

The Brazilian Nutritional Policy of Iodination of Culinary Salt to Control Iodine Deficiency in Population: From the Lack to the Excess

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Abstract

In the 1950's, Brazil adopted the iodination of the cooking salt to defeat chronic iodine deficiency diseases. The Federal government has been performing national inquiries periodically about the occurrence of endemic goiter in schools, adopting the urinary excretion of iodine and the thyroid volume as result indicators. The determination of the iodine concentration in the cooking salt has also been used as a determinant factor in these results analysis. This bibliographic review aims to present the actions taken by the Brazilian government in relation to iodine deficiency since the beginning of iodization policy of culinary salt in the 50's decade, the results achieved and the situation of excess iodine found in the Brazilian population at the present time. These measures systematically adopted by the Brazilian government, supported in laws, ordinances and ministry resolutions, have shown to be efficient instruments in the reduction of endemic goiter. Nowadays, the prevalence of goiter in the Brazilian population is between the parameters established by the World Health Organization, which means less than 5% of the population affected. Nevertheless, the last survey made by the Health Ministry highlighted an excessive ingestion of iodine, exposing the population to other health risks associated to this excess.

Keywords: Iodized salt; Urinary iodine; Hypothyroidism; Excess of iodine; Public health

Introduction

Iodine is an element essential to health, directly related to thyroid gland functioning, to adequate nervous system development and to general body growth [1]. Inadequate iodine ingestion is associated to several diseases identified as Iodine Chronic Deficiency Diseases (ICDD): Neonatal and adult hypothyroidism, multinodular goiter, iodine-induced hyperthyroidism, fertility decrease, fetal malformation, perinatal mortality, deaf-mutism and clinical variants of endemic cretinism [2,3].

Iodized salt for human consumption is considered the most effective measure to achieve appropriate iodine levels for populations. It is the universal strategy adopted in public health, without iodized salt some two billion people would have iodine deficiency, while the actual number is 700 million [4]. Populational programs of iodination of salt in every continent have significantly limited illnesses related to chronic iodine deficiency. However, there are still 266 million children and two billion adults living in the world with insufficient ingestion of iodine [5].

Data from the World Health Organization (WHO), referring to 130 countries, showed that 68% of all residences in the world have access to iodized salt and that 34% of them are in a country with more than adequate iodine ingestion or even excessive, among those countries is Brazil [5]. The Health Ministry has been developing periodic population inquiries to evaluate the impact of this intervention on the Brazilian population. This research has shown a decrease in the prevalence of endemic goiter from 20.7% in 1955 to 1.3% in 1994,

proving the efficacy of the strategy to public health aims. A similar outcome was obtained in another study set in 2000, with prevalence of 1.4% showing control over the endemic in the country [3,6].

However 86.5% of the scholars involved in this study showed high levels of urinary iodine excretion, with urinary iodine above 300 mcg/L and half of these with numbers above 500 mcg/L, showing a new reality concerning excessive iodine consumption [3]. Iodine-induced hyperthyroidism, autoimmune chronic thyroiditis and secondary hypothyroidism are severe illnesses that can affect individuals exposed to an excessive amount of iodine [3].

This article aims to review literature concerning Brazilian strategy to fortify cooking salt with iodine to reduce endemic goiter in the country, its temporal evolution and the results achieved by the national program since its beginning. This article will also highlight the transition from deficiency to excess of corporal iodine and its side effects in the organism.

Methods

Bibliographic review of national and international publications in periodic indexed in the following database: National Library of Medicine (Medline, USA) and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), during the time period between 1980 and 2014 comprising Portuguese, English and Spanish languages that approached the strategies of fortification of cooking salt with iodine recommended by the WHO and implemented in Brazil.

In the search strategy were included publications about the historical evolution of the actions and strategies of combat against iodine deficiency both in Brazil and globally. The descriptors used were:

Goiter, iodine deficiency, iodine excess, urinary iodine, iodized salt, iodine-induced hyperthyroidism, hypothyroidism, autoimmune thyroid disease, isolated or as a combined form. It was selected 40 publications according to the inclusion criteria above. From these, eight publications were excluded for not showing direct relation to the main goal proposed in this article, being 32 publications remained to comprise this review.

History of iodation of salt to control endemic goiter in Brazil

Since the 1920's, most countries have been adapting in order to provide the necessary amount of iodine to their populations. Most countries adopt strategies to guarantee this control and eliminate endemic goiter as a public health issue. The universal iodination of cooking salt has shown to be the most simple and effective of all actions adopted to combat iodine deficiency illnesses [7]. WHO classifies goiter prevalence as severe when prevalence is above 30% in a population and moderate from 20 to 29.9%. Values under, between 5.0-19.9%, are considered as mild and communities with goiter prevalence of 4.9% and lower are considered null prevalence [4]. The Brazilian National Congress and the sanitary authorities have instituted legal mechanisms (Laws, ordinances and ministry resolutions) addressing chronic iodine deficiency in the country [3,8]. Table 1 presents the temporal evolution of goiter prevalence determined by populational inquiries from 1955 to 2000, highlighting the significant reduction of the illness observed in this period.

Reference	Year	Population	Age (years)	Goiter prevalence (%)
National inquiry	1955	86.217	6-14	20.7
National inquiry	1974	42.752	7-14	14.1
National inquiry	1994	178.774	6-14	1.3
Thyromobil project	2000	2.013	6-14	1.4

Font: Knobel and Medeiros-Neto [3]

Table 1: Populational based studies about endemic goiter in Brazil from 1955 to 2000.

In Brazil, since colonial time, there have been iodine deficiencies illnesses reported as an important cause of goiter in European originated populations, in blacks and mixed bloods, although in indigenous population this phenomenon was not discovered, likely related to eating factors of each population [6]. In 1953 there was the implementation of the first national program of salt iodination in endemic goiter areas of the country, with the addition of 10 mg/Kg of iodine in the culinary salt [3,9]. In 1955, the first national inquiry about goiter occurrence revealed a prevalence of 20.7% in the population [10,11].

In August 17th of 1956, the National Decree number 39,814 defined the endemic goiter areas, leading to an extension of salt iodination to the whole country. The Health Ministry became responsible for emphasizing the importance of iodized supplements [3,10]. In 1974, law number 6150 mandated 10 mg/kg of iodine in the salt for human consumption, transferred the expense of iodination to private initiative and required the states, territories and counties to supervise this initiative [3,10]. From 1974 to 1976, the Health Ministry/SUCAM (Superintendências de Campanhas de Saúde Pública) made the second national inquiry with 42,752 scholars from 7 to 14 years old, showing a

goiter prevalence of 14.1% indicating a reduction of only 6.5% of this prevalence in 20 years [11]. Despite the proclamation of new laws and federal decrees, since 1980 Brazil has lived with the inefficiency of these regulatory documents due to the lack of control and supervision in the salt industry, which added to the drastic statistic of over 15 million Brazilians bearing endemic goiter [11].

From 1982 to 1992, researches interested in goiter endemia, salt industries representatives, Health Ministry's and Nutrition and Eating Institute's (NEIN) technicians, agreed to maintain the iodine concentration above 10 mg/kg of salt as a responsibility of the producers. The Health Ministry and the NEIN had the duty of creating a wide net of public laboratories to ensure the appropriate iodine concentration production. This movement established the decrease of goiter in scholars and overall improvement in health for the whole population being worldly recognized and cited as an example of success to be followed by other countries [3,10].

The third national inquiry made in 1994 with 178,774 scholars from 6 to 14 years showed a low prevalence of goiter (<5.0%) in most coastal states, compared to the presence of chronic iodine deficiency illness in states from northern and central regions of the country. This study highlighted the disparity in public health efforts targeted at eliminating iodine deficiency [12]. In 1995 the Health Ministry established the correct iodination of cooking salt with amounts of iodine between 40-60 mg/kg and authorized the potassium iodide supply to salt industries [3]. As NEIN was stopped in 1997, and the National Agency of Sanitary Surveillance (ANVISA) at the end of the 1990's, the boundaries of potassium iodide were liberated to 40-100 mg/kg of salt, exposing Brazilian to an elevated consumption of iodine from 1998 to 2003 [3].

In May and June of 2000, the Thyromobil Project in Brazil, adapted from the model developed in Europe and Latin America, ran 12,000 km from north to south of the country visiting 29 counties from eight states where there were the Sentinels Villages marking the iodine chronic deficiency in the 1995 inquiry [13]. In this project, concentration of the iodine in urinary samples was analyzed in a representative sample made of scholars from 6 to 14 from both genders, aside from the collect of a sample of consumed salt by these scholars to determine the concentration of iodine in the salt. The urinary excretion of iodine was the diagnostic indicator used to determine the nutritional state of iodine in the population, using the established references by WHO [3] according to Table 2.

The obtained results in the project were startling and showed 86.5% of scholars with excessive iodine levels in the urine, above 300 mcg/L, where in half of the researched showed levels above 500 mcg of iodine/L. In 5% of the scholars were detected levels of urinary iodine above 900 mcg/L. Such results show accordance with the fact that 50% of the samples of consumed salt in residences by the scholars showed concentrations of iodine above 60 mg/kg of salt [3,13].

Therefore, in 2003, ANVISA reduced again the levels of concentration of iodine in the salt for human consumption to 20-60 mg/kg of salt in an attempt to correct the situation of excess demonstrated with the nutritional iodine. Table 3 summarizes the fluctuations of iodine in the cooking salt according to the recommended concentrations in the regulatory governmental marks.

In 2006 the Health Ministry made a new national inquiry to collect data about the salt consumed in Brazilian residences, showing that 99% of these had the product for daily use with 95.7% of iodine in the cooking salt analyzed [15]. The lower proportions were in the rural

areas of the north (90.4%) and of the center-west (91.4%). It concluded being necessary permanent actions of orientation e supervising in the steps of production and distribution of salt in the country.

Urinary iodine (µg/L)	Iodine ingestion	Iodine nutrition
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Light iodine deficiency
100-199	Adequate	Great
200-299	More than adequate	Risk of iodine-induced hyperthyroidism in 5 to 10 years of introducing iodized salt with high levels of iodine
>300	Excessive	Risk of developing side effects (iodine-induced hyperthyroidism, chronic autoimmune thyroiditis)

Font: WHO [14]

Table 2: Epidemiologic criteria to evaluate the adequate ingestion of iodine based on the median urinary concentration of iodine in scholars.

Year	Iodine concentration in salt
1953	10 mg/kg
1974	10 mg/kg
1994	40–60 mg/kg
1997	40–100 mg/kg
2003	20–60 mg/kg

Font: Adapted from Knobel and Medeiros-Neto [3]

Table 3: Chronology of fluctuations of iodine concentration in salt-Brazil.

Excessive consumption of iodine and health risks

The insufficient ingestion of iodine or its excessive consumption can lead to illnesses of the thyroid [16]. Esteves [11] reaffirmed that the combined action of assessment of the thyroid volume, preferable by ultrasound, and the determination of urinary excretion of iodine of scholars consists in the best way to monitor the control of the endemic iodine deficiency [11]. Gandra [17] compared the concomitant prevalence of goiter in adults and children considering as vulnerable group scholars from 9 to 14 years old due to their prepubertal biophysiological characteristics related to growth, more prone to the effects both of deficiency and excess of iodine [17].

In Brazil, some studies have been done to better understand and control these problems. Nimer et al. [18] studied 280 students from two schools from fundamental education, one private and the other public, from the Ouro Preto (Minas Gerais State) county, dosing the urinary iodine concentration and the iodine concentration in cooking salt samples. The results showed consumption of cooking salt with levels of iodine below the recommendation in 89.9% in public schools and in 40.9% in private. Around 57.4% of students from public school

showed urinary iodine compatible to light deficiency (35.6%), moderate (12.9%) and severe (8.9%). In the private school's students, 92.2% of them showed levels of urinary iodine among the recommended standard. The inadequate iodine concentration in salt consumed by the scholars contributes to a significant prevalence of iodine deficiency [18].

Pontes, Adan e Costa, in a study with individuals from 3 to 85 years determined the prevalence of thyroid diseases in the county of Cabaceiras (Paraíba State/Brazil). Group 1 was formed by 122 patients from rural areas of the state that made clinical control for diagnostic suspicion of thyroid disease and 88 healthy volunteers formed group 2. Most individuals (79%) were females. Both groups were submitted to serum dosages of TSH, T3, free T4 and antibody anti-microsomal research. Patients from the rural area submitted themselves to ultrasound of the thyroid gland and the ones from group 2, to palpation of the gland. The results found showed high prevalence of thyropathies in groups 1 and 2 (19.8% and 20.4% respectively) associated with genetic and environmental factors, pointing out to the need of epidemiological studies surrounding the excessive consumption of nutritional iodine [19].

A retrospective study of 43 children and adolescents from 1.1 to 17.6 years with Hashimoto thyroiditis (36 female and 7 male subjects) in the Unity of Pediatric Endocrinology of the Hospital das Clínicas/São Paulo University (São Paulo/Brazil) showed possible association between the stimulus to produce antibodies against thyroid components and the high ingestion of iodine, explaining the increase in thyroid autoimmune diseases frequency in the last few years [20].

Duarte et al. selected by random 844 scholars from both genders form 6 to 14 years from six regions of São Paulo state aiming to assess the thyroid volume by ultrasound exam and determine the urinary iodine. The echography of the thyroid showed a prevalence of 16% of goiter. It drew attention to the excessive urinary iodine excretion as 53% of the samples showed numbers above 300 mcg/L. The dosages of iodine in cooking salt showed an excessive iodine concentration in 47.4% of samples. Therefore, a likely increase in salt consumption with high levels of iodine contributed to the occurrence of iodine-induced hyperthyroidism as well as chronic autoimmune thyroiditis, therein this one predominant in females [21].

These effects can be shown in the study of Camargo et al. that evaluated the prevalence of chronic autoimmune thyroiditis, iodine-induced hypothyroidism, clinic and sub-clinical hyperthyroidism and goiter in 1085 subjects selected by random in the São Paulo metropolitan region of Brazil [22]. The female group prevailed with 62.5% of the subjects and the average age was between 24.7 and 81 years. In the male group (37.5%) the average age was between 55, 8 ± 12 years. Dosages of the iodine concentration were performed in urinary samples and in cooking salt. Despite the fact that iodine concentration in the cooking salt were included in the new official parameters (20-60 mg/kg of culinary salt), 45.6% of iodine urinary concentration were at excessive levels (above 300 mcg/L), therein greater than 400 mcg/L in 14.1%. The prevalences were: 3.3% of hyperthyroidism, 8.0% of hypothyroidism and 16.9% of chronic autoimmune thyroiditis [22]. This data, once more, supported the assumption that the excess of iodine consumption by the Brazilian from 1998 to 2003 may have contributed to the increase of these disturbs prevalence in subjects genetically predisposed.

Similar situation to the chronic autoimmune thyroiditis prevalence (Hashimoto's thyroiditis) in two regions of São Paulo Brazilian State:

attached area to the petrochemical pole of Capuava (409 subjects) and control area in São Bernardo do Campo (420 subjects). The prevalence of chronic autoimmune thyroiditis was proportionally elevated in both studied areas, not showing direct epidemiological connection to the proximity to petrochemical pole but probably connection to the elevated ingestion of nutritional iodine that the Brazilian population was submitted to from 1998 to 2003 [23].

Duarte et al. studied the iodine urinary excretion in 964 scholars from both genders in the state of São Paulo-Brazil, iodine-sufficient area. In 76.8% of researched students, the urinary iodine was above 300 mcg/L, with predominance in males. The ultrasound study in this population showed abnormalities in 13.1%; hemi agenesis in 0.5%, nodules in 0.2%, cists in 0.7% and hypo echogenicity in 11.7%. Authors of the study proposed the direct relation between the thyroid alterations and the excessive consumption of iodine [24].

Another cross-sectional study involving 300 students from three schools of different social economic levels from the Ribeirão Preto (São Paulo State/Brazil) county, being considered an iodine-sufficient area, analyzed the urinary iodine and the iodine concentration in cooking salt, as well as a thyroid ultrasound was evaluated in all participants. The iodine urinary excretion was above 300 mcg/L in 59.5% of samples. From the 300 children examined, 15.6% showed abnormalities of the thyroid in the ultrasound exam. Such results revealed that the thyroid gland alterations can be associated to the exposition to excessive amounts of iodine [25].

Furthermore, a regional study evaluated the iodine excretion in 145 students of two schools: One in the urban area and the other in the rural area of the county of Botucatu (São Paulo State/Brazil). At the same time, they dosed the iodine concentration in those children's residences. The results showed that 3.0% of students from the urban schools had urinary iodine below 100 mcg/L and 90.9% above 300 mcg/L. In the rural area group, 3.8% of scholars had some deficiency level of iodine and 60.0% had urinary iodine concentration above 300 mcg/L. As for the iodine concentration in cooking salt, in the urban residences 84.8% of the samples were between 20-60 mg/kg of salt and in the rural area, 59.5%. They came to the conclusion that the iodine deficiency in the population studied was controlled but showed a high prevalence of excessive urinary iodine excretion [26].

Carvalho et al. [27] collected casual samples of urine from 828 scholars from both genders from ages 4 to 13 years from eight schools in the city of São Paulo (Brazil) in order to determine iodine urinary excretion from these participants. Only 1.9% of the children and adolescents presented with urinary iodine values less than 100 mcg/L while 24.6% had urinary iodine between 100-200 mcg/L. Most students (67.1%) had urinary iodine above 300 mcg/L, a result that pointed to excessive consumption of iodine in this population [27].

In Novo Cruzeiro, in the semi-arid region of Minas Gerais State (Brazil), the prevalence of iodine deficiency was investigated in children from 7 to 71 months. A total of 475 children were allocated by probabilistic sampling stratified according to the iodine concentration in salt consumed by the family and urinary iodine excretion. Iodine excretion deficiency occurred in 34.4%, where 23.5% showed light deficiency, 5.9% moderate and 5.0% severe. Difference in the urinary iodine concentration was determined among urban and rural areas ($p < 0.001$). Higher median concentrations of urinary iodine of 150.6 mcg/L were observed in the urban area versus 114.3 mcg/L in the rural area. Elevated deficiencies were observed among children who consumed salt with iodine amounts below the recommendation [28].

The borderline distribution of iodine associated to low levels of iodine in the salt suggested that greater standardization of iodation is needed between the urban and the rural areas.

In a recent study, Boasquevisque et al. determined the iodine concentration in 30 samples of urine and conducted an anatomic-pathological study of 55 thyroids from cadavers from the Forensic Medical Institute in the county of Vitória, Espírito Santo (ES) Brazilian State. Excessive urinary iodine (>300 mcg/L) was found in 96.7% of samples [29]. Histological findings compatible with thyroiditis were identified, which were likely related to the excess of iodine in the studied population and the higher incidence of inflammatory processes of the thyroid.

Final Considerations

Disorders coming from iodine deficiency and main causes of endemic goiter are still major public health issues affecting several regions in the world [4]. In 1993 WHO, UNICEF (United Nations Children's Fund) and the ICCIDD (International Council for Control of Iodine Deficiency Disorders) recommended the universal iodination of cooking salt as a more effective strategy to reach the elimination of iodine deficiency disorders, due to its ease of implementation e lower cost [30]. The American continent stands out worldwide for having reached optimal control of iodine deficiency, despite the cases of setbacks of some countries [6]. The iodination of cooking salt has shown to be an effective and low cost strategy to reduce this endemic.

From a global point of view, different strategies to defeat micronutrients deficiency have been adopted mostly in developing countries. The massive fortification of food from daily use has now been used in several regions of the world, although limited; progress has been attained in the struggle against iron, folic acid, zinc, vitamin A and iodine deficiencies [31].

Brazil has shown positive impact in reducing the prevalence rate of goiter, however there is also evidence of excessive ingest of iodine. This important epidemiological diagnosis draws attention to the need of improving the Brazilian National Program of Prevention and Control of Iodine Deficiency Disorders (Pró-iodo), aiming to monitor the iodine in salt for human consumption, by making a priority strategies of information, education, communication and permanent social mobilization [8,30].

In April 25th of 2013, the Brazilian Official Journal published the RDC 23/3013 with the new standards for iodine addition to salt for human consumption in the Brazilian territory. This decision was based upon the information from the Research of Familiar Budget (RFB-2011) showing that Brazilians consume an average of 10 g of salt per day. Therefore ANVISA started using the concentration of 15-45 mg of iodine per kilogram of salt in substitution to that of 20-60 mg of iodine per kilogram of salt [32].

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References

1. Delange F, de Benoist B, Pretell E, Dunn JT (2001) Iodine deficiency in the world: where do we stand at the turn of the century? *Thyroid* 11: 437-447.

2. Boyages SC (1993) Clinical review 49: Iodine deficiency disorders. *J Clin Endocrinol Metab* 77: 587-591.
3. Knobel M, Medeiros-Neto G (2004) [Disorders associated to chronic iodine deficiency]. *Arq Bras Endocrinol Metabol* 48: 53-61.
4. World Health Organization/United Nations Children's Fund/International Council for the Control of Iodine Deficiency Disorders (2010) Assessment of elimination: a guide for programme managers (6th edn.), Geneva-Switzerland.
5. de Benoist B, McLean E, Andersson M, Rogers L (2008) Iodine deficiency in 2007: global progress since 2003. *Food Nutr Bull* 29: 195-202.
6. Medeiros-Neto G (1982) One hundred and eighty years of endemic goiter in Brazil. *Arq Bras Endocrinol Metab* 30: 226-231.
7. Dunn JT, Crutchfield HE, Gutekunst R, Dunn AD (1993) Two simple methods for measuring iodine in urine. *Thyroid* 3: 119-123.
8. Government of Brazil, Ministry of Health. Department of Health Care (2008) Technical and Operational Manual of the Pro-Iodine: National Programme for Prevention and Control of Iodine Deficiency Disorders by Brasília-DF.
9. Pontes AA, Rocha Ada M, Leite DF, Lessa Ada F, Adan LF (2009) Salt iodination in Brazil, a controversial subject. *Arq Bras Endocrinol Metabol* 53: 113-114.
10. Medeiros-Neto G (2009) Iodine nutrition in Brazil: where do we stand? *Arq Bras Endocrinol Metabol* 53: 470-474.
11. Esteves RZ, Kasamatsu TS, Kunii IS, Furuzawa GK, Vieira JG, et al. (2007) Development of a semi-automated method for measuring urinary iodine and its application in epidemiological studies in Brazilian schoolchildren. *Arq Bras Endocrinol Metabol* 51: 1477-1484.
12. Corrêa Filho H, Vieira JB, Silva YS, Coelho GE, Cavalcante Fdos A, et al. (2002) Endemic goiter prevalence survey in Brazilian schoolchildren 6 to 14 years old, 1994-1996. *Rev Panam Salud Publica* 12: 317-326.
13. Rossi AC, Tomimori E, Camargo R, Medeiros-Neto G (2001) Searching for iodine deficiency disorders in schoolchildren from Brazil: the Thyromobil project. *Thyroid* 11: 661-663.
14. World Health Organization (1994) Indicators for assessing Iodine Deficiency Disorders and their control through sal iodization. Micronutrient Series. Document. Geneva-Switzerland.
15. Ministry of Health, Brazilian Center for Analysis and Planning (2009) National Demographic and Health Children and Women-PNDS-2006. Brasília-DF, Brazil.
16. Teng W, Shan Z, Teng X, Guan H, Li Y, et al. (2006) Effect of iodine intake on thyroid diseases in China. *N Engl J Med* 354: 2783-2793.
17. Gandra YR (1984) Clinical evaluation of endemic goiter. *Rev Saude Publica* 18: 396-404.
18. Nimer M, Silva ME, de Oliveira JE (2002) Relationship between iodized salt and urinary iodine excretion in school children, Brazil. *Rev Saude Publica* 36: 500-504.
19. Pontes AAN, Adan LF, Costa ADM, Benicio AVL, Silva CRA, et al. (2002) Thyroid disease prevalence in a community in northeastern Brazil. *Arq Bras Endocrinol Metabol* 46: 544-549.
20. Szeliga DVM, Setian N, Passos L, Lima TMR, Kuperman H, et al. (2002) Hashimoto's thyroiditis in children and adolescents: a retrospective study of 43 cases. *Arq Bras Endocrinol Metabol* 46: 150-154.
21. Duarte GC, Tomimori EK, Borioli RA, Ferreira JE, Catarino RM, et al. (2004) Echographic evaluation of the thyroid gland and urinary iodine concentration in school children from various regions of the State of São Paulo, Brazil. *Arq Bras Endocrinol Metabol* 48: 842-848.
22. Camargo RYA, Medeiros-Neto G, Tomimori KE, Neves SC, Rubio IGS, et al. (2008) Thyroid and the environment: exposure to excessive nutritional iodine increases the prevalence of thyroid disorders in São Paulo, Brasil. *Eur J Endocrinol* 159: 293-299.
23. Camargo RYA, Tomimori EK, Neves SC, Knobel M, Medeiros-Neto G (2006) Prevalence of chronic autoimmune thyroiditis in the urban area neighboring a petrochemical complex and a control area in São Paulo, Brasil. *Clinics* 61: 307-312.
24. Duarte GC, Tomimori EK, de Camargo RY, Catarino RM, Ferreira JE, et al. (2009) Excessive iodine intake and ultrasonographic thyroid abnormalities in school children. *J Pediatr Endocrinol Metab* 22: 327-334.
25. Alves MLD, Duarte GC, Navarro AM, Tomimori EK (2010) Sonographic evaluation of thyroid, determination of urinary iodine and iodine concentration in table salt used by students from Ribeirão Preto, São Paulo, Brazil. *Arq Bras Endocrinol Metab* 54: 813-818.
26. Navarro AM, Oliveira LA, de Meirelles CJ, Costa TM (2010) Salt iodination and excessive iodine intake among schoolchildren. *Arch Latinoam Nutr* 60: 355-359.
27. Carvalho AL, Meirelles CJ, Oliveira LA, Costa TM, Navarro AM (2012) Excessive iodine intake in schoolchildren. *Eur J Nutr* 51: 557-562.
28. Macedo Mde S, Teixeira RA, Bonomo E, Silva CA, Silva ME, et al. (2012) Iodine deficiency and associated factors in infants and preschool children in an urban community in the semi-arid region of Minas Gerais State, Brazil, 2008. *Cad Saude Publica* 28: 346-356.
29. Boasquevisque PC, Jarske RD, Dias CC, Quintaes IP, Santos MC, et al. (2013) Correlation between iodine urinary levels and pathological changes in thyroid glands. *Arq Bras Endocrinol Metabol* 57: 727-732.
30. Pretell EA, Delange F, Hostalek U, Corigliano S, Barreda L, et al. (2004) Iodine nutrition improves in Latin America. *Thyroid* 14: 590-599.
31. Berti C, Faber M, Smuts CM (2014) Prevention and control of micronutrient deficiencies in developing countries: current perspectives. *Nutrition and Dietary Supplements* 6: 41-57.
32. http://bvsm.sau.de.gov.br/bvs/sau.delegis/anvisa/2013/res0023_23_04_2013.html