

## Original Article

# Iodine concentration in cow's milk and its relation with urinary iodine concentrations in the population<sup>☆</sup>

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## SUMMARY

**Background & aims:** The importance of milk intake to the supply of dietary iodine is not fully known. We therefore undertook a study in Spain of the iodine concentration in cow's milk and the impact of the frequency of milk consumption on urinary iodine concentrations in three study populations.

**Methods:** We studied the iodine concentration in 362 samples of milk from 45 commercial brands and compared it with the milk iodine status in studies undertaken 17 years earlier. The epidemiologic studies were performed in three different places in the south of Spain: two in school-age children ( $N = 757$  and  $N = 1205$  children) and one in adults ( $N = 1051$ ). A milk consumption questionnaire was given and urinary iodine concentrations measured.

**Results:** The mean concentration of iodine in the milk rose from 1991 ( $117 \pm 37 \mu\text{g/L}$ ) to 2008 ( $259 \pm 58 \mu\text{g/L}$ ) ( $P < 0.001$ ). The iodine concentration was greater in skimmed milk ( $273 \pm 52 \mu\text{g/L}$ ) than in semi-skimmed milk ( $254 \pm 57 \mu\text{g/L}$ ) or whole milk ( $251 \pm 61 \mu\text{g/L}$ ) ( $P < 0.0001$ ). The winter samples had a greater concentration of iodine ( $270 \pm 55 \mu\text{g/L}$ ) than the summer samples ( $247 \pm 58 \mu\text{g/L}$ ) ( $P < 0.0001$ ), independently of the type of milk. The urinary iodine concentrations in all three epidemiologic studies were significantly associated with the frequency of milk intake.

**Conclusions:** The concentration of iodine in cow's milk has risen over recent years, and it is higher in skimmed milk. The results also show that cow's milk is a relevant source of dietary iodine.

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## 1. Introduction

An adequate amount of dietary iodine is essential for the production of thyroid hormones. Recent studies have shown that

even a mild degree of iodine deficiency has repercussions on cognitive function and school performance in clinically euthyroid school-aged children.<sup>1,2</sup> Epidemiologic criteria for assessing iodine nutrition based on median urinary iodine concentrations of school-age children and adults are: iodine deficiency,  $<100 \mu\text{g/L}$ ; adequate iodine nutrition,  $100\text{--}199 \mu\text{g/L}$ ; above requirements,  $200\text{--}299 \mu\text{g/L}$ ; excessive,  $\geq 300 \mu\text{g/L}$ .<sup>3</sup> For pregnant women, these median urinary iodine concentrations are higher.<sup>3</sup>

The recommended daily dose of dietary iodine has recently been revised: 1–8 years old,  $90 \mu\text{g/d}$ ; 9–13 years,  $120 \mu\text{g/d}$ ; 14 years and older,  $150 \mu\text{g/d}$ ; pregnant and lactating women  $250 \mu\text{g/d}$ ; and women of reproductive age (15–49 years)  $150 \mu\text{g/d}$ .<sup>3,4</sup> The iodine concentrations in foods of animal origin depend on their biological

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capacity to store the iodine and the external supply received. Spain is known to have areas with an iodine deficiency,<sup>5</sup> though no precise information is available on the evolution of iodine intake over the years. Another point is that the Spanish food composition tables either do not include iodine concentration or vary between the tables, especially concerning the iodine composition of cow's milk (82–150 µg/L).<sup>6–8</sup>

Iodine passes the mammary barrier and is incorporated into the milk. The iodine concentration in animals' milk varies with the varying concentration of iodine in water, different foods, nutritional supplements and drugs given by veterinarians.<sup>9,10</sup> From 100 to 300 µg of iodine per liter of milk is a likely mean value considering the different values of milk iodine.<sup>9</sup> The iodine compounds generally used as disinfectants of the udders or the tools may also be modifying the iodine concentration of the milk.<sup>9,11</sup>

The importance of milk in the supply of iodine for the Spanish is unknown. Among other reasons, this is because the amount of iodine is not stated on packs of milk. Epidemiologic studies carried out over recent years in Spain have found higher urinary iodine concentrations than expected in a country where historically there was a deficiency of iodine,<sup>5,12,13</sup> though no explanation for this has been found.

The aims of this study were 1) to study the iodine concentration in cow's milk obtained from commercial establishments in different parts of Spain at present and one decade ago, and 2) to evaluate the impact of the intake of milk on urinary iodine in three cross-sectional Spanish populations.

## 2. Materials and methods

### 2.1. Iodine composition in cow's milk

We studied 362 samples of milk from 45 commercial brands in 8 different parts of Spain (Malaga  $N = 75$ , Jaen  $N = 33$ , La Seu d'Urgell (Lleida)  $N = 55$ , Alava  $N = 35$ , A Coruña  $N = 51$ , Barcelona  $N = 64$ , Valencia  $N = 31$  and Oviedo  $N = 18$ ). The milk was bought in commercial establishments in these places. The following data were obtained for each sample: place of purchase, date of purchase (February to November 2008), date of expiry, type of milk (whole,  $N = 134$  (37.0%), semi-skimmed,  $N = 121$  (33.5%) and skimmed,  $N = 107$  (29.5%)), as well as whether the milk was plain ( $N = 268$ , 74%) or contained supplement (calcium, vitamins, omega 3 fatty acids or other) ( $N = 94$ , 26%).

In 1991 one of the authors undertook a systematic study of the iodine composition in milk from 31 different brands. The results of this study were never published and are used here as a reference for the evolution in the iodine concentration of milk available on the Spanish market.

### 2.2. Consumption of cow's milk and urinary iodine

This report combines three epidemiologic studies previously undertaken by the authors in three different places in southern Spain. The Axarquía study (1997–1998) was carried out with 757 schoolchildren (4–16 years) in order to determine the prevalence of goiter in the province of Malaga.<sup>14</sup> The Jaen study (2001–2002) involved 1205 schoolchildren (4–16 years) from the province of Jaen, again to determine the prevalence of goiter.<sup>1</sup> The Pizarra study (1996–1998) was done in 1051 adults (18–64 years) from a different part of the province of Malaga and was designed to examine the “nature-nurture” relation to explain the metabolic and cardiovascular risk factors of this population.<sup>15</sup> All three studies involved a standardized food frequency questionnaire to determine the consumption of iodized salt and other sources of iodine, such as the consumption of milk and other dairy products, fish or eggs.

The food surveys were based on questionnaires validated by the authors in previous studies<sup>16</sup> and were carried out by certified dietitians. These surveys also included measurements of urinary iodine concentrations in a casual urine sample from the whole study population.

### 2.3. Procedures

The iodine concentration in the urine and milk was measured by the modified Benotti and Benotti technique.<sup>17</sup> Briefly, the iodine concentration in the urine samples, milk samples and standards were digested with chloric acid solution at 110 °C for 90 min. After the heating, a solution of arsenious acid and ceric ammonium sulphate solution was added to each tube. The absorbance of each sample was measured 30 min later at 420 nm with a spectrophotometer. In urine samples the intra- and inter-assay coefficient of variation (CV) was 3.2% and 3.5%,<sup>18</sup> respectively, and in the milk samples the intra- and inter-assay CV was 3.3% and 8.3%, respectively.

### 2.4. Statistical study

The data are presented as the mean  $\pm$  SD. The hypothesis contrast between two samples was done with the Student *t* test. For more than two samples the comparison was made with one- or two-way ANOVA and the post hoc analysis was done with Duncan's multiple range tests. The probability (Odds Ratio) of an event was calculated with multiple logistic regression models. In all cases the level of rejection of a null hypothesis was  $P \leq 0.05$ . The statistical analysis was done with SPSS (Version 11.5 for Windows; SPSS, Chicago, IL).

## 3. Results

### 3.1. Iodine concentration in cow's milk

The mean iodine concentration in the samples of milk studied was  $259 \pm 58$  µg/L (minimum: 79 µg/L; maximum: 409 µg/L). The frequency distribution of the iodine concentration in the samples of milk studied adjusted to a normal distribution (Kolmogorov–Smirnov  $Z = 0.81$ ,  $P > 0.05$ ). Concerning iodine concentration, 55.8% of the samples had a concentration greater than 250 µg/L, 27.2% had a concentration above 300 µg/L and just 0.3% had a concentration less than 100 µg/L.

The mean time between the date of purchase and the date of expiry was  $2.46 \pm 0.99$  months (minimum 0 months, maximum 5 months). No significant correlation was found between the iodine concentration in the milk and the preservation time ( $r = 0.04$ ; not significant) (data not shown).

The iodine concentration in the milk was lowest in the milks bought in Oviedo ( $214 \pm 27$  µg/L) and highest in those bought in La Seu d'Urgell ( $272 \pm 63$  µg/L) ( $P < 0.0001$ ) (Table 1). Independently of the place of purchase, the iodine concentration was greater in the skimmed milk ( $273 \pm 52$  µg/L) than the semi-skimmed milk ( $254 \pm 57$  µg/L) or the whole milk ( $251 \pm 61$  µg/L) ( $P < 0.0001$ ) (Table 1), without differences between these two last. No interaction was detected between the place of purchase and the type of milk (whole, semi-skimmed and skimmed) ( $P = 0.96$ , not significant).

The winter samples had a greater concentration of iodine ( $270 \pm 55$  µg/L,  $n = 204$ ) than the summer samples ( $247 \pm 58$  µg/L,  $n = 158$ ) ( $P < 0.0001$ ), independently of the type of milk. A gradient was seen in the iodine concentration in the milk depending on the month of purchase ( $P < 0.0001$ ) (Fig. 1), except for June ( $283 \pm 15$  µg/L). A two-way ANOVA showed no significant interaction between

**Table 1**  
Iodine concentration in the milk ( $\mu\text{g/L}$ ) according to the place of purchase and the type of milk.

Place of purchase	Whole milk	Semi-skimmed milk	Skimmed milk	N
N	134	121	107	
Malaga	254 $\pm$ 71	266 $\pm$ 51	288 $\pm$ 48	75
Jaen	256 $\pm$ 67	222 $\pm$ 72	254 $\pm$ 32	33
La Seu d'Urgell	265 $\pm$ 73	261 $\pm$ 55	290 $\pm$ 60	55
Alava	249 $\pm$ 44	265 $\pm$ 56	279 $\pm$ 40	35
A Coruña	252 $\pm$ 69	255 $\pm$ 51	276 $\pm$ 48	51
Barcelona	263 $\pm$ 41	270 $\pm$ 65	266 $\pm$ 53	64
Valencia	214 $\pm$ 38	227 $\pm$ 48	239 $\pm$ 65	31
Oviedo	204 $\pm$ 25	213 $\pm$ 26	225 $\pm$ 28	18

The results are given as the mean  $\pm$  SD. Two-way ANOVA: place of purchase ( $P < 0.0001$ ) and the type of milk ( $p = 0.04$ ). No interaction was detected between the place of purchase and the type of milk ( $P = 0.96$ , not significant). Analyzed individually, in all the cities except two (Jaen and Barcelona), the iodine concentration between different types of milk was significantly different ( $P < 0.05$ ).

the month of purchase and the type of milk in the explanation of the variance in the iodine concentration.

In those commercial brands in which at least 10 measurements were made ( $n = 12$ ), the range (distance between the maximum and minimum values) in the iodine concentration varied from 142  $\mu\text{g/L}$  in one of the brands to 244  $\mu\text{g/L}$  in another. For the other brands with fewer than 10 sample units, the range varied from 23  $\mu\text{g/L}$  in one of the brands to 303  $\mu\text{g/L}$  in another.

In the 1991 cow's milk study of 31 commercial brands, the iodine concentration was significantly lower than at present: 117  $\pm$  37 vs. 259  $\pm$  58  $\mu\text{g/L}$ ,  $P < 0.001$ . Whereas most milks in the present study had an iodine concentration above 200  $\mu\text{g/L}$ , in 1991 they were mostly below 150  $\mu\text{g/L}$ , and even 100  $\mu\text{g/L}$ . Admittedly, the commercial brands were not always the same in the two studies (1991 and 2008), but in 13 cases the brands did coincide. Here a significant increase was confirmed: 277  $\pm$  31 at present vs. 114  $\pm$  44 in 1991,  $P < 0.001$ .

### 3.2. Intake of milk and urinary iodine

#### 3.2.1. Axarquía study

The mean age of the 757 children was 9.69  $\pm$  3.64 years (4–16 years) (boys 48.1% and girls 51.9%). The overall urinary iodine concentration was 119  $\pm$  70  $\mu\text{g/L}$  (median = 120  $\mu\text{g/L}$ ). Milk was consumed at least three times a day by 20.5% of the children, twice

a day by 48.5%, once a day by 20.0%, once a week by 6.6% and never by 4.4%. The likelihood of having an urinary iodine concentration  $\leq 100 \mu\text{g/L}$  was significantly inversely associated with the frequency of milk intake. This association remained significant after adjusting the logistic regression model for other variables that could have influenced the urinary iodine concentrations, such as geographic origin, sex, intake of iodized salt, or source of drinking water (Fig. 2).

#### 3.2.2. Jaen Study

The mean age of the 1205 children studied (boys 51.5% and girls 48.5%) was 10.84  $\pm$  2.96 years. The overall urinary iodine concentration was 119  $\pm$  77  $\mu\text{g/L}$  (median = 90  $\mu\text{g/L}$ ). Milk was consumed at least three times a day by 38.0% of the children, twice a day by 41.5%, once a day by 14.0%, five-six times a week by 5.3%, and never by 1.2% (Fig. 3A). The mean urinary iodine concentration of the children who consumed milk at least three times a day was significantly greater than in the other groups ( $P < 0.001$ ) (Fig. 3A).

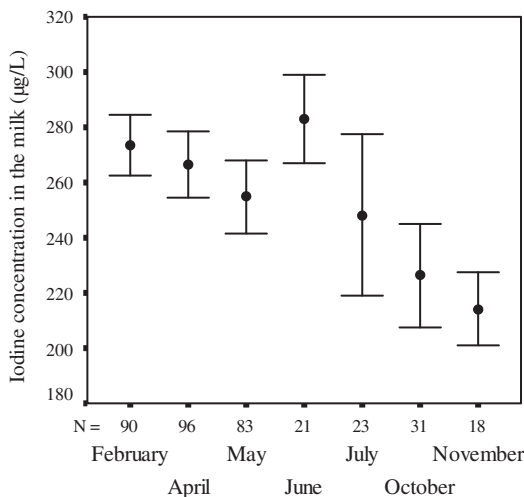
#### 3.2.3. Pizarra Study

The mean age of the 976 adults (men 38.6% and women 61.4%) was 46.1  $\pm$  13.9 years (23–73 years). The overall mean urinary iodine concentration was 125  $\pm$  93  $\mu\text{g/L}$  (median = 110  $\mu\text{g/L}$ ). Milk was consumed at least twice a day by 31.4%, once a day by 15.3%, less than once a day by 19.6%, and never by 33.7%. The urinary iodine concentration was significantly greater in those persons who consumed milk more than once a day ( $P = 0.040$ ). The significant difference remained after adjusting the ANOVA model for age, sex and intake of iodized salt (Fig. 3B).

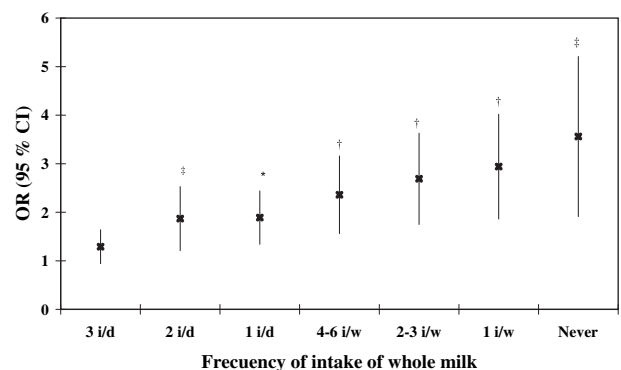
## 4. Discussion

As far as we are aware, this is the first systematic study in Spain of the iodine concentration range in milk. The results show the current composition of iodine in cow's milk available on the Spanish market. The comparison between the 1991 and present samples suggests a significant increase in the milk iodine concentration over this time period. Additionally, the results show that cow's milk is a relevant source of dietary iodine.

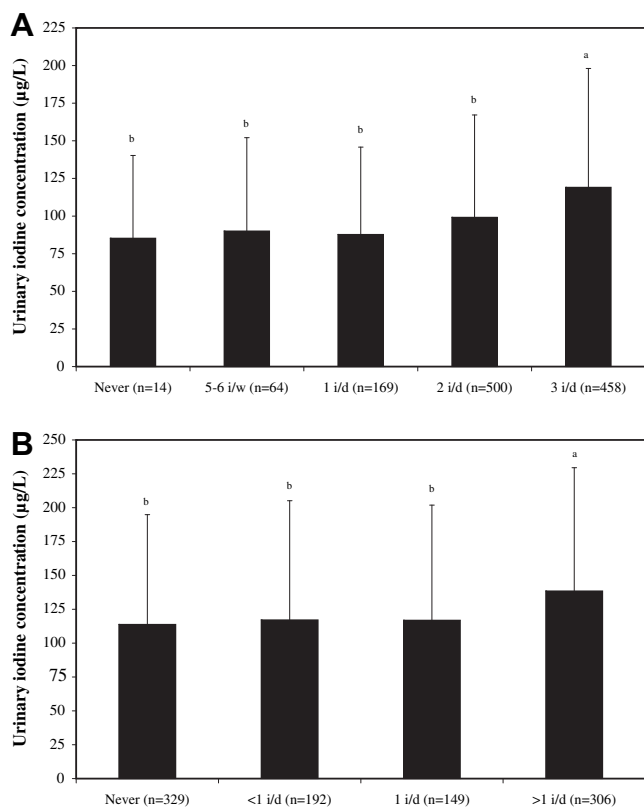
Several studies have shown that the dietary iodine concentration has varied greatly over the years. In the USA, the concentration of iodine in milk fell from 1975 to 1982, and remained relatively stable from 1982 to 1990 with iodine concentrations around 230  $\mu\text{g/L}$  and a CV of 39%.<sup>19</sup> However, an area of Boston has been



**Fig. 1.** Iodine concentration in the milk ( $\mu\text{g/L}$ ) according to the month of purchase ( $P < 0.0001$ ).



**Fig. 2.** Odds Ratio (OR)  $\pm$  95% confidence intervals (CI) of having a urinary iodine concentration lower than 100  $\mu\text{g/L}$  (0,1) in the children of the Axarquía study according to the frequency of intake of whole milk. OR adjusted for age (continuous variable), sex (0,1), consumption of water from a well (no, yes), place (coast, inland), consumption of iodized salt (yes, no) and recent wounds (yes, no). \* $P < 0.05$ ; † $P < 0.01$ ; ‡ $P < 0.005$ . i/d: number of intakes per day; i/w: number of intakes per week.



**Fig. 3.** Urinary iodine concentration ( $\mu\text{g/L}$ ) (mean  $\pm$  SD) according to the frequency of milk consumption after adjusting in an ANOVA model for age, sex and intake of iodized salt. (A) Jaen Study ( $P < 0.001$ ). (B) Pizarra Study ( $P = 0.040$ ). i/d: number of intakes per day; i/w: number of intakes per week. Different letters indicate significant differences between the means of the different groups of subjects ( $P < 0.05$ ).

reported to have mean concentrations of iodine in milk of  $454 \mu\text{g/L}$ .<sup>20</sup> In Australia, the iodine concentration in milk fell from  $593 \mu\text{g/L}$  in 1975 to  $195 \mu\text{g/L}$  in 2004.<sup>21</sup> The authors of this study suggest that, as no active iodine prophylaxis policy exists in Australia (with iodized salt), the reduced amount of iodine in milk is likely to be one of the explanations for the re-emergence of iodine deficiency in Sydney and perhaps elsewhere in Australia. In the Czech Republic, the iodine concentration in cow's milk rose from a mean of less than  $50 \mu\text{g/L}$  in 1982 to over  $300 \mu\text{g/L}$  in 2005, with 16% of samples above  $500 \mu\text{g/L}$ .<sup>22</sup> In Peru, the iodine concentration in cattle milk varies from  $24 \mu\text{g/L}$  in the region of Cajamarca to  $170 \mu\text{g/L}$  in Lima.<sup>23</sup> Iodine deficiency was well-known in Great Britain, at least up to the 1950s. Although Great Britain has never had mandatory iodization of salt and other foods, iodine intake has increased, especially since the 1970s and up to the early 1990s. Increased iodine intake is mainly due to changes in farming practice that have resulted in more iodine in milk and other dairy products.<sup>24</sup>

Studies on the iodine concentration of milk have also been undertaken in other countries over recent years.<sup>25,26</sup> The general conclusion in all these studies is that the iodine composition in milk varies greatly from one sample to another, that changes in the concentration have occurred over time and that this variation has not usually been the result of a policy of regulating the iodine concentration in milk. A few of the causes of this variation are known and common to all the studies. The iodine concentration is higher in winter milk samples than in summer milk samples.<sup>19,20,24,25</sup> This variation was also found in our study, though it was not so marked as that of other studies.<sup>24,27</sup> Another variation found in our study was the greater iodine concentration detected in

skimmed milk; this, too, has been seen elsewhere, though it was not commented on in the results.<sup>27</sup> Nevertheless, the most important variations in the concentration of iodine in milk are random, as shown in our study, with wide variation found within the same brands, with ranges above  $100 \mu\text{g/L}$ . Iodine in cow's milk comes from the iodine consumed by the animal in fodder, as well as the contamination of products used for disinfection and sterilization.<sup>9–11</sup> The milk that can be bought in commercial establishments in Spain is pooled from several dairy farms. Thus, any high iodine concentrations in milk from one farm will be diluted by lower concentrations in milk from other farms. The differences in iodine administration in veterinary practice may also explain part of this variation.<sup>24</sup>

Populations affected by iodine deficiency should be considered as more sensitive to the adverse effects of iodine intake, such as a higher risk of both hyper- and hypothyroidism in the event of acute or chronic exposure to high doses of iodide.

Therefore, in Europe, the Scientific Committee on Food proposed an upper limit of iodine intake in the healthy population and the upper iodine levels in feed for dairy cows is also regulated according to the recommendations of animal nutrition scientists.<sup>28</sup> Reducing iodine to a maximum of  $4 \text{ mg/kg}$  complete feed for dairy cows would result in a satisfactory margin of safety for the consumption of milk.<sup>9</sup>

In children, milk is a very adequate source of iodine. The results of the study undertaken in schoolchildren from the Axarquía show that the frequency of milk consumption is associated in a dose-dependent manner with their urinary iodine concentrations and with the risk (OR) of having urinary iodine concentrations lower than  $100 \mu\text{g/L}$ .<sup>14</sup> This association between milk intake and urinary iodine concentration in children has been found in other studies.<sup>1,26</sup> In the Pizarra study, too, the adults who consumed milk more often had higher urinary iodine concentrations.

Surveys on individual consumption reveal that the consumption of milk and dairy products in the Spanish population is higher in childhood, falling progressively from adolescence.<sup>29,30</sup> A recent study in Spanish university students found that the consumption of milk and dairy products is inadequate.<sup>31</sup> In the Pizarra study, 46.6% of the adults consumed some type of dairy product each day, but 33.7% never consumed milk. The situation in children, however, is different. Over 95% of the schoolchildren in the Axarquía study consumed milk at least once or twice a day. Less information is available concerning the consumption of milk by healthy pregnant women. The Guía de la Alimentación Saludable (Guide to Healthy Eating) drawn up by the Spanish Society of Community Nutrition, recommends a daily intake of two or three rations, or their equivalent, of dairy products. This recommendation is designed to provide an estimated 250–300 mg of calcium (200–300 mL milk, estimating  $1 \text{ g Ca/L}$  milk). However, none of these nutritional recommendations contemplate the importance of dairy products as a source of dietary iodine, even though two glasses of skimmed milk a day could supply 100–150  $\mu\text{g}$  of iodine per day, which is almost the cited daily iodine requirement in the diet of a healthy adult.<sup>34</sup> This is especially interesting in children, with stable consumption of dairy products, and in pregnant women with their higher requirement. Recent studies have shown the very important role of cow's milk as a source of iodine during pregnancy.<sup>32,33</sup>

The international agencies recommend universal iodization of salt as the best way of guaranteeing an adequate amount of iodine in the diet.<sup>34</sup> This measure has led to the eradication of iodine deficiency in most parts of the world. Nevertheless, in Spain and most other industrialized countries, only a part of the population actually consume iodized salt<sup>5</sup> and the increase in the urinary iodine concentration of the population has mostly depended on the presence of iodine in food, even though the risks associated with



this silent, or non systematic iodine prophylaxis have been repeatedly denounced.<sup>3,35</sup> Milk may be a good vehicle to contribute to an adequate iodine intake, but for this case it would be necessary to standardize concentration of iodine and submit it to legal regulation. A concentration of 200–300 µg of iodine per liter of milk would be a recommendable concentration.

### Conflict of Interest

None.

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