Update on Chornobyl and KI Prophylaxis

Lewis E. Braverman

UPDATE ON CHERNOBYL AND KI PROPHYLAXIS

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The ingestion of excess iodine (I), most commonly due to I rich medications and x-ray contrast agents, may cause hypothyroidism and hyperthyroidism in susceptible individuals. Under normal conditions, excess I exposure causes a transient decrease in thyroid hormone synthesis for about 48 hours (the Acute Wolff Chaikoff [W-C] Effect) and normal thyroid hormone synthesis resumes shortly thereafter despite continued ingestion of excess I (Adaptation or Escape from the Acute W-C Effect).[1,2] The transient inhibition of hormone synthesis is most likely due to the generation of an iodinated lipid or an iodolactone which inhibits thyroid peroxidase activity and the subsequent oxidation of I, iodination of tyrosines, and the coupling of the iodinated tyrosines (MIT and DIT) to generate T4 and T3.[3] We postulated in 1963 that escape from the acute W-C effect was due to a decrease in the active transport of I from the blood to the thyroid, thereby decreasing intrathyroidal I and allowing normal thyroid hormone synthesis to resume.[4] The cloning of the Na/I Symporter (NIS) in 1996 by Carrasco et al provided the unique opportunity to restudy the W-C effect in the rat and to test this hypothesis.[5] In 1999, Eng et al reported that, during the first 24 to 48 hours of excess I ingestion, there was a marked reduction in thyroid NIS mRNA and NIS protein which persisted during continued ingestion of iodinated water.[6] Thus, escape from the acute W-C Effect is, at least partially, due to a decrease in NIS and the I trap and a subsequent decrease in intrathyroidal I. Iodine also has a modest effect on decreasing thyroid hormone release from the thyroid, especially in the hyperfunctioning gland.

I intake in the United States has decreased from approximately 300 ug daily in 1971-1974 to approximately 150 ug daily in 1988-1994.[7] Recently, it has been reported that U.S. Peace Corps Workers (PCW) in Niger who were accidentally exposed to inordinate quantities of iodinated drinking water from 1995-1998 developed goiter and small increases in serum TSH concentrations.[8] Following a reduction in the I content in the water supply, the prevalence of goiter decreased, serum TSH values decreased and serumTPO antibodies decreased, the latter suggesting that the excess I may have increased LT in these normal PCWs as has been reported in susceptible animal models, including the BB/Wor rat, the Buffalo rat, the obese strain chicken, and the NOD mouse.

There are clinical situations, however, in which the thyroid fails to escape from the acute W-C effect, resulting in I induced hypothyroidism.

Iodine Induced Hypothyroidism

No underlying thyroid disease

Fetus and neonate, mostly preterm

Secondary to transplacental passage of iodine and exposure of newborn infants to topical or parenteral iodine-rich substances

Infant

Occasionally reported in infants drinking iodine-rich water (China)

Adult
Frequently reported in Japanese subjects with high iodine intake (Hashimoto's thyroiditis has been excluded)
Elderly
Reported in elderly subjects with and without possible defective organification and autoimmune thyroiditis
Chronic nonthyroidal illness
Cystic fibrosis
Chronic lung disease (Hashimoto's thyroiditis was not excluded)
Chronic dialysis treatment
Thalassemia major
Anorexia nervosa

Underlying thyroid disease

Hashimoto's thyroiditis
Euthyroid patients previously treated for Graves' disease by ^{131}I, thyroidectomy, or antithyroid drugs
Subclinical hypothyroidism, especially in the elderly
After transient postpartum thyroiditis
After subacute. painful thyroiditis
After hemithyroidectomy for benign nodules
Euthyroid patients with a previous episode of amiodarone-induced destructive thyrotoxicosis
Euthyroid patients with a previous episode of interferon-alpha-induced thyroid disorders

Iodine plus other potential goitrogens

Lithium

Adapted from Roti, E., Vagenakis, G.: Effect of excess iodide: clinical aspects. Werner and Ingbar's The Thyroid, A Fundamental and Clinical Text, eighth edition, Eds. L.E. Braverman and R.D. Uitger, J. Lippincott Co., Phila., PA, pp. 316-329, 2000.

In contrast to iodine induced hypothyroidism, excess iodine ingestion may induce hyperthyroidism or Iod Baselow's disease, especially in regions of iodine deficiency, including many countries in Continental Western Europe.

Iodine Induced Hyperthyroidism

- Iodine supplementation for endemic iodine-deficiency goiter
- Iodine administration to patients with euthyroid Graves' disease, especially those in remission after antithyroid drug therapy
- Nontoxic nodular goiter
- Autonomous nodule
- Nontoxic diffuse goiter
- Iodine administration to patients with no recognized underlying thyroid disease, especially in areas of mild to moderate iodine deficiency

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As noted, under normal circumstances excess iodide decreases NIS on the thyroid cell surface thereby inhibiting the further entrance of iodide into the thyroid. Therefore, excess iodide administration would decrease the thyroid radioactive iodine uptake (RAIU) by decreasing NIS and also by decreasing the specific activity of the isotope(s). Thus, the marked decrease in the thyroid RAIU by the administration of stable iodine would be extremely useful in preventing internal radiation effects on the thyroid from radioisotopes of iodine emitted from a nuclear accident by inhalation and, more importantly, from the consumption of ^{131}I contaminated foods, especially milk, other dairy products, grains and vegetables.

In normal volunteers, the thyroid uptake of radioactive iodine has been reported to be essentially blocked for at least 24 hours by the administration of 30 to 200 mg stable iodine, as potassium iodide (KI), just prior to and minutes after exposure.[9-11] If KI is given one or three hours after exposure to radioactive iodine, further thyroid radioiodine uptake, above that which is already concentrated in the thyroid, is blocked for at least 24 hours. The inhibitory effect on the thyroid RAIU uptake of a single dose of 100 mg iodide as KI lasts for about 48 hours, decreasing the 24 hour uptake form 28% before KI administration to 8% at 48 hours.

The current recommended dose of KI for different population groups is as follows:

Groups	**Dose of KI**
Adult (over age 40 yrs)	130
Adult (18 to 40 yrs)	130
Pregnant & Lactating Women	130
Adolescent (12 to 18 yrs)	65
Child (4 to 12 yrs)	65
Child/Infant (1 month to 3 yrs)	32.5
Newborn (birth to 1 month)	16.25 mg

In order to facilitate the preparation of KI for infants and children, quartered 65 mg tablets would be preferred. Adults could then take two of these 65 mg tablets.

References

1. Wolff J, Chaikoff IL, Rosenfeld S. 1944. Inhibiting effect of inorganic iodide on the formation *in vitro* of thyroxine and diiodotyrosine by surviving thyroid tissue. J Biol Chem. 154:381-387.

2. Wolff J, Chaikoff IL, Goldberg RC, Meier JR. 1949. The temporary nature of the inhibitory action of excess iodide on organic iodine synthesis in the normal thyroid. Endocrinology. 45:504-513.

3. Pisarev MA, Gartner R. Autoregulatory actions of iodine. In The Thyroid: A Fundamental and Clinical Text, Eighth Edition, L.E. Braverman and R.D. Utiger, pp 85-90, 2000.

4. Braverman LE, Ingbar SH. Changes in thyroidal function during adaptation to large doses of iodide. J Clin Invest. 42:1216-1231, 1963.

5. Dai G, Levy O, Carrasco N. 1996. Cloning and characterization of the thyroid iodide transporter. Nature. 379:458-460.

6. Eng, Peter. H.K., Cardona, G.R.,Fang, S.L., Previti, M., Alex, S., Carrasco, N., Chin, W.W., Braverman, L.E.: Escape from the acute Wolff-Chaikoff effect is associated with a decrease in thyroid sodium/iodide symporter mRNA and protein. Endocrinology 140:3404-3410, 1999.

7. Hollowell, J.G., Staehling, N.M., Hannon, W.H., Flanders, D.W., Gunter, E.W., Maberly, G.F., Braverman, L.E., Pino, S., Miller, D.T., Garbe, P.L., DeLozier, D.M., and Jackson, R.J.: Iodine nutrition in the United States: trends and public health implications. Iodine excretion data from NHANES I and NHANES III (1971-1974 and 1988-1994). J. Clin. Endocrinol. Metab. 83:3401-3410, 1998.

8. Pearce, E.N., Gerber, A.R., Gootnick, D.B., Khan, L.K., Li, R., Pino, S., Braverman, L.E. Effects of chronic iodine excess in a cohort of long-term American workers in West Africa. J Clin Endocrinol Metab. 87:5499-5502, 2002.

9. Sternthal, E., Lipworth, L., Stanley, B., Abreau, C., Fang, S., and Braverman, L.E.: Suppression of thyroid radioiodine uptake by various doses of stable iodide. New Engl. J. Med. 303:1083-088, 1980.

10. Blum M, Eisenbud M. Reduction of thyroid irradiation from ^{131}I by potassium iodide JAMA. 1967;200:1036-40.

11. Ramsden D, Passant FH, Peabody CO, Speight RG. Radioiodine uptakes in the thyroid studies of the blocking and subsequent recovery of the gland following the administration of stable iodine. Health Phys. 1967;13:633-46.