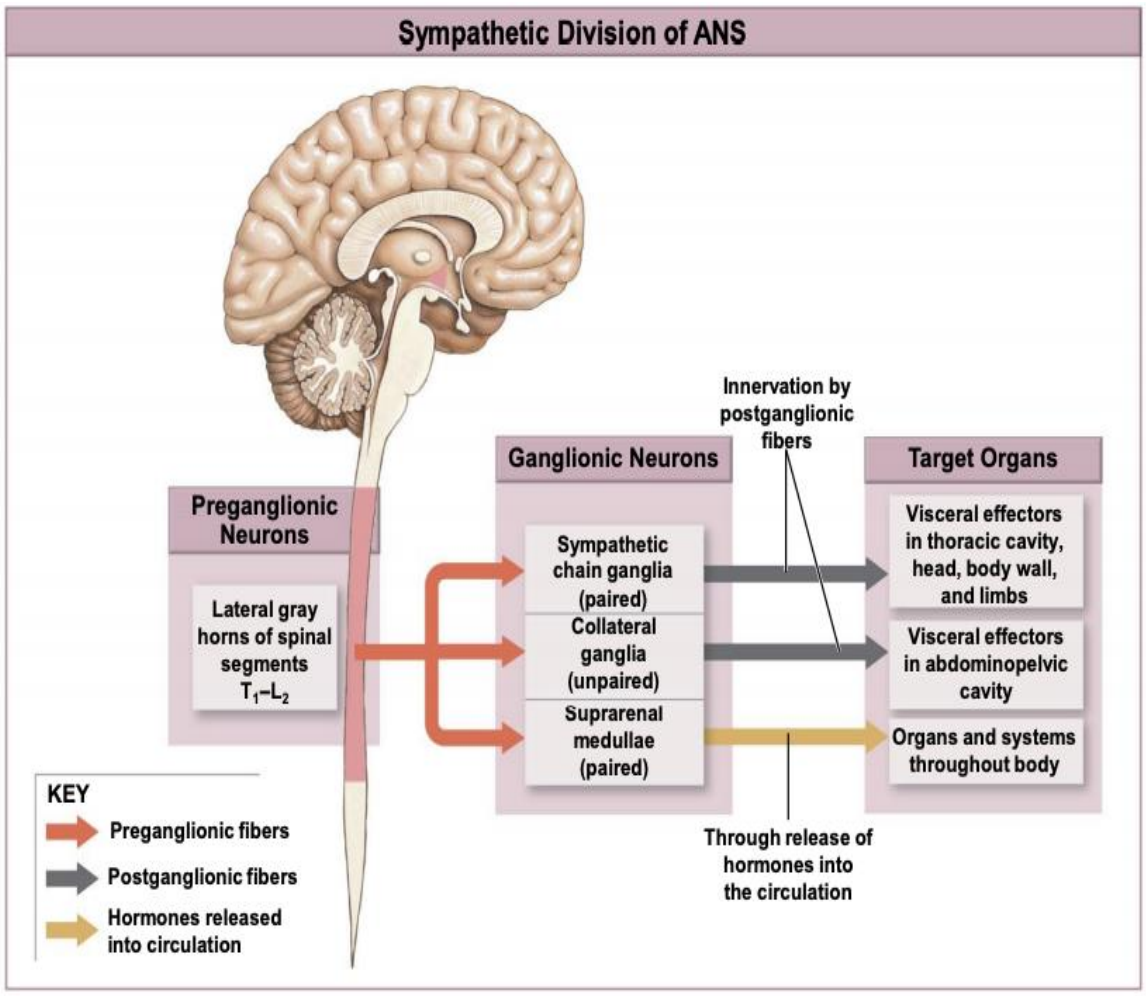


Figure 5 - Organization of the Sympathetic Division of the ANS (26)

Sympathetic system increases the heart rate & force of contractions and dilates airway to make breathing easier. It releases stored energy. Muscular strength is increased. Palms sweat, pupils dilate and piloerection occurs. Other body processes such as digestion that are less important in emergencies are slowed down.

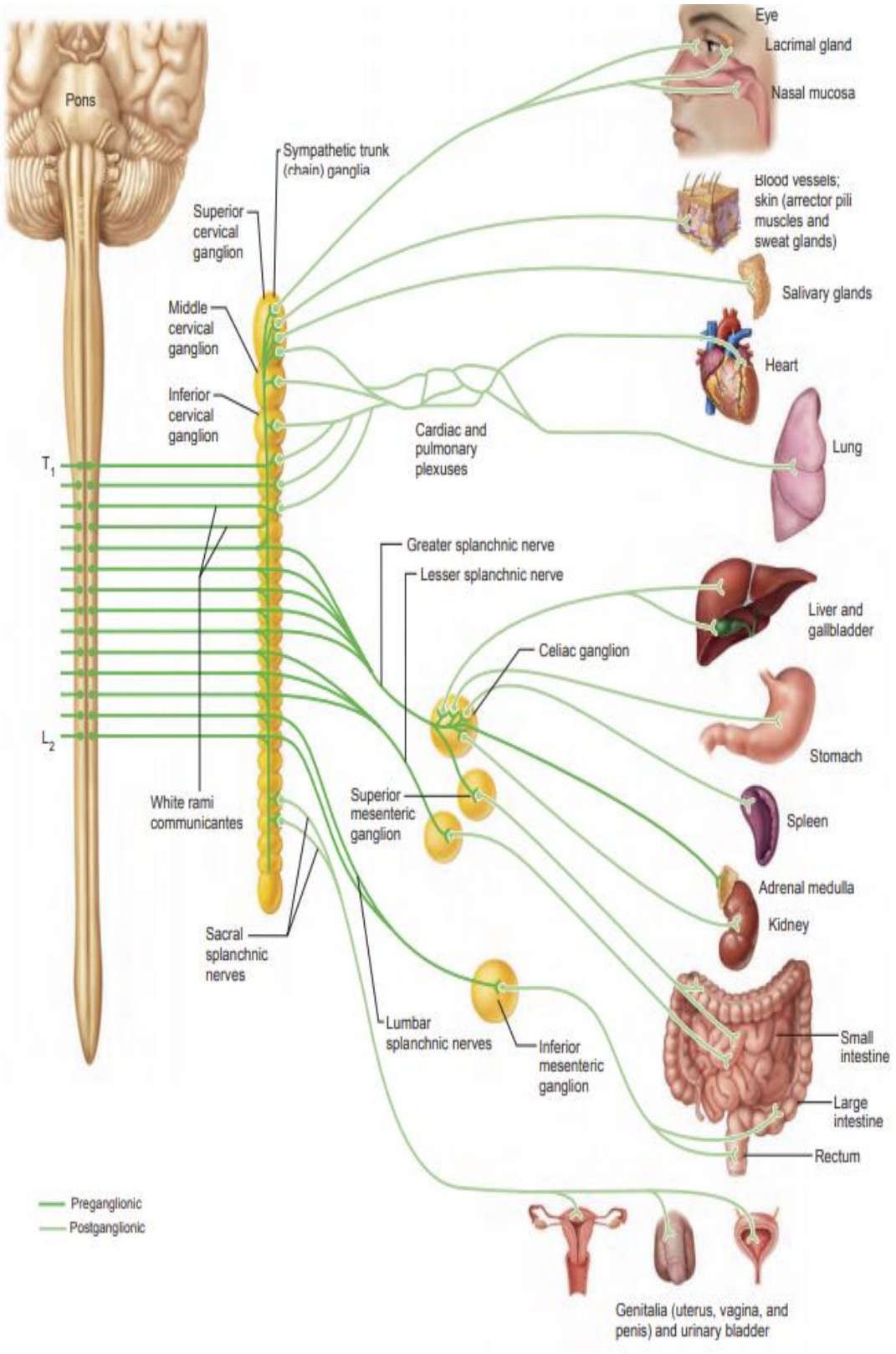


Figure 6 - Sympathetic division of the ANS. (27)

The **parasympathetic division** does the following:

- Control body processes during ordinary situations.

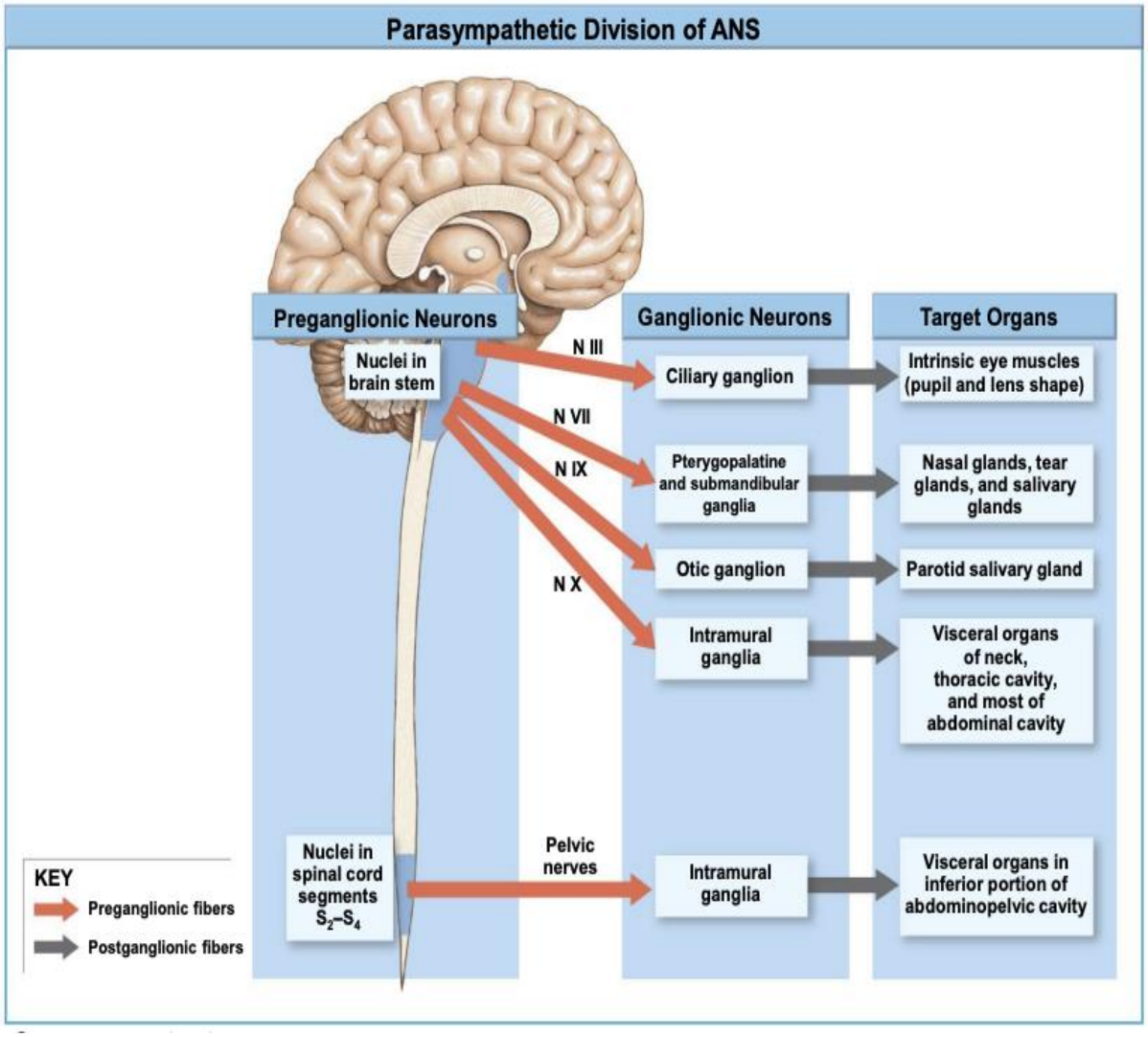


Figure 7 - Organization of the Parasympathetic Division of the ANS (26)

The Parasympathetic system on the other hand, conserves and restores. It slows down the body processes and decreases the heart rate and blood pressure. It also stimulates the digestive tract to process food and eliminates waste. Energy processed is used to restore and build tissues.

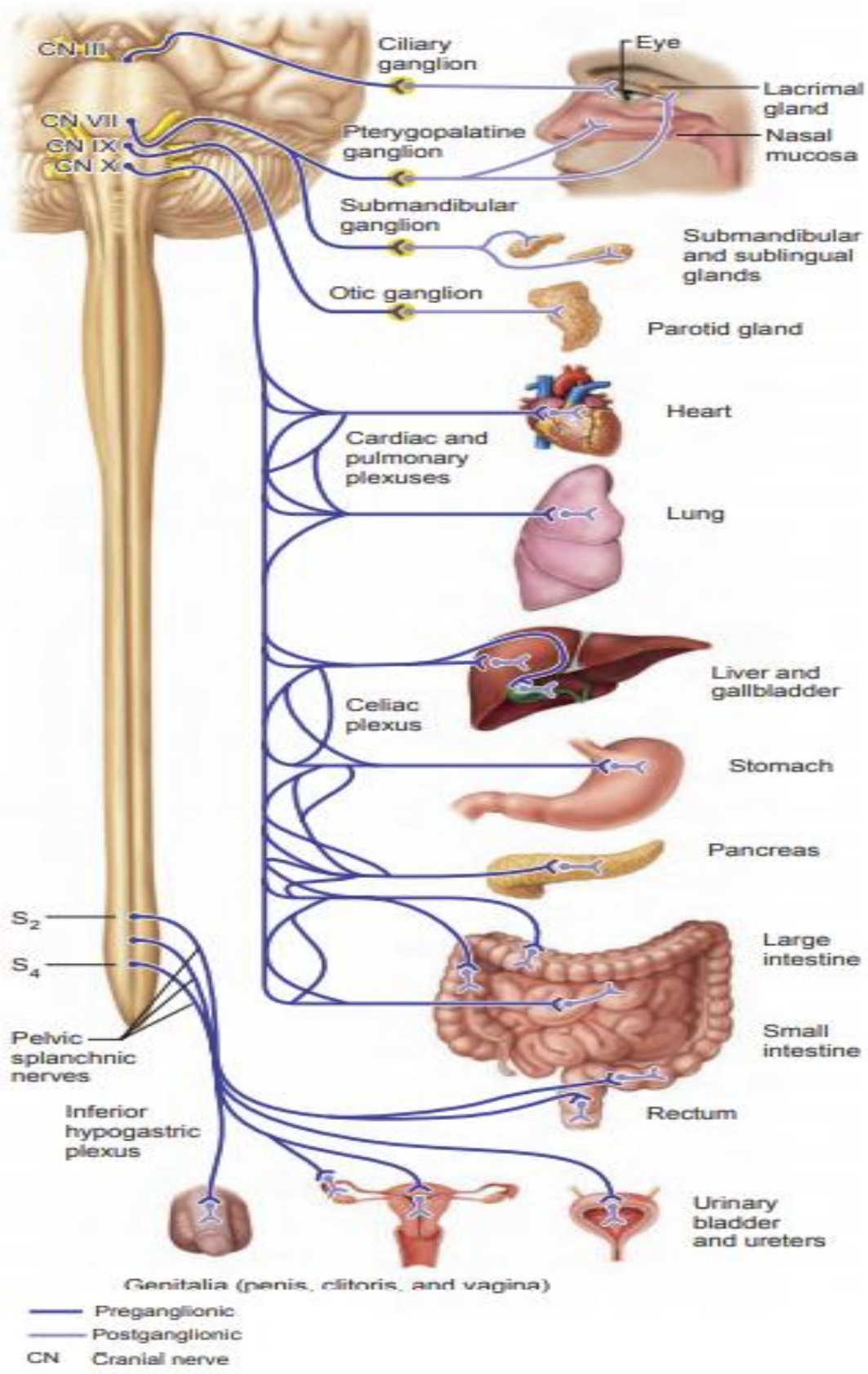


Figure 8 - Parasympathetic division of the ANS. (27)

Neurotransmitters in the ANS:

- Acetylcholine
- Norepinephrine

Nerve fibers that release acetylcholine are called cholinergic fibers. And fibers that release norepinephrine are called adrenergic fibers. Usually, acetylcholine has parasympathetic (inhibiting) effects and norepinephrine has sympathetic (stimulating) effects. However, acetylcholine has some sympathetic effects. For example, it sometimes stimulates sweating or piloerection.

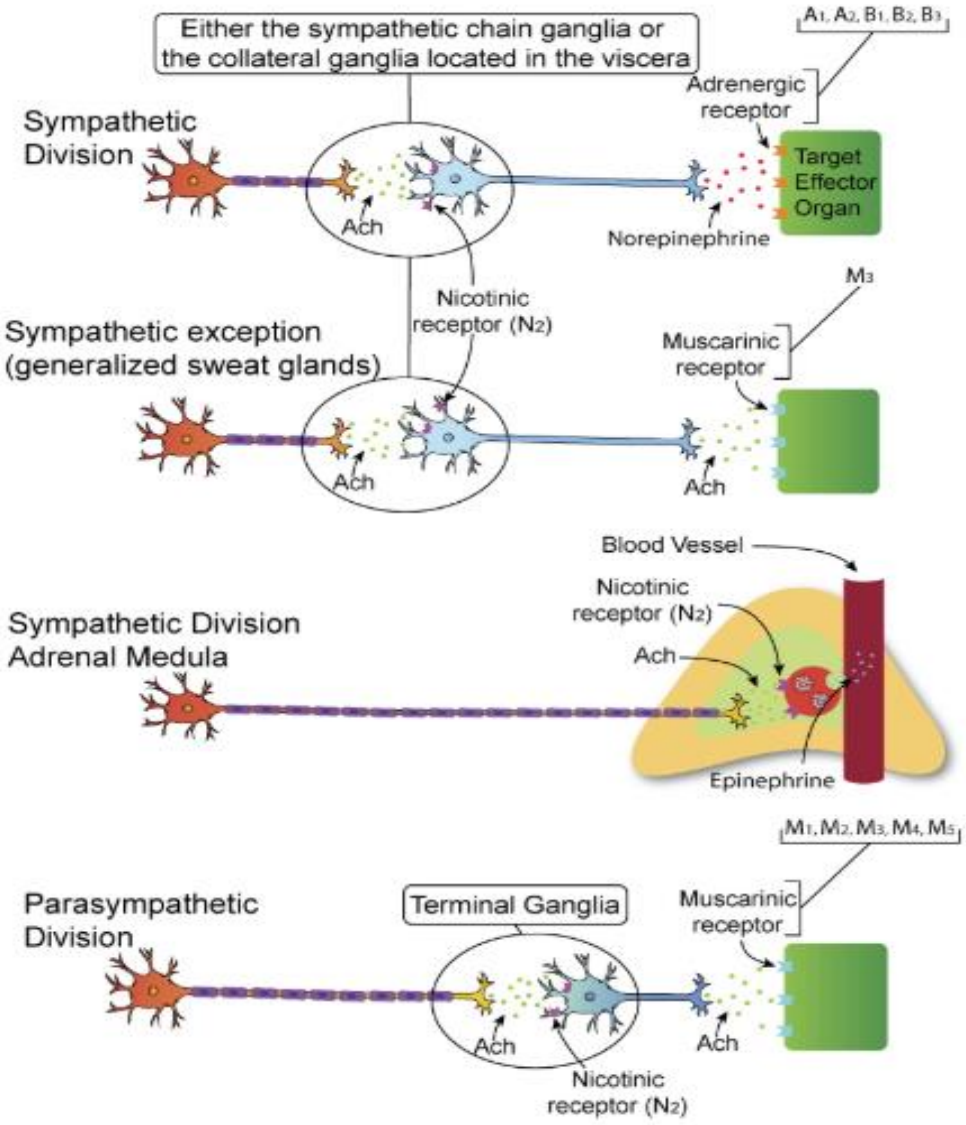


Figure 9 - Acetylcholine at different receptors

Cholinoceptors:

Two classes of receptors for Ach are recognized.

➢ MUSCARINIC RECEPTORS- (G protein-coupled receptor) These are stimulated by muscarine and blocked by atropine. They are located primarily on autonomic effector cells in the heart, blood vessels, smooth muscles, eye and glands of respiratory, gastrointestinal and urinary tracts, sweat glands etc.,and in the CNS. subtypes-M1 to M5.

➢ NICOTINIC RECEPTORS- (ligand-gated) These are activated by nicotine and blocked by tubocurarine or hexamethonium.

Types-NM, NN

NM-located at the skeletal muscle endplate. They mediate contraction of the skeletal muscle.

NN-present on ganglion cells, adrenal medullary cells, brain & spinal cord.

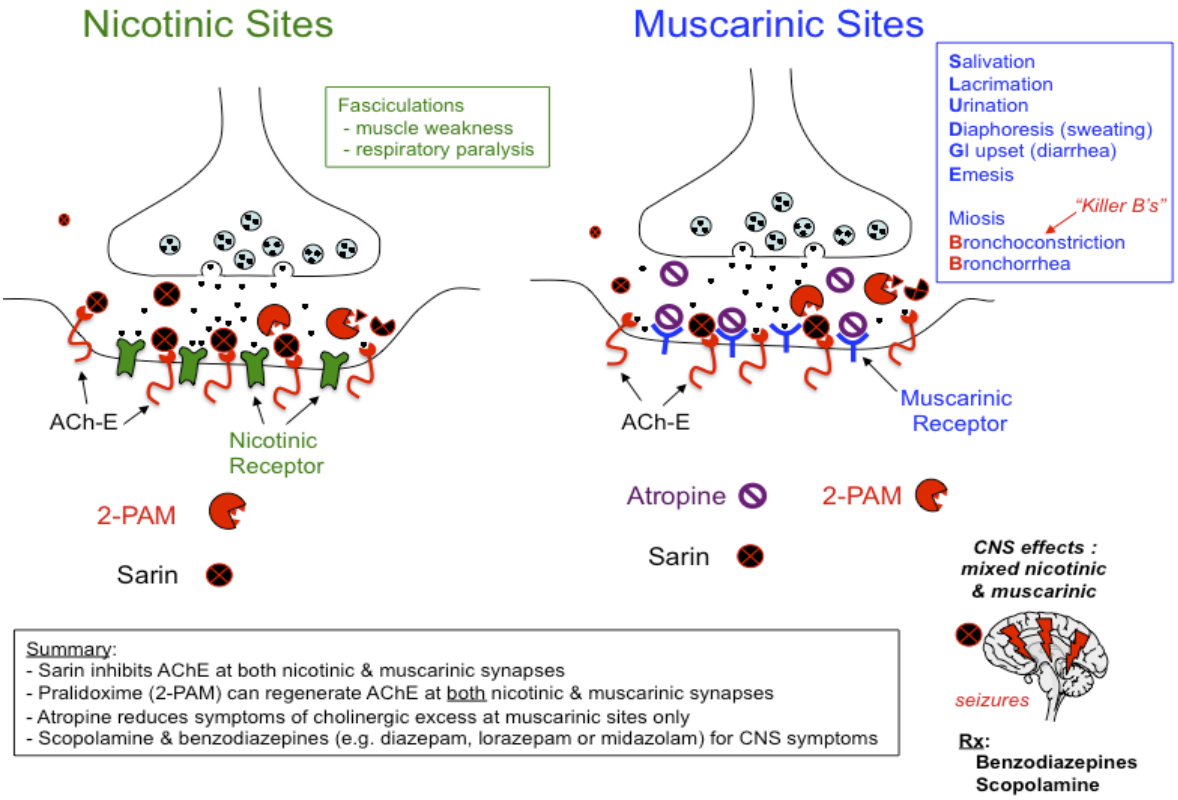


Figure 10 – Cholinoceptors

Table 6 - Cholinergic and Adrenergic Receptors (28)

Cholinergic and Adrenergic Receptors			
Neuro Transmitter	Receptor type	Major locations	Effect of binding
Acetylcholine	Cholinergic		
	Nicotinic	All ganglionic neurons; adrenal medullary cells and neuromuscular junctions of skeletal muscle.	Excitation
	Muscarinic	All parasympathetic organs	Excitation mostly, inhibition of cardiac muscle
		Some sympathetic targets: • Eccrine sweat glands • Blood vessels in skeletal muscles	Activation Vasodilation
Norepinephrine (and epinephrine released by adrenal medulla)	Adrenergic		
	β1	Heart, kidney and adipose tissue	Increases heart rate and stimulates renin release by kidneys
	β2	Lungs blood vessels supplying the heart, liver and skeletal muscle	Inhibitory→ dilates blood vessels and bronchioles; relaxes smooth muscle walls of the urinary, uterus, digestive, & visceral organs.
	β3	Adipose tissue	Stimulates lipolysis in fat cells
	α1	Blood vessels sympathetic organs except for the heart	Constricts blood vessels and visceral organ sphincters; dilates pupils of the eyes
	α2	The membrane of adrenergic axon terminals; pancreas; blood platelets	Inhibits NE release from adrenergic terminals; inhibits insulin secretion promotes blood clotting

Specific features of ANS:

1. It supplies all the organs.
2. The distal most synapse located outside in the ganglia.
3. Preganglionic are myelinated and postganglionic are non- myelinated.
4. It has peripheral plexus formation.
5. The efferent neurotransmitter is Ach, Noradrenaline
6. There is no denervation atrophy after nerve section in ANS.

Control of Autonomic Functioning

Although the ANS is not usually considered to be under voluntary control, its activity is regulated by CNS controls in the spinal cord, brain stem, hypothalamus, and cerebral cortex. Hypothalamus controls lower CNS centers. Although the cerebral cortex may modify the workings of the ANS, it does so at the subconscious level and by acting through limbic system structures on hypothalamic centers.

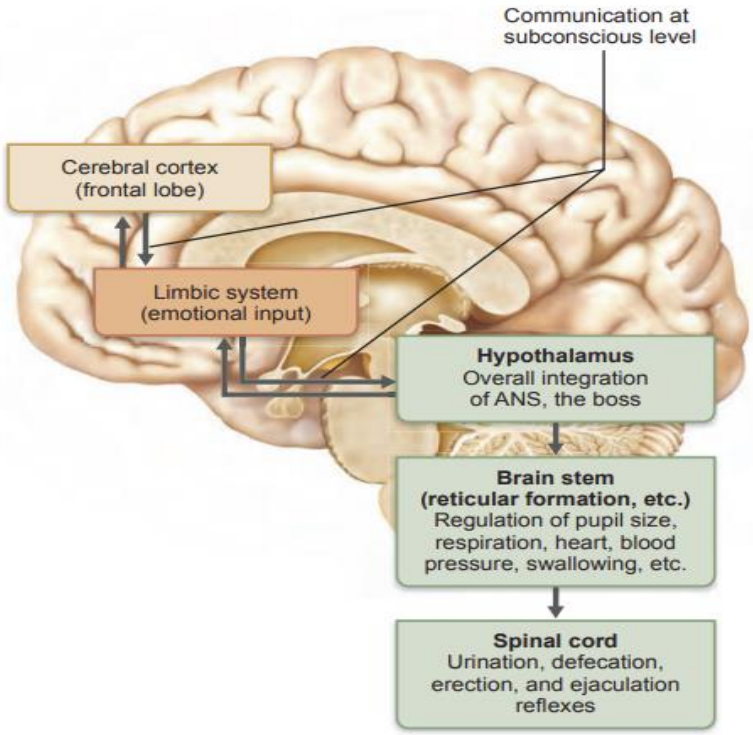
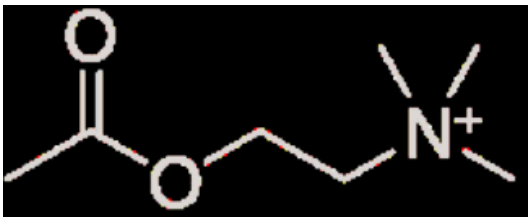


Figure 11- Levels of ANS control.

The hypothalamus stands at the top of the control hierarchy as the integrator of ANS activity, but it is influenced by subconscious cerebral inputs via limbic system connections. (28)

ACETYLCHOLINE: (29)



Acetylcholine (Ach), first synthesized by BAYER in 1867, is a neurotransmitter. It was first recognized as a potent pharmacological substance by HUNT in 1906.(20)

The various stages of acetylcholine formation and release at neuromuscular junction occur as follows.

1. Golgi apparatus forms small vesicles measuring about 40 nm in the cell body of the motor neuron at the spinal cord.
2. These vesicles are transported through the core of the axon from the central body of spinal cord to neuromuscular junction by a method called "streaming".The number of vesicles at the nerve terminals is about 3,00,000 at a single skeletal muscle endplate.

Acetylcholine is synthesized in the cytosol of the terminal nerve fibers and then transported through membranes of the vesicles to their interior, where it is stored in highly concentrated form with about 10,000 molecules of acetylcholine in each vesicle.

Neuromuscular Junction

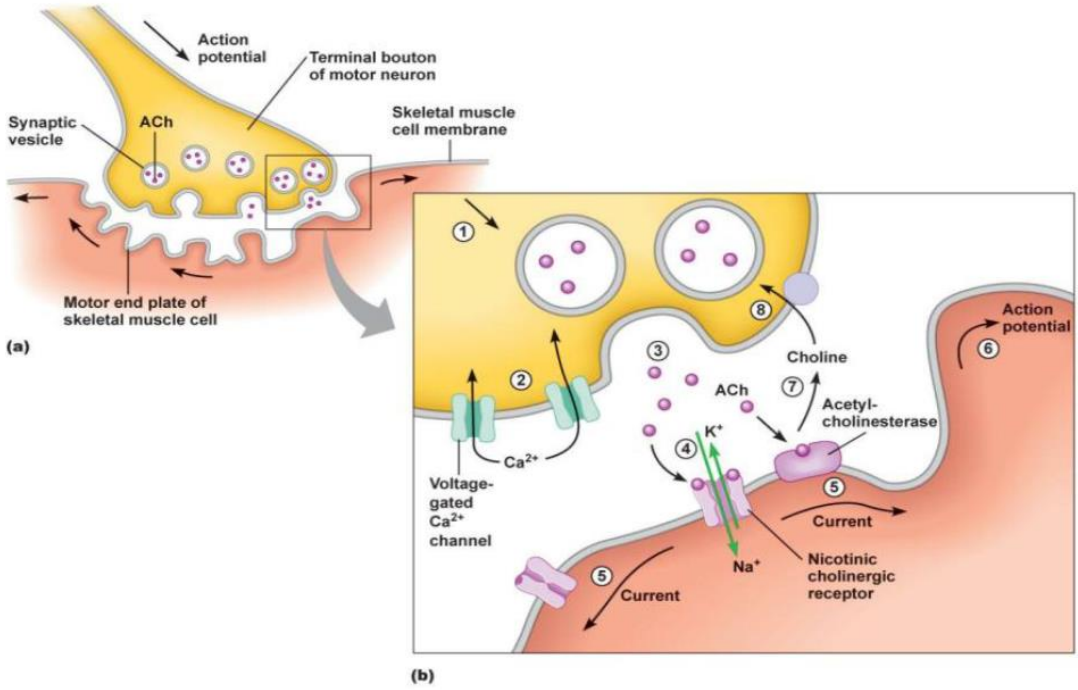


Figure 12. : Neuromuscular Junction

The neuromuscular junction (NMJ) is a synapse that develops between a motor neuron and a muscle fiber and is made up of several components: the presynaptic nerve terminal, the postsynaptic muscle membrane, and the intervening cleft (or gap). The vertebrate NMJ is the focal point of contact where motor neurons transmit impulses to skeletal muscle fibers in a 1:1 ratio. NMJ functions as an impedance adapter between the motor neuron (high impedance) and the muscle fiber (low impedance).

The integrity of neuromuscular transmission is dependent on a highly orchestrated mechanism involving:

1) Synthesis, storage, and release of acetylcholine (ACh) from motor nerve endings (presynaptic region) at the NMJ, and ACh reuptake into the nerve terminal. (30)
2) Binding of ACh to nicotinic receptors on the muscle membrane (postsynaptic region) and generation of action potentials.
3) Rapid hydrolysis of ACh by the enzyme acetylcholinesterase.

SYNTHESIS, STORAGE AND RELEASE OF ACETYLCHOLINE: (30,31,32)

When a nerve impulse reaches the nerve terminal, it opens many calcium channels at the nerve terminal causing the release of acetyl choline into the synaptic space. On average 125 vesicles are ruptured with each action potential.

Duration of acetylcholine is curtailed since it is hydrolyzed by the enzyme acetylcholinesterase, which is bound in collagen and glycosaminoglycans in the local connective tissue. The choline is reabsorbed actively into the neural terminal to be reused in forming new acetylcholine.

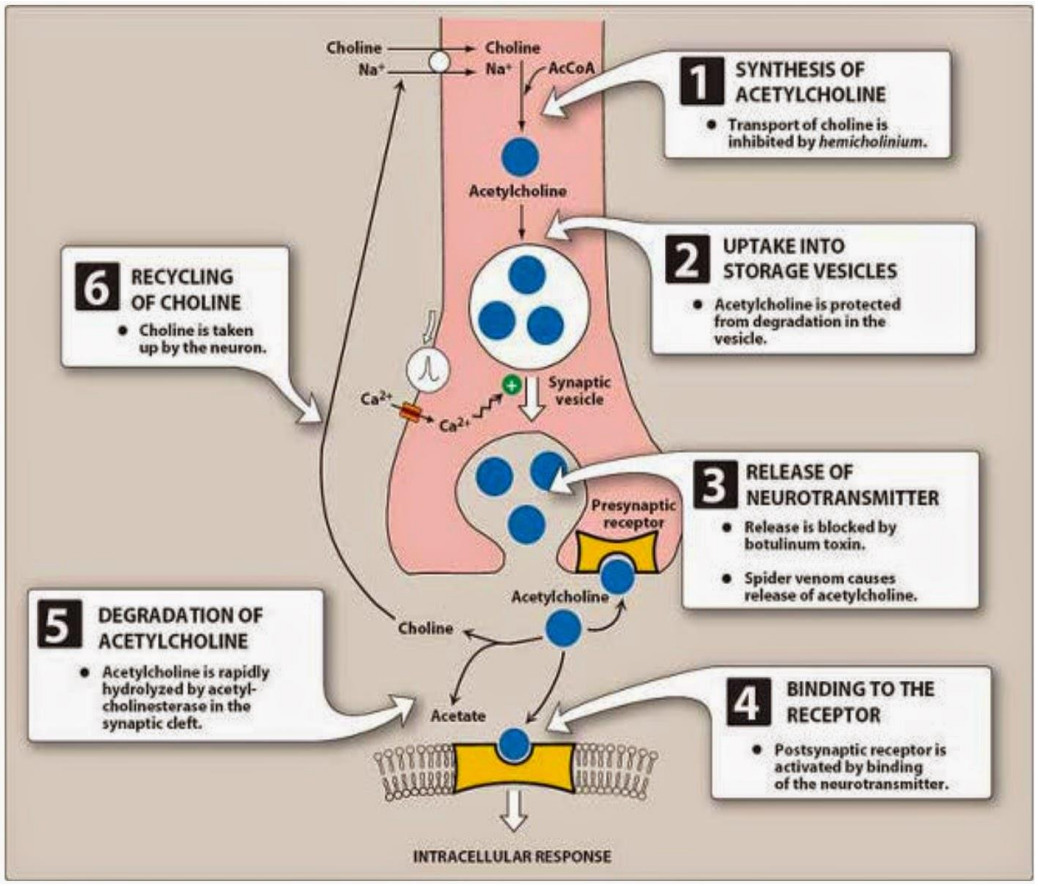


Figure 13 – Synthesis & Degradation of Ach

Once its function in the synapse is over, synaptic acetylcholine esterase breaks it back down into acetate anions and choline. This hydrolysis takes less than a millisecond. The acetate goes back into the Krebs cycle and the choline is taken back presynaptically. This reuptake is the rate-limiting step in acetylcholine synthesis. (30,31,32)

ACETYLCHOLINESTERASE(AChE):

History of Acetylcholinesterase(AChE):

In 1968, Walo Leuzinger et al from Columbia University, NY first purified and crystallized acetylcholinesterase.

Ach is present in three forms:

Brain acetylcholinesterase:

Brain ach is like RBC esterase. In the brain, it is a tetramer (G4) form & monomer (G1) form.

RBC acetylcholinesterase

- Specific or true acetylcholinesterase
- Red cell, nervous tissue, skeletal muscle.

Plasma acetylcholinesterase

- Butryl or Pseudo cholinesterase
- Plasma, liver, heart, pancreas, brain

Table 7 - Causes of cholinesterase level abnormalities:

Abnormalities	RBC cholinesterase	SERUM cholinesterase
Low level	1. Antimalarial drugs 2. Oral contraceptives 3. Anemias mainly pernicious anemia	1. Acute infections 2. Benzalkonium salts 3. Carbon disulphide 4. Chronic disease 5. Codeine, cocaine 6. Dermatomyositis 7. Morphine, malnutrition 8. Pregnancy, pills

AchE is a protein which is attached to the basement membrane of the muscle, motor end plates and the nerve terminal. Each molecule of the enzyme can bind and hydrolyze several molecules of acetylcholine.

The biological effects of OP is due to the accumulation of endogenous acetylcholine at sites of cholinergic transmission. Ion binding is by which enzyme AChE is inhibited, but eventually progressively phosphorylated by covalent bonding a process normally takes 24-48 hrs. This process is called "Ageing" and this period is known as the "critical interval" because during this time administration of antidote is still effective in reversing the process. Once ageing is completed the enzyme cannot be reactivated.

Plasma AChE recovers quickly within 4 weeks. Red cell AChE takes longer and may not be restored. Affected AChE recovers at the rate of 1% per day. Restoration of AChE activity occurs by slow denovo synthesis of free enzyme and also to some extent as a result of spontaneous dephosphorylation of the inhibited enzyme.

The inactivation (phosphorylation) and reactivation (dephosphorylation) vary considerably with different OP compounds, which account for differences in toxicity. Ageing is important to assess toxicity and treatment outcome. Oximes cannot reactivate aged phosphorylated enzyme.

Changes in acetylcholinesterase levels during poisoning and treatment:

Serum cholinesterase inhibition depends on the concentration of the inhibitor, as this is subject to continuous unknown fluctuations and it is not possible to predict the time course of inhibition. Enzyme inhibition will proceed until a steady state is reached and spontaneous reactivation is achieved.

True cholinesterase activity is restored instantly and completely which is long lasting, but that of serum cholinesterase is transient and variable after oximes. The oximes restore true acetylcholinesterase activity & relieves symptoms. True cholinesterase level indicates effectiveness and serum cholinesterase levels indicate the prior presence of cholinesterase inhibitor.(33,34)

Time of ingestion & relation to serum cholinesterase activity: the longer time of ingestion lower is serum cholinesterase activity. It case of doubtful ingestion or bizarre clinical presentation or if more than one poisonous substance is ingested, the estimation of serum cholinesterase activity is important for diagnosis.

Serum cholinesterase is reduced in acute myocardial infarction, liver diseases and dermatomyositis. Nephrotic syndrome patients have increased levels of serum cholinesterase.

Disadvantages of serum cholinesterase estimation:

True cholinesterase levels indicate effectiveness of the oxime therapy and pseudocholinesterase levels indicate the presence of cholinesterase inhibitor priorly. Hence pseudocholine esterase is not used to assess the effect of oxime therapy.

The level of AchE in the blood is not constant but continuously changes as the enzyme inhibition & spontaneous reactivation takes place simultaneously

OPC inhibits AchE in synapses and on RBC membranes & pseudocholinesterase in plasma. (35) Although no clinical features are seen on inhibition of pseudocholinesterase, inhibition of AchE results leads to Ach accumulation and overstimulation of Ach receptors. (35)

Table 8 – Difference between acetylcholinesterase and butyrlcholinesterase.

Features	Acetylcholinesterase	Butyrylcholinesterase
1. Distribution	All cholinergic sites, RBC, grey matter	Plasma, liver, intestine, white matter
2. Hydrolysis Ach	Very fast (micro seconds)	Slow
3. Inhibition	Sensitive to physostigmine	Sensitive to OP
4. Function	Termination of Ach action	Hydrolysis of esters
5. Structure	Tetramer	Tetramer, 342 KD weight
6. Half life		12 days
7. Carbohydrate content	16%	24%

CLINICAL FEATURES

The clinical features depend upon the end points where sustained cholinergic stimulation takes place namely

a. Post ganglionic parasympathetic hollow end organ (muscarinic)
b. Sympathetic and parasympathetic ganglionic and somatic neuro muscular junction (nicotinic)
c. Central nervous system affection

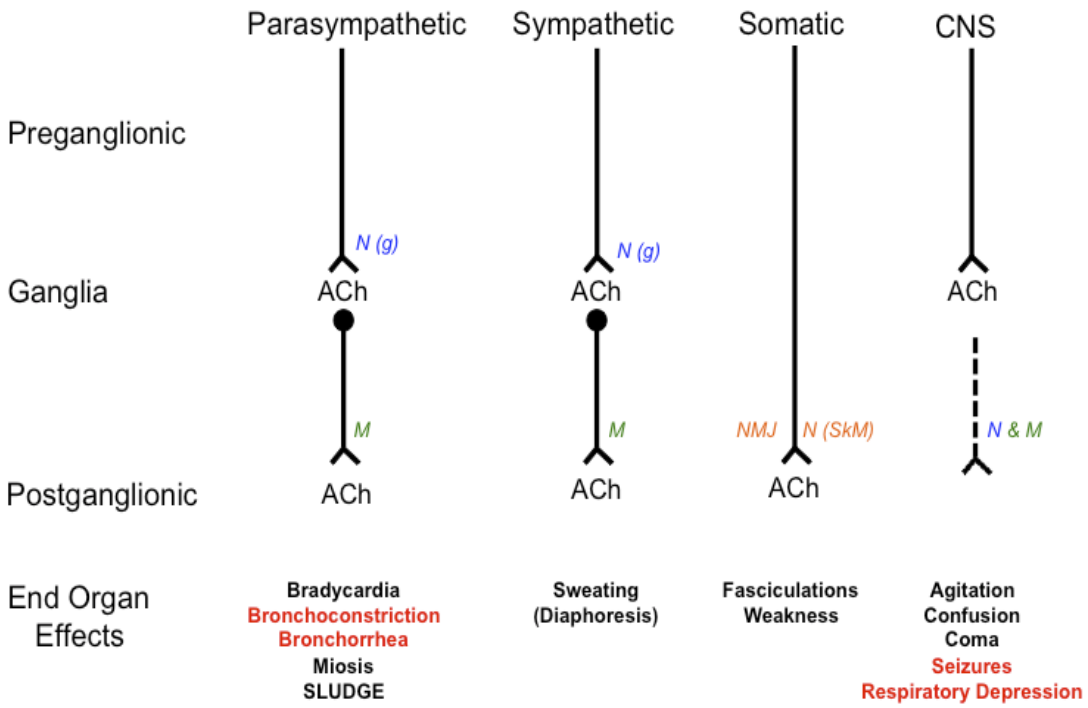


Figure 14 – Ach as a neurotransmitter at various synaptic terminals

Following exposure to OPC, toxic features appear within 30 minutes to 3 hours. In some cases it is delayed depending on systemic absorption. Toxicity is due to rapid absorption of the OPC through the GI, Skin & respiratory tracts. The clinical symptoms and signs are non-specific and will depend on the specific agent, the quantity and the route of entry.

Multi-system manifestations like gastrointestinal, respiratory, and cardiovascular and nervous systems, as well as the involvement of skeletal muscle, other organs and metabolic effects such as hypo or hyperglycemia. Mortality is high within the first 24 hours and those who recover usually do so within 10 days.

Cardiac manifestations: (36) - The commonest cardiac manifestations following poisoning are hypotension (with warm, dilated peripheries), and bradycardia. Patients rarely present with hypertension and tachycardia predominantly due to nicotinic receptor blockade. Cardiac manifestations are often the cause of serious complications and fatality. (19)

The mechanism of cardiac toxicity though unclear has been postulated as:

- A direct toxic effect on the myocardium
- Over activity of cholinergic or nicotinic receptors causing hemodynamic alteration
- Hypoxia
- Acidosis
- Electrolyte abnormalities
- Atropine in High doses.

The more common mnemonic of the muscarinic effects of OP poisonings is DUMBELS:

- **D** = Defecation/diaphoresis
- **U** = Urination
- **M** = Miosis
- **B** = Bronchospasm/bronchorrhea
- **E** = Emesis
- **L** = Lacrimation
- **S** = Salivation.

Table 9. Clinical features in organophosphorous poisoning		
Muscarinic receptors	Nicotinic receptors	Central receptors
<u>Cardiovascular</u> • Bradycardia • Hypotension <u>Respiratory</u> • Rhinorrhoea • Bronchorrhoea • Bronchospasm • Cough <u>Gastrointestinal</u> • Nausea/vomiting • Increased salivation • Abdominal cramps • Diarrhea • Faecal incontinence <u>Genitourinary</u> • Urinary continence <u>Eyes</u> • Blurred vision • Increased <u>Lacrimation</u> • Miosis <u>Glands</u> • Excessive salivation	<u>Cardiovascular</u> • Tachycardia • Hypertension <u>Musculoskeletal</u> • Weakness • Fasciculation • Cramps • Paralysis	<u>General effects</u> • Anxiety • Restlessness • Ataxia • Convulsions • Insomnia • Dysarthria • Tremors • Coma • Absent reflexes • Respiratory depression • Circulatory collapse

Gastrointestinal manifestations: Symptoms such as vomiting, diarrhea and abdominal cramps occur after the oral ingestion of the OP compound.

Respiratory manifestations: (36) - Bronchorrhoea, rhinorrhoea, bronchospasm and laryngeal spasm. This is due to the action of the OP on muscarinic receptors. Excessive secretions compromise the integrity of the airway. Weakness and subsequent paralysis of respiratory and oropharyngeal muscles occur due to nicotinic effects. This leads to both airway obstruction and aspiration of gastric contents. Finally causes central neurological depression leading to respiratory arrest.

Neurological manifestations: (36) A large number of patients, following acute exposure to organophosphorous compounds, require prolonged ventilator support in the ICU due to neuromuscular weakness. Therefore neurological manifestations are of the prime focus of interest. There has been an emphasis on reducing the incidence of neuromuscular respiratory failure. Three different types of paralysis are:

- Type 1 paralysis:

  Acute paralysis is seen in the initial cholinergic phase. This is when both muscarinic and nicotinic receptors are occupied by acetylcholine, leading to persistent depolarization at the NMJ. Fasciculation, cramps, twitching and weakness can be seen. Respiratory depression and arrest occurs due to the respiratory muscle weakness & the patient may require ventilator support.

- Type 2 paralysis or Intermediate syndrome:

  This was first described in 1974 by Wadia et al [37] as type 2 paralysis & subsequently termed "The Intermediate Syndrome" by Senanayake. The syndrome develops 24-96 hours after poisoning. This occurs following recovery from the acute cholinergic crisis, and before the onset of delayed neuropathy.

  The cardinal features are muscle weakness affecting the proximal limb muscles and neck flexors. The distal muscle group is relatively spared. Cranial nerves supplying the extra-ocular muscles are mostly involved, with a lesser effect on VII and X. This syndrome goes on for about 4-18 days and most of the patients survive unless infection or cardiac arrhythmias complicates their course.

- Type 3 paralysis or organophosphate- induced delayed polyneuropathy (OPIDP):

  OPIDP is a pure motor or predominantly motor axonal neuropathy. Wrist drop and foot drop with minimal or no sensory loss is characteristic, which occurs 7-20 days after OP exposure. (38,39) OPIDP is a rare cause of peripheral neuropathy. The cardinal feature is the weakness that appears initially in distal leg muscles and small muscles of the hand. Later it may extend proximally. Clinical involvement of the corticospinal tracts and the dorsal columns becomes apparent when the peripheral neuropathy improves.5 The prognosis in mild neuropathy is good but with severe neuropathy, partial recovery with deficits like claw hand, foot drop, ataxia can occur in 6 – 12 months. (5,6) The pathogenesis of OPIDN is presumed to be phosphorylation & ageing of an enzyme in axons called neurotoxic esterase or neuropathic target esterase (NTE). Inhibition of NTE causes degeneration of predominantly long axons, with loss of myelin and macrophage accumulation in nerves leading to motor axonal neuropathy. (38,40) Thiamine and high dose methylprednisolone has been beneficial in experimental animals. However Senanayake found that only physiotherapy was helpful.

Table 10 – Other effects of opc may include (36)	
Neuropsychiatric effects	Impaired memory, confusion, irritability, lethargy, psychosis Chronic OP- induced neuropsychiatric disorders
Extra pyramidal effects	Dystonia, Cogwheel rigidity - Parkinsonian features
Other neurological and psychological effects:	Guillain-Barré–like syndrome Isolated bilateral recurrent laryngeal nerve palsy
Eyes	Optic neuropathy, Retinal degeneration Defective vertical smooth pursuit, Myopia and miosis
Ears	Ototoxicity

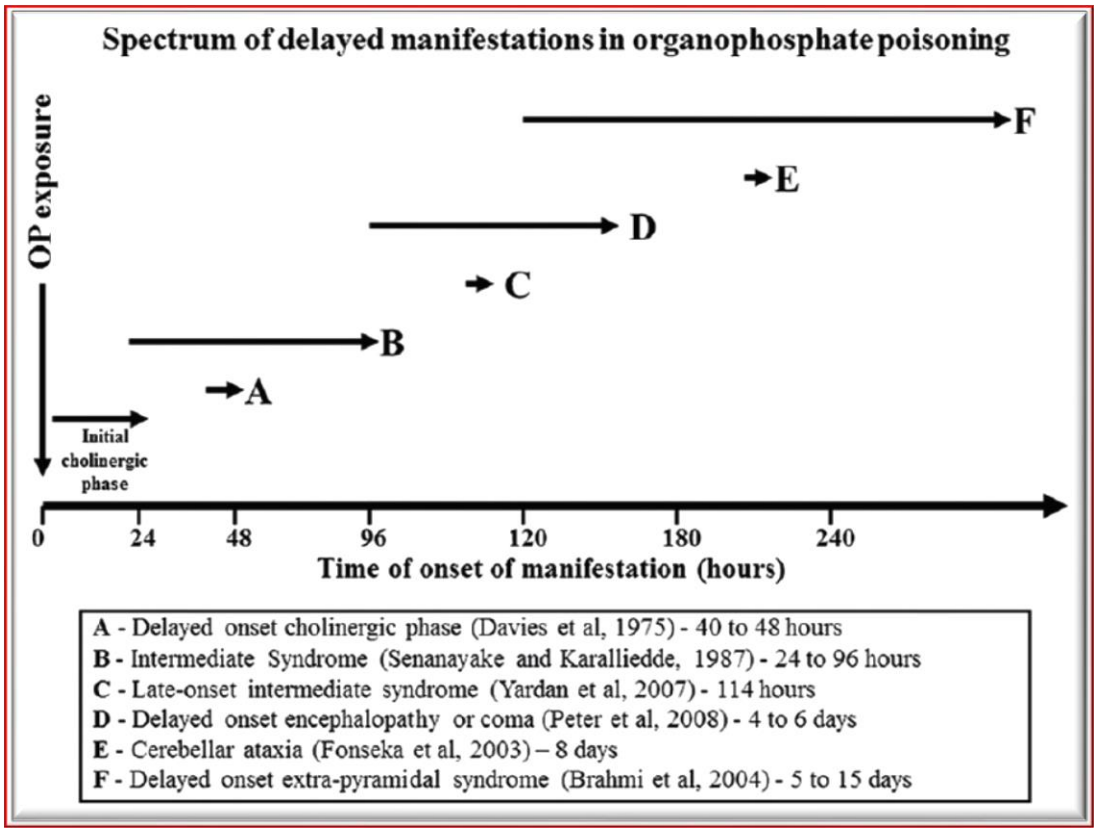


Figure 15 - Spectrum of delayed manifestations in OP poisoning - delayed onset cholinergic symptoms occurs 40-48 h following poisoning

a. Intermediate syndrome
b. Typically occurs 24-96 h following poisoning up to 114-h
c. Delayed onset coma or encephalopathy
d. Occurs about 4-day after poisoning, generally after a period of normal conscious state. Cerebellar ataxia
e. Has been reported to occur 8-day after poisoning and extrapyramidal manifestations
f. after 5-15 days (reproduced with permission) (41)

MODIFIED DREISBACH' CLINICAL CRITERIA – KARNIT [42]

GRADE I - Mild symptoms related to the portal of entry.

Nausea, vomiting in case of ingestion Cough, burning sensation in the chest in case of inhalation Mild systemic symptoms like headache, dizziness, and weakness.

GRADE II - Moderate systemic intoxication

Abdominal pain and diarrhea in case of ingestion.

Tightness in chest, difficulty in breathing in case of inhalation Salivation, Lacrimation, sweating, papillary changes. Bradycardia, confusion, tremor, restlessness.

GRADE III - Severe systemic intoxication

Respiratory depression, generalized weakness Cyanosis, peripheral circulatory failure, Convulsion, coma.

DIAGNOSTIC CRITERIA [43]

ESTIMATION OF CHOLINEESTERASE LEVELS: Organophosphate (OP) toxicity is a clinical diagnosis. OP Confirmation is based on the measurement of cholinesterase activity.

True and pseudo cholinesterase levels should be measured before oximes are started. Serial monitoring can determine the response to therapy.

True AChE is similar to that found in neuronal tissue. therefore, a more useful marker of OP poisoning & gives an accurate measurement of AchE.

Plasma cholinesterase is an acute-phase protein in the liver that circulates in the blood plasma. It is found in CNS white matter, the pancreas, and the heart. Factors affecting the levels are pregnancy, infection, and medical illness.

True cholinesterase is more accurate, but pseudocholinesterase is easier and readily available. Cholinesterase levels do not correlate with severity of clinical symptoms.

Baseline level are measured in patients, so the diagnosis can be confirmed by increasing trend of the cholinesterase levels until the values plateau over time.

False low levels of erythrocyte cholinesterase can be found in pernicious anemia, hemoglobinopathies, use of antimalarial drugs, and oxalate blood tubes.

False low levels of pseudo cholinesterase is seen in liver dysfunction, low-protein conditions, neoplasia, hypersensitivity reactions, use of certain drugs (succinylcholine, codeine, and morphine), pregnancy, and genetic deficiencies.

Other laboratory findings include leukocytosis, hemoconcentration, metabolic acidosis, hyperglycemia, hypokalemia, and hypomagnesemia.

IMAGING STUDIES:

A chest radiograph may reveal pulmonary edema. Electrocardiographic manifestations include Q-Tc prolongation, ST segment elevation, T wave inversion and PR prolongation. Rhythm disturbances such as sinus bradycardia, ventricular extra-systoles, ventricular tachycardia and fibrillation are also seen. Ludomirsky et al described three phases of cardiac toxicity following organophosphate poisoning:

- **Phase I**: Increased sympathetic tone for a brief period.
- **Phase II**: Prolonged parasympathetic activity including AV node blockade
- **Phase III**: Q-T prolongation followed by torsades de pointes, ventricular tachycardia and ventricular fibrillation [(44)]

Patients are categorized as mild, moderate and severe poisoning depending on symptoms, signs for management, prevention of complications & to improve prognosis. To determine severity many scales are used of which PARADENIYA ORGANOPHOSPHOROUS POISONING SCALE is one.

Table 11 - Paradeniya Organophosphorus Poisoning scale(POP): (45)

Parameter	Score
MIOSIS	
Pupil size > 2mm	0
≤ 2mm	1
Pinpoint	2
FASCICULATIONS	
None	0
Present but not generalized	1
Generalized and continuous with central cyanosis	2
RESPIRATION	
RR ≤ 20/min	0
RR > 20/min	1
RR > 20/min with central cyanosis	2
BRADYCARDIA	
PR > 60/min	0
PR 41-60/min	1
PR ≤ 40/min	2
LEVEL OF CONSCIOUSNESS	
Conscious and rational	0
Impaired, and responds to oral commands	1
Impaired and no response to oral commands (if fits present add 1)	2
Total	11

Score	Grade
<4	Mild
4-7	Moderate
>7	Severe

Grading of Fasciculation:

Grading is done by giving 1 point each to anterior chest, posterior chest, anterior abdomen, posterior abdomen, right arm, left arm, left thigh, right thigh, right leg and left leg.

Standard and non-standard therapy:

Atropine & oximes along with other supportive measures is the standard treatment of OP poisoning.(46) however the of oximes use is controversial.(47)

Non-regular antidotes include clonidine, FFP, activated charcoal, MgSo4,(9) NAC,(48) milk, gacyclidine,(49) haemoperfusion, (50) alkalization of blood plasma and certain other home remedies,(50,51) but their efficacy is not established yet.(10)

Principles of therapy:

Resuscitation

Oxygen inhalation

Muscarinic antagonist – atropine

Fluids

Acetylcholinesterase reactivator - Oximes

Respiratory support

Gastric decontamination (after the patient has been fully resuscitated and stabilized)

Summary of treatment: (52,53,54)

- Airway, breathing, and circulation is established. To avoid the risk of aspiration the patient is placed at a head low & left lateral position. High flow oxygen & Intubation if the airway/ breathing is compromised.
- IV access is obtained and 1–3 mg of IV atropine bolus is given, followed by infusion.
- Record pulse, BP, secretions, pupil size, & auscultatory findings at first atropine dose. Assess again after & every 5 mins and double atropine dose if there is no improvement. Once there is some improvement (HR is > 80 bpm, SBP is >80 mm Hg and the chest is clear) then stop doubling the dose.
- PAM at 2 g IV over 20–30 min followed infusion @ 0.5–1 g/hr in 0.9% normal saline and continued for 48hrs.
- Tachycardia is multifactorial therefore it is not a contraindication for atropine use. The pupils commonly dilate, but fully dilated pupils indicate atropine toxicity.
- In severe hypotension vasopressors may benefit. The use of vasopressors v/s atropine at higher doses is not clear.(55,56)
- Cholinergic features re-emerge if the dose of atropine is low.
- At excess dose, patients become pyrexial, agitated, bowel sounds are absent & urinary retention occurs. Infusion is stopped for 30–60 min before starting infusion at lower rate.
- Intubate & ventilate patients if tidal volume is < 5 mL/kg or vital capacity is < 15 mL/kg, or any apnoeic spells occur, or PaO is < 60 mm Hg with FiO2 of > 60%.
- Neck lift against resistance is often assessed. Any sign of weakness imples development of intermediate syndrome Tidal volume is assessed every 4 hours.
- Agitation is treated by dose adjustment of atropine, physical restraint or sedation with benzodiazepines.

- Frequent Monitoring for cholinergic crises is done as OP from fat stores are released. This occur for several days to weeks after ingestion. Restart atropine and oxime if cholinergic features recurr. Atropine & oximes were rapidly introduced in 1950s (57,58) so the ideal regimens is unknown.

Efficacy of treatment and outcome:

Factors affecting the outcome in OP poisoning

1. Toxicity
2. Impurities
3. Formulation
4. Alkyl subgroups: OP have either two methyl or two ethyl groups. Acetylcholinesterase ages faster fin dimethyl poisoning than for diethyl poisoning.
5. Need for activation of inactive compounds.
6. Speed of activation and AChE inhibition
7. Duration of effect—fat solubility and halflife

Muscarinic antagonist drugs:

Atropine is the main treatment,(59) other antimuscarinic are studied in animals.(59) Based on penetration of the drug into the CNS.(60)

Glycopyrronium and hyoscine do not enter the CNS.

The important side effect of atropine is delirium in patients who received high dose.(59) Some physicians prefer glycopyrronium to treat the peripheral effects of OP without causing confusion. Since it has poor CNS it is ineffective at countering coma and reduced respiration seen in cholinergic syndrome. A small RCT compared glycopyrronium & atropine & showed no significant difference in ventilation rates/ mortality.(61)

Hyoscine was used to treat severe extrapyramidal features. (62) However, seizures & extrapyramidal effects are not common in OP poisoning.(13,20)

Atropine is the antimuscarinic agent of choice till a high quality RCT shows another muscarinic antagonist which is widely available, affordable & moderately able to penetrate into the CNS.

Early therapy is effective in reversing cholinergic features and improving cardiac and respiratory function. A study (63) recorded benefit from an infusion of atropine to repeated bolus doses. Infusions reduce fluctuation of atropine concentration, frequent observation is reduced.

Oximes:

Oximes reactivates AchE inhibited by OP. (22) PAM was discovered in 1950s by Wilson and colleagues, and was soon introduced into clinical practice.(46) Other oximes obidoxime and trimedoxime were also developed, but pralidoxime is used widely. It has four salts: chloride, iodide, metilsulfate, and mesilate.(64)

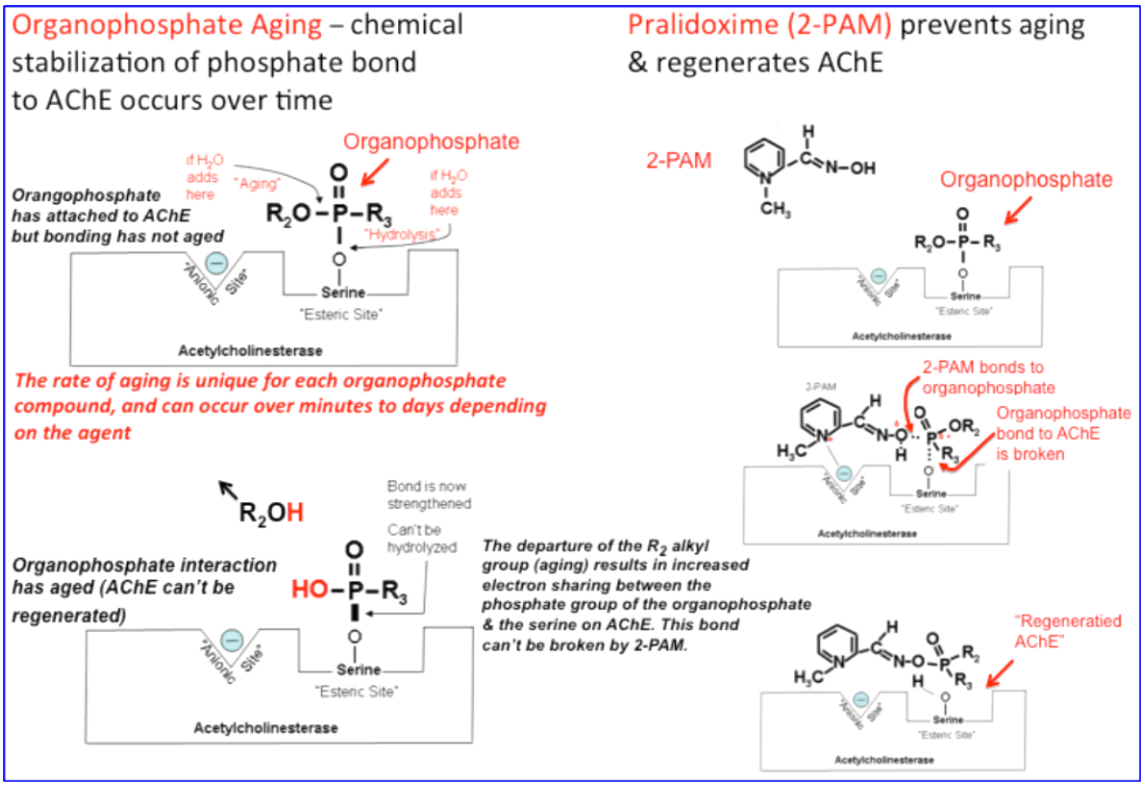


Figure 16: Ageing

Pralidoxime at high dose for long period can cause thyroid toxicity.(65) Despite initially benefit seen with pralidoxime, its role is much debated in Asia.(66,67,68)

In particular, two RCTs in Vellore, India in the early 1990s showed that pralidoxime infusions might cause harm.(69,70)

The absence of clinical benefit could be due to trial design (suboptimum dose, or bias in allocation). Pralidoxime is ineffective, perhaps this may be due to specific pesticide or amount ingested, or delayed presentation.(71,72)

A Cochrane review included two RCTs (70,71) that reported no clear evidence of harm/benefit.

A RCT in India (73) studied the effect of high dose PAM in 200 patients with moderate to severe OP poisoning. The high dose regimen was associated with decreased case fatality, fewer cases of pneumonia, and decreased mechanical ventilation.

At larger dose, PAM may have benefit if the patient is treated early and have good supportive care. Another Observational study, reverse of acetylcholinesterase by oximes varies with the pesticide ingested.(13,71,74)

AchE inhibited by parathion and quinalphos (diethyl) are effectively reactivated by oximes, but achE inhibited by monocrotophos or oxydemetonmethyl (dimethyl) respond poorly. And some like Salkyl-linked organophosphorus, such asprofenofos, is not reactivated by oximes at all. This difference is because of variation in the speed of achE ageing induced by these different pesticides.

Gastrointestinal decontamination:

Gastric lavage is the first intervention poisoned patients receive on presentation to hospital, sometimes before the antidote.(75) No benefit of gastric decontamination was seen in OP. Gastric decontamination is done after the patient is stabilised and treated with oxygen, atropine, and an oxime.(75)

The time window for effective lavage is short. Guidelines suggest that lavage is done within 1 hour of ingesting poison.(76)

Ipecacuanha is not used in OP poisoning.(77) Patients poisoned with OP can rapidly become unconscious, risking aspiration if ipecacuanha has been given.

Mechanically induced emesis with large quantities of water risks pushing fluid through the pylorus and into the small bowel, which might increse the rate of absorption.(77)

A RCT of single and multiple doses of superactivated charcoal in Sri Lanka failed to find a significant benefit of either regimen over placebo in more than 1000 patients poisoned with pesticides.(78) Because activated charcoal binds organophosphorus in vitro,(79) no effect is noted due to rapid absorption of OP into the blood.

Other therapies:

Current therapy have only a few mechanisms.(80) Several new therapies are studied but results were inconclusive. Future studies may reveal several therapies working at separate sites, at affordable price that could complement present treatments.

Sodium bicarbonate - It has been suggested that IV infusion of sodium bicarbonate produces moderate alkalinization (blood pH between 7.45 and 7.55) in OP pesticide poisoning. (6,7) The alkalinization products of nerve agents such as soman are shown to be less toxic and hence, the IV infusion of sodium bicarbonate may even be more beneficial in nerve agents poisoning.

Magnesium Sulfate - IV $MgSO_4$ given with 24 hrs of consumption has shown to decrease hospitalization and improve outcomes in patients with OP poisoning. (9)

Benzodiazepines - In animal studies with OP there is evidence of increased CNS activity, seizures and increased phrenic nerve activity with sudden cessation of activity. Pretreatment with diazepam in animal models of OP poisoning reduced respiratory depression and improved outcomes.1

Ketamine – (Neuro protective Drug) is a noncompetitive NMDA Receptor antagonist, can be used until 1 hour following nerve agent-induced seizures specially, when administered in combination with midazolam or diazepam.

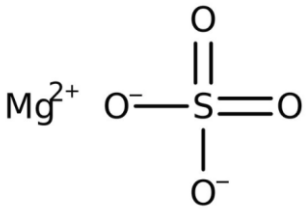
Cathartics - These speed up the passage of poisons in general out of the gastrointestinal tract. Reduced transit time reduces the absorption of poison.

Gacyclidine - antiglutamatergic found to be beneficial in conjunction with atropine, pralidoxime, and diazepam in nerve agents poisoning. EEG findings demonstrated gacyclidine-inhibited seizures that were induced by soman. (81)

Antioxidants – Increase in reactive oxygen radicals, decrease in antioxidant capacity, increased thiobarbituric reactive substances and lipid peroxidation occur in OP poisoning. Thus, antioxidants treatment may be beneficial in these patients. In rats, vitamin E was reported beneficial in OP induced oxidative stress in rat erythrocytes.

New Treatments - Removal of organophosphates from blood by using hemodialysis, hemoperfusion or hemofiltration is not clear. In a recent study, it was noted that hemofiltration after dichlorvos poisoning was beneficial. (50)

Magnesium Sulfate: Magnesium is 4th most common cation in the body, and the 2nd most common intracellular cation after potassium. It has a fundamental role in more than 300 enzymatic reactions as a co-factor involving energy metabolism and nucleic acid synthesis. It helps in hormone receptor binding, gating of calcium channels, transmembrane ion flux and regulation of adenylate cyclase, muscle contraction, neuronal activity, control of vasomotor tone, cardiac excitability and neuro- transmitter release. In its actions it is similar to a physiological calcium antagonist.



Mechanism of Action: It depresses Central nervous system, blocks peripheral NMJ transmission and produces anticonvulsive effects.

It inhibits the calcium channels presynaptically and decreases acetylcholine released at NMJ by motor nerve impulse and reduced CNS overstimulation mediated via NMDA receptor activation. (82)

SA node impulse formation rate is slowed in myocardium and prolongs conduction time

It stabilizes excitable membrane by in and out movement of calcium, potassium, and sodium.

It also helps in bowel evacuation by osmotic retention of fluid in colon, causing distention and increased peristaltic activity.

Other uses include:

- Oral magnesium sulfate - saline, osmotic laxative. (82)
- Replacement therapy in magnesium deficiency
- Magnesium sulfate is for torsades de pointes and quinidine-induced arrhythmias.(83)

- As a bronchodilator in severe exacerbations of asthma,(84) magnesium sulfate can be nebulized to reduce the symptoms of acute asthma.(84) It is commonly administered via the intravenous route.
- In ecclampsia, IV magnesium sulfate is used to prevent and treat seizures. It reduces the SBP but doesn't alter the DBP, so fetal blood perfusion isn't compromised. It is commonly used for eclampsia, gives better results compared to diazepam or phenytoin. (85,86)

Adverse Effects (87)

- Circulatory collapse
- Respiratory paralysis
- Hypothermia
- Pulmonary edema
- Depressed reflexes
- Hypotension
- Flushing
- Drowsiness
- Depressed cardiac function
- Diaphoresis
- Hypocalcaemia
- Hypophosphatemia
- Hyperkalemia
- Visual changes

PREVENTION AND EDUCATION

Improving the regulation on availability of pesticides, strict regulation of vendors, and modifying the package system of pesticides may all help reduce the use of organophosphates as poisons. Public awareness, regular training of health care providers, better availability of drugs / antidotes and the establishment of poison information centers will help in reducing the morbidity & mortality related to OP poisoning. Insecticides should be kept away from children, to prevent accidental poisoning. Standard precautions should be taken to prevent accidental ingestion and inhalation during agricultural spraying. The greatest incidence of organophosphorous poisoning was reported from Japan where there were 19,436 cases over a period of 17 years (1953-1969). Approximately 19 countries have reported 5,00,000 cases of pesticide poisoning annually. Of these 99% belong to third world countries (88). The estimate has risen from 75,000 cases annually to 3million in 2 years with a majority under 30 (89). Pesticide poisoning accounts for > 40% of cases in Poison Centre GGH Chennai. The mortality rate due to this poison is 42.29% (case register 2001-2004). The victims are farmers of rural South India.

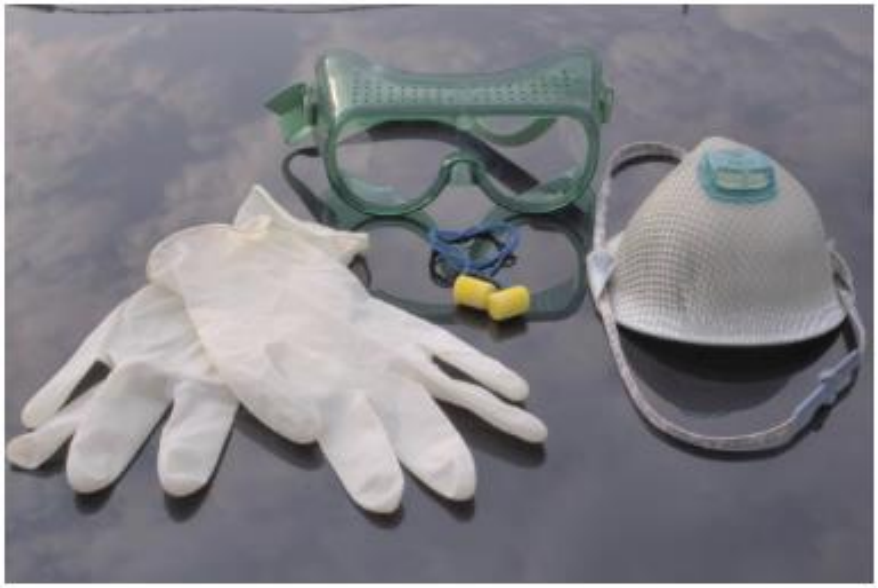


Figure 17- Personal protective gears, including gloves, a mask, and goggles, may help to prevent organophosphate poisoning.

MATERIALS & METHODS

MATERIAL AND METHODS:

4.1 Source Of Data:

The study included 80 patients with alleged history of Organophosphorus compound consumption who presented to RLJ Hospital Kolar attached to SDUAHER during February 2018 - June 2019.

4.2 Inclusion Criteria:

1. Patients above 18 years.
2. Patients admitted with history of OP compound poisoning within 24 hours of consumption (presence of characteristic symptoms and signs of muscarinic and nicotinic involvement, and reduced levels of AChE) and classified as moderate/severe op according to POP scale.
3. Patients/attenders who are willing to give written informed consent.

4.3 Exclusion Criteria:

1. Pregnant women.
2. Patients with mild Organophosphorus poisoning
3. Patients with other comorbidities like renal, cardiac and pulmonary dysfunction.
4. Organophosphorus compound mixed with other compounds.
5. Contraindications for $MgSo_4$ therapy like heart block.

4.4 Methods:

Patients were only included in this study after giving verbal and written consent. Patient confidentiality was maintained. And were informed about the study, procedures involved, relative risks, and benefits of the study.

- All patients with history of OP poisoning were included in the study.
- Decontamination of skin and gastrointestinal tract was done.

- Injection Atropine intravenous (IV) bolus and infusion was given.
- Inj pralidoxime IV bolus and infusion for 48 h was given.
- Patients who developed acute respiratory failure and neuromuscular weakness were intubated and mechanically ventilated.

4.5 Sampling Procedure

Emergency department at R.L.Jalappa hospital offers clinical expertise for management of various types of poisoning On an average 3-4 poisonings and 60% of which are OP are attented to in the casualty.

Consecutive recruitment (total enumerative sampling) of study participants was used. Investigator attended casualty and ICU on respective days targeting to recruit sampled OP poisoning patients.

4.6 Sample size:

Sample size is estimated based on the mortality observed in MgSO4 treated (15.9) and not treated (31.25) in acute OP poisoning in a study by Philomena J et al. Considering confidence interval of 95%, 80% power with an effect size of 60%reduction in mortality in MgSO% treated group. The sample size is 80.

4.7 Specimen Collection And Processing

Blood specimen 10ml was collected from a peripheral vein (antecubital venipuncture). The area was cleaned with methylated spirit and allowed to dry. A tourniquet was applied a few centimeters above the antecubital fossa to distend veins. Blood was taken using a sterilized 10 ml syringe and 21 G needle. The blood sample was transferred into a plain bottle and allowed to stand for about 30 minutes to clot and then centrifuged at 4000rpm for 10 min. The serum was separated and transferred into a Bijou (sample) bottle. The specimen that would not be assayed within 24hours due to logistic problems was frozen at -20^{o}c until time for analysis.

The following laboratory tests were done:

1. CBC,

2. RFT,
3. Serum electrolytes - Sodium, potassium, magnesium.
4. RBS
5. Chest X ray
6. ECG
7. Pseudocholine esterase (on day 1 , 3 and 7) * optional

4.8 Method

"Peradeniya Organophosphorus Poisoning Scale" was calculated.

Based on which patients with a score of 0 to 3 were considered as mild poisoning, 4 to 7 as moderate poisoning and 8 to 11 as severe poisoning.

2 groups were divided

Group 1 (Moderate poisoning were allotted to this group) - cases received 4g of MgSO4 controls did not receive MgSO4.

Group 2 (Severe poisoning were allotted to this group) - cases received 8g of MgSO4 controls did not receive MgSO4.

Consecutive patients were administered IV magnesium Sulphate infusion in 100ml of NS over 1hr

Cases and controls were matched according to the severity of poisoning.

Intensive monitoring of heart rate, blood pressure, oxygen saturation (SpO2), and electrocardiogram was done throughout the stay.

Primary outcomes measures which will be observed are atropine requirement per day, number of patients requiring intubation and mechanical ventilation, day of intubation, duration of mechanical ventilation, ICU stay, and mortality.

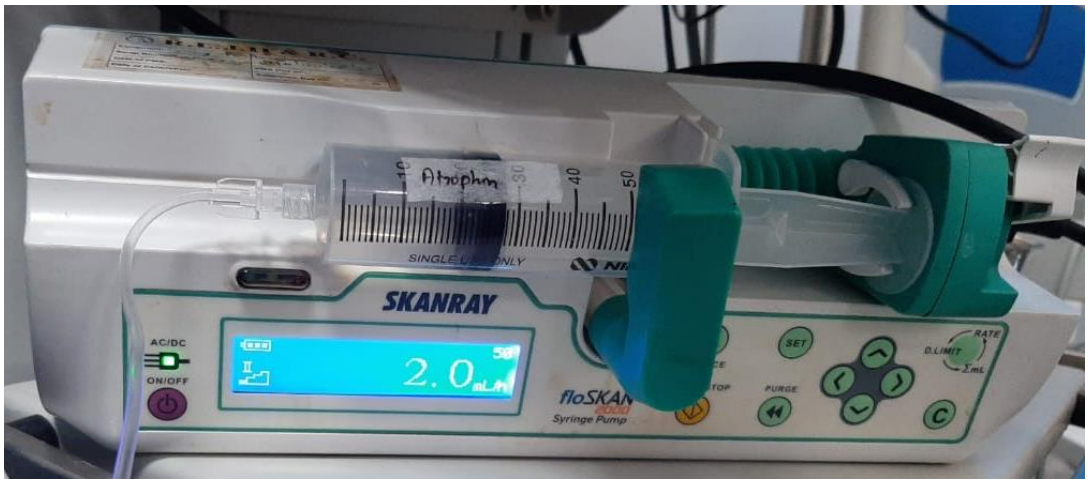


Figure 18 – Atropine infusion

Figure 19 – PAM infusion

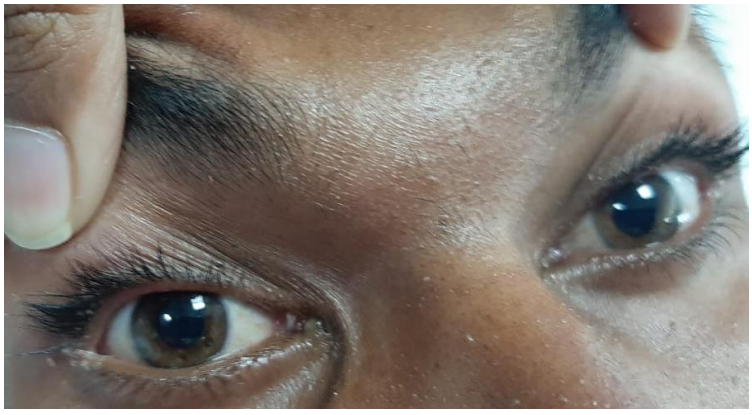


Figure 20 – Dilated pupils after atropine infusion

Figure 21 – Assessing neck lift in OP poisoning

Figure 22 – MgSo4 ampoules

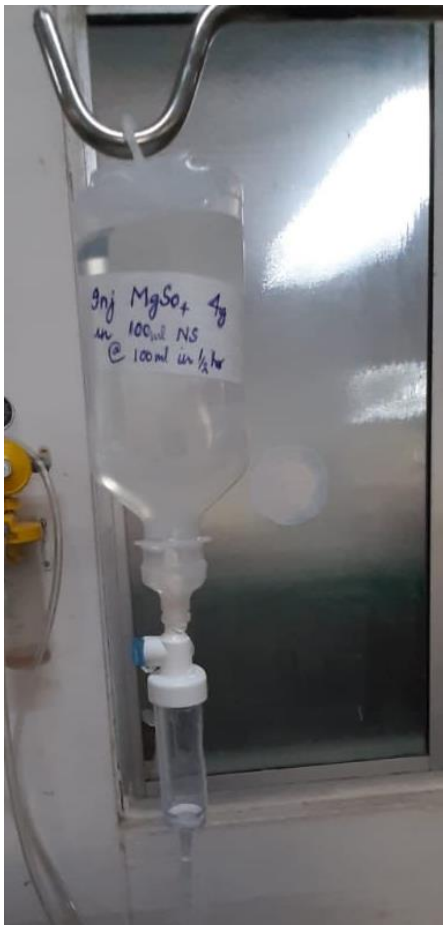


Figure 23 – 4g MgSo4 in 100ml NS infusion

4.9 Study Design:

It is a Comparative interventional study in which 80 patients were included.

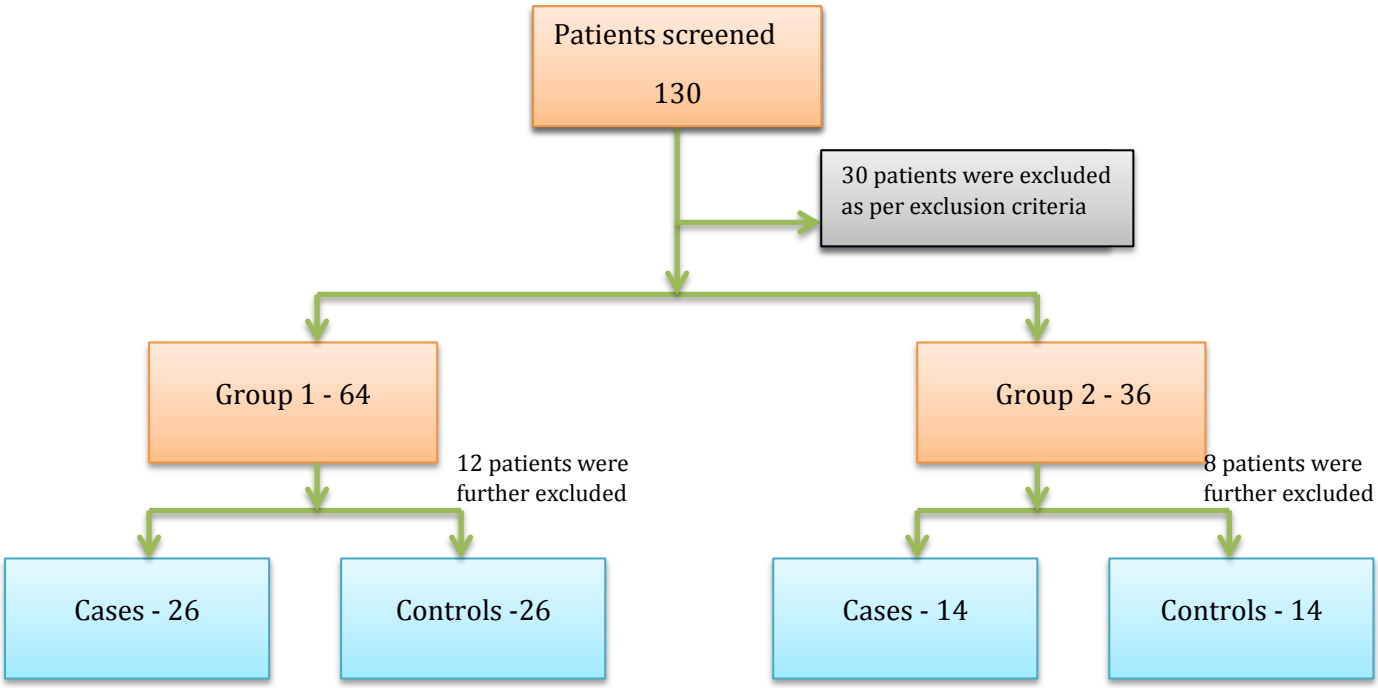


Figure 24 – number of patients screened, included and analyzed

4.10 Statistical analysis: (90,91,92,93)

Data was entered into Microsoft excel data sheet & analyzed using SPSS 22 version software. Categorical data were represented in the form of Frequencies & proportions. **Chi-square test** was used as test of significance for qualitative data. Continuous data were represented as mean and SD. **Independent t test or Mann Whitney U test** was used as test of significance to identify the mean difference between two quantitative variables & qualitative variables respectively.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

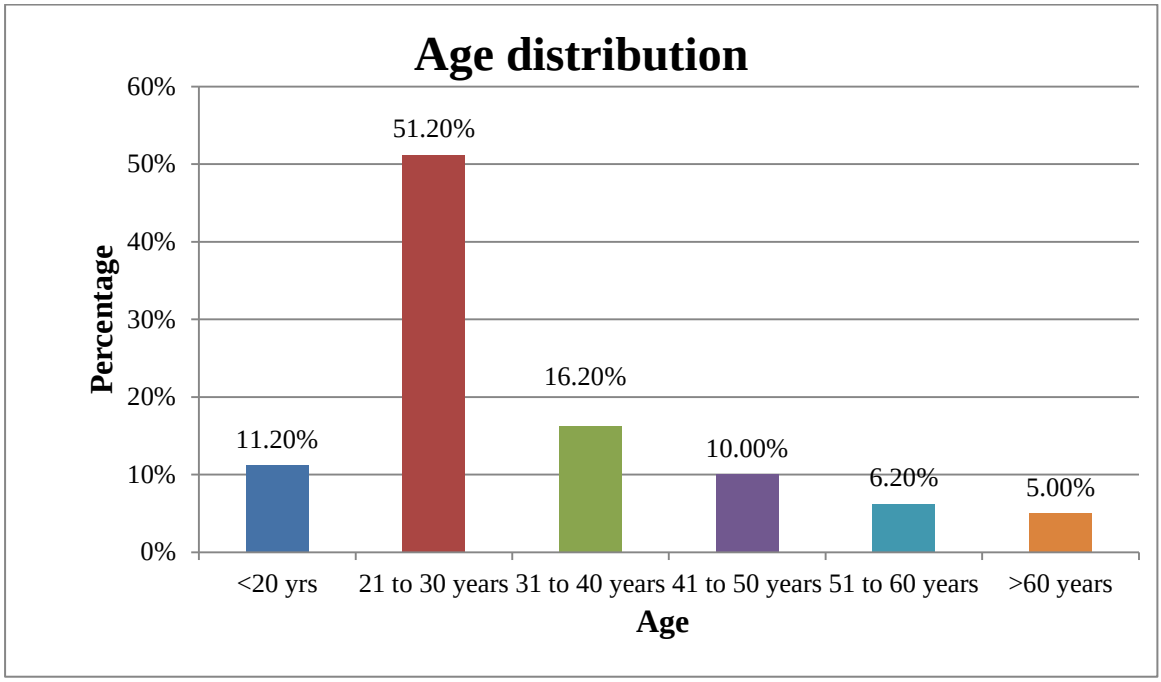
RESULTS:

Table 12: Age distribution of study subjects

		Count	%
Age	<20 yrs	9	11.2%
	21 to 30 years	41	51.2%
	31 to 40 years	13	16.2%
	41 to 50 years	8	10.0%
	51 to 60 years	5	6.2%
	>60 years	4	5.0%
	Total	80	100.0%

32.46 ± 13.089 years

In this study majority of the subjects belonged to the age group ranging from 21 to 30 years (51.2%).

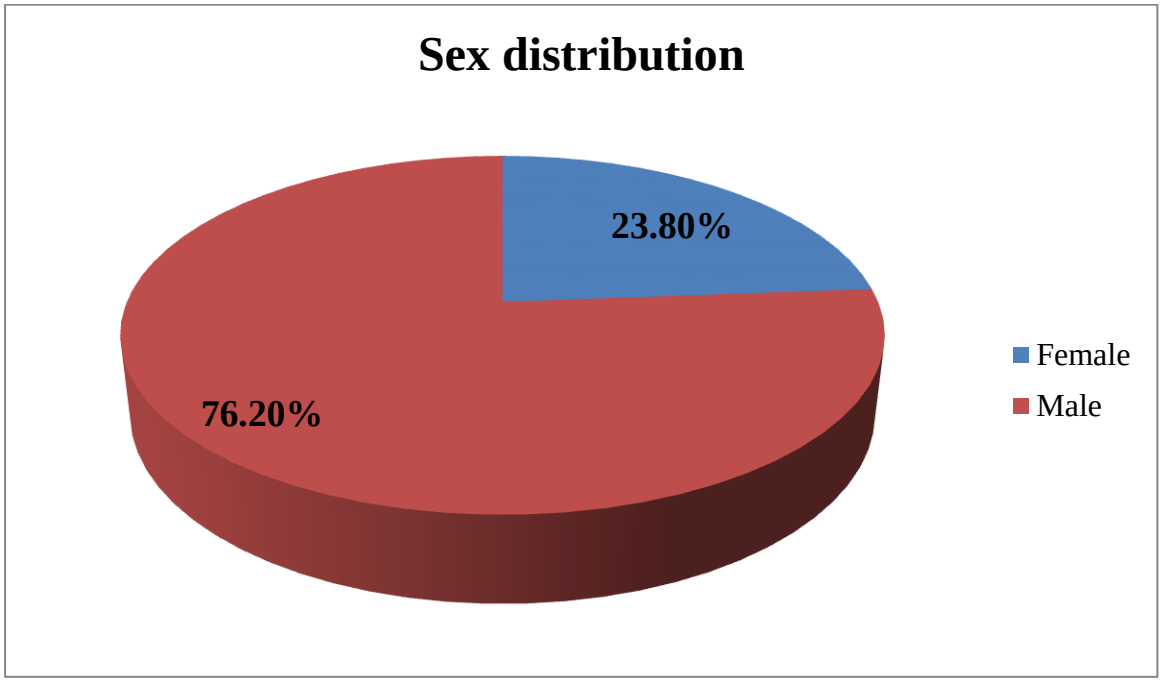


Graph 1: Bar diagram showing Age distribution of study subjects

Table 13: Sex distribution of study subjects

		Count	%
Sex	Female	19	23.8%
	Male	61	76.2%
	Total	80	100.0%

In this study majority of the study subjects were Males 61 (76.2%) and 19 (23.8%) were Females

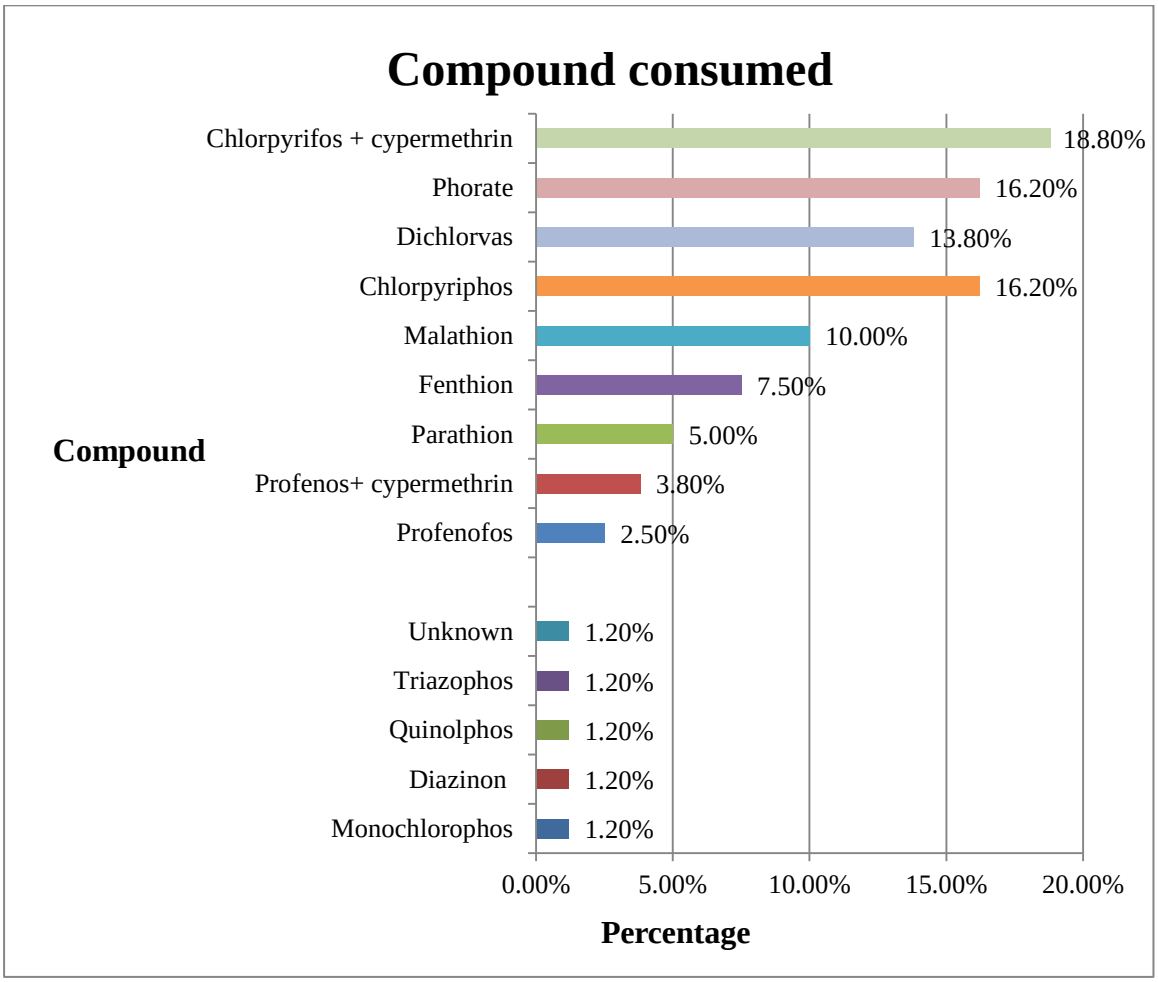


Graph 2: Pie diagram showing Sex distribution of study subjects

Table 14: Compound consumed among study subjects

		Count	%
Compound	Chlorpyrifos + cypermethrin	15	18.8%
	Chlorpyriphos	13	16.2%
	Dichlorvas	11	13.8%
	Fenthion	6	7.5%
	Monochlorophos	1	1.2%
	Malathion	8	10.0%
	Diazinon	1	1.2%
	Parathion	4	5.0%
	Phorate	13	16.2%
	Profenofos	2	2.5%
	Profenos+ cypermethrin	3	3.8%
	Quinolphos	1	1.2%
	Triazophos	1	1.2%
	Unknown	1	1.2%

In the given study subjects majority of them had consumed Chlorpyrifos+ Cypermethrin 15(18.8%), followed by Chlorpyriphos (16.2%), Dichlorvas (13.8%) and others as shown in above table.

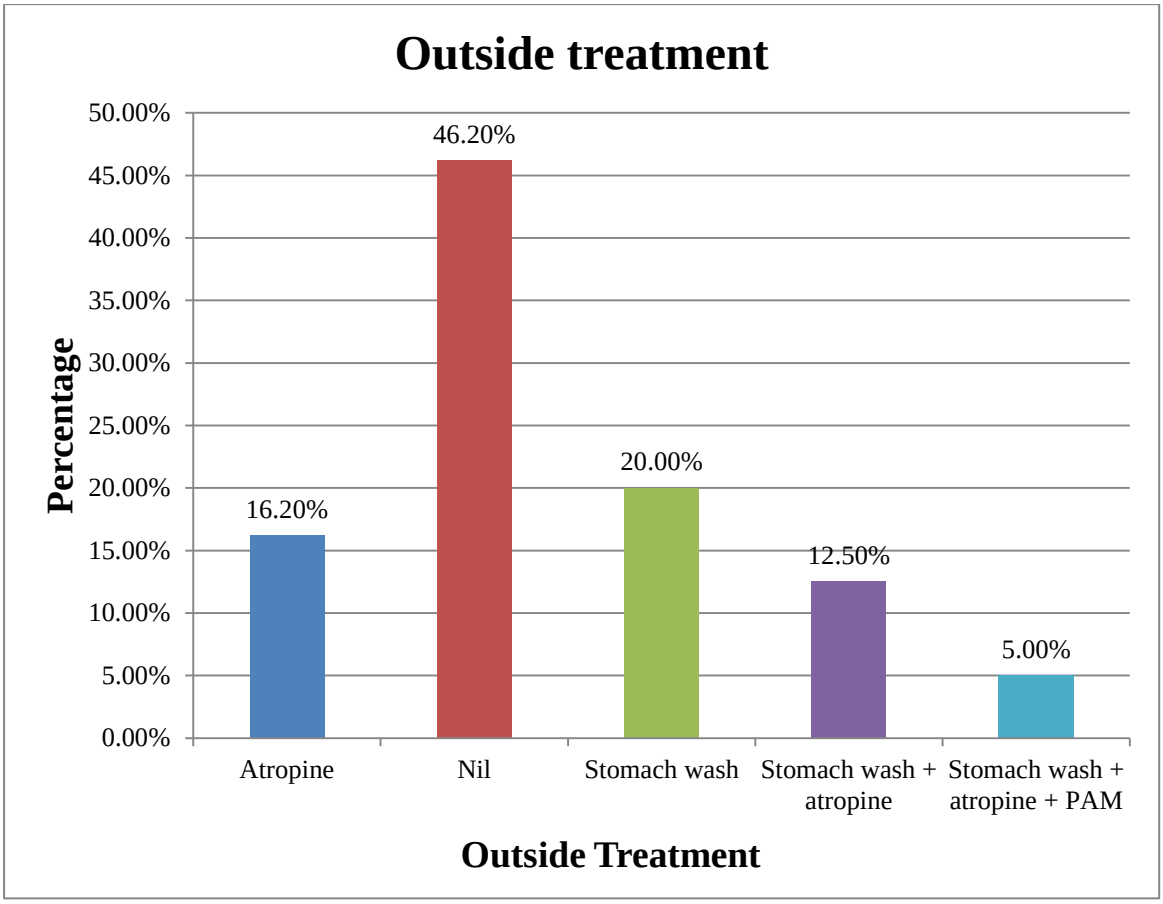


Graph 3: Bar diagram showing Compound consumed among study subjects

Table 15: Outside treatment distribution among study subjects

		Count	%
Outside treatment	Nil	37	46.2%
	Atropine	13	16.2%
	Stomach wash	16	20.0%
	Stomach wash + atropine	10	12.5%
	Stomach wash + atropine + PAM	4	5.0%

In the given study subjects 37 (46.2%) of them did not receive any treatment outside. Majority of the study subjects were given stomach wash 16 (20.0%)

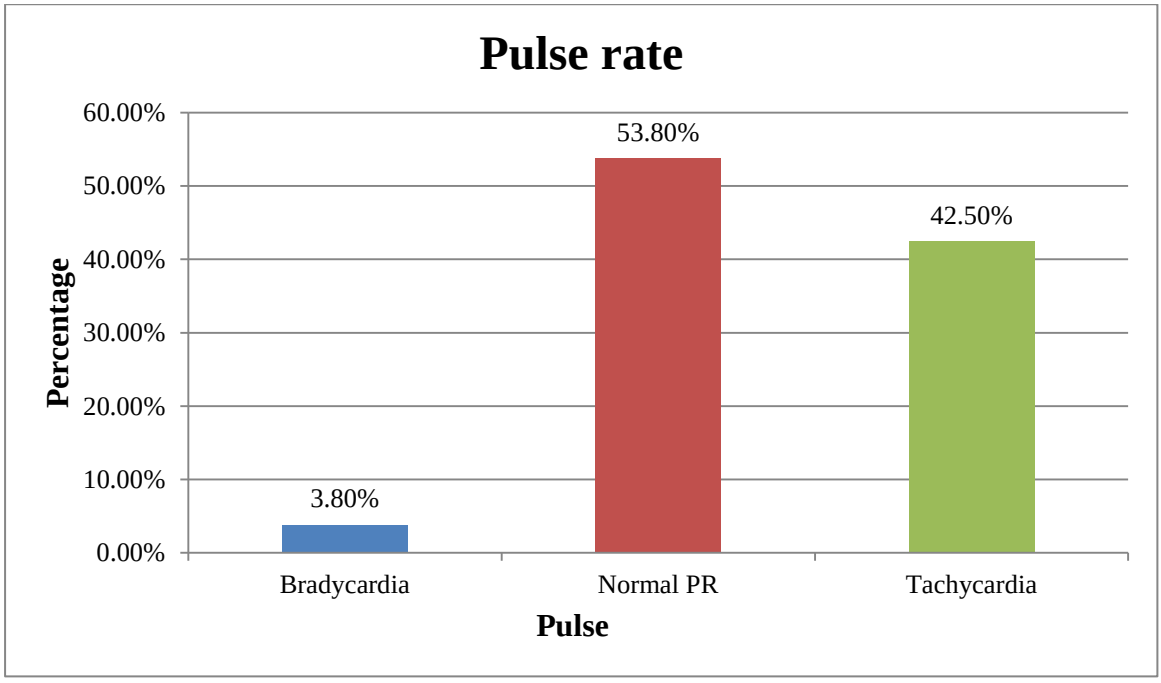


Graph 4: Bar diagram showing outside treatment distribution among study subjects

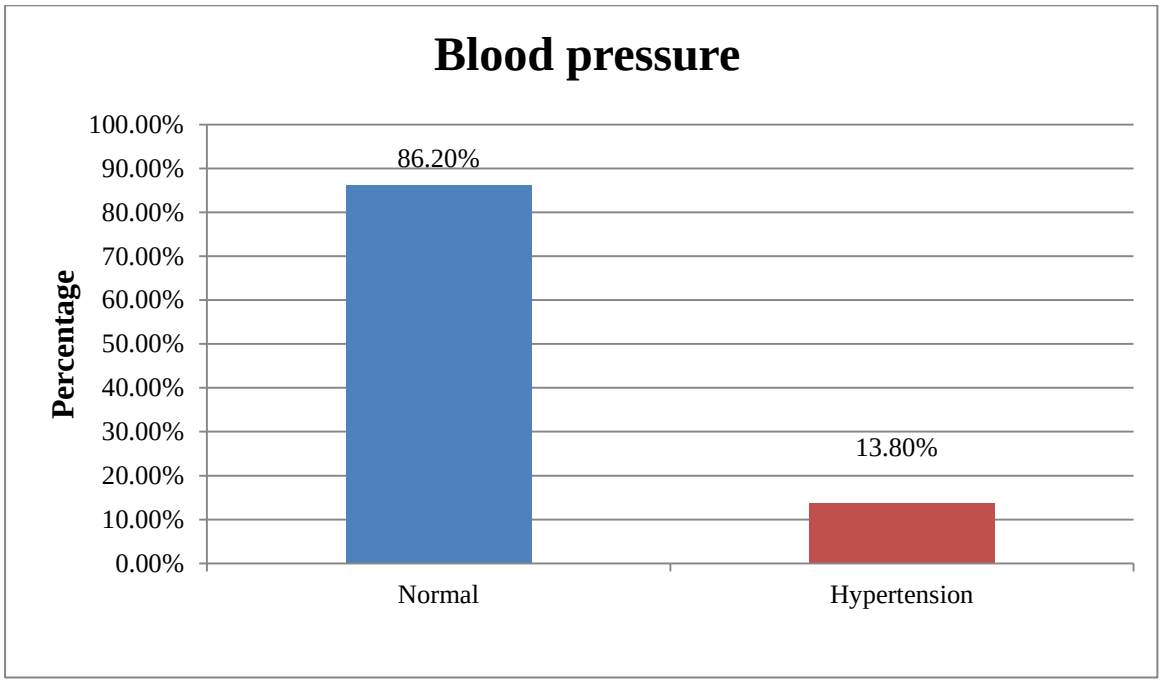
Table 16: Pulse rate and Blood pressure distribution among study subjects

		Count	%
PR	Bradycardia	3	3.8%
	Normal PR	43	53.8%
	Tachycardia	34	42.5%
BP	Normal	69	86.2%
	Hypertension	11	13.8%

In the given study subjects 34 (42.5%) of them had Tachycardia and 3 (3.8%) of them had Bradycardia and 11 (13.8%) of the study subjects had Hypertension.



Graph 5: Bar diagram showing Pulse rate distribution among study subjects

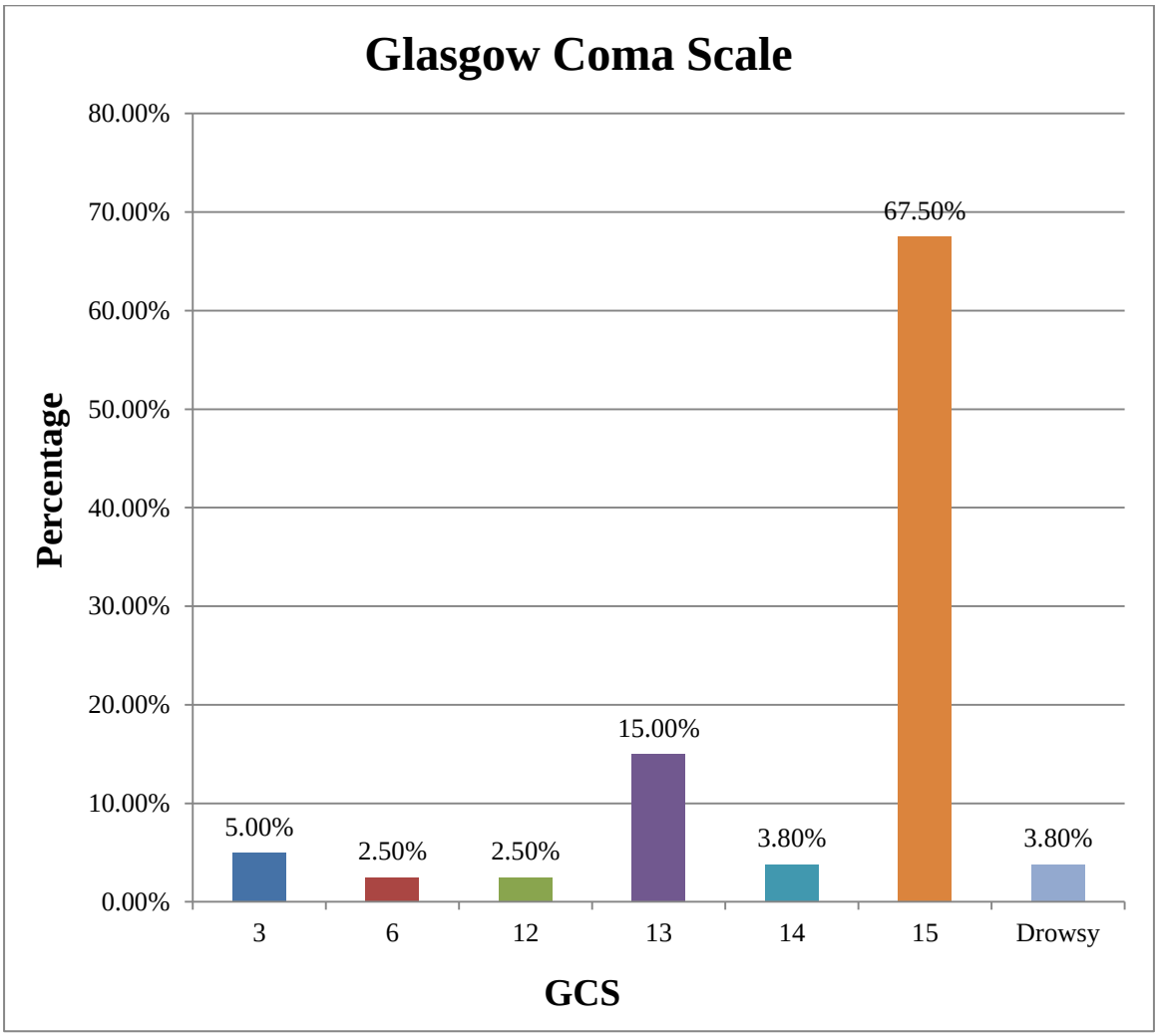


Graph 6: Bar diagram showing Blood pressure distribution among study subjects

Table 17: GCS distribution among study subjects

		Count	%
GCS	3	4	5.0%
	6	2	2.5%
	8	3	3.8%
	12	2	2.5%
	13	12	15%
	14	3	3.8%
	15	54	67.5%

In the given study majority of the study subjects had Glasgow Coma Scale of 15 (67.5%).

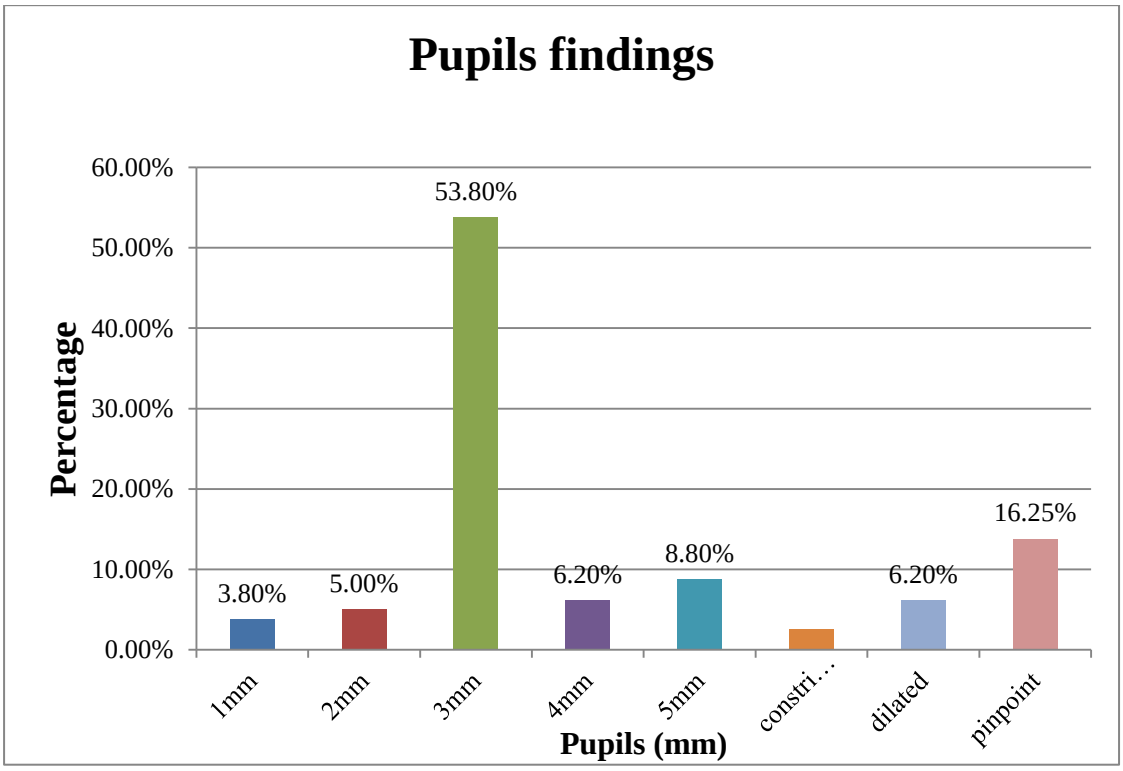


Graph 7: Bar diagram showing GCS distribution among study subjects

Table 18: Pupils findings distribution among study subjects

		Count	%
Pupils (mm)	1mm	3	3.8%
	2mm	4	5.0%
	3mm	43	53.8%
	4mm	5	6.2%
	5mm	7	8.8%
	Dilated	5	6.2%
	Pinpoint	13	16.25%

In the given study majority of the study subject's pupils measured 3mm (53.8%).

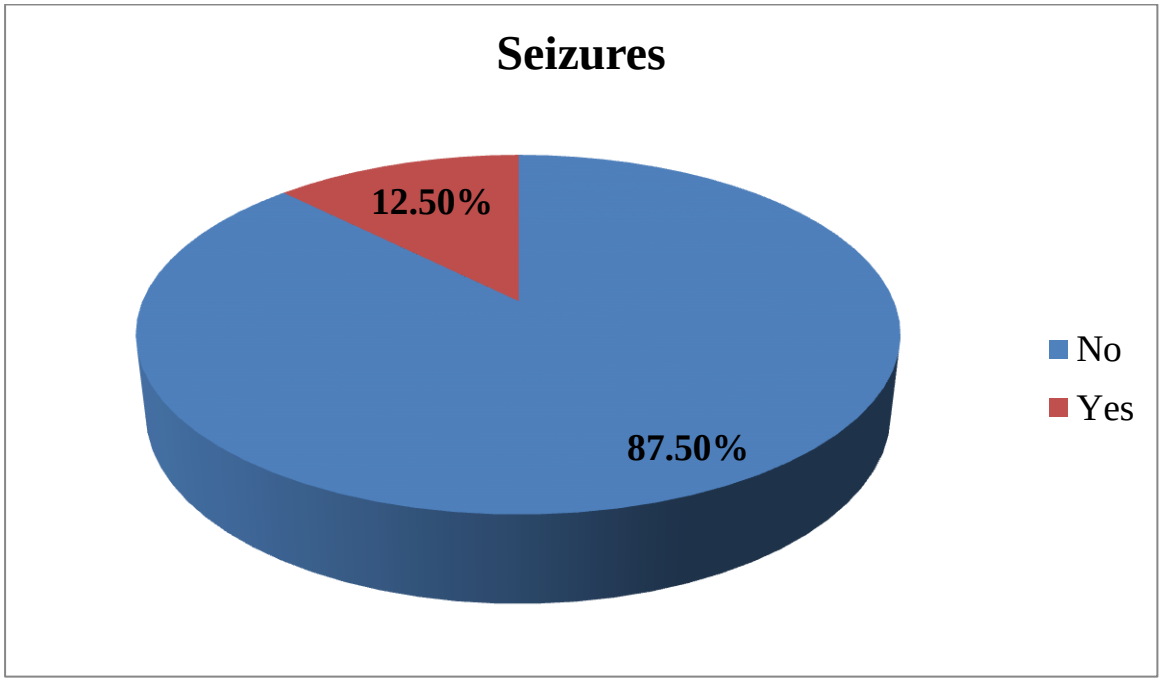


Graph 8: Bar diagram showing Pupils findings distribution among study subjects

Table 19: Seizures and Fasciculation's distribution among study subjects

		Count	%
Seizures	No	70	87.5%
	Yes	10	12.5%
Fasciculation's	No	49	61.3%
	Yes	31	38.8%

In the given study 10(12%) of the study subjects had Seizures and 31(38.8%) of them had Fasciculation.



Graph 9: Pie diagram showing Seizures distribution among study subjects

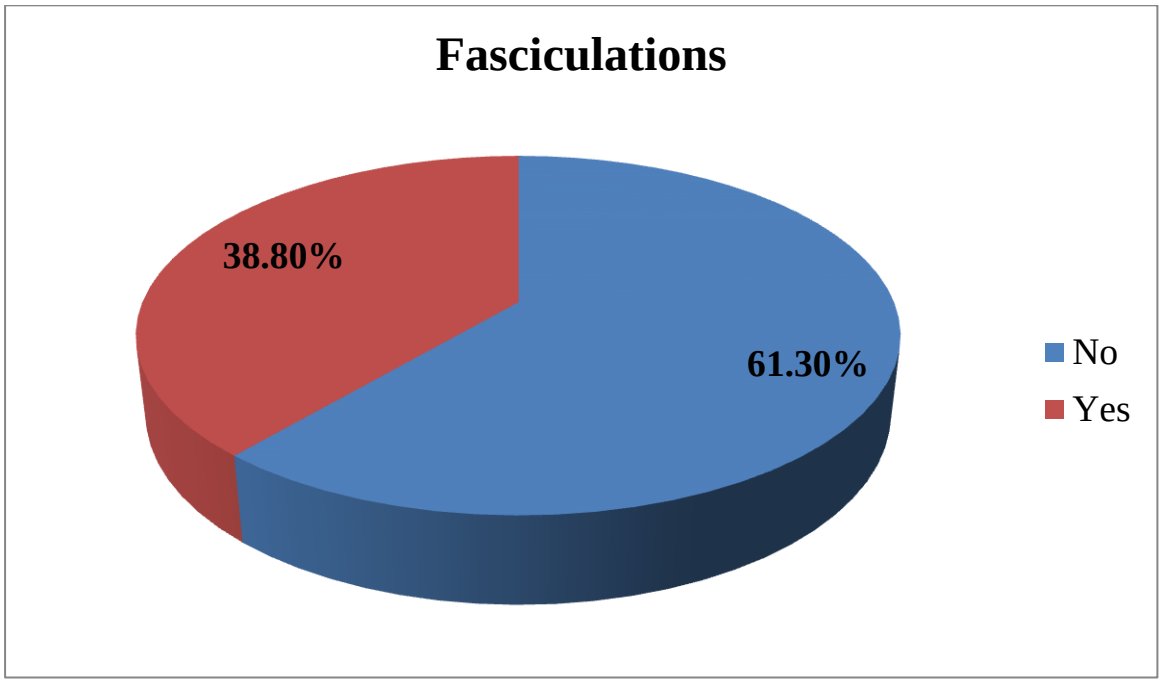
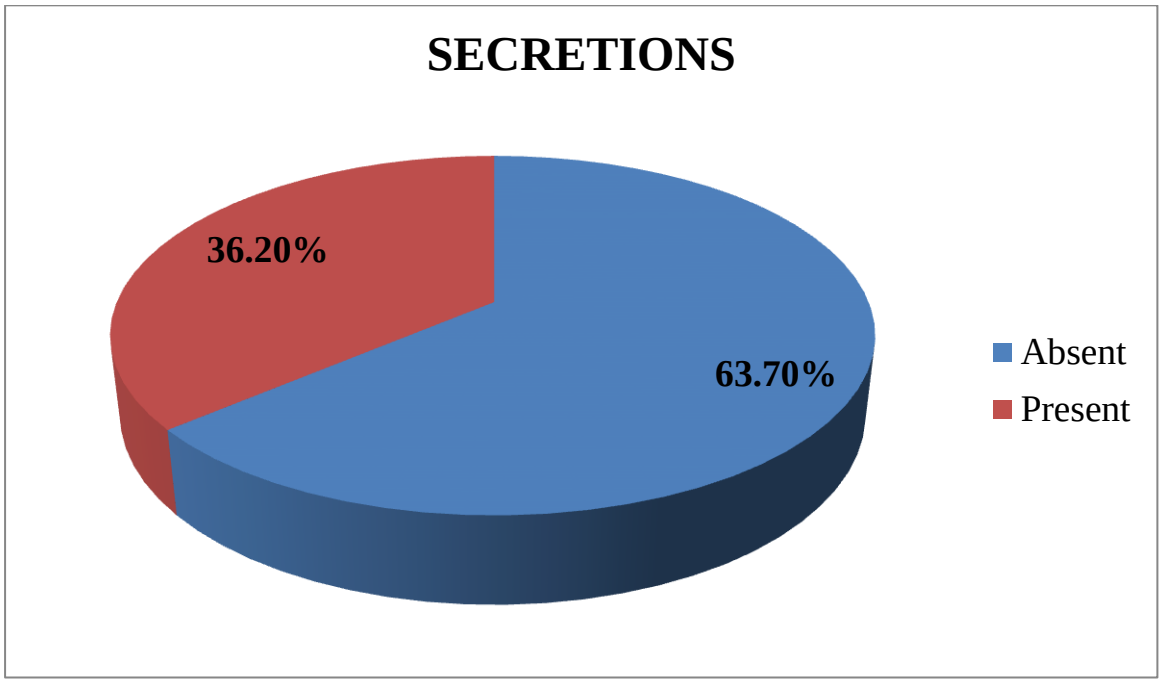


Figure 10: Pie chart showing Fasciculation's distribution among study subjects

Table 20: Secretions distribution among study subjects

		Count	%
Secretions	Absent	51	63.7%
	Present	29	36.2%

In the given study 29 (36.2%) of the study subjects had secretions at presentation.



Graph 11: Pie Chart showing Secretions distribution among study subjects

Table 21: Systemic examination findings distribution among study subjects

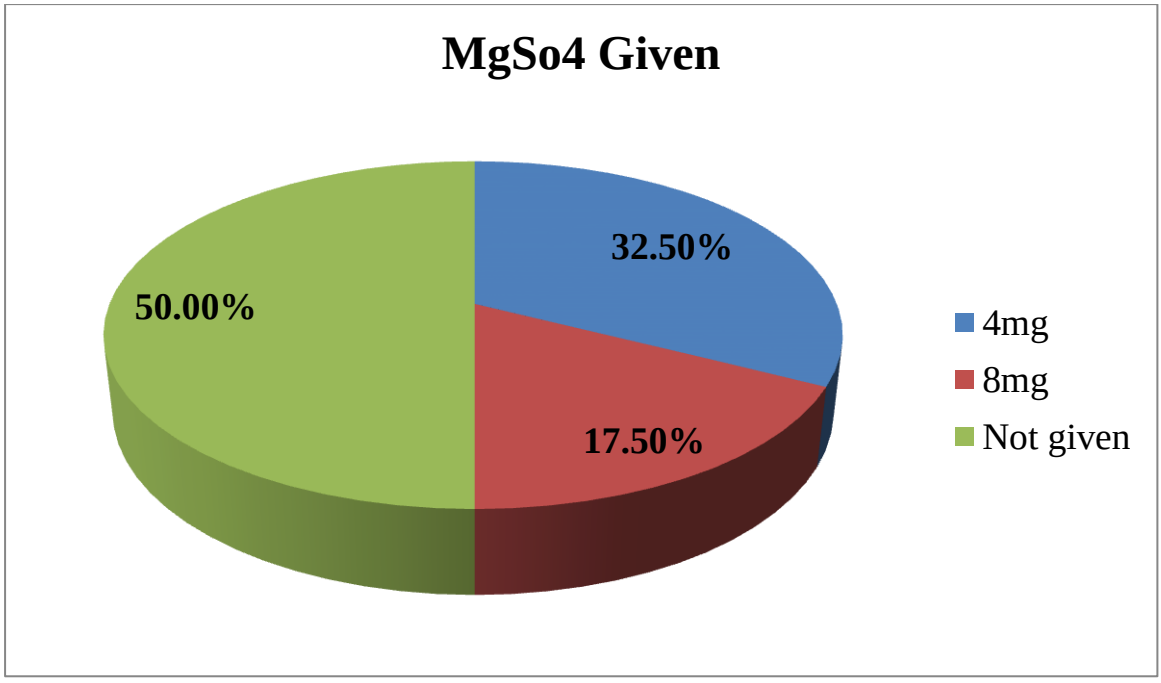
		Count	%
CVS	S1 S2 normal	80	100.0%
RS	Normovesicular breath sounds	58	72.5%
	B/L crepts +	22	27.5%
CNS	Atropinized	2	2.5%
	B/L flaccid paralysis	1	1.2%
	Delirious	1	1.2%
	Drowsy	12	15.0%
	Drowsy, Fasiculations+	5	6.2%
	Fasiculations	2	2.5%
	Irritable	1	1.2%
	NFND	53	66.2%
	Restless, fasiculations	1	1.2%
	Unresponsive	2	2.5%
PA	Soft	80	100.0%

In the study on CVS examination none of them had abnormality, on RS examination 27.5% had Crepitations, On CNS examination, 15% were drowsy, and On PA examination, 100% had soft abdomen.

Table 22: MgSo4 treatment distribution among study subjects

		Count	Percentage
MgSo4 given	4mg	26	32.5%
	8mg	14	17.5%
	Not given	40	50.0%

In the given study 26 (32.5%) of the study subjects received 4mg of MgSo4 and 14(17.5%) of them received 8mg of MgSo4.

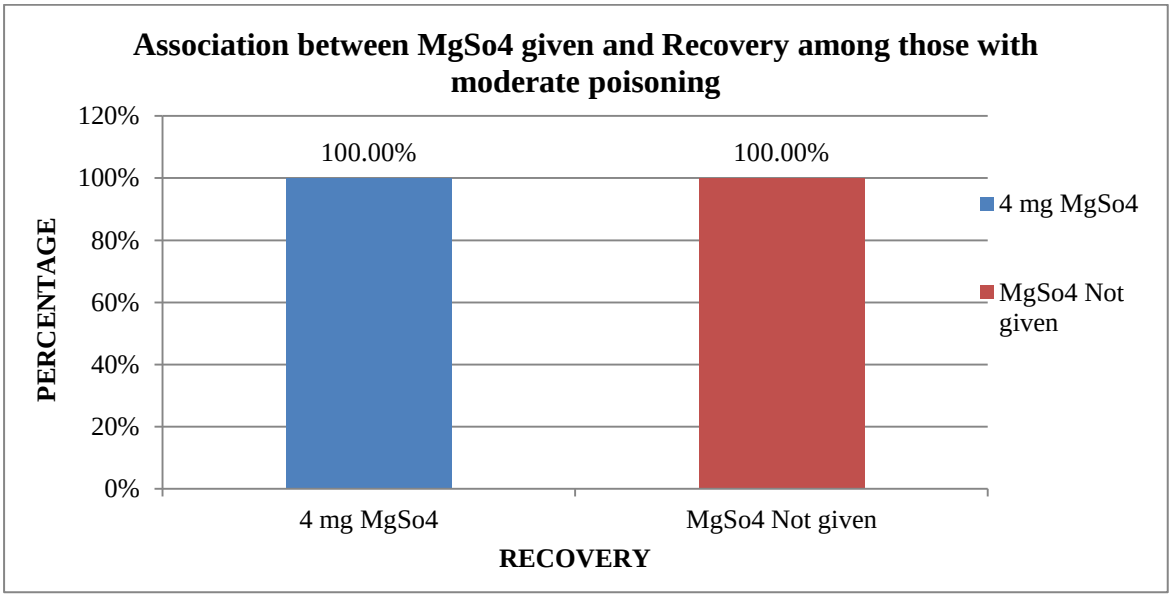


Graph 12: Pie chart showing MgSo4 treatment distribution among study subjects

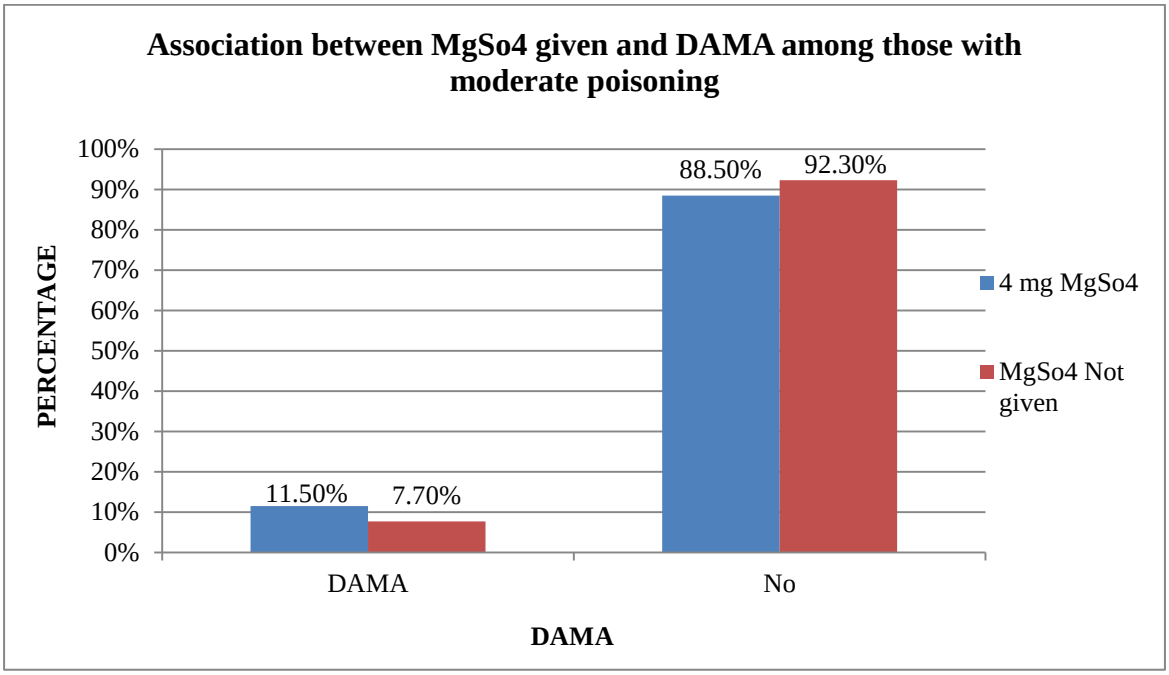
Table 23: Association between MgSo4 given and Outcome among those with moderate poisoning

		MgSo4				P value
		4 mg MgSo4		MgSo4 Not given		
		Count	%	Count	%	
Recovery	Recovered	26	100.0%	26	100.0%	-
DAMA	DAMA	3	11.5%	2	7.7%	0.638
	No	23	88.5%	24	92.3%	
Death	No	26	100.0%	26	100.0%	-

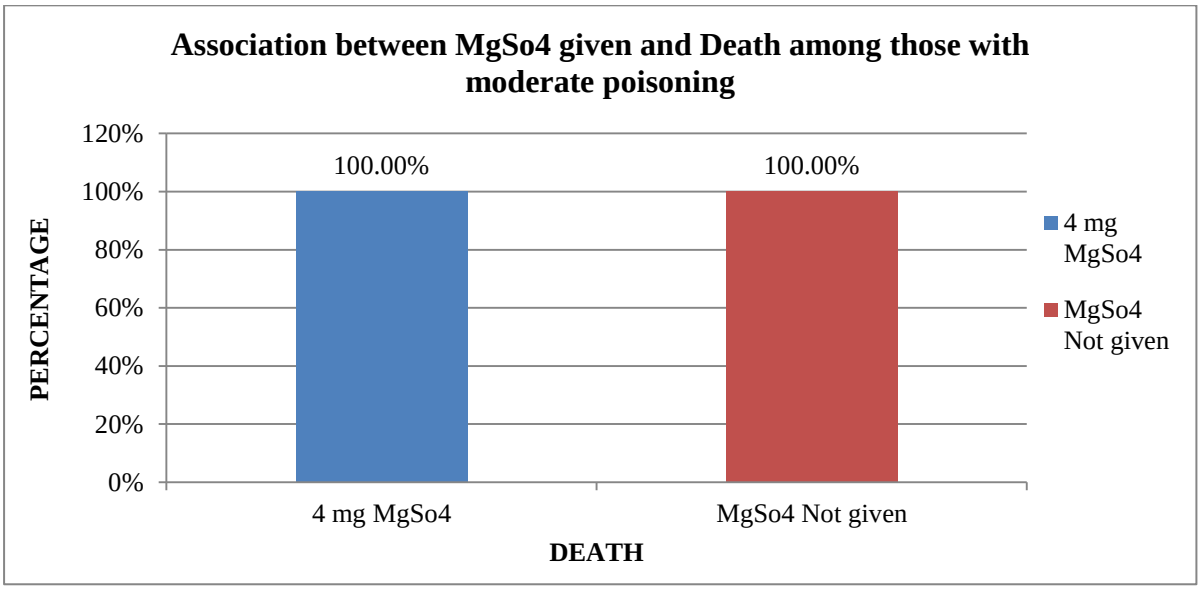
In the study among those with moderate poisoning, there was no difference in outcome between those who received 4 MgSo4 and who did not receive MgSO4.



Graph 13: Bar diagram showing association between MgSo4 given and recovery among those with moderate poisoning in study subjects



Graph 14: Bar diagram showing association between MgSo4 given and DAMA among those with moderate poisoning in study subjects



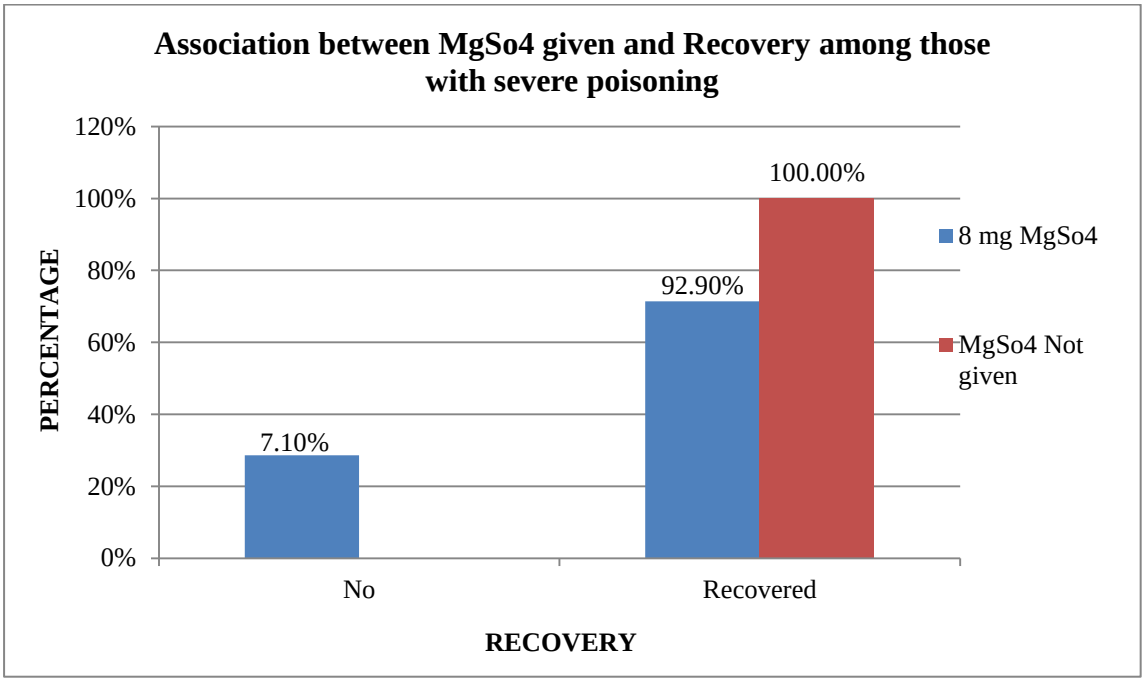
Graph 15: Bar diagram showing association between MgSo4 given and death among those with moderate poisoning in study subjects

Table 24: Association between MgSo4 given and Outcome among those with severe poisoning

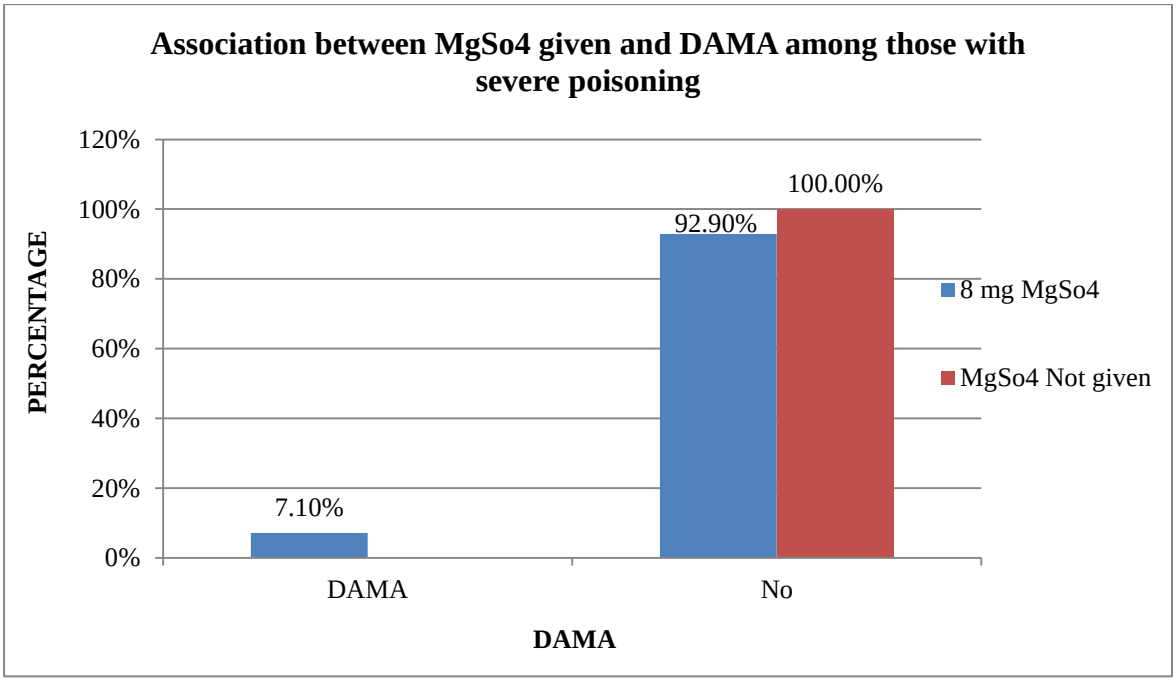
		MgSo4				P value
		8 mg MgSo4		MgSo4 Not given		
		Count	%	Count	%	
Recovery	No	1	7.1%	0	0.0%	0.309
	Recovered	13	92.9%	14	100.0%	
DAMA	DAMA	0	0.0%	0	0.0%	-
	No	14	100.0%	14	100.0%	
Death	Death	1	7.1%	0	0.0%	0.309
	No	13	92.9%	14	100.0%	

In the study among those with severe poisoning, there was no significant difference in recovery among those who received 8 MgSo4, 92.9% recovered and 7.1% did not recover, among those who did not receive MgSo4,100% recovered.

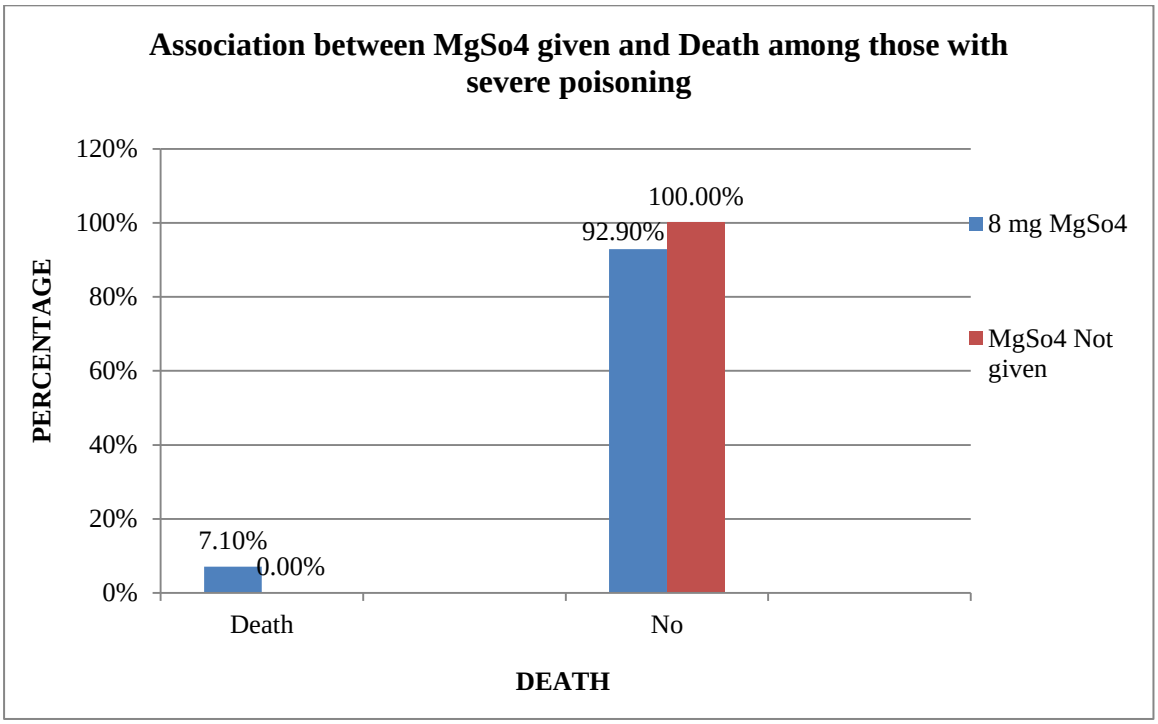
There was no significant difference in DAMA and death between those who received 8 MgSo4 and who did not received MgSo4.



Graph 16: Bar diagram showing association between MgSo4 given and recovery among those with severe poisoning in study subjects



Graph 17: Bar diagram showing association between MgSo4 given and DAMA among those with severe poisoning in study subjects



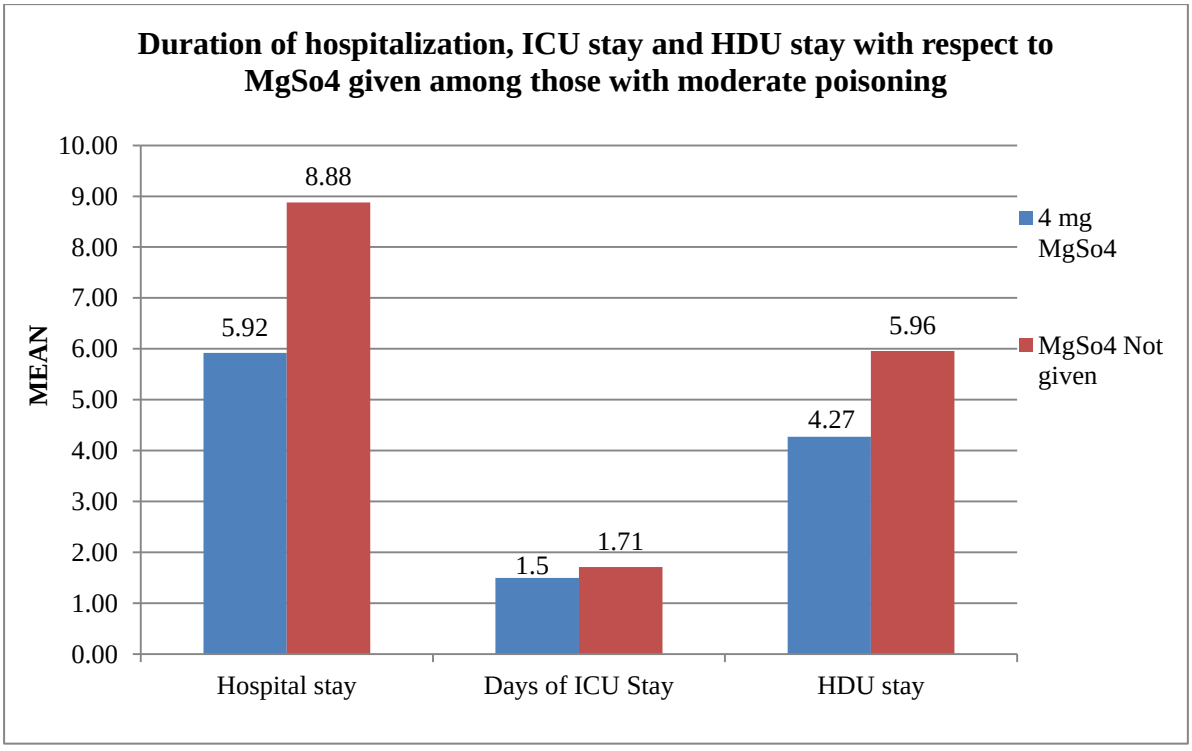
Graph 18: Bar diagram showing association between MgSo4 given and death among those with severe poisoning in study subjects

Table 25: Duration of hospitalization, ICU stay and HDU stay with respect to MgSo4 given among those with moderate poisoning

	MgSo4				P value
	4 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Hospital stay	5.92	1.26	8.88	3.64	<0.001*
Days of ICU Stay	1.50	.58	1.71	1.11	0.732
HDU stay	4.27	1.40	5.96	2.72	0.007*

In the study among those with moderate poisoning, there was significant difference in duration of stay in hospital and HDU stay between those who received MgSo4 and who did not received MgSo4.

Duration of stay and HDU stay was less among those who received 4 MgSo4 compared to those who did not receive MgSo4.

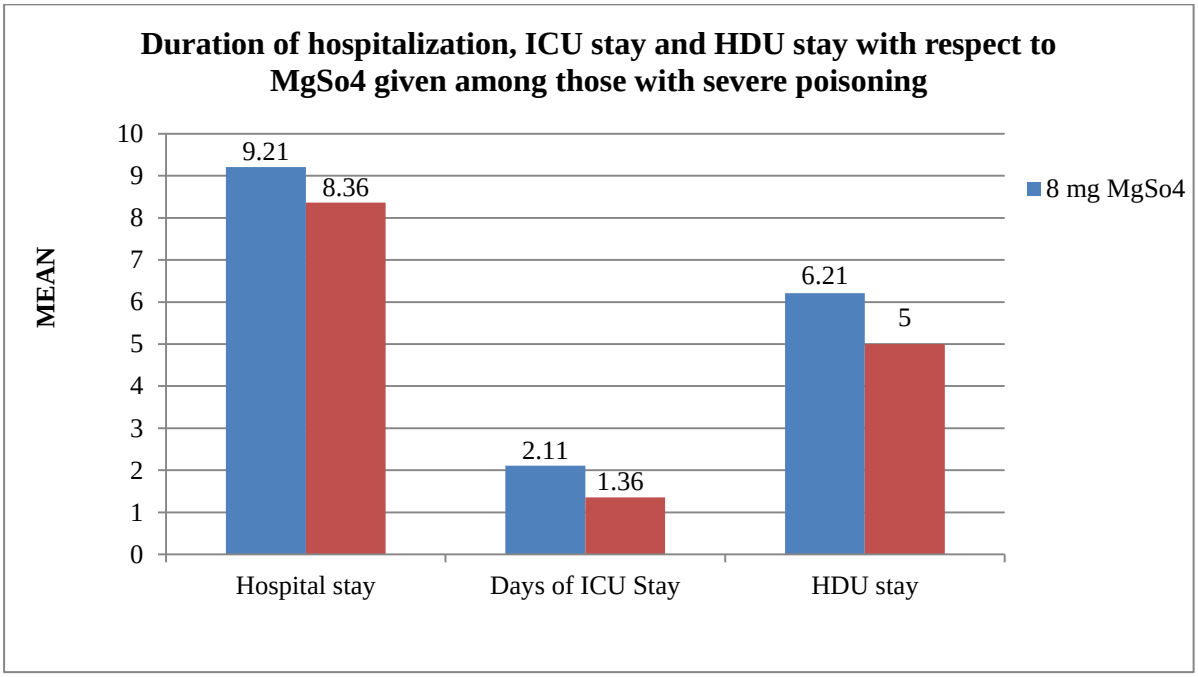


Graph 19: Bar diagram showing duration of hospitalization, ICU stay and HDU stay with respect to MgSo4 given among those with moderate poisoning in study subjects

Table 26: Duration of hospitalization, ICU stay and HDU stay with respect to MgSo4 given among those with severe poisoning

	MgSo4				P value
	8 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Hospital Stay	9.21	4.06	8.36	2.10	0.489
Days of ICU Stay	2.11	1.05	1.36	0.67	0.07
HDU stay	6.21	2.49	5.00	1.47	0.128

In the study among those with severe poisoning, there was no significant difference in duration of stay in hospital, ICU stay and HDU stay between those who received MgSo4 and who did not received MgSo4.



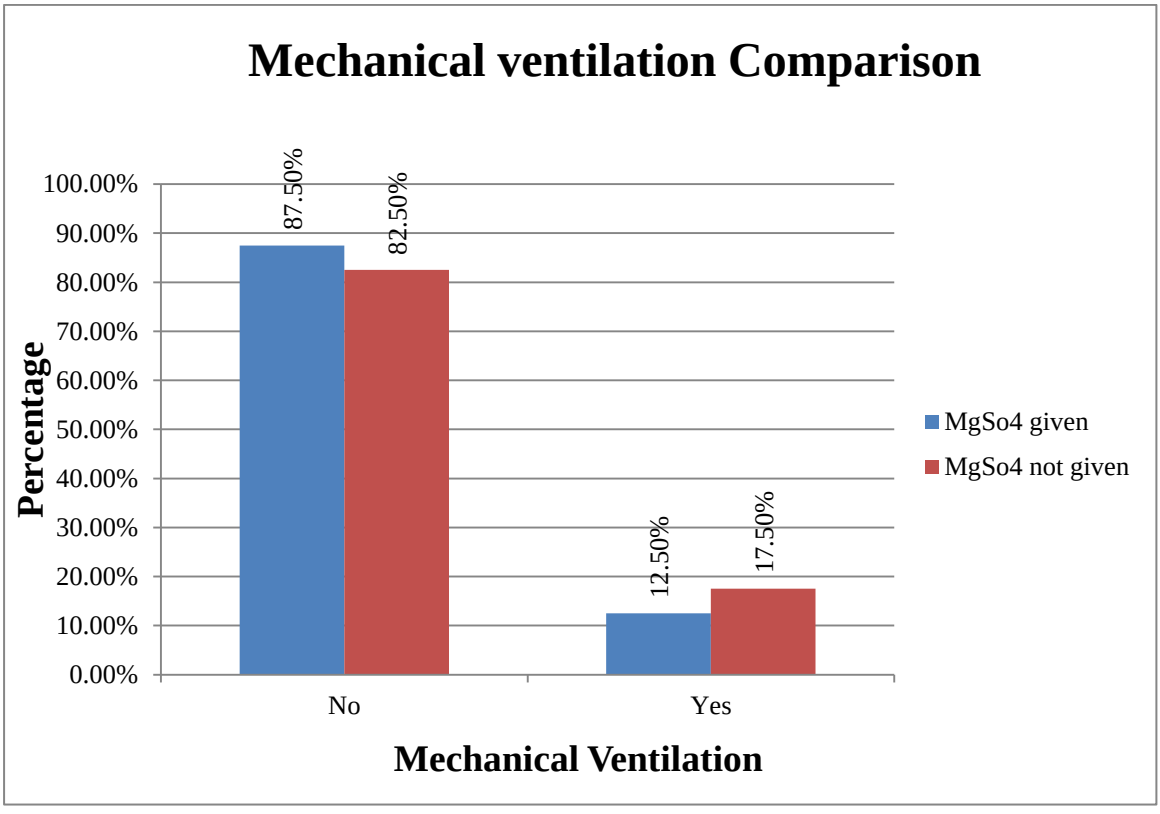
Graph 20: Bar diagram showing duration of hospitalization, ICU stay and HDU stay with respect to MgSo4 given among those with severe poisoning in subjects

Table 27 : Mechanical ventilation comparison between MgSo4 treated and not treated subjects

		MgSo4			
		8mg MgSo4 given		MgSo4 not given	
		Count	%	Count	%
Mechanical ventilation	No	35	87.5%	33	82.5%
	Yes	5	12.5%	7	17.5%

Z= -0.62 , p = 0.528

In the study among those who received MgSo4 12.5 % were intubated and mechnically ventilated and 17.5% were in intubated in patients who did not receive MgSo4. There was no difference in Mechanical ventilation.

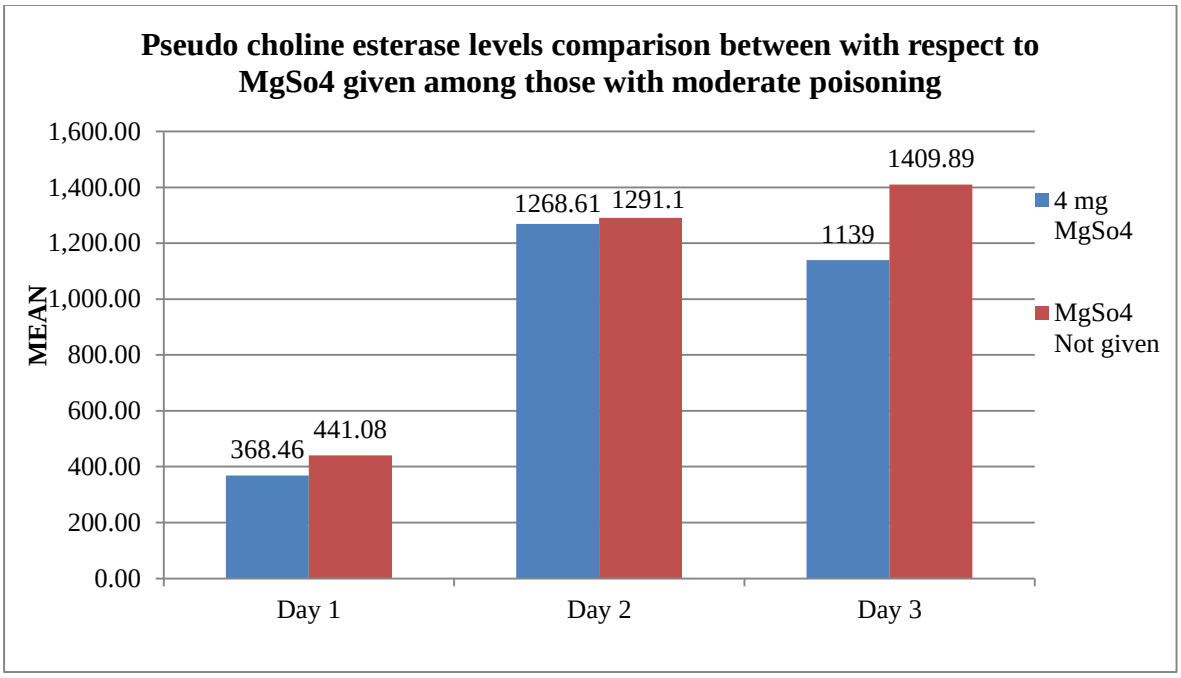


Graph 21: Bar diagram showing Mechanical ventilation comparison between MgSo4 treated and not treated subjects

Table 28: Pseudo choline esterase levels comparison between with respect to MgSo4 given among those with moderate poisoning

	MgSo4				P value
	4 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Day 1	368.46	216.39	441.08	358.71	0.381
Day 2	1268.61	1351.20	1291.10	1947.40	0.965
Day 3	1139.00	658.02	1409.89	1137.23	0.585

In the study among those with moderate poisoning, there was no significant difference in Pseudo choline esterase levels between those who received 4mg MgSo4 and who did not received MgSo4.

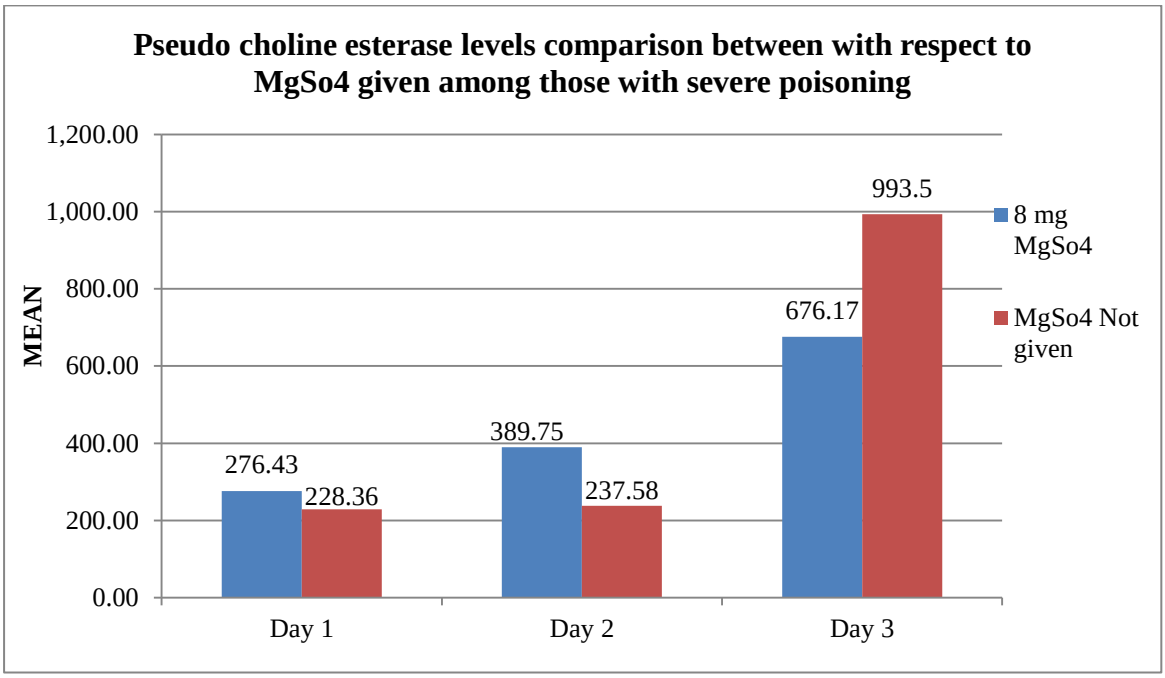


Graph 22: Bar diagram showing pseudo choline esterase levels comparison between with respect to MgSo4 given among those with moderate poisoning in study subjects

Table 29: Pseudo choline esterase levels comparison between with respect to MgSo4 given among those with severe poisoning

	MgSo4				P value
	8 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Day 1	276.43	206.05	228.36	43.42	0.401
Day 2	389.75	359.08	237.58	55.22	0.161
Day 3	676.17	549.05	993.50	1015.32	0.516

In the study among those with severe poisoning, there was no significant difference in Pseudo choline esterase levels between those who received 8mg MgSo4 and who did not received MgSo4.

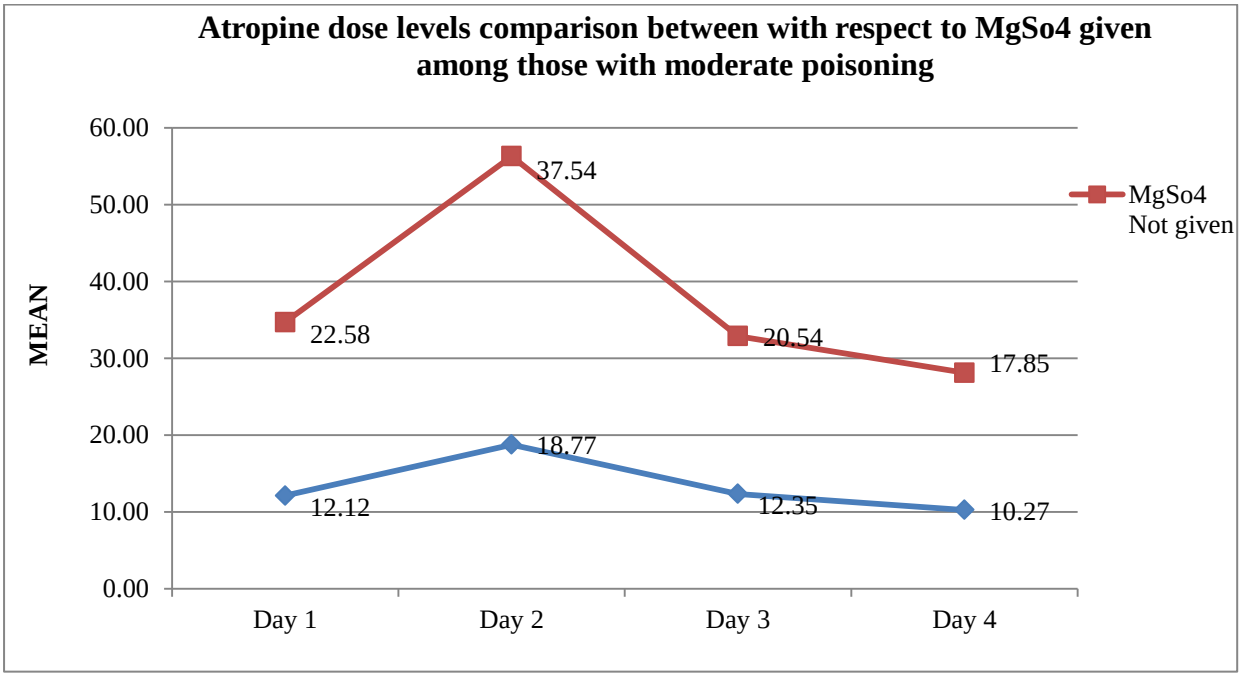


Graph 23: **Bar diagram showing pseudo choline esterase levels comparison between with respect to MgSo4 given among those with severe poisoning in study subjects**

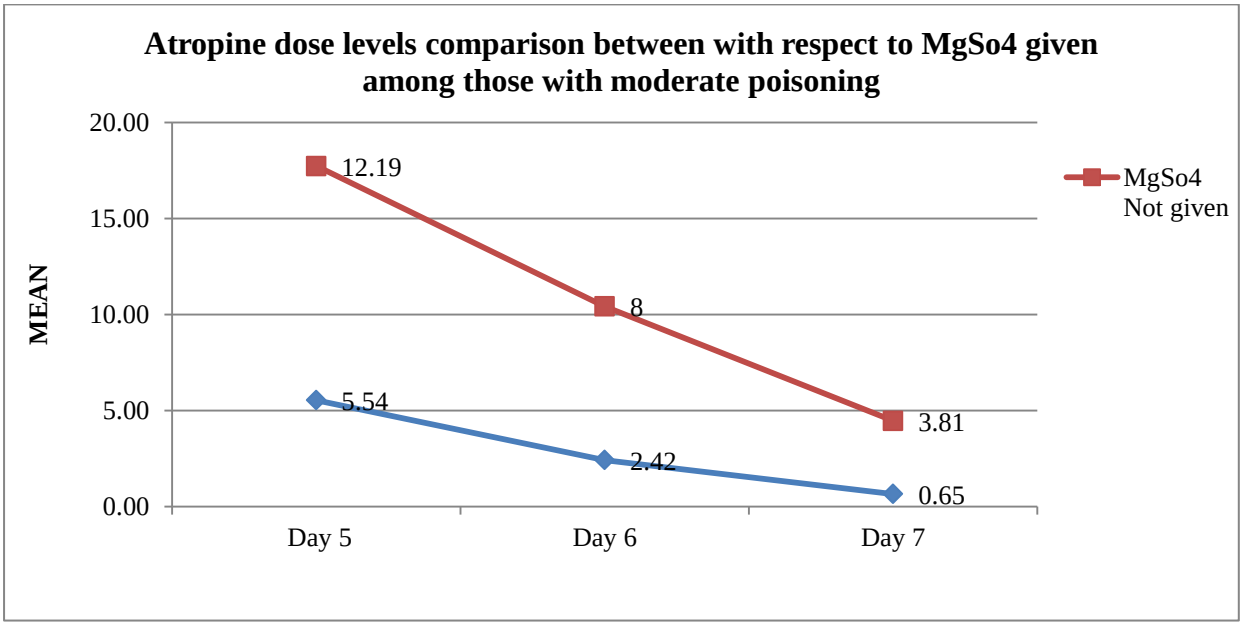
Table 30: Atropine dose levels comparison between with respect to MgSo4 given among those with moderate poisoning

	MgSo4				P value
	4 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Day 1	12.12	5.98	22.58	14.48	0.001*
Day 2	18.77	6.85	37.54	14.43	<0.001*
Day 3	12.35	5.77	20.54	7.67	<0.001*
Day 4	10.27	4.99	17.85	7.30	<0.001*
Day 5	5.54	4.61	12.19	4.37	<0.001*
Day 6	2.42	3.07	8.00	4.06	<0.001*
Day 7	0.65	1.60	3.81	4.22	0.001*

In the study among those with moderate poisoning, there was significant difference in Atropine dose levels between those who received 4mg MgSo4 and who did not received MgSo4 from Day 1 to Day 7.



Graph 24: Line diagram showing atropine dose levels comparison between with respect to MgSo4 given among those with moderate poisoning in study subjects

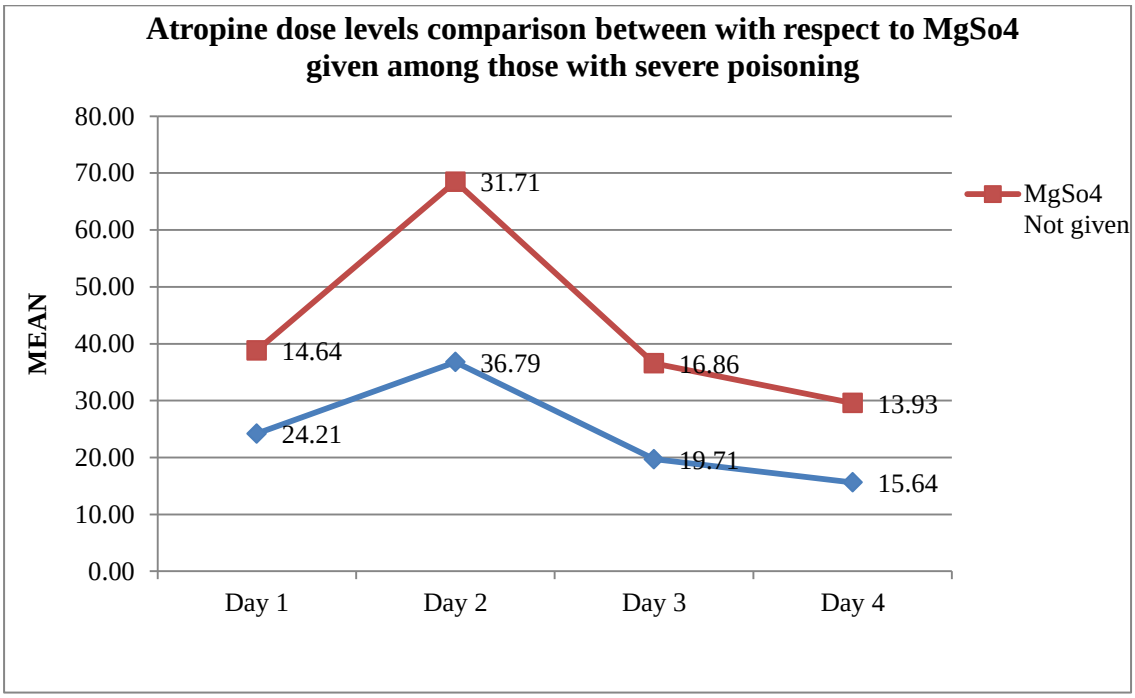


Graph 25: Line diagram showing atropine dose levels comparison between with respect to MgSo4 given among those with moderate poisoning in study subjects

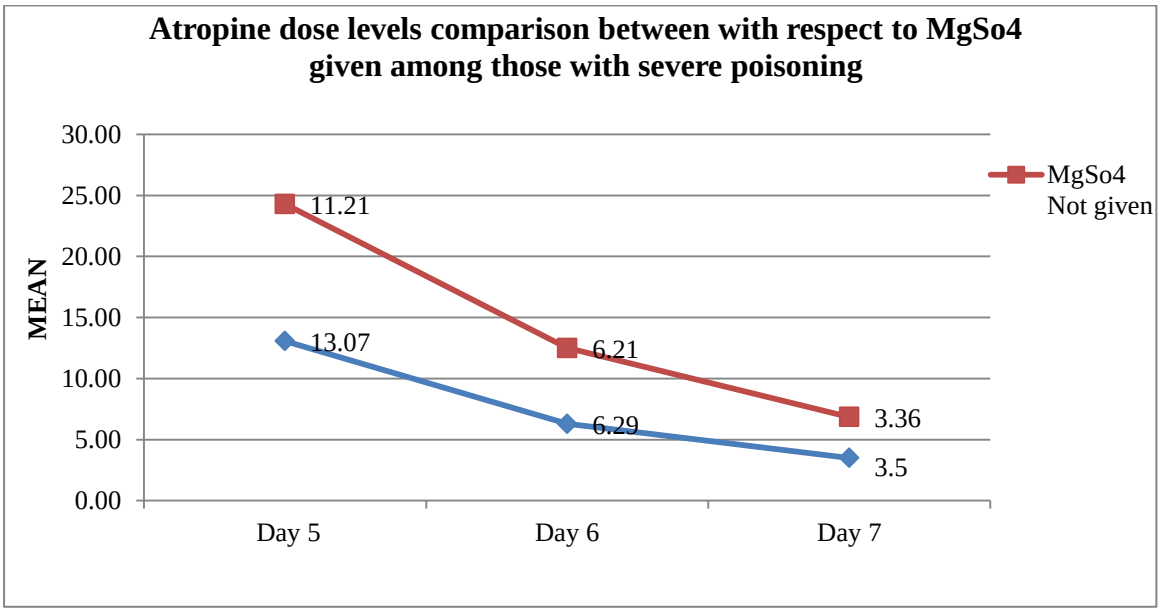
Table 31: Atropine dose levels comparison between with respect to MgSo4 given among those with severe poisoning

	MgSo4				P value
	8 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Day 1	24.21	10.74	14.64	10.24	0.023*
Day 2	36.79	11.83	31.71	10.92	0.249
Day 3	19.71	8.81	16.86	5.20	0.306
Day 4	15.64	8.44	13.93	3.56	0.490
Day 5	13.07	12.45	11.21	3.07	0.592
Day 6	6.29	3.87	6.21	3.53	0.960
Day 7	3.50	2.65	3.36	2.21	0.878

In the study among those with severe poisoning, there was significant difference in Atropine dose levels between those who received 8mg MgSo4 and who did not received MgSo4 Day 1 n day 1. And on other days there was no significant difference in Atropine dose requirement between two groups.



Graph 26: Line diagram showing atropine dose levels comparison between with respect to MgSo4 given among those with severe poisoning in study subjects

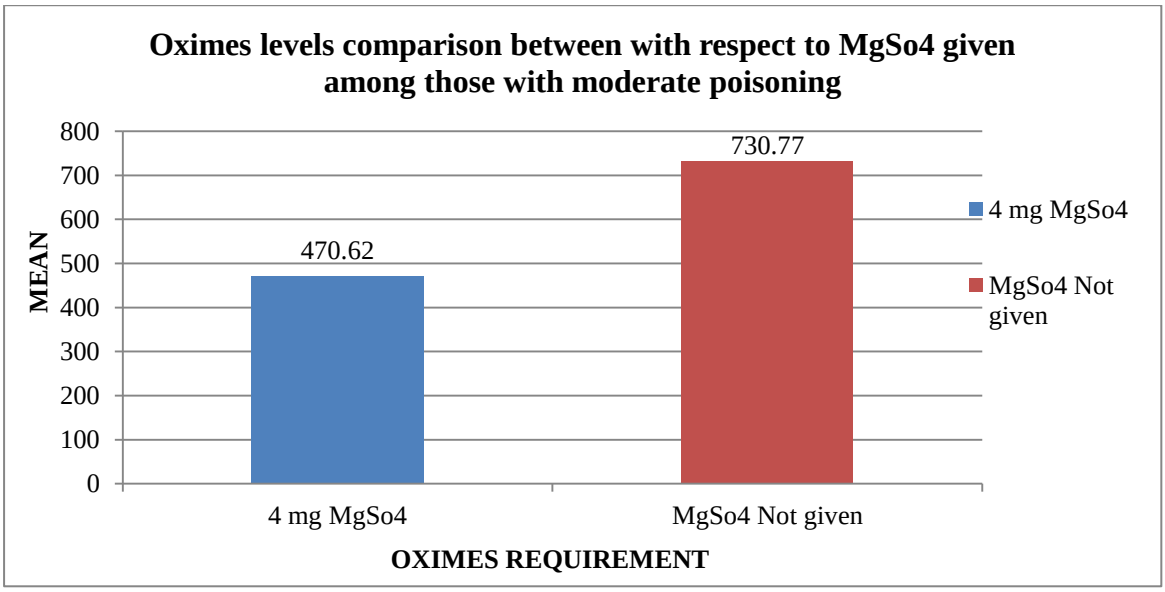


Graph 27: Line diagram showing atropine dose levels comparison between with respect to MgSo4 given among those with severe poisoning in study subjects

Table 32: Oximes levels comparison between with respect to MgSo4 given among those with moderate poisoning

	MgSo4				P value
	4 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Oximes requirement	470.62	379.91	730.77	268.86	0.006*

In the study among those with moderate poisoning, there was significant difference in mean Oximes requirement among those who received 4 mg MgSo4 and who did not receive MgSo4. Oximes requirement was low among those who received 4 mg MgSo4 group.

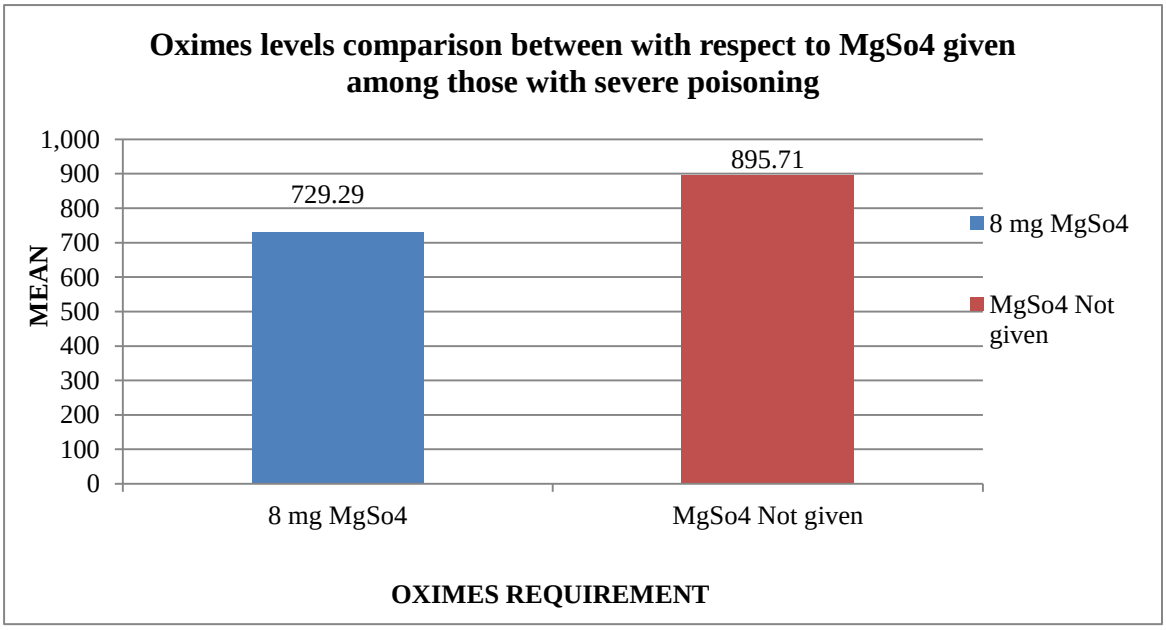


Graph 28: Bar diagram showing oximes levels comparison between with respect to MgSo4 given among those with moderate poisoning in study subjects

Table 33: Oximes levels comparison between with respect to MgSo4 given among those with severe poisoning

	MgSo4				P value
	8 mg MgSo4		MgSo4 Not given		
	Mean	SD	Mean	SD	
Oximes requirement	729.29	281.11	895.71	240.54	0.104

In the study among those with severe poisoning, there was no significant difference in mean Oximes requirement among those who received 8 mg MgSo4 and who did not receive MgSo4.

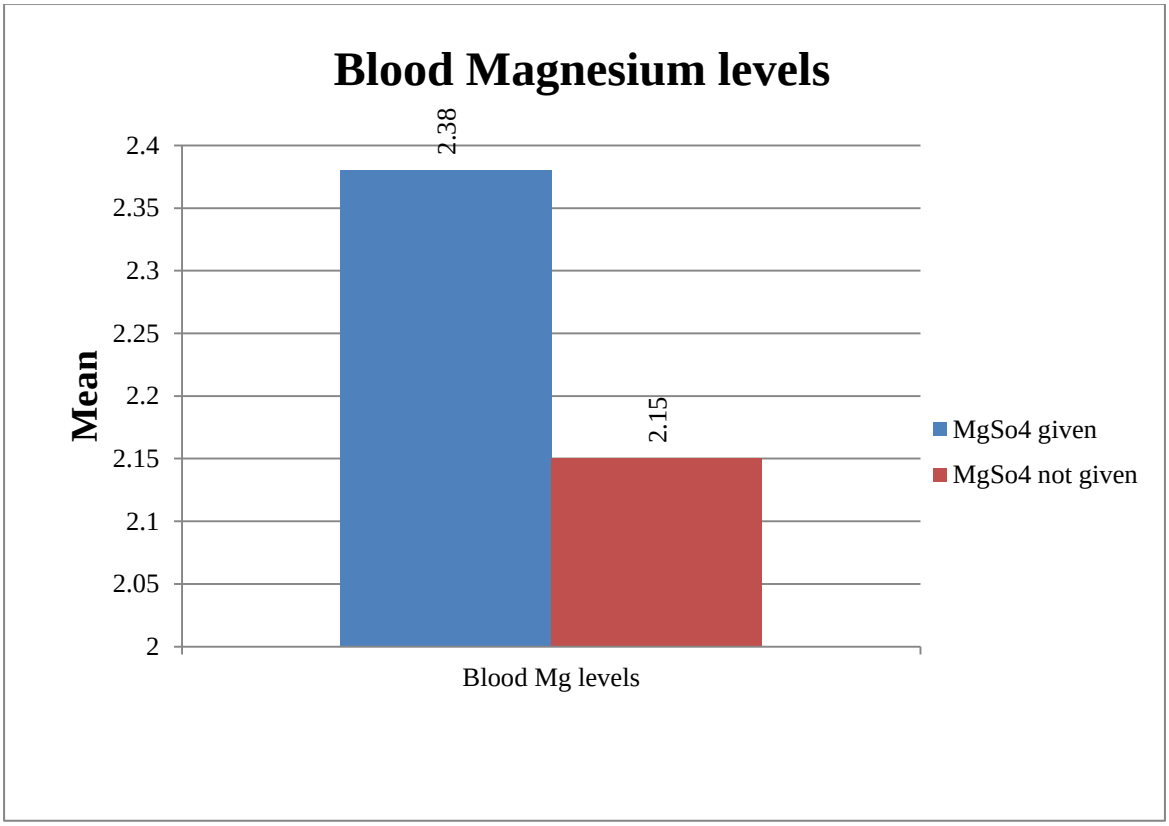


Graph 29 : **Bar diagram showing oximes levels comparison between with respect to MgSo4 given among those with severe poisoning in study subjects**

Table 34: Blood Mg levels between MgSo4 treated and not treated subjects

	MgSo4						P value
	MgSo4 given			MgSo4 not given			
	Mean	SD	Median	Mean	SD	Median	
Blood Mg levels	2.38	2.73	2.00	2.15	1.96	2.00	0.673

Blood Magnesium levels among those who received MgSo4 were 2.38±2.73 and those who did not receive MgSo4 were 2.15±1.96. However there was no significant difference between the two groups.



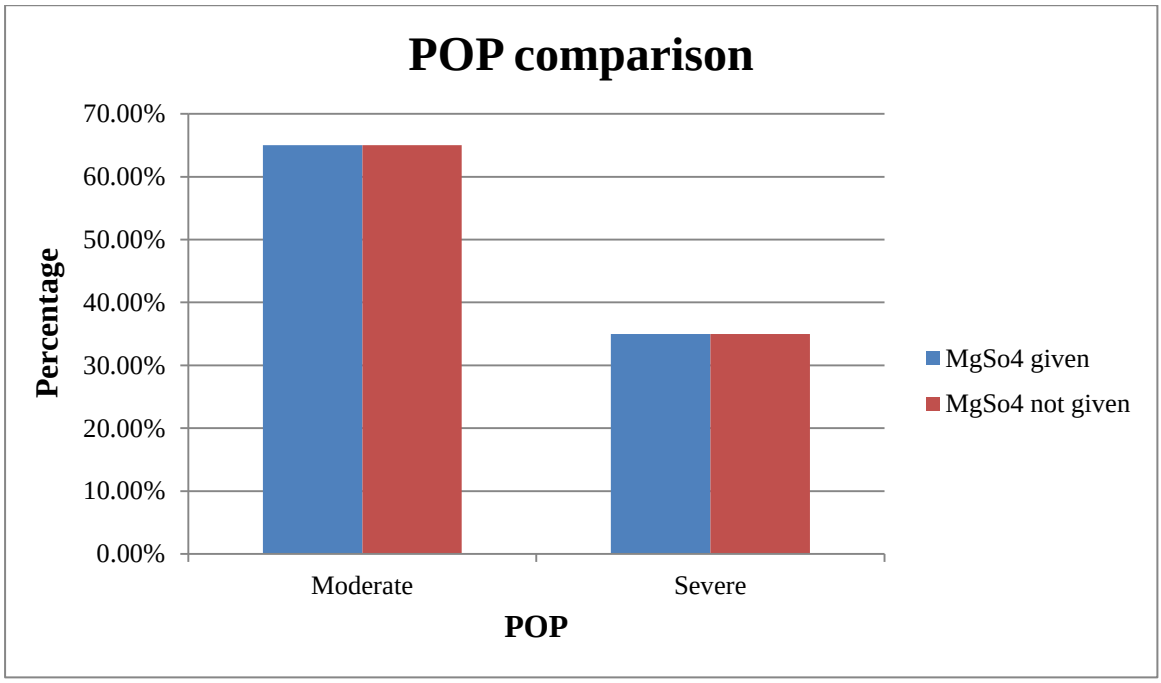
Graph 30: Bar diagram showing Blood Mg levels between MgSo4 treated and not treated subjects

Table 35: POP comparison between MgSo4 treated and not treated subjects

		MgSo4			
		MgSo4 given		MgSo4 not given	
		Count	%	Count	%
POP	Moderate	26	65.0%	26	65.0%
	Severe	14	35.0%	14	35.0%

$\chi 2 = 0.000$, df =1 , p =1.000

In the given study among those who received and did not receive MgSo4, 65% had moderate and 35% had Severe POP. There was no significant difference in POP between two groups.



Graph 31: Bar diagram showing POP comparison between MgSo4 treated and not treated subjects

DISCUSSION

DISCUSSION :

The causes of the high morbidity & mortality in OP poisoning are multifactorial and includes the increased toxicity of domestically available poisons, late presentation to the hospital, lack of health care workers compared with the large numbers of patients, lack of facilities including ICU care, antidotes and trained personnel for OP poisoning management.(94,95)

In this study, 51.2% of patients belong to 21-30 years of age (cream of the society). Other studies have also shown that working class is burdened. (96,07,98). Since we excluded mild poisoning, our study showed men (76.2%) preponderance. Overall 5.6% reported lifetime suicide attempts (6.9% of women and 4.3% of men). Generally, Non fatal deliberate self-harm' is more common in women.

Severe and fatal poisoning is commonly seen in men.

In the present study, poisoning with suicidal intent was more common (98.75%). This is similar to studies conducted in Nepal,[99] Turkey,[100] Gulbarga[101] where poisoning with suicidal intent where 95.24%, 75.9% & 97.25% of OP poisoning. Patient who presented within 24hrs after OP consumption were included in the study. In studies conducted at Chennai,[102] most patients (89.69%) presented within 6 hours.

Chlorpyrifos was common (35%) type of poisoning followed by Phorate(16.2%) and Diclorvos (13.8%). In a study conducted in Nepal,[99] methyl parathion (64.62%) was common then Baygon spray, malathion, dichlorvos. Methyl parathion was also one of the common poison in studies conducted in Chennai.[102] However, in a study conducted in Turkey,[100] dichlorvos was the commonest. Diffenrent types of poison consumed may due to the regional availability of the pesticide in different countries.

Clinical presentation is different in different OP poisoning. It depends on the specific OP consumed, the quantity absorbed, deposition into fat cells & the type of exposure.

About half of the patients (53.8%) were treated outside either by atropine, PAM or stomach wash and referred to us. Clinical presentation in these patients was different

with respect to heart rate, pupil size, and conscious levels. The patient was then assessed based on clinical judgment. The POP scale was used to grade severity and divide the groups based on severity.

Currrent different studies are assessing the efficacy of FFP, beta-adrenergic agonist, nicotinic receptor antagonist, organophosphorus hydrolases, lipid emulsions & magnesium in the management of OPCP.[6,103] In an animal study, MgSO4 showed benefit by reducing cholinergic stimulation after OPCP.[104] Magnesium is also useful in cardiac arrhythmias due to OPCP.[105]

Group 1 had 52 patients of moderate OP poisoning. 26 cases and controls were equally divided and matched. Group 1 patients were given 4g of MgSO4 within the first hour of presentation. 28 patients of group 2 had severe OP poisoning. 14 cases and controls were divided and were matched equally. Patients of group 2 were given 4g of MgSo4 within the first hour of presentation and another 4g was repeated after 6hrs.

MgSo4 dose of 4 g and 8g was chosen for our study, due to its ease of administration and less intense monitoring of magnesium levels. Even though a mild increase in magnesium levels was seen after MgSo4 administration none of the patients had any side effects related to magnesium like diminished knee reflex or hypotension. [9,12]

Most of the studies done, used only 4g of MgSo4 except a phase II study n which magnesium was given at a total dose of 4g, 8g, 12g and 16g in different groups of patients and Outcome was measured for effect of OP toxicity including respiratory failure, death and the total atropine used. Six patients died in the control group, 3 in 4g, 2 in 8g and 1 in 12g group. No mortality was seen in 16g group. Magnesium was well tolerated. The study was done on a small group & the cases & controls were not matched in the study.

Pseudo choline esterase was estimated on day 1,3 & 7. There was no significant difference in the mean pseudo choline esterase in cases & controls.

There is conflicting evidence regarding the effect of magnesium on atropine requirements. [9,12]

In our study, Atropine need was lower in patients receiving 4mg MgSo4 in moderate poisoning on all the days compared to their controls. In a study conducted in Bengaluru, the atropine need was less in MgSo4 treated group.

In severe poisoning atropine requirement reduced only in the first few days whilw on other days the reduced need was insignificant compared to controls.

Atropine need was more on day 2 compared to day 1. Poisoning was observed in late in the evening or night.

Oximes requirement was less in 4g MgSo4 treated group. No significant difference in oximes requirement in 8g MgSo4 treated group compared to controls was noted.

Average oximes requirement per patient during their complete stay did not differ in both groups as patients were given oximes for a fixed period of 48hrs or till atropine was given. There are some side effects of oximes in neuromuscular recovery,[106] but its reactivation of enzyme acetylcholinesterase is also questionable. Many studies have questioned the effectiveness, dosing, timing and in fact, in some, it was found to be harmful.[7]

The need for intubation and mechanical ventilation depends on the severity of OP poisoning.[107] Our study showed no statistical difference in intubation and mechanical ventilation between cases & controls. However earlier studies have shown a significant reduction in intubation & mechanical ventilation in the Magnesium treated group. This is due to a decrease in acetylcholine release and facilitating, the metabolism of OPCP, which the intermediate syndrome.[12] This may be the reason for the reduction in the need for intubation after an initial 24 h in the magnesium group.

The average duration of mechanical ventilation in our study did not differ in the cases & controls; this is similar to few earlier studies. [106,108,109] A single dose of MgSO4 is not enough to keep a sustained therapeutic level, which may influence the duration of mechanical ventilation. [12]

Reducing the atropine and PAM requirement has reduced the duration of hospital stay in m gnesium treated patients, which further supports the beneficial role of magnesium in the management of OPCP.

No mortality benefit was noted between the groups in our study. Basher *et al*. noted reduced mortality with increasing doses of MgSO4.[12]

A clinical study showed a reversion of the neuroelectrophysiological defects due to OPCP.[110] In an earlier study, 4 g of MgSO4 when administered with in the first 24 h of OPCP consumption, reduced mortality, and duration of hospitalization.[9]

In moderate poisoning, Duration of hospital stay and HDU stay was less among those who received 4mg MgSo4 compared to those who did not receive MgSo4. Whereas the ICU stay had no statistical difference.

In severe poisoning, there was no significant difference in duration of stay in hospital, ICU stay and HDU stay between those who received MgSo4 and who did not received MgSo4.

SUMMARY

SUMMARY

- In this study about 51.2% patients belonged to age group of 21-30.
- A male preponderance (76.2%) was observed.
- OP poisoning with suicidal intent was more common (98.75%).
- Chlorpyrifos (35%) was comman type of poisoning followed by Phorate(16.2%) and Diclorvos (13.8%).
- About half of the patients (53.8%) were treated outside either by atropine, PAM or stomach wash and were referred to us.
- Group 1 had 52 patients of moderate OP poisoning. 26 cases were given 4g of MgSO4.
- Group 2 had 28 patients of severe OP poisoning. 14 cases were given 8g of MgSo4.
- Pseudo choline esterase was repeated on day 1,3 & 7. There was no difference in mean pseudo choline esterase between cases and controls in both the groups.
- In moderate poisoning, Atropine requirement was lower in MgSo4 treated patients on all the days compared to those who didn't receive it.
- Where as the in severe poisoning the initial days atropine requirement only reduced and other days decrease was not significant.
- Oximes requirement was low among those who received 4 mg MgSo4 group. But no significant difference in mean Oximes requirement among those who received 8 mg MgSo4 and who did not receive MgSo4.
- There was no reduction in the need for intubation and mechanical ventilation.
- The duration of hospital stay and HDU stay in moderate poisoning was less in patients receiving magnesium, as atropine requirement was less. There was no difference in ICU stay.
- In severe poisoning there was no difference in ICU & hospital stay.
- There was no significant mortality difference between the groups.

CONCLUSION

CONCLUSION

Addition of MgSO4 to standard therapy has shown significant clinical improvement of moderate OPC poisoning by reducing the atropine & oxime requirement and its side effects. Duration of hospital stay was reduced after MgSo4 administration. It does not influence need for intubation, the duration of ICU stay, mechanical ventilation and mortality. The adverse side effects of MgSo4 were not noted with single dose of 4g of MgSo4.

However in severe poisoning, there is no influence of MgSo4 on primary outcomes like atropine & oxime requirement, hospital stay, need for intubation and mechanical ventilation, ICU stay and mortality.

RECOMMENDATIONS

- Along with the standard care of OPC poisoning, this study recommends MgSO4 to be added to the standard management.
- Future multicentric studies with larger sample size are required.
- Studies should be carried on daily and different dosing of magnesium.
- Frequent measurement of magnesium levels to maintain the therapeutic levels, may be needed to fully assess the effect of magnesium on outcome in OPCP.
- Delayed complications like neuropathy should also be followed up.
- Magnesium along with other modalities like fresh frozen plasma, nicotinic receptor antagonist, beta-adrenergic agonist, lipid emulsions, organophosphorus hydrolases in addition to standard treatment must be evaluated.

LIMITATION

The study had certain limitations.

- A relatively smaller small sample size
- Confirmation of exposure by analysis & identification of the specific organophosphate should be done.
- Patient's delay in seeking medical attention and alcohol also influences the outcome.
- The patients were followed up only during their stay and hence we are not able to comment on delayed complications.
- As the primary focus of this study was to observe the effect of $MgSO_4$ on the need for mechanical ventilation and ICU stay, it is not sufficiently powered to comment on the effect of $MgSO_4$ on mortality.
- MgSo4 was given to patient who presented with 24hrs of OP consumption only.

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ANNEXURES

Title: *MgSO4 in acute OP poisoning*

PROFORMA

Name: Date:

Age / Sex:

Residential Address:

Mobile No:

Case History:

Other known Illness:

Outside treatment given:

On admission BP: Pulse rate: GCS:
Pupils: Neck lift: secretions:

Daily follow up					
DATE					
BP					
HR					
Pupils					
Neck lift					
secretions					

CVS- RS-

P/A- CNS-

MgSO4 gms.					
Pseudo cholinesterase					
Daily atropine requirement					
Oximes usage					
Blood Mg level					
Hospitalization (days)					
Mechanical ventilation					
Recovery					
Signature					

PATIENT INFORMATION SHEET

Study Title: **Study of Effect of Magnesium Sulphate in Acute Organophosphorus Poisoning**

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Aim: To assess the effect of MgSO4 on the outcome in acute OP poisoning patients admitted to medical wards.

Organophosphorus poisoning (OP) is the most common poisoning in India because of its easy availability. There are pproximately about 26- 35 cases of OP poisoning every month in our institute. There are more than 3,00,000 deaths each year in developing countries.

MgSO4 along with conventional therapy has shown to reduce mortality, need for intubation and duration of hospitalization.

This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The Institutional Ethics Committee has reviewed this study and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you

will get will not change if you don’t wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

CONSENT FORM

*I ---------- participant, hereby give consent to participate in the study entitled "**Study of Effect of Magnesium Sulphate in Acute Organophosphorus Poisoning**"*

I have been explained that;

1. *I would have to provide a blood sample for the study purpose.*
2. *MgSO4 will be given as per requirement and study.*
3. *I have to answer the questionnaires related to project.*
4. *If need arises I give consent for intubation and ventilator support.*
5. *I do not have to incur any additional expenditure on my inclusion into the study.*
6. *The data generated from my clinical examination and laboratory tests and other reports will be used in the study (which may be subsequently published) without revealing my identity in any manner.*

I affirm that I have been given full information about the purpose of the study and the procedures involved and have been given ample opportunity to clarify my doubts in my mother tongue. In giving my consent, I have not faced any coercion. I have been informed that, notwithstanding this consent given, I can withdraw from the study at any stage.

For any further clarification you can contact the study investigator: Dr.Rumaisa Ahmed

Signature of participant: *Place:*

Name of participant: *Date:*

ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ: ತೀವ್ರ ಆರ್ಗೋನೋಫಾಸ್ಫೋರಸ್ ವಿಷಪೂರಿತದಲ್ಲಿ ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್ನ ಪರಿಣಾಮದ ಅಧ್ಯಯನ

ಸ್ಟಡಿ ಸೈಟ್: ಆರ್.ಎಲ್.ಎಲ್ ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆ, ತಮಾಕಾ, ಕೋಲಾರ್.

ಗುರಿಯು: ವೈದ್ಯಕೀಯ ವಾರ್ಡ್ಗಳಲ್ಲಿ ಒಪ್ಪಿಕೊಂಡ ತೀವ್ರ ಓಪನ್ ವಿಷ ರೋಗಿಗಳ ಫಲಿತಾಂಶದ ಬಗ್ಗೆ MgSO4 ಪರಿಣಾಮವನ್ನು ನಿರ್ಣಯಿಸಲು.

ಆರ್ಗನೋಫಾಸ್ಫೊರಸ್ ವಿಷ (ಒಪಿ) ಭಾರತದಲ್ಲೇ ಅತ್ಯಂತ ಸಾಮಾನ್ಯವಾದ ವಿಷವಾಗಿದೆ ಏಕೆಂದರೆ ಇದು ಸುಲಭ ಲಭ್ಯತೆಯಿಂದಾಗಿ. ನಮ್ಮ ಇನ್ಸ್ಟ್ಯೂಟ್ನಲ್ಲಿ ಸುಮಾರು ತಿಂಗಳಿಗೆ 26 ರಿಂದ 35 ಪ್ರಕರಣಗಳು ಒಪಿ ವಿಷಕಾರಿಯಾಗಿವೆ. ಅಭಿವೃದ್ಧಿಶೀಲ ದೇಶಗಳಲ್ಲಿ ಪ್ರತಿ ವರ್ಷವೂ 3, 00,000 ಕ್ಕಿಂತ ಹೆಚ್ಚು ಸಾವುಗಳು ಸಂಭವಿಸುತ್ತವೆ.

ಸಾಂಪ್ರದಾಯಿಕ ಚಿಕಿತ್ಸೆಯೊಂದಿಗೆ MgSO4 ಮರಣದ ಪ್ರಮಾಣವನ್ನು ಕಡಿಮೆ ಮಾಡಲು ತೋರಿಸಿದೆ, ಆಸ್ಪತ್ರೆಗೆ ಸೇರಿಸುವಿಕೆ ಮತ್ತು ಅವಧಿಯ ಅವಶ್ಯಕತೆ.

ಈ ಮಾಹಿತಿಯು ನಿಮಗೆ ಅಧ್ಯಯನದ ಸಾಮಾನ್ಯ ಹಿನ್ನೆಲೆ ನೀಡಲು ಉದ್ದೇಶಿಸಿದೆ. ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪಿಕೊಂಡರೆ ನಾವು ನಿಮ್ಮಿಂದ (ಮಾಹಿತಿ ಪ್ರಕಾರ) ಮಾಹಿತಿಯನ್ನು ಅಥವಾ ನಿಮ್ಮ ಅಥವಾ ಎರಡಕ್ಕೂ ಜವಾಬ್ದಾರರಾಗಿರುವ ವ್ಯಕ್ತಿಗಳನ್ನು ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ಇತಿಹಾಸವನ್ನು ತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಕಟಣೆಗಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿರಿಸಲಾಗುವುದು ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನವು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯಿಂದ ಪರಿಶೀಲಿಸಲ್ಪಟ್ಟಿದೆ ಮತ್ತು ನೀವು ಸಂಸ್ಥೆಯ ಎಥಿಕ್ಸ್ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತವಾಗಿರುತ್ತೀರಿ. ಈ ಅಧ್ಯಯನಕ್ಕೆ ಒಪ್ಪಿಗೆ ನೀಡಲು ಯಾವುದೇ ಕಡ್ಡಾಯವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಳ್ಳುವುದಾದರೆ ಮಾತ್ರ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆಗೆ ನೀವು ಸಹಿ / ನೀಡಬೇಕಾಗಿದೆ.

ಒಪ್ಪಿಗೆ ಪತ್ರ

ನಾನು ---------- ಪಾಲ್ಗೊಳ್ಳುವವರು, ಅದರ ಮೂಲಕ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪಿಗೆ ನೀಡಿ "ಪರಿಣಾಮದ ಅಧ್ಯಯನ ತೀವ್ರ ಆಗ್ನೇಯಫಾಸ್ಫೋರಸ್ ವಿಷಪೂರಿತ ಮೆಗ್ನೀಸಿಯಮ್ ಸಲ್ಫೇಟ್"

ನಾನು ಅದನ್ನು ವಿವರಿಸಿದೆ;

1. ನಾನು ಅಧ್ಯಯನದ ಉದ್ದೇಶಕ್ಕಾಗಿ ರಕ್ತ ಮಾದರಿಯನ್ನು ಒದಗಿಸಬೇಕಾಗಿದೆ.

2. ಅಗತ್ಯತೆ ಮತ್ತು ಅಧ್ಯಯನಕ್ಕೆ ಅನುಗುಣವಾಗಿ MgSO4 ನೀಡಲಾಗುವುದು.

3. ನಾನು ಯೋಜನೆಗೆ ಸಂಬಂಧಿಸಿದ ಪ್ರಶ್ನಾವಳಿಗಳಿಗೆ ಉತ್ತರಿಸಬೇಕು.

4. ಅಗತ್ಯವಿದ್ದರೆ ನಾನು ಒಳ ಮತ್ತು ಗಾಳಿ ಪೂರೈಕೆ ಬೆಂಬಲಕ್ಕಾಗಿ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ.

5. ನಾನು ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಸೇವೆಗಾಗಿ ಯಾವುದೇ ಹೆಚ್ಚುವರಿ ಖರ್ಚು ಮಾಡಬೇಕಾಗಿಲ್ಲ.

6. ನನ್ನ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸದೆ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ವೈದ್ಯಕೀಯ ಪರೀಕ್ಷೆ ಮತ್ತು ಪ್ರಯೋಗಾಲಯ ಪರೀಕ್ಷೆಗಳು ಮತ್ತು ಇತರ ವರದಿಗಳಿಂದ ಉತ್ಪತ್ತಿಯಾಗುವ ಡೇಟಾವನ್ನು (ತರುವಾಯ ಪ್ರಕಟಿಸಬಹುದು).

ನಾನು ಅಧ್ಯಯನದ ಉದ್ದೇಶ ಮತ್ತು ಪೂರ್ಣಗೊಳಿಸಿದ ಕಾರ್ಯವಿಧಾನಗಳ ಬಗ್ಗೆ ಪೂರ್ಣ ಮಾಹಿತಿ ನೀಡಲಾಗಿದೆ ಎಂದು ನನ್ನಲ್ಲಿ ದೃಢಪಡಿಸಿದೆ ಮತ್ತು ನನ್ನ ಮಾತೃಭಾಷೆಯಲ್ಲಿ ನನ್ನ ಅನುಮಾನಗಳನ್ನು ಸ್ಪಷ್ಟಪಡಿಸಲು ಸಾಕಷ್ಟು ಅವಕಾಶವನ್ನು ನೀಡಲಾಗಿದೆ. ನನ್ನ ಒಪ್ಪಿಗೆ ನೀಡುವಲ್ಲಿ, ನಾನು ಯಾವುದೇ ದಬ್ಬಾಳಿಕೆಯನ್ನು ಎದುರಿಸಲಿಲ್ಲ. ಈ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡಿದ್ದರೂ, ಯಾವುದೇ ಹಂತದಲ್ಲಿ ನಾನು ಅಧ್ಯಯನದಿಂದ ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು ಎಂದು ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

ಮತ್ತಷ್ಟು ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ನೀವು ಅಧ್ಯಯನದ ತನಿಖೆದಾರರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು: Dr. ರುಮೈಸಾ ಅಹ್ಮದ್

ಭಾಗವಹಿಸುವವರ ಸಹಿ: *ಸ್ಥಳ:*

ಪಾಲ್ಗೊಳ್ಳುವವರ ಹೆಸರು: *ದಿನಾಂಕ:*

KEY TO MASTER CHART

B/L NVBS – bilateral normo vesicular breath sounds

BP – blood pressure

CNS – central nervous system

CVS – cardiovascular system

DAMA – discharge against medical advice

F - female

GCS – glasgow coma scale

HDU – high dependency unit

ICU - intensive care unit

IP No. – in patient number

M - male

mg – milli gram

mm – milli meter

NFND – no focal neyrological deficit

PA – per abdomen

POP

RS – respiratory system

S1 S2 – 1^{st} and 2^{nd} heart sounds

Sl No. – serial number

sl no.	IP no.	name	age	sex	compound	outside treatment	pulse	BP	GCS	pupils	neck lift	seizures	fasciulations	secretions	CVS	RS	CNS	PA	MgSo4 given	pseudo choline esterase	2	3		atropine requirement	day1	day 2	day3	day4	day5	day6	day7	oximes requirmnet	Blood Mg levels	days of hospitalization	mechanical ventilation	ICU stay	HDU stay	recovery	DAMA	Death	POP
1	610108	manjunath	18	M	cypermethrin	nil	110	110/80	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	200	200	2116	15	56	5	17	9	9	12	4	0	60	1.6	6	no	no	4	recovered	no	nil	moderate
2	611154	Santhosh kumar	34	M	dichlorvas	stomach wash + atropine + PAM	110	150/100	14/15	4mm	poor	no	yes	present	S1 S2 normal	B/L NVBS	drowsy	Soft	NG	800	3287		15	96	9	30	15	15	10	9	8	960	1.6	8	no	no	7	recovered	no	nil	moderate
3	611615	Srinivas	28	M	profenos+ cypermethrin	1 day treatment with atropine	170	140/90	13/15	5mm	present	no	no	absent	S1 S2 normal	B/L NVBS	B/L flaccid paralysis	Soft	NG	200	239	1967	15	183	18	55	28	32	15	10	9	60	1.7	12	no	1	10	recovered	no	nil	moderate
4	610162	Vinod Kumar	26	M	parathion	atropine	120	100/60	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	456	657	1200	15	67	13	20	15	11	8	0	0	60	1.7	5	no	no	4	recovered	no	nil	moderate
5	613398	manjunath naidu	45	M	Malathion	atropine	60	100/60	6\15	2mm	poor	no	no	present	S1 S2 normal	B/L crepts+	drowsy	Soft	8mg	200			15	66	16	20	14	10	6	0	0	60	1.3	5	no	3	2	recovered	no	nil	severe
6	614686	Venkataramappa	30	M	chlorpyrifos + cypermethrin	stomach wash	86	120/80	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	265	232	15	254	76	88	44	26	12	6	2	960	2.1	7	no	1	5	recovered	no	nil	moderate
7	617526	manjunath	25	M	chlorpyrifos + cypermethrin	stomach wash + atropine	112	110/70	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	480	2213		15	57	12	14	8	15	3	3	2	960	1.8	7	no	no	6	recovered	no	nil	moderate
8	619862	Kumar	25	M	fenthion	stomach wash	76	110/80	15/15	3mm	present	no	no	present	S1 S2 normal	B/L NVBS	NFND	Soft	NG	690			15	98	16	30	15	12	11	9	5	960	1.6	8	no	no	5	recovered	no	nil	moderate
9	620354	kakanna	55	M	fenthion	stomach wash	65	120/80	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	200			15	48	12	15	11	8	2	0	0	960	2.1	5	no	no	4	recovered	no	nil	moderate
10	616170	sudeep	19	M	dichlorvas	nil	65	130/90	15/15	3mm	poor	yes	yes	present	S1 S2 normal	B/L crepts +	NFND	Soft	NG	240	200	780	15	164	34	43	34	23	15	11	4	420	1.4	8	no	1	7	recovered	no	nil	severe
11	619159	bhagyamma	36	F	parathion	nil	87	150/100	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	890			15	169	36	45	36	32	15	5	0	960	1.5	6	no	no	4	recovered	no	nil	moderate
12	620171	janaki	19	F	chlorpyrifos + cypermethrin	stomach wash	112	130/90	15/15	3mm	present	no	yes	present	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	650	2300		15	48	5	15	10	12	4	2	0	960	1.5	6	no	no	5	recovered	yes	nil	moderate
13	626247	naveen	25	M	phorate	stomach wash + atropine + PAM	115	120/80	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	236		15	133	36	55	30	12	0	0	0	960	2	4	no	no	4	no	yes	no	severe
14	622872	parvathamma	45	F	parathion	stomach wash + atropine	119	100/60	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	205	340		15	70	11	23	24	12	0	0	0	960	1.9	4	no	no	4	recovered	no	nil	moderate
15	530534	seenappa	45	M	phorate	nil	113	130/70	6/15	1mm	poor	no	no	present	S1 S2 normal	B/L crepts+	unresponsive	Soft	8mg	337	232	2980	15	156	15	46	23	18	15	11	4	960	1.9	10	no	1	8	recovered	no	nil	severe
16	530542	hemavathi	22	F	chlorpyrifos + cypermethrin	nil	120	110/70	15/15	2mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	406	200	200	15	60	10	18	12	12	6	2	0	960	1.6	7	yes 1 day	2	6	recovered	no	nil	moderate
17	539378	roja	25	F	profenos+ cypermethrin	stomach wash + atropine	126	110/70	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	250	214	780	15	68	14	20	10	10	9	5	0	960	1.7	6	no	no	5	recovered	no	nil	moderate
18	541974	babu	25	M	fention	nil	86	100/60	15/15	3mm	present	no	no	present	S1 S2 normal	B/L NVBS	NFND	Soft	NG	229	200	1960	15	108	29	32	21	17	9	0	0	960	1.9	5	no	no	4	recovered	yes	nil	moderate
19	544895	savithramma	45	F	dichlorvas	stomach wash	121	130/70	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	240	2990		15	20	3	10	7	0	0	0	0	960	1.8	6	no	no	4	recovered	yes	nil	moderate
20	549458	sukanya	20	F	phorate	nil	61	130/70	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	8mg	210	214		15	96	10	30	18	12	15	8	3	960	1.4	7	yes 1 day	1	5	recovered	no	no	severe
21	561904	vinodh	32	M	phorate	stomach wash + atropine	120	180/100	drowsy	pinpoint	poor	no	no	present	S1 S2 normal	B/L crepts +	drowsy, fasiculations+	Soft	NG	200			15	140	42	40	26	15	9	5	3	960	2	7	yes 2 day	4	3	no	no	no	severe
22	576164	raghu ram	43	M	dichlorvas	nil	87	130/90	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	200	440		15	36	9	11	9	4	3	0	0	60	1.6	5	no	no	4	recovered	no	nil	moderate
23	576194	imanna	65	M	chlorpyrifos + cypermethrin	stomach wash	76	100/60	15/15	3mm	present	no	yes	present	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	234	200	1430	15	88	23	26	21	18	0	0	0	60	1.5	4	no	no	3	recovered	no	nil	moderate
24	588727	sarawathi	35	F	fenthion	atropine	126	130/90	13/15	4mm	poor	no	yes	present	S1 S2 normal	B/L crepts +	drowsy	Soft	NG	200	1406		15	300	45	60	26	32	19	16	16	960	1.6	12	1	4	7	recovered	no	nil	moderate
25	589154	madhuri	18	F	chlorpyrifos + cypermethrin	stomach wash + atropine	114	114/80	drowsy	3mm	poor	no	no	absent	S1 S2 normal	B/L crepts +	drowsy	Soft	4mg	240	2178		15	120	21	28	26	19	11	9	6	60	1.9	9	1	2	7	recovered	no	nil	moderate
26	589137	raghavendra	22	M	chlorpyrifos + cypermethrin	stomach wash + atropine + PAM	121	126/90	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	340	2235		15	48	5	15	10	12	4	2	0	60	2	6	no	nil	5	recovered	yes	nil	moderate
27	594745	Santhosh	22	M	phorate	nil	76	130/80	3\15	5mm	poor	no	no	present	S1 S2 normal	B/L crepts +	unresponsive	Soft	NG	200	206		15	88	36	52	0	0	0	0	0	400	1.9	2	yes 2 days	2	4	no	no	no	severe
28	597664	yalappa	30	M	diazinon	nil	77	110/90	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	450			15	20	5	9	3	3	0	0	0	960	1.6	4	no	nil	1	recovered	no	nil	moderate
29	598850	Shamshu khan	55	M	phorate	stomach wash	64	90/60	drowsy	5mm	poor	yes	yes	present	S1 S2 normal	B/L crepts +	drowsy, fasiculations+	Soft	NG	960	780	200	15	210	30	56	32	39	53	0	0	270	1.4	5	yes 1 day	2	3	no	no	death	severe
30	600166	manjunath	40	M	chlorpyrifos + cypermethrin	stomach wash	76	90/70	15/15	3mm	present	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	230	240		15	46	15	14	9	8	0	0	0	60	1.5	4	no	nil	2	recovered	no	nil	moderate
31	605783	Rafiq	40	M	chlorpyrifos + cypermethrin	nil	113	100/60	15/15	3mm	present	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	240			15	20	5	9	3	3	0	0	0	60	1.6	7	no	1	3	recovered	no	nil	moderate
32	403747	gangaraj	30	m	chlorpyriphos	nil	86	120/80	twelve	3mm	poor	yes	yes	present	S1 S2 normal	crepts+	drowsy	Soft	8mg	200	200		15	190	46	62	30	23	14	9	6	960	2.1	10	yes	1	4	recovered	no	nil	severe
33	185294	subhash	24	m	quinolphos	stomach wash	102	120/80	15/15	5mm	good	no	no	no	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	228	1178		15	106	20	32	15	13	15	10	1	480	2.1	7	no	1	4	recovered	no	nil	moderate
34	592472	chandra shekar	22	m	malathion	stomach wash + atropine	120	110/70	twelve	dilated	poor	yes	yes	present	S1 S2 normal	crepts	delirious	Soft	8mg	200	237	598	15	75	8	22	12	12	14	3	4	960	14	14	yes	2	6	recovered	no	nil	severe
35	530846	sathish kumar	26	m	chlorpyrifos + cypermethrin		62	130/70	15/15	1mm	poor	yes	yes	present	S1 S2 normal	crepts	fasiculations	Soft	8mg	200	200	200	15	120	26	32	18	17	10	7	2	960	1.2	9	yes 1 day	1	4	recovered	no	nil	severe
36	535080	chamaraju	18	m	profenofos	stomach wash	78	110/70	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	440	2210		15	21	6	7	5	2	1	0	0	460	1.6	7	no	no	5	recovered	no	nil	moderate
37	509091	ramappa	65	m	chlorpyriphos	stomach wash + atropine	65	126/90	15/15	4mm	good	no	yes	present	S1 S2 normal	B/L NVBS	NFND	Soft	NG	241			15	138	31	66	23	18	0	0	0	480	1.7	4	no	no	2	recovered	DAMA	nil	moderate
38	602429	manjunath	28	m	chlorpyriphos	nil	80	130/90	15/15	dilated	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	793	900	1645	15	70	12	21	14	12	9	2	0	400	2	6	no	no	4	recovered	no	nil	moderate
39	580713	manjunath	35	m	phorate	nil	112	110/70	15/15	3mm	poor	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	370	373		15	96	19	30	18	15	9	5	0	480	1.8	6	no	no	4	recovered	no	nil	moderate
40	587468	venkataramappa	55	m	unknown	nil	86	130/80	15/15	2mm	poor	no	no	present	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	200	1461	15	106	21	31	16	13	11	6	4	480	2.2	14	yes 2 days	3	5	recovered	no	nil	severe
41	314926	tanveer	30	m	chlorpyriphos	nil	88	150/100	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	200	200	15	120	21	31	16	13	11	6	8	480	2.1	17	no	1	11	recovered	no	nil	severe
42	592494	pillamma	80	F	monochlorophos	nil	99	130/90	15/15	4mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	240	200		15	90	19	31	16	13	7	4	0	480	1.4	6	no	no	5	recovered	no	nil	moderate
43	572273	nethravathi	24	f	phorate	nil	85	130/70	13/15	3mm	poor	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	200	992	15	96	15	32	15	12	11	7	4	960	1.6	18	no	no	14	recovered	no	nil	moderate
44	492971	deevaraj	25	M	malathion	nil	86	110/90	13/15	constricted	poor	no	no	present	S1 S2 normal	crepts	drowsy	Soft	NG	200	1295		15	150	27	41	22	12	9	9	8	960	1.2	9	yes 2 days	3	4	recovered	no	nil	severe
45	594095	nethravathi	27	f	phorate	nil	122	90/60	15/15	dilated	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	515	808	2414	15	126	26	35	21	12	11	8	8	680	2.2	14	no	no	10	recovered	no	nil	modetare
46	512755	srinivas	21	M	chlorpyrifos + cypermethrin	nil	128	140/90	14/15	constricted	poor	yes	yes	absent	S1 S2 normal	B/L NVBS	restless, fasiculations	Soft	NG	200	200	247	15	150	30	32	21	19	15	9	3	960	2.3	14	no	2	9	recovered	no	nil	severe
47	555314	Santhosh kumar	28	m	chlorpyrifos + cypermethrin	nil	77	130/90	13/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	irritable	Soft	NG	200	200	378	15	96	10	36	15	12	11	8	4	960	1.5	15	yes 1 day	2	5	recovered	no	nil	moderate
48	98151	narayana swamy	42	m	chlorpyriphos	nil	120	130/70	15/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	570		15	200	30	30	30	28	21	16	12	960	1.9	13	no	1	9	recovered	no	nil	moderate
49	624819	ramappa	55	m	chlorpyriphos	nil	86	120/80	15/15	2mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	200		15	116	11	35	18	23	12	8	5	480	2	10	no	no	7	recovered	no	nil	moderate
50	625731	nagesh	21	m	dichlorvas	nil	102	100/60	15/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	468		15	140	21	31	29	15	11	12	7	960	1.6	12	no	no	8	recovered	no	nil	moderate
51	620737	chittemma	26	F	malathion	atropine	120	180/100	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	atropinized	Soft	4mg	240	558		15	72	7	22	11	17	7	5	3	558	1.4	7	no	no	4	recovered	no	nil	moderate
52	622859	ayanna	60	m	chlorpyriphos	stomach wash + atropine	62	110/90	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	200	455	15	96	10	30	15	14	11	12	4	480	1.5	8	no	no	5	recovered	no	nil	moderate
53	615960	mohan	35	m	chlorpyriphos	nil	78	120/80	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	drowsy	Soft	NG	200	200		15	106	10	34	17	19	15	9	2	490	1.6	13	no	no	9	recovered	no	nil	moderate

sl no.	IP no.	name	age	sex	compound	outside treatment	pulse	BP	GCS	pupils	neck ilft	seizures	fasciulations	secretions	CVS	RS	CNS	PA	MgSo4 given	pseudo choline esterase	2	3		atropine requirement	day1	day 2	day3	day4	day5	day6	day7	oximes requirmnet	Blood Mg levels	days of hospitalization	mechanical ventilation	ICU stay	HDU stay	recovery	DAMA	Death	POP
54	626911	gangadhar	20	m	phorate	nil	65	120/80	15/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	660	5461		15	96	9	30	16	11	15	10	5	480	1.3	8	no	2	3	recovered	no	nil	moderate
55	570505	srinivas	48	m	malathion	nil	80	110/70	15/15	3mm	good	yes	yes	absent	S1 S2 normal	crepts	NFND	Soft	NG	200	200		15	106	11	35	15	18	15	7	5	960	2.3	9	yes 1 day	1	7	recovered	no	nil	severe
56	362647	chikkamuniyappa	65	m	malathion	nil	112	130/70	15/15	5mm	poor	yes	yes	present	S1 S2 normal	crepts	fasiculations	Soft	8mg	260	348	1073	15	104	10	38	18	12	12	10	4	960	2.4	8	no	no	6	recovered	no	nil	severe
57	261253	nagesh	21	m	dichlorvas	nil	86	110/70	15/15	4mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	200	560		15	87	19	26	14	15	13	0	0	80	14	5	no	no	3	recovered	no	nil	moderate
58	286460	harish s	28	m	triazophos	atropine	88	90/60	15/15	dilated	poor	no	yes	present	S1 S2 normal	B/L NVBS	atropinized	Soft	4mg	918	200		15	60	19	21	9	5	4	2	0	500	1.2	6	no	no	6	recovered	no	nil	moderate
59	470120	venkatesh	25	m	dichlorvas	nil	99	140/90	13/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	870			15	104	22	32	15	13	11	11	0	960	1.6	6	no	1	3	recovered	no	nil	moderate
60	411294	seenappa	26	m	dichlorvas	nil	85	130/90	13/15	1mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	309	200	602	15	87	17	26	18	13	9	4	0	60	1.2	6	no	no	5	recovered	no	nil	moderate
61	450721	prasad	25	m	chlorpyrifos + cypermethrin		86	130/70	15/15	5mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	300	3637		15	78	10	17	15	11	11	9	5	500	2.1	8	no	no	6	recovered	no	nil	moderate
62	526283	srinivasappa	45	m	chlorpyriphos	atropine	122	120/80	14/15	5mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200			15	96	24	26	19	11	9	7	0	480	1.6	6	no	no	4	recovered	no	nil	moderate
63	558181	pratika	20	f	chlorpyriphos	stomach wash	128	100/60	13/15	3mm	poor	yes	yes	present	S1 S2 normal	crepts+	drowsy	Soft	NG	200	200		15	116	13	34	16	14	11	9	6	480	1.9	11	no	no	9	recovered	no	nil	severe
64	312525	benedic arun kumar	37	m	dichlorvas	stomach wash	77	180/100	15/15	3mm	poor	no	no	present	S1 S2 normal	B/L NVBS	NFND	Soft	NG	1740	2574	3578	15	140	29	39	21	29	22	0	0	960	1.4	5	no	no	6	recovered	no	nil	moderate
65	545578	shilpa	25	f	chlorpyriphos	nil	120	110/90	15/15	3mm	good	no	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	4mg	891	5128		15	72	18	21	17	10	6	0	0	558	1.9	5	no	no	2	recovered	no	nil	moderate
66	599333	shilpa	30	f	malathion	stomach wash + atropine	88	120/80	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	260	520	713	15	96	9	25	17	15	13	9	5	480	1.4	8	no	no	6	recovered	no	nil	moderate
67	5502257	roopa	30	f	phorate	atropine	66	120/80	15/15	dilated	poor	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	600			15	106	21	35	16	13	11	10	0	490	14	6	no	no	4	recovered	no	nil	moderate
68	461116	gayathri	22	f	phorate	atropine	77	110/70	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	640	7263		15	96	10	27	12	11	10	7	3	480	1.8	9	no	no	5	recovered	no	nil	moderate
69	582746	parashuram	25	m	profenofos	stomach wash	56	130/70	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	200	206		15	106	27	31	11	13	15	9	0	960	1.9	6	no	no	4	recovered	no	nil	moderate
70	10208	nagaveni	33	f	phorate	atropine	87	110/70	15/15	3mm	good	no	no	absent	S1 S2 normal	B/L NVBS	NFND	Soft	NG	563	1182		15	104	24	32	21	14	8	5	0	960	2.1	6	no	no	5	recovered	no	nil	moderate
71	740917	madhusudan	39	m	cypermethrin	nil	110	130/70	15/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	drowsy	Soft	NG	200	200		15	100	15	18	18	16	14	11	4	960	2.2	10	no	no	6	recovered	no	nil	severe
72	742151	rajesh	25	m	dichlorvas	stomach wash + atropine + PAM	110	110/70	15/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	NFND	Soft	8mg	200	340		15	96	12	31	11	11	9	4	3	960	2.1	8	no	1	5	recovered	no	nil	severe
73	741744	prakash	24	m	profenos+ cypermethrin	1 day treatment with atropine	170	90/60	3\15	pinpoint	poor	no	no	absent	S1 S2 normal	B/L NVBS	drowsy, fasiculations+	Soft	NG	430	760	1169	15	87	13	26	16	13	11	6	2	960	2.1	10	no	no	8	recovered	no	nil	severe
74	740094	vijay kumar	30	m	parathion	atropine	120	140/90	3\15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	drowsy	Soft	8mg	290	200		15	78	8	24	14	12	9	5	3	960	1.4	9	yes 1 day	2	3	recovered	no	nil	severe
75	740932	raghavendra	27	m	malathion	atropine	60	130/90	13/15	pinpoint	poor	yes	yes	absent	S1 S2 normal	B/L NVBS	NFND	Soft	8mg	200			15	89	9	26	21	17	13	2	1	960	2.1	7	no	no	5	recovered	no	nil	severe
76	735283	rahul	33	m	chlorpyrifos + cypermethrin	stomach wash	86	130/70	13/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	drowsy, fasiculations+	Soft	8mg	260	200		15	94	16	29	11	14	13	7	4	960	1.9	7	no	no	6	recovered	no	nil	severe
77	734353	syed suleman	32	m	chlorpyrifos + cypermethrin	stomach wash + atropine	112	120/80	3\15	pinpoint	poor	no	no	absent	S1 S2 normal	B/L NVBS	drowsy	Soft	8mg	240	200	430	15	106	11	31	14	13	12	12	9	960	2.1	8	no	1	6	recovered	no	nil	severe
78	733880	pavan	20	m	fenthion	stomach wash	76	100/60	13/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	drowsy, fasiculations+	Soft	8mg	200	200		15	88	9	26	17	12	9	5	2	960	1.3	8	no	1	5	recovered	no	nil	severe
79	733836	ravi	21	m	fenthion	stomach wash	65	180/100	13/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	drowsy	Soft	8mg	200	280	680	15	93	9	27	15	12	6	4	2	960	2.4	7	no	1	5	recovered	no	nil	severe
80	731611	someshekar	30	m	dichlorvas	nil	65	110/90	15/15	pinpoint	poor	no	no	present	S1 S2 normal	crepts+	NFND	Soft	NG	240			15	77	10	21	14	12	9	9	2	960	2.5	9	no	no	7	recovered	no	nil	severe