



Urine Iodine
October 2010

Indications

Iodine is required in small amounts by humans, the current RDA being 150 micrograms per day; the only known function of iodine in man is as a component of the secretions of the thyroid gland, principally tri-iodothyronine and thyroxine. Iodine is one of the halogen series of elements (along with fluorine, chlorine and bromine); it was formerly used as an antiseptic, but is now regarded as too toxic for that purpose.

80 – 90% of the total serum iodine is incorporated into thyroxine, which is largely protein bound; the remainder (5 – 15%) of the serum iodine is in the form of iodide (the plasma inorganic iodide) and it is this fraction that is filtered at the glomerulus and passes into the formed urine. Regulation of body iodine does not occur via changes in the glomerular filtration rate (as occurs with other essential elements) but via iodine uptake into the thyroid gland.

A common method for correction of iodine deficiency is salt iodization – the addition of potassium iodate to salt for human and livestock consumption to give a concentration of c. 15 ppm of iodine – with the urinary iodine concentration as the principal indicator of effect. Measurement of thyroid size has a more limited role as an indicator because it reflects chronic rather than immediate iodine deficiency.

Interpretation

The urine iodine concentration is recommended as the best single indicator of iodine nutrition, with the following stratification of reference values [1]:

Urine iodine $\mu\text{mol/L}$	Urine iodine $\mu\text{g/L}$	Iodine intake	Iodine nutritional status
0–0.15	< 20	Insufficient	Severe deficiency
0.16–0.38	20-49	Insufficient	Moderate deficiency
0.40–0.78	50-99	Insufficient	Mild deficiency
0.79–1.56	100-199	Adequate	Optimal
1.57–2.36	200-299	More than adequate	Risk of iodine-induced hyperthyroidism
$\geq 2.37 \mu\text{mol/L}$	≥ 300	Excessive	Risk of hyperthyroidism and autoimmune thyroid disease

Urine creatinine can be co-analysed with iodine to correct for urine dilution in a short collection (6 hours, early morning urine or random urine collection). Expressed in this way, the reference interval for urine iodine is 0.16 – 0.42 mmol/mol creatinine [2].

The potential hazards of large iodine doses.

Normally there is a high tolerance to ingested iodine with a wide safety margin [3,4,5,6]. An upper dietary limit of 2 mg per day has been proposed, which is exceeded only exceptionally. On a high seaweed diet in Japan, intakes of up to 5 mg per day cause no ill-effects and some individuals are reported to tolerate as much as 30 mg per day.

It is, however, not correct to assume that the administration of iodine is entirely non-hazardous, as it can have profound and variable effects on thyroid gland function. Iodine is a known goitrogen at high intake levels, an action which is used in clinical medicine in a number of circumstances.

Substantial increases in the dietary intake of iodine can have paradoxical and counter-intuitive effects. Common causes of iodide toxicity include heavy applications of iodine (for example as povidone-iodine) to open wounds, large injections of iodine radio-contrast media and amiodarone treatment for cardiac arrhythmias (amiodarone contains 75 mg of iodide per 200mg tablet and both hypothyroidism and hyperthyroidism are listed as potential adverse effects of its use).

In such cases there is a definite progression of events:

- a rapid decrease in release of T3 and T4 from thyroglobulin;
- decreased I^- uptake by the thyroid gland;
- decreased organification of I^- and hence decreased T3 and T4 synthesis.

These changes will culminate in hypothyroidism, with low plasma T3 and T4 and a high TSH.

If the thyroid gland was normal before excess iodine administration, then, as the iodide level in the gland falls in response to decreased iodine uptake, normal thyroid function is restored. However, if there was previous thyrotoxicosis or Hashimoto's disease, permanent hypothyroidism with goitre may result.

Conversely, thyrotoxicosis may result from excess iodine administration if the gland was previously adenomatous. In such a case T4 may then be given until the urine iodine excretion has fallen to within the reference interval. In adults with a goitre due to iodine deficiency, iodine supplementation may also precipitate thyrotoxicosis (the Jod Basedow phenomenon).

The thyroid-suppressive action of iodine is still used as an acute therapeutic intervention (iodine solution is given orally to control thyrotoxicosis pre-operatively), in thyrotoxic crisis ('thyroid storm') and for thyroxine cardiotoxicity. In the "pre-carbimazole" era, 10 mg per day of iodine was regularly used as a long term treatment for hyperthyroidism.

Though there is often tolerance to high doses of iodine (as it reported from Japan) adverse effects can occur as a result of either high supplemental doses or following modest increases in intake in populations after the introduction of iodised salt. In the UK the Guidance Level for iodine supplements was set at 500 μ g per day (i.e. 0.5 mg) by the Food Standards Agency in 2003, which could result in a maximum Total Safe Intake of 940 μ g per day (0.94 mg). The equivalent US Tolerable Upper Intake Level from all sources is 1,100 μ g (1.1 mg). Both the UK Reference Nutrient Intake and the US RDA are 150 μ g (0.15 mg). However, the US Institute of Medicine advises that those with autoimmune thyroid disease or nodular goitre may respond adversely to doses of iodine within this range and considerable caution should be used. The mild iodine deficiency that is now seen in the UK can be easily corrected by emphasis on iodine-rich foods (cow's milk and goat's milk products, fish - especially mackerel - and the use of iodised salt), together with modest supplements of 150 to 300 μ g (0.15 – 0.30 mg) per day for several months.

The adverse effect of very high intakes of supplemental iodine on thyroid function was observed in Peace Corp workers in West Africa who demonstrated a high rate of thyroid dysfunction and goitre after using iodine-treated water [7]. Their estimated daily iodine intakes for several months were in the region of 50 mg per day. Observed effects included goitre, raised TSH levels and raised levels of thyroid peroxidase antibodies. The prevalence of these abnormalities substantially reduced when high iodine intakes ceased.

To emphasise that significant changes in thyroid function can result from even modest increases in iodine intake, a recent Danish study [8] reported on the increased incidence of overt hypothyroidism in subjects

in the age range of 20 – 59 years following on the iodine fortification of salt. This measure was introduced in Denmark in 1998 and resulted in an across-the-board increase in iodine intake in the Danish population. Possible causes of the observed increase in the incidence of hypothyroidism were suggested as:

- an increase in autoimmune thyroid disease, provoked by excess iodine,
- intra-thyroidal synthesis of iodinated arachidonic acid derivatives, which normally acts as a negative feedback protection against a sudden iodine load,
- an iodine-induced increase in the rate of apoptosis of thyroid follicular cells.

Conclusions

High-dose iodine (greater than 2 mg per day) has a number of medical uses and practitioners should consider this carefully before they recommend high dose nutritional supplementation with iodine. There are a number of potential effects on thyroid function that may derive from increasing the amount of iodine ingested; even marginal increases in intake over long periods of time have been shown to adversely affect thyroid function in some subjects.

Patient preparation

The patient should dis-continue nutritional supplements and medication the day before the collection of a basal urine iodine sample (iodine is a component of the material used in pharmaceutical capsules).

Specimen requirements

A 24 hour urine collection with an accurate total volume is the preferred sample; alternatively, a 6 hour collection, an early morning urine or a random urine sample can be supplied. The WHO reference intervals [1], quoted above, are based on a random urine specimen.

Postal samples should reach Biolab within 48 hours of collection.

Methodology

Iodine is measured by inductively coupled plasma-mass spectrometry (ICPMS).

Turn around time

3-4 working days.

References

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