

## Commentary

In the article, entitled “Mania following organophosphate poisoning”<sup>[1]</sup> the authors reported occurrence of a neuropsychiatric condition, mania in a 33-years old female followed by acute organophosphorus compound (OPC), chlorpyrifos (CPF) poisoning. A similar case report was presented by Bradwell 1964<sup>[2]</sup> in a farm exposure with demeton-S-methyl, an OPC. It was the first reported case of organic bipolar affective disorder following chronic OP poisoning. Bipolar disorder causes extreme mood swings from very high energy (mania) to depression. Neuropsychiatric and other neuronal disorders by OPC poisoning have been reported mainly in chronic exposures. There are different groups of OPCs and not necessarily all the OPCs show similar effect as CPF. CPF is moderately

toxic OPC; however, chronic exposure in humans is linked to developmental and autoimmune disorders with neurological effects. Exposure during pregnancy retards the mental development of children. CPF use in homes has been banned since 2001 in the United States. However, the compound is still widely applied as agrochemicals throughout the world. Different groups and organizations in the USA are trying to completely ban the usage of this compound.

Evidences regarding non-cholinergic effect of OPC, particularly with neurological disorders have been demonstrated in the literature.<sup>[3,4]</sup> Cognitive disorders were found associated with acute and chronic exposures, and psychiatric disorders mostly

with poisonings.<sup>[5]</sup> Bayrami *et al.*<sup>[6]</sup> concluded that oxidative stress and inhibition of acetylcholinesterase can be seen in chronically OPC exposed people but incidence of neuropsychological disorders seems a complex multivariate phenomenon that might be seen in long-term high-dose exposure situations. Wani *et al.*<sup>[7]</sup> reported that dichlorvos, another OPC can induce oxidative stress leading to the caspase-dependent nigrostriatal dopaminergic neuronal cell death. The OPC-induced neurological disorders include multiple sclerosis, motor disability, Alzheimer, Parkinson, depression, schizophrenia, mood disorders and bipolar disorders etc., They all are reported to be due to increased levels of pro-inflammatory cytokines.<sup>[8]</sup>

Now, it has been established that OPC is not merely act as anticholinesterases rather exhibit multitoxic effect. Their inhibitory effect interacts concurrently with adrenergic, dopaminergic and cholinergic sites. The acetylcholine released during the acute toxicity may lead to augmented discharge of biogenic amines like histamines, serotonin and catecholamines. An excess of biogenic amines is dangerous if unchecked. Fatehyab *et al.*<sup>[9]</sup> showed significant alterations in the levels of dopamine, noradrenaline and serotonin in rat brains after administration of dichlorvos. Thus, link between OPC effects in the brain and subsequent changes in neurotransmitter mechanisms is known to be important in the control of mood and behavior.

In short, it can be concluded that the use of OPC and long-term brain damage, could have global significance, particularly in many developing countries where adequate protective measures are lacking.

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## References

1. Mohapatra S, Rath N. Mania following organophosphate poisoning: A rare case report. *J Neurosci Rural Pract* 2014;5:S86-8.
2. Bradwell RH. Psychiatric sequelae of organophosphorous poisoning: A case study and review of the literature. *Behav Neurol* 1994;7:117-22.
3. Terry AV Jr. Functional consequences of repeated organophosphate exposure: Potential non-cholinergic mechanisms. *Pharmacol Ther* 2012;134:355-65.
4. Androutsopoulos VP, Hernandez AF, Liesivuori J, Tsatsakis AM. A mechanistic overview of health associated effects of low levels of organochlorine and organophosphorous pesticides. *Toxicology* 2013;307:89-94.
5. Blanc-Lapierre A, Bouvier G, Gruber A, Leffondré K, Lebailly P, Fabrigoule C, *et al.* Cognitive disorders and occupational exposure to organophosphates: Results from the PHYTONER study. *Am J Epidemiol* 2013;177:1086-96.
6. Bayrami M, Hashemi T, Malekiran AA, Ashayeri H, Faraji F, Abdollahi M. Electroencephalogram, cognitive state, psychological disorders, clinical symptom, and oxidative stress in horticulture farmers exposed to organophosphate pesticides. *Toxicol Ind Health* 2012;28:90-6.
7. Wani WY, Sunkaria A, Sharma DR, Kandimalla RJL, Kaushal A, Gerace E, *et al.* Caspase inhibition augments Dichlorvos-induced dopaminergic neuronal cell death by increasing ROS production and PARP1 activation. *Neuroscience* 2014;258:1-15.
8. Nurulain SM, Adeghate E, Shamsulislam A, Yasin J, Kamal MA, Sharma C, *et al.* Sub-chronic exposure of no-observable adverse effect dose of terbufos sulfone may cause neuroinflammation. *CNS Neurol Disord Drug Targets*. 2014 Oct 23. [Epub ahead of print].
9. Ali SF, Hasan M, Tariq M. Levels of dopamine, norepinephrine and 5-hydroxytryptamine in different regions of rat brain and spinal cord following chronic administration of organophosphate pesticide dichlorvos. *Indian J Exp Biol* 1979;17:424-6.

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