High day-to-day variability of urinary iodine excretion despite almost universal salt iodization in Switzerland

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Iodine in 21 consecutive morning urine samples of 11 volonteers in Switzerland varied widely from day to day in any given individual, being e.g. 40 µg/l on one day and 159 µg/l the next. Thus, despite almost universal salt iodization, a single urinary iodine measurement is not representative of an individual's iodine nutritional status. Urinary iodine, however, retains its value when used in cross-sectional epidemiological surveys in population samples of appropriate size.

1. INTRODUCTION

Salt has evolved worldwide as the most suitable carrier to supplement iodine in deficient populations. To establish the presence of iodine deficiency and to monitor the effects of supplementation thereupon, iodine measurements in urinary spot samples in about 100 persons per site are performed [1]. At any given site, persons with a urinary iodine below 50 µg and 20 µg per liter are considered mildly and severly iodine-deficient respectively [2]. Our investigations suggest that this latter conclusion is incorrect; persons with a low iodine excretion on one day may well have a high excretion the next day, and thereby achieve on average a normal excretion.

2. METHODS

Urinary spot morning samples were collected on 21 consecutive days from 11 healthy volunteers (5 women, 6 men, agend 15 to 85 years). The samples were collected in early 1998 in the Solothurn area, when salt iodine content in Switzerland was still 15 mg/kg (in later 1998 it was raised to 20 – 30 mg/kg). Iodine was measured according to Pino [3]. The interassay coefficients for samples with a low, medium and high iodine content were 0.15, 0.04 and 0.07 respectively. Sodium was measured by flame photometry, creatinine by a Jaffé-type method on a Hitachi analyzer.

3. RESULTS

The 21-day average (±SD) urinary iodine for all 11 volonteers was 103 ± 39 µg/l or 105 ± 30 µg/g creatinine. The respective medians were 106 µg/l and 91 µg/g creatinine. The highest 21-day average was 185 µg/l, the lowest 28 µg/l. The latter figure illustrates an individual where (probably due to high fluid intake) the urinary iodine in µg/l misleadingly suggests severe iodine deficiency. When related to creatinine, this individual's iodine excretion was 84 µg/g creatinine, i.e. virtually normal.

Figures 1 and 2 show the daily iodine excretions in a typical subject. For all eleven subjects the mean coefficient of day-to-day variation was 39 % (range 15 to 75 %) for µg/l, and 33 % (range 18 to 82 %) for µg/g creatinine.

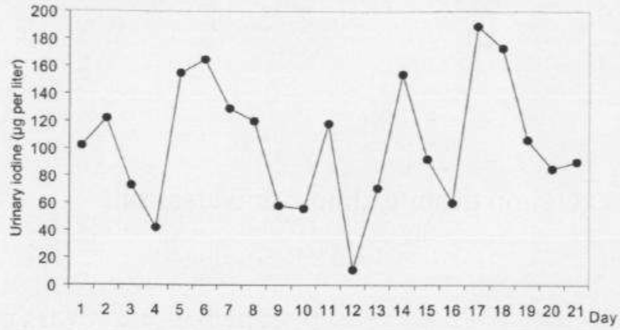

Figure 1. Urinary iodine in spot morning urine samples over 21 consecutive days in a typical subject (number 5), expressed in µg/l. The 21-day mean is 103 µg/l, the coefficient of variation is 44 %.

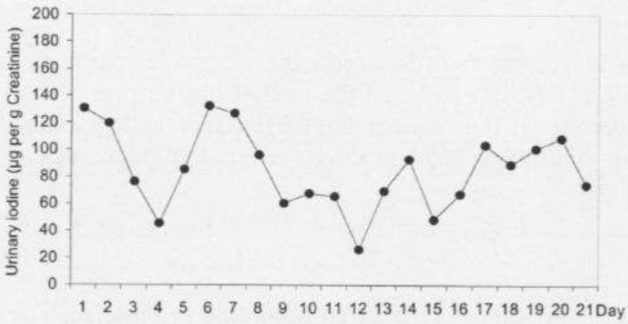

Figure 2. Urine iodine in same subject as figure 1, expressed in µg/g creatinine. The 21-day mean is 85 µg/g creatinine, the coefficient of variation is 34 %.

Figures 3 and 4 show that the day-to-day variations are smoothed out when the daily values of the 11 volunteers are averaged. Urinary iodine and sodium concentrations were highly correlated (figure 5).

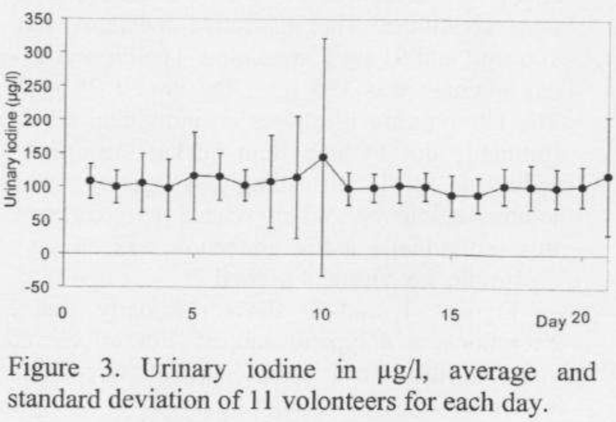

Figure 3. Urinary iodine in µg/l, average and standard deviation of 11 volonteers for each day.

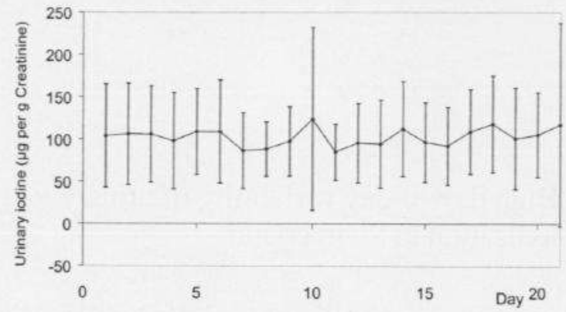

Figure 4. Urinary iodine in µg/g creatinine, same subjects as figure 3.

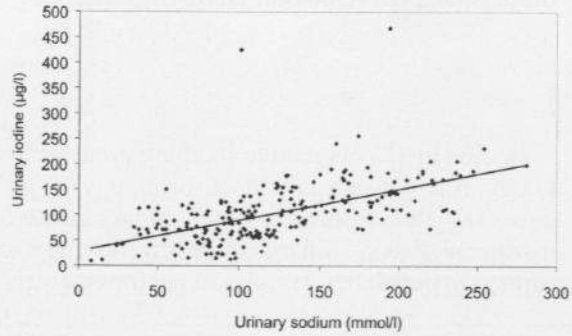

Figure 5. Urinary iodine plotted against urinary creatinine concentration for 231 urine samples of 11 volonteers. $r = 0.575$; $p < 0.001$.

4. DISCUSSION

The major and surprising finding of this work is that despite almost universal salt iodization (92 % of household salt, 75 % of salt for food industry) urinary iodine excretion shows enormous day-to-day variations, with coefficients of variation reaching up to 82 % in certain individuals (figure 1). The day-to-day variations are only partly smoothed out when corrected for fluid intake by relating iodine to creatinine (figure 2); they disappear when the values of the 11 volunteers are averaged (figures 3 and 4); the standard deviation, however, remains high, e.g. for day 10. Thus, it is probably wise to include 50 – 100 persons per site in a cross-sectional epidemiological survey to obtain a reliable estimate of the true mean [1]. This mean (or median) value of course remains a valid tool in epidemiological surveys. While some investigators are aware of this day-to-day variability, others are not and incorrectly suggest that individuals with a urinary iodine below a certain threshold (e.g. 50 μg/l) are iodine deficient [2]. Our study shows that such individuals often have high urinary iodines on other days, thus achieving a normal average over a certain period of time. With its capacity to store a large surplus of iodine in thyroglobulin, the thyroid gland is well suited to adapt to such variations in iodine supply. The variation in cross-sectional single-urine studies is due in at least 50 % to day-to-day variations.

Similar high day-to-day variations of iodine excretion have so far been shown in severly iodine-deficient Malawi, while they were much less (2 – 18 %) in an iodine-sufficient area of Sicily [4, 5]. Modest day-to-day variations are present even in volonteers on an iodine-constant diet [6]; they remain unexplained. The very high variability in Switzerland must be due to widely fluctuating iodine content of food. The strong correlation between iodine and sodium excretion (figure 5) suggests that variations of salt intake are the cause of the varying iodine intake in Switzerland, and also that salt remains the main source of iodine in the diet. Similar variations in Denmark (where iodized salt was not available) are attributed to the highly variable iodine content of sea food [7].

Recently the traditional iodine to creatinine ratio in urine has been claimed to be an inferior index than the simple urinary iodine concentration [2, 4, 5, 8, 9]. This is certainly true for developing countries with low protein intakes and consequently low creatinine excretion, and for measurements in children. On the other hand, urinary creatinine is a quite reliable marker in industrialized countries, especially if corrections of daily creatinine excretion are applied for sex [6] and age [7]. One of our 11 volonteers (probably with a high fluid intake) had a very low urinary iodine concentration suggesting marked iodine deficiency; iodine to creatinine ratio however indicated at best borderline deficiency. One should therefore consider to reintroduce the creatinine measurement in field studies, at least in industrialized countries.

In conclusion, our studies show that the daily urinary iodine excretion varies widely from day to day in any given individual, and this despite almost universal salt iodization. This varying iodine excretion is highly correlated with sodium excretion, suggesting that variations in (iodized) salt intake are the main cause of the iodine fluctuations. Biologically the thyroid gland, with its large hormone and iodine stores in the colloid, is well equipped to handle large day-to-day variations of iodine supply.

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