Acute off-target toxicity and chronic toxicity of organophosphorus compounds

Dear Editor,

We appreciate the authors' valuable work in elucidating the rare manifestation of hyperglycemic ketoacidosis in acute poisoning with organophosphorus compound (OPC).[1] However, it is important to exercise caution and emphasize that more research is required in this area. This approach is necessary to rule out the possibility of random occurrences and biological variability. The history of chronic starvation has to be ruled out thoroughly in all such cases, which could also have partly contributed to the presenting picture because it was a case of suicidal ingestion.

As mentioned by the authors, OPC ingestion causes dysregulation of glucose homeostasis in multiple ways of endocrine disruption by increasing adrenaline levels, reducing lipolysis, increasing glycogenolysis, and reducing glycogenesis. However, the nicotinic receptor stimulation leading to high adrenaline concentration has been recognized as one of the most plausible mechanisms for hyperglycemia in an acute OPC poisoning scenario. Although the sympathetic surge and the transient dysfunction of pancreatic beta cells on prolonged stimulation by acetylcholine seem to partly explain the hyperglycemia in a case of acute OPC poisoning, the exact pathophysiology behind its transition to ketoacidosis remains elusive. In the present case, there is also a possibility of preexisting ketoacidosis due to some other reason, such as starvation, which may have presented incidentally combined with hyperglycemia due to the exposure to OPC. Usually, OPCs are manufactured or sometimes mixed with certain other diluents and solvents, such as xylene and toluene, which may also contribute to hyperglycemia with ketoacidosis.

Chronic exposure to OPC, including several other highly hazardous pesticides (enlisted in the top ten toxic compounds of global concern by the World Health Organization (WHO)), is a risk factor for metabolic syndrome. Pesticides have long been identified as endocrine disruptors affecting human health in general and maternal–fetal health in particular.[2] The proposed pathways for pesticide-induced metabolic syndrome include, but are not limited to, impairment of insulin signaling, dysfunction of pancreatic beta cells, dysregulation of glucose metabolism, secretion of pro-inflammatory mediators, release of adipokines, excess of free fatty acids, induction of oxidative stress, feedback effects of glucocorticoids, and dysbiosis of the gut microbiota.[3]

Within the Indian medical landscape, it is regrettable that the off-target acute toxicity of various poisonings (like in the present case where the toxicity was exerted on glucose homeostasis, but the actual target is the cholinergic system), alongside the latent, chronic morbidities stemming from poisoning, is frequently relegated to the periphery of our collective medical focus. For example, because there is no comprehensive poison incident reporting database, it is difficult for us to have the chance to monitor the long-term health consequences experienced by poisoning survivors. Furthermore, it is challenging to keep and organize all the health records for these cases using our current infrastructure. There is a need for a national policy on this matter.

It is clear that farmers, pesticide applicators, and agricultural laborers as a community face an elevated risk of coming into contact with pesticides due to their occupation. This exposure can have a substantial impact on their health because they often have limited knowledge about the proper use of personal protective equipment, and financial constraints may further hinder their access to such equipment. Besides, OPC residues are known to be present in food, posing potential health risks for the general population, which is a growing concern.

In cases where a patient presents with symptoms of mild cholinergic symptoms but lacks a clear history of pesticide exposure, primary care physicians should consider the possibility of accidental poisoning with OPCs rather than immediately suspecting myasthenia gravis. Similarly, there have been instances of homicide attempts by spraying OPC on a person's face, leading to dermal and inhalational exposure as well, although they were not reported in the literature. A primary care physician should also be aware of the fact that exposure to OPC occurs by all possible routes, including intravenous ingestion, intraperitoneal injection, and not just ingestion.[4]

The silent epidemic of increasing metabolic disorders, such as diabetes, among the Indian agricultural rural population needs to be seriously investigated, bearing in mind the risk factors of occupational and environmental exposure to highly hazardous pesticides, as was done in other countries.[5] It is high time we adopted and implemented the International Code of Conduct on Pesticide Management in our country to reduce the preventable hazards of pesticide use. The incidence of hyperglycemia with ketoacidosis in cases of acute exposure to OPC compounds is very unlikely unless the exposure is chronic. Moreover, a chemical analysis of the gastric lavage contents would have confirmed the ingestion of OPC and might have also revealed the concomitant ingestion of any other toxic substance as

well. Once again, we are thankful to the authors for discussing something about the morbidity of chronic pesticide poisoning in their scientific work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Received: 17-09-2023 **Revised:** 22-11-2023
Accepted: 22-11-2023 **Published:** 04-04-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1555_23

How to cite this article: Kattamreddy AR, Nishanth VS. Acute off-target toxicity and chronic toxicity of organophosphorus compounds. J Family Med Prim Care 2024;13:1137-8.