Commentary

Organophosphate (OP) compounds remain a significant cause of self-harm in developing countries. OP poisoning produces different forms of acute, subacute or delayed neurotoxicity that causes critical complications in life via neuromuscular, respiratory, and cardiac paralysis. An epidemiological pattern of poisoning reveals momentous variation in the form of poisoning and the number of deaths. Treatment and outcome of these patients may differ considerably between the developed world and resource-limited countries, often with scanty hospital infrastructure, shortage in Intensive Care Unit (ICU)-capacities, with sparse options for mechanical ventilation, as well as the cost of treatment. Several classes of OPs have different toxicokinetic and aging characteristics that are increasingly recognized.[1] Many patients die during the full-blown cholinergic crisis despite early, aggressive, and effective treatment.[2] Approximately 20% of the patients may experience Intermediate Syndrome (IMS), which is also a major contributor to the high morbidity and mortality.[3] Many complications that develop in the later period are indirectly preconditioned through the early phase of poisoning where initiation of organ damage commonly occurs (e.g., hypoxia, aspiration, and hypotension).[4]

There has been controversy in the toxicology world concerning the true definition and existence of a different neurological phase, as a separate entity. Acute paralysis is observed secondary to continued depolarization at the neuromuscular junction during the cholinergic phase.[5] The intermediate syndrome develops usually 24-96 hours after resolution of the initial phase and is characterized by weakness of the proximal muscles followed by respiratory and cranial nerve palsies.[5,6] Extrapyramidal symptoms, such as, rigidity, resting tremors, akinesia, and impairment of speech are a rare occurrence in OP poisoning in the intermediate or in the initial phase.[5] A literature search shows that there have been reports of a few patients with extrapyramidal symptoms in OP poisoning, of which most are children.[7]

The pathophysiology leading to basal ganglia impairment complicating organophosphate insecticide poisoning is perhaps complex and multifactorial. The resultant imbalance between dopamine and acetylcholine in basal ganglia and substantia nigra may cause the extrapyramidal syndrome.[7] It is thought that a certain low critical threshold of acetylcholine is required to regulate dopaminergic neurotransmission within the basal ganglia, and once this threshold is overcome by an abundance of acetylcholine (Ach), a clinical syndrome of basal ganglia impairment may follow.[7] Some authors suggested that increased Ach concentration in the cholinergic interneurons of the striatum has the ability to stimulate the efferent enkephalin-containing glutaminergic receptor in the subthalamic nucleus and a decline in the cortical glutamate stimulation that reduces striatal activity, resulting in decreased cortical glutamate excitation that clinically mimics a dopamine-deficiency state.[8] The functional threshold is probably genetically determined and is not predictable by sex, ethnic background, or even by the actual dose of the poison.[7,8] The relatively immature brain of children may also put them at risk for crossing this threshold early on to develop Parkinsonian symptoms.[8]

Early diagnosis and prompt treatment may prevent long-term impairment of the basal ganglia function in prone patients, especially children, acutely exposed to organophosphate insecticides. Extrapyramidal manifestations have disappeared even without treatment, but the time taken for recovery may be longer.[6] Very few patients may remain with Parkinsonism, suggesting that the path of basal ganglia impairment complicating

organophosphate insecticide poisoning may not be as favorable and transitory.[6] The usage of amantadine, which possibly enhances neurotransmission, may be beneficial to avoid severe long-term impairment.[7] Extrapyramidal symptoms following OP poisoning are rare, may be often overlooked, and masked by other complications, or misinterpreted as a severe affective disorder. More detailed clinical observations of organophosphate-poisoned patients are needed and detailed studies on the biological functions of acetylcholinesterase, including the influence on the nigrostriatal dopaminergic system, are considered necessary.

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