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 1445 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, 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 (BAC) 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, 11 427 μg/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 29 000 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 (PJE and MMJ). 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
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 the product from sale in Australia. This brand of soy milk manufactured with seaweed, November 2008 to December 2009.*

**Discussion**

Iodine toxicity causes a spectrum of thyroid disorders, ranging from hyperthyromimia to hypothyromimia. The adults described here did not appear to have autoimmune thyroid disease, and amount and duration of iodine ingestion is variable; effects are unclear, but may relate to age, pre-existing health, 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, was also reported in New Zealand in 2005. 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 source, was also reported in New Zealand in 2005.

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. 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

### 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*

<table>
<thead>
<tr>
<th>Sex; age (years)</th>
<th>Serum TSH level (mIU/L)</th>
<th>Serum fT4 level (pmol/L)</th>
<th>Serum fT3 level (pmol/L)</th>
<th>Serum TRAb test result</th>
<th>Serum TPO/Tg Ab test result</th>
<th>Technetium uptake on thyroid scan</th>
<th>Serum iodine level (μg/L)</th>
<th>Thyroid ultrasound result</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR</td>
<td>0.4–3.5</td>
<td>9–19</td>
<td>2.5–5.7</td>
<td>Not done</td>
<td>Negative</td>
<td>Not done</td>
<td>&lt;200</td>
<td>Not done</td>
</tr>
<tr>
<td>Patient 1</td>
<td>F; 36</td>
<td>4.63</td>
<td>9.7</td>
<td>Not done</td>
<td>Negative</td>
<td>Negative</td>
<td>4445</td>
<td>Normal</td>
</tr>
<tr>
<td>Patient 2</td>
<td>M; 38</td>
<td>&lt; 0.02</td>
<td>59.4</td>
<td>16</td>
<td>Negative</td>
<td>Negligible</td>
<td>1278</td>
<td>Normal size, single nodule (3 mm diameter), normal vascularity</td>
</tr>
<tr>
<td>Patient 3</td>
<td>F; 46</td>
<td>&lt; 0.005</td>
<td>50</td>
<td>39</td>
<td>Negative</td>
<td>Negative</td>
<td>&lt; 0.5%</td>
<td>11 427</td>
</tr>
<tr>
<td>Patient 4</td>
<td>F; 36</td>
<td>&lt; 0.04</td>
<td>30</td>
<td>12</td>
<td>Negative</td>
<td>Negative</td>
<td>0.5%</td>
<td>777</td>
</tr>
<tr>
<td>Patient 5†</td>
<td>F; 37</td>
<td>&lt; 0.0005; 12.4</td>
<td>29; &lt; 5</td>
<td>5.6; 3.4</td>
<td>Negative</td>
<td>Not done</td>
<td>6 208</td>
<td>Normal</td>
</tr>
<tr>
<td>Patient 6‡</td>
<td>F; 29</td>
<td>0.04</td>
<td>16</td>
<td>4.9</td>
<td>Negative</td>
<td>Negative</td>
<td>0.5%</td>
<td>48</td>
</tr>
<tr>
<td>Patient 7</td>
<td>F; 33</td>
<td>0.08</td>
<td>18</td>
<td>6.6</td>
<td>Negative</td>
<td>Negative</td>
<td>1.3%</td>
<td>5 022</td>
</tr>
<tr>
<td>Patient 8</td>
<td>M; 47</td>
<td>0.07</td>
<td>17</td>
<td>4.9</td>
<td>Negative</td>
<td>Negative</td>
<td>0.1%</td>
<td>320</td>
</tr>
</tbody>
</table>

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 6 ceased consumption of the Bonsoy milk about 2–3 months before testing.
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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