Systematic review of studies evaluating urinary iodine concentration as a predictor of 24-hour urinary iodine excretion for estimating population iodine intake

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ABSTRACT

Objective. To examine the usefulness of “spot” urine iodine concentrations (UICs) in predicting 24-hour urine iodine excretion (UIE) for estimating average population iodine intake.

Methods. An electronic literature search was conducted for articles published through 19 May 2013 in MEDLINE (from 1950), EMBASE (from 1980), and the Cochrane Library (from 1993) using the terms “urinary excretion (timed or spot or random) and (24 h or 24 hour),” “iodine (iodine deficiency),” “iodine (intake),” and “urine (timed, spot, random, 24-hour).” Full-text articles about studies that examined ≥40 healthy human subjects and measured UIE using the 24-hour urine collection method and UIC and/or UIE using one alternative method (spot (random), timed, and “overnight” (first morning urine), fasting or not fasting) were selected and reviewed.

Results. The review included data from 1,434 participants across the six studies that met the inclusion criteria. The main statistical methods for comparing data from the 24-hour urine collections with the values obtained from the alternative method(s) were either regression (β) or correlation (r) coefficients and concordance analysis through Bland–Altman plots. The urine samples collected using the alternative methods were subject to greater intra-individual and inter-individual variability than the 24-hour urine collections. There was a wide range in coefficient values for the comparisons between 24-hour UIRE measured in 24-hour urine collection and 24-hour UIE estimated using the alternative sampling methods. No alternative sampling method (spot, timed, or “overnight”) was appropriate for estimating 24-hour UIE.

Conclusions. The results of this systematic review suggest current data on UICs as a means of predicting 24-hour UIE for estimating population sodium intake are inadequate and highlight the need for further methodological investigations.

Key words Iodine; iodine, urine; urine specimen collection; population.
be a global public health priority (1). Measures to control iodine deficiency, particularly the provision of iodine through iodized salt, are used in countries worldwide. Until the early 1990s, WHO used total goiter prevalence to estimate prevalence of iodine deficiency. However, given the slow response of goiter to changes in iodine status, and its very low current prevalence, urinary iodine excretion (UIE) is now recommended as a more sensitive indicator of recent intakes of iodine in populations. At least 90% of ingested iodine is excreted in the urine within 24 hours. Knowing total UIE for a 24-hour period thus allows for a good estimate of recent iodine intake (2). Therefore, measurement of UIE is the preferred tool for monitoring and surveillance of iodine intake as well as estimation of the associated iodine status of populations and their response to implementation of iodization programs (3).

Total 24-hour UIE is measured or predicted through 1) 24-hour urinary collection (collection of all urine produced throughout one day to determine actual 24-hour UIE) or 2) alternative methods such as spot (random), timed (mid-morning, afternoon, and/or evening), and “overnight” (first morning urine) sampling, whether fasting or not. While the alternative sampling methods are considered easier and more practical, diurnal variation in urine iodine levels and short-term fluctuations related to diet and water ingestion make them less reliable than 24-hour urine collection for estimating daily iodine intake (4, 5). Therefore, the alternative sampling methods are often used to determine urinary iodine concentrations (UICs), by measuring urinary iodine as a proportion of single urine samples (μg/L), to predict 24-hour UIE. Estimated 24-hour UIE can then be used as an indicator of overall population iodine intake. Determining iodine intake for individuals is more complex than determining iodine intake for a population as a whole because iodine intake varies from day to day as well as seasonally, so accurate measurement requires urine collection over several days.

Epidemiological criteria for assessing iodine nutrition adopted by both the International Council for Control of Iodine Deficiency Disorders (ICC IDD) and WHO are based on median UIC obtained from spot urine samples, predominantly from schoolchildren 6–12 years old (3). Adequate iodine status is defined as median UIC > 100 μg/L (1). Higher median UIC (> 150 μg/L) is recommended for pregnant women (3). Given these criteria, this review aimed to systematically evaluate all studies that compared UIE measured in 24-hour urine collection with UIE estimates derived by UIC or urinary iodine/creatinine ratios (I/Cr) measured using alternative methods (spot, timed, and “overnight” samples) in adults and children. To the best of the authors’ knowledge, the review reported here is the first systematic assessment of studies examining validation of UIC as a predictor of 24-hour UIE.

MATERIALS AND METHODS

Literature search

A search strategy was developed to identify studies that reported the association between UIE measured by 24-hour urine collection and UIE estimated using an alternative method of urine sampling (spot, timed, or “overnight”), applying a method used in a previous similar systematic review (6). The authors searched for articles published through 19 May 2013 in MEDLINE (from 1950), EMBASE (from 1980), and the Cochrane Library (from 1993) using the terms “urinary excretion (timed or spot or random) and (24 h or 24 hour),” “iodine (iodine deficiency),” “iodine (intake),” and “urine (timed, spot, random, 24-hour).” Reference lists of original and review articles were also reviewed to identify additional studies. Only full-text articles were considered. No language restriction was applied. Only studies in humans were included.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: 1) described in a full-text article; 2) involved human subjects; 3) conducted across a specific population or large group; and 4) reported UIE measurements via 24-hour urine collection plus one or more alternative methods (spot, timed, or “over-night” sampling). Studies were excluded if they 1) were reported via an abstract only; 2) had a sample size < 40; 3) were conducted in a special patients group (e.g., renal or heart failure, congenital heart defect, diabetes, etc.); and/or 4) did not report UIE based on 24-hour urine collection plus one of the alternative methods. If multiple published reports from the same study were available, only the one with the most detailed information for both exposure and outcome was included. One study that had a sample size < 40 but assessed UIE using 24-hour urinary collection and spot sampling on multiple occasions, providing more than 40 comparisons, is summarized below but was excluded from Table 1 to avoid changing the a priori criteria.

Data extraction

Two investigators (CJ and TL) extracted the study data independently and differences were resolved by discussion and consensus with a third party (FPC or NRC). Relevant data included the first author’s surname; year of publication; country of origin of the population studied; population type, age group, and sample size; description of the urine sampling method; mean or median UIE obtained via the 24-hour collection and alternative method(s); and the outcome measures (regression or correlation coefficients and concordance analysis through Bland–Altman plots).

RESULTS

Study characteristics

Eleven studies met the inclusion criteria. Of those, five studies were excluded after reading the full-text articles due to lack of data. In two of the five studies, the actual sample size of participants providing UIE levels via both 24-hour urinary collection and alternative-method sampling was < 40 (7, 8). The other three studies only reported UIE via either 24-hour urinary collection or alternative-method sampling but not both (9–11). Therefore, a total of six studies were included in the final review (Figure 1). Of those, four studies were conducted in the adult population (12–15), one in adolescents (16), and one in both adults and children (17). Collectively, the six studies (one from Brazil, one from China, one from Côte d’Ivoire, one from Norway, and two from New Zealand) included data for 1434 subjects. All six studies recruited both male and female participants. Details about the six studies are provided in Table 1.
Summary of the six included studies

Frey et al. (12) studied a group of healthy Norwegian physicians and nurses. The urine samples were collected on an ordinary working day. The authors regressed the urinary iodine / creatinine ratio (I/Cr) (μg/g) estimated from single spot afternoon urine samples against total iodine collected in the 24-hour sample (μg/day) for men and women. Both relationships were significant (regression coefficient (β) value of 0.50 for men and 0.76 for women). The coefficients were then applied to a specific population group to estimate average population iodine intake. The authors recommended using the urinary I/Cr from the single (afternoon) sample for estimating 24-hour UIE rather than a theoretical value that would not take into account diurnal variations in iodine excretion.

Thomson et al. (13) studied the association of UIE estimated from UICs from a single fasting urine sample and a single non-fasting (spot or random) urine sample with UIE measured in 24-hour urine collection in a group of volunteers in New Zealand. The single fasting sample was collected one day before the 24-hour urine collection (and was therefore an independent sample). The single random sample was obtained from the 24-hour urine collection (and was therefore a dependent sample). The authors reported a higher association between the UIE estimated from the one-time random sample UIC and the UIE measured in the 24-hour sample (r = 0.58) versus the UIE estimated from the fasting spot sample UIC (r = 0.34). Although both correlations were significant, the authors concluded that 24-hour urine collection was necessary for diagnosing low iodine intake.

In another study in New Zealand, two groups of people were recruited from two blood transfusion centers. Thomson et al. (14) compared UIE measured in 24-hour samples with UIE estimates based on I/Cr ratios from two types of single fasting “overnight” (first morning urine) samples: single-voided (SV) and double-voided (DV). The correlation coefficient values for the UIE estimates based on the I/Cr ratios from the two types of samples were similar in both study groups (0.492 and 0.475 for the first group and 0.587 and 0.597 for the second), but due to the low degree of correlation for both types of samples the authors of the study concluded that 24-hour urine collection is necessary for estimating iodine intake.

Vanacor et al. (15) conducted a study in a group of Brazilian men and women in which UIE in each of four continuously collected samples (morning, afternoon, evening and overnight) were correlated with the UIE measured in 24-hour urine collection. The estimate based on the afternoon sample had a higher correlation with actual 24-hour UIE (r = 0.78) compared to the other three samples.
### TABLE 1. Characteristics of six studies comparing 24-hour urine collection with alternative urine sampling methods for measuring / predicting urinary iodine excretion (UIE) to estimate average population iodine intake, selected countries

<table>
<thead>
<tr>
<th>Lead author, date, and reference</th>
<th>Country</th>
<th>Population</th>
<th>Sample (n)</th>
<th>Age (years)</th>
<th>Type of urine sampling</th>
<th>Urinary iodine (mean)</th>
<th>Independent</th>
<th>Measure</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frey et al. (12)</td>
<td>Norway</td>
<td>Physicians</td>
<td>33 men</td>
<td>22–64</td>
<td>24-hour collection versus single timed collection (afternoon)</td>
<td>24-hour: 216 µg/day Afternoon I/Cr: 114 µg/g</td>
<td>No</td>
<td>UIE estimates based on afternoon sample I/Cr versus UIE measured in 24-hour sample; ( \beta = 0.50 ) for physicians and 0.76 for nurses</td>
<td>Auto-analyzer technique</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nurses</td>
<td>29 women</td>
<td>20–57</td>
<td>24-hour: 165 µg/day Afternoon I/Cr: 125 µg/g</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thomson et al. (13)</td>
<td>New Zealand Volunteers</td>
<td>31 men</td>
<td>18–56</td>
<td>18–58</td>
<td>24-hour collection versus single fasting collection and single spot (random) collection</td>
<td>24-hour: 0.45 µmol/day, 0.34 µmol/L Fasting: 0.34 µmol/L Non-fasting spot: 0.34 µmol/L</td>
<td>Fasting samples only (spot samples were taken from the 24-hour samples)</td>
<td>UIE estimates based on UIC from fasting samples versus UIE measured in 24-hour sample: ( r = 0.34 ) for physicians and ( r = 0.39 ) for nurses</td>
<td>Sandell-Kolthoff reaction method; 24-hour urine samples are necessary for diagnosis of iodine deficiency in individuals</td>
</tr>
<tr>
<td></td>
<td>New Zealand Otago Blood Transfusion Centre</td>
<td>102 men, 86 women</td>
<td>18–68</td>
<td></td>
<td>24-hour urine collection versus single fasting SV &quot;overnight&quot; collection versus single fasting DV &quot;overnight&quot; collection</td>
<td>24-hour: 60 µg/day, 42 µg/L SV fasting &quot;overnight&quot;: 43 µg/L DV fasting &quot;overnight&quot;: 43 µg/L</td>
<td>No</td>
<td>24-hour UIC versus 24-hour UIE: ( r = 0.697 )</td>
<td>Sandell-Kolthoff reaction method; UICs comparable across the three samples but poorly associated with 24-hour UIE; Bland–Altman plot indicated unsatisfactory agreement</td>
</tr>
<tr>
<td>Waikato Blood Transfusion Centre</td>
<td>67 men, 77 women</td>
<td>19–72</td>
<td></td>
<td></td>
<td>24-hour: 76 µg/day, 53 µg/L SV fasting &quot;overnight&quot;: 50 µg/L DV fasting &quot;overnight&quot;: 45 µg/L</td>
<td></td>
<td></td>
<td>24-hour UIC versus 24-hour UIE: ( r = 0.833 )</td>
<td>Sandell-Kolthoff reaction method; UIC in afternoon sample best reflected 24-hour UIC</td>
</tr>
<tr>
<td>Vanacor et al. (15)</td>
<td>Brazil</td>
<td>Volunteers</td>
<td>17 men, 43 women</td>
<td>33.7</td>
<td>24-hour collection versus &quot;overnight&quot; and (mid-morning, afternoon, and evening) collection</td>
<td>24-hour: 292 µg/day Mid-morning: 182 µg/L Afternoon: 201 µg/L Evening: 238.4 µg/L &quot;Overnight&quot;: 253.1 µg/L</td>
<td>No</td>
<td>UIE estimates based on mid-morning samples versus UIE measured in 24-hour samples: ( r = 0.544 )</td>
<td>Sandell-Kolthoff reaction method; UIE in afternoon sample best reflected 24-hour UIC</td>
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<table>
<thead>
<tr>
<th>Lead author, date, and reference</th>
<th>Country</th>
<th>Population</th>
<th>Sample (n)</th>
<th>Age (years)</th>
<th>Type of urine sampling</th>
<th>Urinary iodine (mean)</th>
<th>Independent</th>
<th>Measure</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hess et al. (16)</td>
<td>Côte d’Ivoire</td>
<td>Adults, urban</td>
<td>30 men, 22 women</td>
<td>30.6</td>
<td>24-hour collection</td>
<td>443 µg/day</td>
<td>Yes</td>
<td>NA</td>
<td>Sandell-Kolthoff reaction method; no comparison because alternative-method and 24-hour samples were obtained from different study subjects</td>
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<tr>
<td></td>
<td></td>
<td>Adults, rural</td>
<td>28 men, 21 women</td>
<td>29.0</td>
<td>Single spot (random) collection</td>
<td>166 µg/day</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Children, urban</td>
<td>110</td>
<td>10.0</td>
<td>488 µg/L</td>
<td></td>
<td></td>
<td></td>
<td>Ceric ion-arsenious acid reaction; no comparison because alternative-method and 24-hour samples were obtained from different study subjects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children, rural</td>
<td>103</td>
<td>9.3</td>
<td>263 µg/L</td>
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<tr>
<td></td>
<td></td>
<td>Pregnant women, urban</td>
<td>72</td>
<td>25.9</td>
<td>351 µg/L</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Pregnant women, rural</td>
<td>66</td>
<td>23.0</td>
<td>136 µg/L</td>
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<tr>
<td>Wong et al. (17)</td>
<td>China (Hong Kong)</td>
<td>Students (12–18 years)</td>
<td>476 (randomly selected, 25 with goiter); single timed (mid-morning) collection; 80 (none with goiter); 24-hour collection</td>
<td>15.3 (single mid-morning samples); 15.1 (24-hour samples)</td>
<td>24-hour collection versus single mid-morning collection</td>
<td>24-hour: 189 µg/day, 170 µg/L; mid-morning: 190 µg/L</td>
<td>Yes</td>
<td>NA</td>
<td>Ceric ion-arsenious acid reaction; no comparison because alternative-method and 24-hour samples were obtained from different study subjects</td>
</tr>
</tbody>
</table>

1 Range or mean value depending on the study.
2 Alternative-method sample(s) were independent of the 24-hour collection.
3 Median values unless specified.
4 I/Cr: iodine/creatinine ratio.
5 Regression correlation coefficient.
6 UIC: urinary iodine concentration.
7 SV: single-voided.
8 DV: double-voided.
9 NA: not available.
an UICs above 100 μg/L, suggesting—with goiter). Both study groups had med- 
iples were from 80 other students (none thyroiditis). The 24-hour collection sam-
ples were collected from 476 randomly reported. The single, mid-morning sam-
amples were taken from two different groups of 

potable water. In Hong Kong. The 24-hour collection sam-

tion in schoolchildren 12–18 years old in 

estimation; "complete" (24-hour) urine 

duced was supplied through salt (the 

urinary sodium (Na) were 0.89 in 


tation between the 24-hour UIE estimates 

values for the correlation 

To calculate the cost-effectiveness of 

of iodine in diet because more than 90% of 

(overnight,” *r* = 0.77; mid-morning, *r* = 0.54; and evening, *r* = 0.37). The Bland– 

Altman plot indicated UIE values from 

the afternoon sample generated the most 

accurate estimates of 24-hour UIE. Values from the other three samples generated under- and over-estimates of 

24-hour UIE, particularly the evening and “overnight” samples, which under-

estimated UIE lower-bound values and over-estimated upper-bound values.

Therefore, the authors concluded the after-

tnoon sample was the best of the four urine samples in predicting 24-hour UIE 

and for estimating average population iodine status.

Hess et al. (16) studied populations of 

children and adults (including pregnant women) in urban and rural areas of Côte d’Ivoire (Abidjan and northern villages) to study the effect of iodized salt consumption; “complete” (24-hour) urine samples were obtained from men and non-pregnant women, and single spot (random) urine samples were taken from pregnant women and children. Only 40 of the 50 adults of whom 24-hour urine samples were requested submitted a complete 24-hour sample. In the northern villages, adults had a median 24-hour UIE of 166 μg/day; based on the spot samples, children had a median UIC of 263 μg/L, and pregnant women had a median UIC of 136 μg/L. In Abidjan, adult 24-hour median UIC was 443 μg/day; based on the spot samples, children had a median UIC of 488 μg/L and pregnant women had a median UIC of 351 μg/L. The values for the correlation coefficients between urinary iodine and urinary sodium (Na) were 0.89 in Abidjan and 0.53 in the northern villages (not shown). The high I–Na correlations found in Abidjan suggest most iodine intake was supplied through salt (the main source of sodium) versus food intake.

Wong et al. (17) studied iodine excretion in schoolchildren 12–18 years old in Hong Kong. The 24-hour collection samples and the spot (mid-morning) samples were taken from two different groups of students, so no correlation values were reported. The single, mid-morning samples were collected from 476 randomly selected students, of whom 25 had goiter (mostly colloid goiter or autoimmune thyroiditis). The 24-hour collection samples were from 80 other students (none with goiter). Both study groups had median UICs above 100 μg/L, suggesting—according to WHO criteria—that the population was iodine sufficient. The UICs did not vary between males and females, but females had a lower creati- 

nine excretion.

Notable study that did not meet apriori inclusion criteria

König et al. (18) collected either multiple (10) fasting “overnight” urine samples or 24-hour urine samples from 22 women, resulting in 177 “overnight” samples and 341 24-hour urine samples. For subjects contributing 10 “overnight” samples, 24-hour UIE was estimated based on I/Cr (adjusted for expected 24-hour creatinine excretion by sex and age). Intra-individual variation (mean coefficient of variation) was similar for the 24-hour UIE estimates based on the adjusted I/Cr values from the “overnight” samples and UIE measured in the 24-hour collection (33% versus 32%). For the population that was studied, either 10 “overnight” samples or 24-hour samples were needed to assess individual iodine status with 20% precision. As both types of samples were used in the study, additional analytical work was needed to adjust the data, reducing the cost-effectiveness of the alternative method (the “overnight” samples). In addition, when the 10 “overnight” urine samples were used to estimate 24-hour UIE, based on the adjusted I/Cr, total (24-hour) urine (μg) was underestimated by 16%, possibly due to circadian effects. Therefore, the authors did not recommend the use of adjusted I/Cr from fasting “overnight” samples for estimating UIE.

DISCUSSION

This review was the first systematic assessment of studies comparing esti-

mates of 24-hour UIE based on UIC and UIE values from spot, timed, and “over-
night” urine samples and UIE measured in 24-hour urine collections. Very few 

studies met the inclusion criteria. The six studies that were included in the review 

differed in terms of their objectives, methods for measuring or estimating 

UIE, types of urine collection, study pop-

ulations, and measures for comparison and protocols, and reported a more than twofold range in the values for correlation between the 24-hour UIE estimates based on the alternative-method sampling and 24-hour UIE measured in 24-hour collection. The reasons for the wide variation in correlations across the stud-

ies were unclear.

Advantages and disadvantages of alternative urine sampling methods

UIE is a sensitive indicator of recent iodine intake because more than 90% of ingested iodide is excreted in the urine within 24 hours (19, 20). While 24-hour urine collection is a good standard for estimating average population dietary iodine intake, it has three main disadvantages: high participation burden, high cost, and lack of objective proof of completeness (no quality assurance tool for assessing completeness of urine collection has been widely used in iodine measurement). Spot, timed, and “overnight” urine sampling methods may have a lower participation burden and a lower cost, but share the quality assurance limitation concerning completeness of urine collection. For example, of the four studies reported here that compared I/Cr (12), UIE (15), and UIC (13, 14) measured in spot, timed, and/or “overnight” urine samples to UIE measured in 24-hour urine collection, only one (15) reported validating urine collection completeness using a standard method (measuring 75% of 24-hour urinary creatinine). In the study by Frey et al. (12), completeness of urine collection was self-reported. The remaining two studies (13, 14) did not report any method of assessing completeness of urine collection. This lack of quality assurance suggests potential inaccuracies in the 24-hour UIE values determined through 24-hour urine collection. Uncertainties about the completeness of urine samples from 24-hour collections are not easily overcome in population studies, and there is no current consensus on the best quality assurance method. The use of para-aminobenzoic acid (PABA)—an exogenous marker—and assessment of its recovery in the urine may not be feasible in large population studies (6). Other methods of evaluating the completeness of urine collection include self-report of incomplete collection, measurements of total urinary volume (conventionally volumes < 300 mL/24h are considered low and an indication of
under-collection), and assessment of urinary creatinine excretions (21–23). None of these methods are satisfactory when used in isolation (24). Therefore, rigorous methods to minimize over- and under-collection of urine should be implemented (25).

Comparison of alternative sampling methods

Three studies used spot UIC to estimate 24-hour UIE. The UIC values were estimated from spot, morning, afternoon, evening, overnight, and timed samples. I/Cr ratio was also used in one study (12). Correlation coefficients were commonly used for comparisons between spot UIC and 24-hour UIE. The results varied. Vanacor et al. (15) found that the UIC from an afternoon sample had the strongest correlation with UIE from 24-hour urine collection. Two New Zealand studies (13, 14) reported weak correlations between the UIC from overnight and DV fasting samples and UIE from 24-hour collection. Two of the four included studies (14, 15) used Bland-Altman plot to examine the agreement of UIC in spot samples and UIE in 24-hour urine collection. Using the Bland–Altman plot instead of correlations, the performance improved in accuracy. However, both studies produced unsatisfactory results according to the plots. In one study, the plots showed under- or over-estimation in all (morning, afternoon, evening and overnight) urine samples. In particular, these overestimated values may misclassify individual and population iodine status, exposing more individuals than expected to the risk of iodine deficiency.

One study used urinary I/Cr to estimate 24-hour UIE (12). However, spot urinary creatinine varies considerably across populations, ethnic, and age groups and by gender (21, 22). Thus, creatinine correction will require the estimation of adjustment factors for each condition.

Limitations

This review had some limitations. First, the number of studies that met the inclusion criteria was too low to allow for conclusive comparisons between 24-hour UIE estimated according to UIC and UIC or I/Cr ratios measured in alternative types of urine sampling (spot, timed, and “overnight”) and UIE measured in 24-hour collections. Second, in most of the studies, the alternative method urine samples were taken from—or included in—the 24-hour urine collections. As this dependence inevitably increases the resulting strength of the correlation, the ideal methodology would be the use of spot, timed, or “overnight” samples independent of the 24-hour collection. Third, validation of 24-hour urine completeness did not appear to be a common practice in the six included studies. Incomplete or excess urine collection could lead to biased estimation of 24-hour UIE. Future studies could include one (or a combination) of the most effective methods for validating completeness of urine collection (e.g., PABA). Fourth, there were some concerns about 1) the reliability and reproducibility of the alternative methods of urine sampling used in the adult population and 2) the generalizability of the results (in terms of policy-making). Finally, none of the six included studies conducted valid comparisons between UIE estimates based on UIE and UIC or I/Cr ratios from alternative-method sampling and UIE measured in 24-hour collection in newborns, young children, and pregnant and lactating women—the populations most vulnerable to iodine deficiency—so their results may not be applicable to those populations, the main targets of population iodization programs. Studies specifically designed for those vulnerable populations are needed to answer the questions posed in this review.

Recommendations

Further comparison of the association between estimated UIE based on UIC or UIC and I/Cr ratios from spot, timed, and “overnight” urine samples and UIE measured in 24-hour collection is desirable. Because UIE is affected by circadian rhythm (11), spot measures of UIE and UIC or I/Cr ratios could vary across a 24-hour time frame. In addition, UIE and UIC (μg/L) and I/Cr (μg/g) are influenced by hydration level, fluid intake, and diuresis, unlike 24-hour UIE (μg/day). Estimated 24-hour UIE based on UIC or UIC or I/Cr ratios measured in spot sampling is also open to other variations and inaccuracies and potential bias. Further research is needed to provide better understanding of these issues and to improve the quality of reporting on iodine intake and iodine status with proper protocols for assessments of validity and reliability (26). The use of spot, timed, and “overnight” urine samples in predicting 24-hour UIE for estimating iodine intake brings up another issue: the lack of consensus on the best indicators for determining proper iodine nutrition. WHO defines optimal iodine status as a median UIC of 100–199 μg/L, which is assumed to correspond to the definition of optimal average iodine intake as 150 μg/day for adults (3, 4).

Population policies of salt iodization to reduce IDD and dietary salt reduction to prevent cardiovascular diseases are important, efficacious, and cost-effective ways to reduce the burden of very common diseases worldwide (27, 28). However, some concerns have been raised about the potential unintended adverse mutual impacts of these policies (27–29), and initiatives have been put in place to help coordinate public health programs to optimize both programs (30, 31).

Conclusions

The results of this systematic review suggest current data on UICs as a means of predicting 24-hour UIE for estimating population sodium intake are inadequate and highlight the need for further methodological investigations. Given the extent of iodine deficiency worldwide and its importance as a global health issue, additional research should be carried out to determine the best ways to assess iodine intake in individuals and across different populations, including those most vulnerable to iodine deficiency (pregnant and lactating women and children). Research questions should include 1) optimum timing of spot urine sampling for measuring UIC and UIE and 2) the advantages of using UIC measurements versus UIE measurements to estimate iodine intake across different populations.

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**REFERENCES**


RESUMEN

Revisión sistemática de estudios que evalúan la concentración urinaria de yodo como factor predictivo de la excreción urinaria de yodo de 24 horas para calcular la ingesta de yodo en la población

Objetivo. Analizar la utilidad de la concentraciones urinarias de yodo en una muestra puntual de orina como predicción de la excreción urinaria de yodo de 24 horas para calcular la ingesta promedio de yodo en la población.

Métodos. Se realizó una búsqueda de bibliografía electrónica de artículos publicados hasta el 19 de mayo del 2013 en MEDLINE (desde 1950), EMBASE (desde 1980) y la Biblioteca Cochrane (desde 1993) que utilizaran los términos “urinary excretion (timed or spot or random) y (24 h or 24 hour)”, “iodine (iodine deficiency)”, “iodine (intake)”, y “urine (timed, spot, random, 24-hour)” (“excreción urinaria [programada o puntual o aleatoria] y [24 h o 24 horas]”, “yodo [carencia de yodo]”, “yodo [ingesta]”, y “orina [programada, puntual, aleatoria, 24 horas]”). Se seleccionaron y analizaron artículos de texto completo acerca de estudios que hubieran examinado como mínimo a 40 personas sanas y medido la excreción urinaria de yodo mediante la recolección de orina de 24 horas, y la concentración urinaria de yodo o la excreción urinaria de yodo mediante un método alternativo (recolección puntual [aleatoria], programada y “de toda la noche” [primera orina de la mañana], en ayunas o no).

Resultados. La revisión incluyó datos de 1 434 participantes de los seis estudios que reunieron los criterios de inclusión. Los principales métodos estadísticos utilizados para comparar los datos de las recolecciones de orina de 24 horas con los valores obtenidos a partir de los métodos alternativos fueron los coeficientes de regresión ($\beta$) o correlación ($r$) y los análisis de concordancia mediante el gráfico de Bland-Altman. Las muestras de orina recolectadas mediante métodos alternativos presentaron una mayor variabilidad interpersonal y para una misma persona que las recolecciones de orina de 24 horas. Se observó una amplia gama de valores de los coeficientes en las comparaciones entre la excreción urinaria de yodo de 24 horas medida mediante la recolección de orina de 24 horas y la excreción urinaria de yodo de 24 horas calculada mediante métodos de muestreo alternativos. Ningún método de muestreo alternativo (puntual, programado o “de toda la noche”) resultó apropiado para calcular la excreción urinaria de yodo de 24 horas.

Conclusiones. Los resultados de esta revisión sistemática indican que los datos actuales en cuanto a la concentración urinaria de yodo como factor predictivo de la excreción urinaria de yodo de 24 horas para calcular la ingesta de yodo en la población son inadecuados y subrayan la necesidad de nuevas investigaciones metodológicas.

Palabras clave Yodo; yodo, orina; toma de muestras de orina; población.