Iodine toxicity from soy milk and seaweed ingestion is associated with serious thyroid dysfunction

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We report a series of cases of thyroid dysfunction in adults associated with ingestion of a brand of soy milk manufactured with kombu (seaweed), and a case of hypothyroidism in a neonate whose mother had been drinking this milk. We also report two cases of neonatal hypothyroidism linked to maternal ingestion of seaweed made into soup. These products were found to contain high levels of iodine. Despite increasing awareness of iodine deficiency, the potential for iodine toxicity, particularly from sources such as seaweed, is less well recognised. ***(MJA 2010; 193: 413-415)***

Clinical records

Cases of thyroid dysfunction associated with ingestion of soy milk

In November 2008, a 36-year-old woman (Patient 1, Box 1) presented with a mildly elevated serum thyroid-stimulating hormone (TSH) level detected during screening for in vitro fertilisation. As she tested negative for thyroid antibodies, her urinary iodine level was measured to exclude iodine deficiency; this level was markedly elevated at 4445 µg/L (reference range [RR], < 200 µg/L). The source of the excess iodine was unclear until the patient did an internet search and identified that the soy milk she had been drinking (Bonsoy) contained kombu[1,2] — a type of seaweed. The patient ceased drinking the soy milk, which resulted in rapid normalisation of her TSH level. Three months later, a 38-year-old man (Patient 2, Box 1) presented with florid thyrotoxicosis. Minimal uptake of technetium on a thyroid scan and absence of TSH receptor antibodies essentially excluded Graves disease. The scan result, in combination with his elevated urinary iodine level (1278 µg/L), indicated that iodine toxicity was the most likely cause of the thyrotoxicosis. He drank brands of soy milk other than Bonsoy, but also drank Bonsoy in takeaway coffee. After he ceased drinking all soy milk, his symptoms rapidly abated and his serum TSH level normalised 3 months later.

No further cases of suspected iodine toxicity were seen until approximately 1 year later, when six additional patients presented to one of us (B A C) over a 6-week period (Patients 3–8, Box 1). These patients presented with thyroid conditions ranging from subclinical hyperthyroidism to florid thyrotoxicosis. Patient 3 had already been diagnosed with thyrotoxicosis due to underlying iodine toxicity (urinary iodine level, 11 427µg/L); however, the source of excess iodine was not identified until she sought a second opinion. One month after she ceased consuming Bonsoy milk (which she had been consuming for the previous 8 years), her serum TSH level normalised.

An aliquot of Bonsoy milk was analysed for iodine content using a plasma mass spectrometer (Department of Biochemistry, Royal Prince Alfred Hospital, Sydney, NSW), which showed an iodine concentration of 25 000 µg/L. In comparison, the levels of iodine in other soy milks that were analysed ranged from 15 µg/L to 281 µg/L (Box 2).

Two weeks later, the same laboratory received a second aliquot of Bonsoy milk for analysis, due to a case of neonatal hypothyroidism. The newborn screening program had identified a baby with an elevated TSH level (28 mIU/L; RR, < 20 mIU/L; heel-prick blood sample). Additional testing 19 days after birth showed further elevation of the baby's serum TSH level (163 mIU/L), as well as a low level of serum free thyroxine (3.7 pmol/L; RR, 10–25 pmol/L). Exposure to exogenous iodine from a maternal source was suspected because of the marked rise in serum TSH level. Urinary iodine levels were subsequently found to be elevated in both the mother (5415 µg/L) and the baby (9797 µg/L). During the last trimester of pregnancy, the mother had been drinking about 500 mL of Bonsoy milk daily. She had been breastfeeding since delivery. The iodine concentration of the second aliquot of this soy milk (27 580 µg/L) was similar to that of the previously analysed sample. The baby was initially treated with thyroxine but, after the mother ceased ingesting the soy milk, the baby's thyroid function normalised. Independent analysis of the soy milk (Division of Analytical Laboratories, NSW Health, Sydney, NSW) again revealed an extremely high iodine concentration (31 000 µg/L).

Cases of neonatal hypothyroidism associated with maternal ingestion of seaweed soup

Two cases of neonatal hypothyroidism related to maternal ingestion of seaweed have been reported recently by two of us (P J E and M M J).[3] The first case involved a Korean mother who, during pregnancy and the puerperium, consumed soup made with overseas-bought dried seaweeds. Her baby, born at 36 weeks' gestation, had a normal TSH level at the time of newborn screening (heel-prick blood sample). However, the baby subsequently developed jaundice and, at 3 weeks of age, a repeat TSH test showed elevation of the baby's serum TSH level (39 mIU/L; RR, 0.4–5.0 mIU/L) as well as a low level of serum free thyroxine (9.7 pmol/L; RR, 13–30 pmol/L) and an elevated urinary iodine level (690 µg/L). The baby was initially treated with thyroxine but, after the mother ceased ingesting seaweed soup, the baby's thyroid function normalised. Dried samples of two different seaweed compounds, analysed by a commercial pathology company (Sullivan Nicolaides Pathology, Brisbane, QLD), showed iodine concentrations of 291 µg/g and 424 µg/g.

The second case involved an infant born at 27 weeks' gestation who had a normal TSH level at the time of newborn screening, and an elevated serum TSH level (24 mIU/L; RR, 0.06–7.14 mIU/L) when a routine repeat TSH test was carried out at 1 month of age. This infant's mother had also been ingesting seaweed soup — made with Heng Fai seaweed, imported from China, to increase her breast milk supply. The baby's urinary iodine level at the time

1 Characteristics of a cluster of eight adult patients in whom thyroid dysfunction was attributed to consumption of Bonsoy, a brand of soy milk manufactured with seaweed, November 2008 to December 2009*

	Sex; age (years)	SerumTSH level (mIU/L)	Serum fT4 level (pmol/L)	Serum fT3 level (pmol/L)	Serum TRAb test result	Serum TPO/Tg Ab test result	Technetium uptake on thyroid scan	Urinary iodine level (μg/L)	Thyroid ultrasound result
RR		0.4–3.5	9–19	2.5–5.7			0.5%–3.5%	< 200	
Patient 1	F; 36	4.63	9.7	Not done	Not done	Negative	Not done	4 445	Not done
Patient 2	M; 38	< 0.02	59.4	16	Negative	Negative	Negligible	1 278	Normal size, single nodule (3 mm diameter), normal vascularity
Patient 3	F; 46	< 0.005	50	39	Negative	Negative	< 0.5%	11 427	Mild enlargement, reduced vascularity
Patient 4	F; 36	< 0.04	30	12	Negative	Negative	0.5%	777	Normal
Patient 5†	F; 37	< 0.0005; 12.4	29; < 5	5.6; 3.4	Negative	Negative	Not done	6 208	Normal
Patient 6‡	F; 29	0.04	16	4.9	Negative	Negative	0.5%	48	Tiny nodules (< 3 mm diameter)
Patient 7	F; 33	0.08	18	6.6	Negative	Negative	1.3%	5 022	Normal
Patient 8	M; 47	0.07	17	4.9	Negative	Negative	0.1%	320	Single nodule (5 mm diameter)

TSH = thyroid-stimulating hormone. fT4 = free thyroxine. fT3 = free triiodothyronine. TRAb = TSH receptor antibody. TPO/Tg Ab = thyroid peroxidase and thyroglobulin antibodies. RR = reference range. F = female. M = male. * Reported daily intake of Bonsoy milk ranged from < 100 mL/day to 1000 mL/day. † Patient 5 had blood tests for thyrotoxicosis performed at 5.5 months postpartum, and repeated at 7 months postpartum (when she had developed hypothyroidism). ‡ Patient 6 ceased consumption of the Bonsoy milk about 2–3 months before testing. ◆

of maternal seaweed ingestion was elevated (454 μg/L).The iodine concentration in the mother's breast milk at the time of seaweed ingestion was elevated at 878 μg/L; 4 weeks after she ceased consuming the seaweed, the concentration dropped to 188 μg/L. NSW Health was notified and testing of the Heng Fai seaweed by the NSW Food Authority revealed high levels of iodine (4450 μg/g), which resulted in voluntary withdrawal of Heng Fai seaweed by the importers in March 2010.[4]

Discussion

Iodine toxicity causes a spectrum of thyroid disorders, ranging from hyperthyroidism to hypothyroidism.[5,6] Reasons for the variable effects are unclear, but may relate to age, pre-existing autoimmune thyroid disease, and amount and duration of iodine ingestion.[5,6] The adults described here did not appear to have underlying nodular goiters or Hashimoto disease (Box 1). In iodine toxicity, thyroid technetium uptake scans usually show absent or low technetium uptake in thyrotoxicosis and increased technetium uptake in neonatal hypothyroidism. Graves disease and autonomous nodular thyroid disease are more common causes of thyrotoxicosis but can be excluded primarily by scan results, lack of a goitre and absence of TSH receptor antibodies. However, as urinary iodine levels are not routinely measured in clinical practice, iodine toxicity may be underdiagnosed.

This series of cases of thyroid dysfunction led to a national recall of Bonsoy milk on 24 December 2009,[7] and the distributer agreed to voluntary withdrawal of the product from sale in Australia. This brand of soy milk was fermented in seaweed, which is thought to improve the flavour, and is promoted as having wide-ranging health benefits.[1] The NSW Health alert for Bonsoy milk stated that in a child, ingestion of only 5 mL, and in an adult, only 30 mL, would exceed the safe upper limit of iodine intake.[8,9] It is unclear whether changes to the manufacturing process of the Bonsoy product may have increased its iodine content. However, after removal of kombu from the manufacturing process, the iodine content was reduced markedly (15 μg/L) and the product returned to the Australian market in April 2010.

The World Health Organization was notified of the iodine toxicity of the Bonsoy milk, which was withdrawn from sale in a number of other countries.[10] Between January and June 2010, 48 retrospective Australian cases of thyroid dysfunction associated with this brand of soy milk were also notified to local public health authorities (Katrina Knope, Coordinating Epidemiologist, OzFoodNet, Office of Health Protection, Department of Health and Ageing, June 2010, personal communication). A cluster of cases of thyrotoxicosis, linked to iodine toxicity from an unidentified soy milk, was also reported in New Zealand in 2005.[11]

The common practice by women from Japan and Korea of ingesting seaweed made into soup, sometimes in large quantities, to promote wellbeing in the mother and stimulate breast milk supply, does not appear to be widely known in the medical community. However, due to iodine transmission through breast milk, transient or even persistent hypothyroidism has been reported in neonates born to mothers who undertake this practice.[12,13] If left undiagnosed and untreated, neonatal hypothyroidism can have devastating clinical consequences, including impaired intellectual development. Although newborn screening tests will help to identify hypothyroidism during the

2 Iodine concentration in various milks, assayed in December 2009*

Brand	Iodine (μg/L)
Soy milks	
Bonsoy	25 000, 27 580
Sanitarium So Nice	27
Vitasoy	19
Coles Soy Drink	19
So Natural Original	15
Other milks	
Woolworths Lite (low-fat cows milk)	281
Pura Milk (full-fat cows milk)	215
So Good Rice Milk	29

* All testing was carried out at the Department of Biochemistry, Royal Prince Alfred Hospital, Sydney, NSW. ◆

first week of life, there is no subsequent routine screening of thyroid function in term babies whose TSH level may not increase until after 1 week of age, as seen in one of the neonatal cases described here and in a Korean study of preterm infants.[12]

Our findings demonstrate the importance of:

- considering iodine toxicity in patients who present with thyrotoxicosis in the absence of TSH receptor antibodies and low or absent uptake on a thyroid technetium uptake scan;
- measuring urinary iodine level in cases where thyrotoxicosis is not explained by conditions such as autoimmune or nodular thyroid disease; and
- actively seeking a history of maternal seaweed consumption during pregnancy and lactation in cases of neonatal hypothyroidism.

Finally, although iodine deficiency is a documented and serious concern in Australia,[14,15] these cases highlight the risks of excess iodine intake from dietary sources. The food industry is not strictly regulated (eg, imported products are not usually tested to confirm their contents), and contamination of food and drink is only detected when unusual or severe clinical events ensue. There is a strong public health argument for monitoring iodine levels in imported foods and commercially available seaweed preparations.

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Competing interests

None identified.

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