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ORGNOPHOSPHATE POISONING AND ITS NEUROLOGICAL MANIFESTATIONS

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ABSTRACT
Organophosphate (OP) compounds are one of the common cause poison related hospital admission in India with varying morbidity and mortality. These poisons cause various clinical manifestations due to inactivation of acetylcholine esterase enzyme at muscarinic, nicotinic and central nervous system. Multiple types of neurological disorders are associated with OP compound poisoning, such as Acute cholinergic crisis, Intermediate syndrome (IS), Organophosphate induced delayed polyneuropathy (OPIDN), Chronic organophosphate induced neuropsychiatric disorder (COPIND) and very rarely Guillain-Barre syndrome (GBS). Early diagnosis and management can reduce morbidity and mortality.

INTRODUCTION

Organophosphate compounds are commonly used as poisons for suicidal purpose in India [1]. particularly in central and south India [2-4]. Major reason being due to free availability of OP compounds in the shops and commonly used everywhere in agriculture as insecticide. About 2 million suicidal poisoning occurs due to insecticide every year in the world according to WHO (World health organisation) and most deaths are occurring in developing countries [5]. The morbidity and mortality depends upon the type and quantity of preparation consumed

OP compound poisoning causes various clinical manifestations due to acetylcholine esterase enzyme inactivation. Among this manifestation, the neurological features cause more morbidity and mortality. Organophosphate poisoning can cause 4 different types of neurological syndromes such as acute cholinergic crisis, Intermediate syndrome, Organophosphate induced delayed polyneuropathy, and Chronic organophosphate induced neuropsychiatric disorders. Recently OP poison induced Guillain Barre syndrome has been documented [6].

Acute Cholinergic Crisis: also known as type-1 paralysis [7]. It is seen during early phase of OP poisoning and recovers over 2-3 days.

Mechanism: due to Acetyl cholinesterase (AchE) enzyme inhibition by OP compound, causing more and more accumulation of Acetyl choline (Ach) at nerve endings. This results in initial excessive stimulation and later exhaustion of cholinergic synapses.

Clinical features: Stimulation of Muscarinic receptors (Postganglionic parasympathetic) causes – Nausea, vomiting, diarrhoea, urination, salivation, lacrimation, bronchospasm, rhinorrhea, bronchorrhoea, headache, bradycardia, miosis, conjunctival hyperemia and blurring of vision. Stimulation of Nicotinic receptors (Neuromuscular junction) causes – Fasciculations and

muscle paralysis (Depolarisation and desensitization block). Stimulation of Central nervous system causes – Emotional irritability, mental obtundation, cognitive impairment, convulsion and coma.

Electro-physiological studies – Compound muscle action potentials (CMAPS) – During initial phase of weakness, with supra maximal stimulation shows repetitive discharges (due to excessive Ach) with decremental and incremental phenomenon [8,9]. During progression of weakness, these potentials show decremental response.

Single fibre electromyography shows jitter [10] (due to failure of transmission of impulse at motor end plate).

Treatment: Mainly the decontamination of exposed surface (skin) and gastrointestinal tract and administration of atropine as antidote. Atropine can be used either as boluses or as infusion. In case of bolus strategy, 2-4 mg of atropine given every 5-15 minutes (IV) till the signs of atropinisation is achieved (Pulse rate >90bpm, systolic blood pressure >90mmHg, pupils no more constricted, drying of axilla and secretions). In case of Infusion strategy of atropine 0.02-0.08 mg/kg/hr is also found to be effective. Oximes (especially Pralidoxime) are also been used during the cholinergic phase. These drugs act by reactivation of Acetylcholine esterase enzyme. Pralidoxime can also been given as bolus form (30mg/kg bolus followed by 1gm every 8^{th} hourly) or as continuous infusion (500mg/hr) with equal benefit [11].

INTERMEDIATE SYNDROME

Also known as type-2 paralysis [7] or Nicotinic syndrome. The term IS was coined by Senanayake and Karelliedde in 1987 [12]. Since this syndrome occurs after cholinergic phase and before OPIND hence called as intermediate syndrome. Incidence is about 20 to 68% [13]. Onset seen between 1 to 4 days of ingestion of OP compound [14] and recovery is seen over 4 to 18 days.

Mechanism: multiple factors are involved, like down regulation of Ach receptors, nicotinic paralysis [15], gross reduction of serum Ach esterase [16], prolonged action of Ach on nicotinic receptors and prolonged suppression of Ach esterase enzyme.

Clinical features: Initially the ocular, bulbar and neck muscles followed by proximal limb muscles and respiratory muscles in that order of severity. During recovery proximal limb muscles are last to recover. Sensory function will be normal. Deep tendon reflexes are depressed and pyramidal tract involvement has also been reported [17]. Agents involved in IS are fenthion, monocrotophos, dimethoate, methyl parathion (Most common), diazinon, ethyl parathion, malathion and sumithion.

Diagnosis: Electro-physiological studies include repetitive response for a single supramaximal electrical stimulus, decremental-incremental response or decremental response to high frequency repetitive nerve stimulation (30-50Hz). In case of decremental response, the ratio of amplitude of ninth compound muscle action potential (CMAP) to first CMAP is considered as the severity marker of decremental response and as electrodiagnostic marker for the intermediate syndrome [18]. These electrophysiological studies are influenced by pancuronium, oximes and magnesium sulfate.

Treatment: mechanical ventilation for respiratory muscle weakness. No role of atropine in this phase.

ORGANOPHOSPHATE INDUCED DELAYED POLYNEUROPATHY

Seen in patients who consume Thiortho cresyl phosphate (due to weak anticholinesterase activity). The onset is delayed up to 7-21 days of exposure. In case of mild neuropathy – the outcome is good, where as in severe neuropathy – patients develop foot drop, claw hand, atrophy, spasticity or ataxia.

Mechanism: due to phosphorylation and ageing of axonal enzyme called neuropathy target esterase [19,20] and causes degeneration of long axons with loss of myelin and Schwann cell proliferation.

Clinical features: Earliest symptoms are paresthesias and calf pain. Initially it starts with weakness of distal leg muscle (foot drop), later on with involvement of proximal leg muscles and the trunk muscles. Involvement of proximal muscles of hand can cause claw hand. Deep tendon jerks are absent. Cranial nerves and autonomic nervous system are not involved (cortico-spinl tracts and dorsal column involvement will be apparent when peripheral neuropathy improves).

CHRONIC ORGANOPHOSPHATE INDUCED NEUROPSYCHIATRIC DISORDERS

Usually seen between 4-40 days.

Mechanism: due to exposure of patients to high levels of OP compound, prolonged exposure to low dose of OP compounds or due to the sequelae of convulsion, anoxia, arrhythmias and respiratory failure which occur due to complication of OP compound during cholinergic crisis.

Clinical features: lethargy, depression, confusion, drowsiness, anxiety and irritability. Other features like schizophrenia, dystonic reactions, cogwheel rigidity and choreoathetosis.

Electrophysiological findings such as jitter has been seen in patients who were exposed to OP compounds for prolonged period.

GUILLAIN BARRE SYNDROME (GBS)

Guillain-Barr'e syndrome is one of the causes of

neuro-muscular paralysis. The annual incidence is about 1.2-2.3 / 100000 people [21], and men are affected more than women [22]. Caused by infection with C.jejuni, Cytomegalo virus, Epstein-bar virus, M.Pneumonia and H.Influenza. Diagnosed based on progressive symmetrical weakness in both arms and legs over days to 4 weeks, areflexia, and albumino-cytological dissociation.

Mechanism: Infection causes immune response where antibodies produced cross react with various gangliosides of peripheral nerves.

Treatment is either Plasma exchange (PE) or Intravenous Immunoglobulin (IV-Ig) with no difference among these two and no better outcome if both are combined. Very rarely organo-phosphate compound can cause demyelinating polyneuropathy [6] have reported a case of GB syndrome where patient on 26th day of consumption of OP compound (Chloropyrifos) developed weakness of lower limbs (ascending in nature). Patient was treated successively with methylprednisolone and plasmapharesis. Patient recovered fully over 15 days.

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DECLARATION OF INTEREST

None declared.

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