

## Oxidative stress and hyperglycemia in aluminum phosphide poisoning

Aluminum phosphide (AIP) poisoning via rice tablet ingestion can be fatal, as there is no effective antidote. The exact AIP' mechanism of action remains poorly understood, although appears to induce oxidative stress and increase extramitochondrial release of free oxygen radicals resulting in lipid peroxidation and protein denaturation of cellular membranes in various organs.<sup>[1]</sup> Meanwhile, hyperglycemia has been a known prognostic factor in severe AIP poisoning cases.<sup>[2]</sup> In our previous study, patients admitted to emergency room (ER) with glucose levels above 140 mg/dL had an increased risk of death, suggesting involvement of other mechanisms such as impaired mitochondrial respiratory function or insulin resistance and  $\beta$ -cell dysfunction.<sup>[3]</sup> Moreover, oxidative stress is a common finding in AIP poisoning and reportedly there has been a significant increase in lipid peroxidation in AIP intoxication patients along with a reduction in total antioxidant capacity and total thiol molecules.<sup>[4]</sup> However, it is unknown whether hyperglycemia induces oxidative stress or hyperglycemia is a result of oxidative stress in AIP poisoning. Some consequences oxidative stress in AIP poisoning include the development of insulin resistance, pancreatic  $\beta$ -cell dysfunction, glucose tolerance impairment, and mitochondrial dysfunction, which all end up with hyperglycemic state. Animal and human studies have shown an inverse association between insulin sensitivity and levels of reactive oxygen species.<sup>[5]</sup> Moreover, oxidative stress can activate a series of pathways involving a family of serine/threonine kinases, which in turn have a negative effect on insulin signaling.<sup>[5]</sup> On the other hand, hyperglycemia causes increased oxidative stress through several pathways, of

which a main mechanism seems to be overproduction of superoxide ( $O_2^-$ ) through mitochondrial electron transport chain.<sup>[6]</sup> Thus, oxidative stress can be possibly ameliorated by management of hyperglycemia and changes or disruptions in these mechanisms may reduce the risk of insulin resistance and the development of hyperglycemia and, furthermore, may have a potential role in its treatment. Meanwhile, the use of antioxidants may present a useful role in the treatment of oxidative stress and hyperglycemia. The purpose of this communication was to alert toxicologists to these related mechanisms of AIP-induced toxicity and to propose further studies to elucidate other factors involved in such.

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