A review of oculotoxicity in iodine overdose

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Introduction

Iodine is a trace chemical element primarily found in oceans as a highly water-soluble iodide ion. It is an important molecule used for industrial purposes. It is also used in clinical medicine as a drug and as a substance for radiological investigations. Iodine compounds are commonly used in contrast media and in chemotherapy for thyroid disorders. Potassium iodate (KIO_3) is an iodized salt used for iodine supplementation in areas endemic for goiters.

Iodine is a vital micronutrient required at all stages of life. Fetal life and early childhood being the most critical phases of requirement. It is an essential element required to produce thyroid hormones. Thyroid hormones are important for normal growth and differentiation of cells, fetal growth, nervous system development, bone formation, reproductive tract development and general wellbeing. They are important for intermediary metabolism of virtually all tissues and is of fundamental importance for the development of the central nervous system in the fetus and the newborn (1). Therefore, iodine deficiency due to a lack of dietary iodine is a leading cause for developmental delays, mental retardation, endemic goiter, and many other health problems (2). Iodine deficiency disorders are a preventable public health problem with a simple and inexpensive solution, the iodine supplementation. Universal salt iodization (USI) is a global strategy recommended by the UNICEF and WHO in 1994 to prevent iodine deficient disorders (3).

Although iodine is beneficial for humans, there are risks involved in iodine excess such as hypothyroidism, hyperthyroidism, cancers, and autoimmune thyroid diseases (4,5,6). Iodine toxicity occurs due to excess iodine results from chronic consumption or from acute toxicity. Acute iodine toxicity results from ingestion of iodide compounds accidently or from attempted deliberate self-harm with iodine containing substances. Iodine excess and toxicity which occurs from regional dietary sources that are naturally rich in iodine often goes unrecognized. Drinking water with high levels of iodine, application of iodine-containing water-purification tablets, nutritional supplements such as multivitamin tablets are common sources (7,8,9,10,11).

Iodine excess also occurs from iodine-rich medications and from iodinated contrast agents used for diagnostic radiology. A single dose of iodinated contrast usually contains hundreds to thousands of times higher iodine than the recommended daily dose.

Iodine excess has been observed much more frequently since iodide supplementation by USI was initiated. However, due to the variable iodine content in edible salt, poor monitoring of production and social iodine status, salt iodine sometimes can exceed the adequate level for a community (3). Most health authorities preferentially recommend iodate as an additive to salt for correcting iodine deficiency. The recommended level of iodine is between 20 mg to 80 mg per kilogram of salt. Even though this results in a low exposure of at most 1700 mg/day, doubts have recently been raised whether the safety of iodate has been adequately documented (12). Several studies have shown that overconsumption of iodized salt in food with iodine excess associates with thyroid disorders in Mexico, Somalia, China, Bulgaria, Brazil, and African countries (3). Excessive iodine intake has also been reported in Sri Lanka (13) (14).

Regardless of the iodine source, daily diet or one-time incident of exposure to excessive levels of iodine, can easily occur without awareness. Extensive recovery time may be needed to restore the normal level of iodine, a period during which thyroid functions can be significantly disturbed (3).

Radioactive iodine is one of the corner stone of treatment for hyperthyroidism and an adjuvant treatment of differentiated thyroid carcinoma. Iodine-131 (I-131) treatment gives rise to early complications ranging from gastrointestinal symptoms, radiation thyroiditis, sialadenitis, and bone marrow suppression. Dry eyes and nasolacrimal duct obstruction are some of the ocular complications seen with I-131 (15).

Acute iodine poisoning results in an oculotoxicity which will end up with serious visual impairment. The ocular toxicity occurs at doses of 600 to 1200mg/kg per individual, which is a much higher dose than used in iodized salts (12). Animal studies and few human case reports have shown that the retinal pigment

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epithelium (RPE) and the photoreceptors are the primary targets of iodate toxicity, and this toxicity is associated with the oxidizing properties of iodate (12, 16, 17). The damage threshold is lowered by oxidizers and raised by antioxidants (18). The retinal damage can be reduced by antioxidants like glutathione, but they must be given shortly before, or combined with, iodate. Glutathione cannot protect the retinal pigment epithelium even when it is given within 30 minutes following an intravenous bolus of iodate. This prevents the use of glutathione as an antidote for iodine poisoning (12). In a study of five cases of potassium iodate toxicity in humans, the retinal toxicity was shown by damage to retinal pigment epithelial layer and the photoreceptor cells. The fundi of these patients have shown bilateral extensive areas of retinal pigment epithelial window defects. There was marked impairment of generation of visual evoked potentials. The recovery of retinal function depends on the amount of chemical absorption, the regeneration of RPE and the recovery function of photoreceptor cells (17).

The pathophysiology of retinal toxicity from iodine in humans is not fully understood. Almost all the evidence regarding the experimental pathogenesis of oculotoxicity has come from animal studies.

Instillation of the conjunctival surface with povidone iodine is a common practice in ocular surgeries. In rabbits it has shown that up to 0.5% of povidone iodine is tolerated without detectable adverse effects (19). When 5% povidone iodine is applied to ocular surfaces of rabbits there was a reduction in goblet cell density, histopathological and ultrastructural changes of conjunctiva and cornea, in a time-dependent manner (20). In vitro study of povidone iodine effects on human corneal endothelial cells, had shown a significant endothelial cell damage with a povidone iodine concentration of 0.1% compared to 0.05% or less (21). Alp, et. al. demonstrated povidone iodine in both 5% and 10% concentrations induced severe endothelial toxicity in rabbit eyes when one drop of either concentration is placed directly into the anterior chamber (22).

When 5% povidone iodine was injected to the vitreous cavity of rabbits, the eyes developed full thickness retinal necrosis (19). In rats it has been shown that intravenous administration of sodium iodate can produce retinal toxicity that damages RPE and photoreceptor cells. In these rats the retinal pigment epithelial cells showed delay in phagocytosis, decrease in proliferation and metaplasia into fibroblast like cells (23). When given intravenously to rats or when added to whole blood or tissue homogenates in vitro or to foodstuff, iodate is quantitatively reduced to iodide by nonenzymatic reactions thus becomes available to the body as iodide. Therefore, exposure of tissues to iodate might be minimal, except perhaps for the gastrointestinal mucosa (12).

Another study in rabbits has shown that the retinotoxic effect of iodine is not due to the accumulation of iodate in eye tissues rather due to the biochemical mechanisms involved in reduction of iodate to iodine (24).

In summary, iodine toxicity is rare but becoming an increasing health problem. The devastating almost permanent blindness with acute iodine toxicity needs attention of the health care workers and public. When povidone iodine is used in ophthalmic surgeries to prevent septic endophthalmitis, eye surgeons must be careful regarding the concentration of the povidone iodine solution and must take all the precautions to prevent inadvertent leakage of povidone iodine into the anterior chamber.

Povidone iodine solution has become a most commonly used item of first aid boxes at homes, schools, and workplaces. The school children, teachers, public and individuals working with iodine preparations, including contrast media must be clearly warned regarding the toxicity of iodine and the serious visual impairment associated with iodate toxicity.

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