British Journal of Nutrition (2011), **106**, 1630–1631
doi:10.1017/S0007114511005514

Invited Commentary

Time to refine the use of urinary iodine to assess iodine intakes in populations

(First published online 11 October 2011)

Iodine is essential for normal development, and its deficiency can cause growth retardation and irreversible brain damage[1]. Nowadays, the main source of iodine is iodised salt[2]. However, in many countries discretional use of salt (cooking and table salt) is increasingly being replaced by salt from processed foods[3]. This situation has raised concern about the risk of iodine inadequacy if the food industry does not use iodised salt. The study by Johner *et al.*[4] published in this issue of the *British Journal of Nutrition* was motivated by such concern.

High intake of salt has been linked to high blood pressure and hence CVD[5]. For addressing this preventable health risk, the WHO has recommended reducing salt intake to less than 5 g/d in adult populations[6]. Reduction of dietary salt should not jeopardise the supply of iodine if the content of this mineral is adjusted upward to compensate for lower salt intakes[7]. However, in order to implement any change in the iodine content of salt, it is important to monitor intakes of both salt and iodine. A practical way to measure those intakes is through their 24-h excretion in urine[8,9].

Salt is not consumed independently from foods but as part of meals; therefore daily intake is directly correlated with energy intake. Consequently, iodine delivered through salt keeps direct correlation with energy intake. This direct association with total energy intake explains why daily excretions of iodine are greater in males than in females[10,11], and why the differences among groups disappear when the 24-h excretion is divided by the daily energy intake[11]. Johner *et al.*[4] confirmed such findings. The difference in daily iodine excretion between groups could be maintained in terms of urinary iodine concentration (UIC) only if daily urinary volumes were also similar. This was the case in this study with German boys and girls aged 6–12 years: both the 24-h iodine excretion and UIC revealed differences between the groups. If the daily urinary volumes are different, as for example between school-age children and reproductive-age women, the UIC value depends on the urinary volume rather than on the 24-h iodine excretion. This is the reason why the National Health and Nutrition Examination Survey of the USA found that children aged 6–11 years and adults older than 70 years showed the highest values of UIC[12].

A way to compensate for the urine dilution is dividing the iodine content by the creatinine content. This may work in theory, because creatinine is excreted according to muscle activity, which is closely associated to energy intake. However, the intra-individual variations of both iodine and creatinine excretions make the results of UIC/creatinine very difficult to interpret. Results from African populations with low protein intake, and hence lower than common urinary creatinine excretion, forced WHO/UNICEF/ICCIDD to recommend the use of UIC in absolute terms[2]. A population median of 100 μg/l was selected as the reference point at which a population may be at risk of iodine inadequacy. This simple criterion has been very useful to start programmes and to monitor their performance worldwide[13].

For children aged 6–12 years, who are frequently used as the reference to assess the iodine intake of the population, a median of 100 μg/l as the UIC means an average intake of 78 μg/d, assuming a daily urinary volume of 0·7 litres and 90 % excretion of this iodine intake through urine. This iodine intake is just slightly above the estimated average requirements (EAR) for this age group (65–73 μg/d)[9]. However, for women (1·9 litres of urinary daily volume), a median of 100 μg/l of UIC predicts a daily iodine intake of 211 μg/d, which is 2·2 times larger than the corresponding EAR value (95 μg/d)[9]. These calculations exemplify that direct comparisons of UIC are neither valid among cohorts nor valid for populations living under different climatic conditions, because the daily urinary volumes can vary greatly.

The WHO[14] introduced the value of 150 μg/l as the specific UIC reference median to identify iodine inadequacy in pregnant women, based on the higher iodine requirements for this physiological stage (160 μg/d)[9]. This criterion has already been used to assert that some subgroups of reproductive-age women in the USA may be at risk of iodine deficiency[15]. Regardless of the potential risk of iodine inadequacy in segments of the US population, the results presented by Johner *et al.*[4] illustrate the weakness of using UIC values without additional supporting evidence. The median UIC of German children was 110 μg/l in 2004–6, and 98 μg/l in 2007–9, a statistically significant difference. If the WHO recommendation is applied strictly, Germany would have passed from iodine sufficiency to iodine insufficiency in such a short time period. However, based on the 24-h iodine excretion, the median iodine intake decreased only from 86 to 83 μg/d in the 2-year periods that were compared,

and the percentage of children with iodine intakes lower than the corresponding EAR increased from 12·75 % to 15·50 %. These results suggest that indeed the iodine intake somewhat declined but not in the magnitude that would have been inferred using the current WHO criteria.

The determination of the UIC in urine spot samples only permits the estimation of the population median when the sample size is large enough[16], but it fails to reflect the distribution of iodine excretions. The WHO/UNICEF/ICCIDD[17] are very well aware of the limitation of the UIC results; thus they have suggested making inferences only based on the median value. However, the need for having some idea of distributions to estimate the prevalence of inadequacy moved the WHO to use the median as a cut-off point and interpret the proportion of cases below the median as the percentage of individuals with low iodine intakes[13]. Consequently, this practice has produced an overestimation of iodine inadequacy worldwide.

Ideally, iodine excretion should be measured in 24-h urine samples. Nevertheless, UIC in spot samples may still be useful. However, different reference points should be determined for each age, sex and physiological group and studied under different climatic conditions and lifestyles. The specific median UIC should be associated with a low proportion of cases below the EAR iodine intake of each group as estimated by 24-h measurements. The study by Johner *et al.*[4] provides inputs in this direction.

Conflict of interest

Omar Dary is a member of the PAHO/WHO Expert Group to prevent CVD through the reduction of dietary salt.

Omar Dary

Project A2Z
Academy of Educational Development (AED)
1825 Connecticut Avenue NW #800
Washington DC 20009
USA
email omardaryphn@gmail.com

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British Journal of Nutrition