Effects of prophylaxis with iodised salt in an area of endemic goitre in north-eastern Sicily

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ABSTRACT. In developed countries, the use of iodised salt represents the best prophylaxis of endemic goitre in areas exposed to iodine deficiency. In the present study we re-evaluated goitre prevalence and iodine intake 10 years after the introduction of iodised salt in an area of goitre endemicity in north-eastern Sicily (Italy), and we compared these results with those obtained in previous surveys. Three centres with known moderate goitre endemicity (Bronte, Nicosia, and Gagliano) and three other smaller ones with severe goitre endemicity (Sperlinga, Villadoro, and Maniace) were studied. We surveyed 697 schoolchildren. Goitre prevalence was assessed by thyroid palpation and by a thyroid ultrasound scan. Iodine urinary excretion was also measured. Iodised salt consumption was 44% of total salt consumption. Goitre prevalence assessed by thyroid palpation was significantly decreased in all towns studied compared to previous surveys. However, the persistence of a mild goitre endemicity was observed in some small rural centres (5.8% in Sperlinga/Villadoro, and 11.4% in Maniace). Goitre prevalence evaluated by thyroid ultrasound scan was greater than 5% in all centres of the endemic area and was always greater than that assessed by thyroid palpation. Iodine urinary excretion was above 100 µg/l in all localities studied. In conclusion, our studies indicate a progressive reduction in goitre prevalence over a period of about 30 years in schoolchildren in a well-characterised endemic area in north-eastern Sicily. The decrease in goitre prevalence was associated with a significant increase in urinary iodine excretion. However, it may be speculated that iodine deficiency is the pre- eminent, but not the exclusive cause of goitre endemicity in this area.


INTRODUCTION
Nutritional deficiency of iodine represents the most important factor for the development of thyroid diseases. In the last decades, several studies have emphasised the severity and high frequency of iodine deficiency-related disorders (1, 2). The most common of these is endemic goitre. In order to assess the goitre prevalence in a given population, thyroid ultrasound has replaced the simple thyroid palpation (3). Daily urinary iodide excretion is generally used to evaluate iodide intake. The combination of these two indexes defines the degree of the goitre endemicity.

In Italy, epidemiological surveys carried out in all Italian regions have revealed the presence of a goitre endemicity in several areas (4). In Sicily, epidemiological studies were carried out in the seventies and were mainly performed in schoolchildren in some centres in the north-eastern part of the island. These studies detected a goitre prevalence of 10-70% in schoolchildren and a direct relationship between goitre prevalence and iodine deficiency (5, 6). In addition to iodine deficiency, other factors, like thiocyanates, were supposed to contribute to goitre pathogenesis in our studies (5) as well as in other studies (7). In developed countries it has been demonstrated that the best prophylaxis is based on the use of iodised salt (8). Dietary iodine supplementation has always been able to reduce both iodine deficiency and related disorders. However, a complete eradication can be obtained only with nation-wide programs (9-15).

In Sicily, a pilot prophylaxis program was carried out in the years 1979-1987, by the addition of iodine to the drinking water in the district of Troina (16). Subsequent epidemiological surveillance revealed a reduction of 90% in goitre prevalence after 5 years. However, in other endemic areas of the same territory, goitre prevalence spontaneously decreased by 60% without any planned intervention over 15 years (17). This improvement has been attributed to the "silent prophylaxis" (18), due to socioeconomic changes, and increased diffusion and consumption of industrial iodine-enriched foods.

Up to 1996, the use of iodised salt in Sicily was less than 1% of the total salt consumed (unpublished observations). Since then, educational campaigns were started, aimed at the promotion of the use of iodised salt.

The objectives of the present study, carried out 10 years after the initiation of this campaign, are to assess the increase in iodised salt consumption and to re-evaluate goitre prevalence and iodine intake in the population of the endemic area previously studied.

PATIENTS AND METHODS
Area studied
Epidemiological surveys were carried out in an area of goitre endemicity in north-eastern Sicily (Italy), which had already been characterised prior to 1996, and in a control area (Catania) with sufficient iodine intake and absence of goitre endemicity. The
study was conducted in three different towns with moderate endemic goitre (Bronte, Nicosia and Gagliano), and in three smaller rural communities, geographically close to the previous ones and with a severe goitre endemic at previous observation in the late seventies (Sperlinga, Villadoro, and Maniace). Both Bronte and Maniace are located on a volcanic ground, on the north-west side of Mount Etna, a very active volcano, whereas the other centres are at a distance of approximately 50 km from the main crater and are not in the volcanic area. In Bronte, Nicosia, and Gagliano, people live on a mixed economy (rural, commercial, and small family enterprises), and the socio-economic level is similar to the mean Sicilian level. In the other three centres (Sperlinga, Villadoro, and Maniace), a rural economy predominates, associated with a slightly lower socio-economic level than the average regional standard.

Campaign for the implementation of iodised salt consumption

Since 1996, several alimentary educational campaigns have been conducted, which included seminars addressed to local health care and school authorities and employees, as well as to organisations involved in the production, distribution, and sale of iodised salt. Posters, illustrations, and advertising materials were diffused in that area, particularly in schools, outpatient clinics, health care offices, and markets. Mass-media and communication networks actively contributed to the diffusion of information to consumers. A specific law promoted by the Italian Ministry for Health, issued on March 21, 2005 (19), markedly supported such iodine prophylaxis campaigning. It described the rules aimed at the prevention of endemic goitre.

In the area of goitre endemicity, iodised salt distribution and marketing was also assessed directly in supermarkets, stores, and door-to-door. The availability of iodised salt in shops and markets, salt iodide compositions (amount of iodide per kg of salt), and the annual rate of iodised salt sales compared to common non-iodised salt sales, were assessed in each centre examined.

Subjects studied

The subjects examined were 697 (349 females and 348 males), ages in the range 11-14 years. Of these, 180 were from the control area, and 517 were from the endemic area. This number represented approximately 35% of subjects from the endemic area. For each subject, personal data were recorded, and body weight (kg) and height (cm) were measured, in order to calculate total body surface. Thyroid palpation and a thyroid ultrasound scan were performed in all subjects. In addition, a morning urinary sample for the measurement of urinary iodine excretion was obtained from 601 subjects. An informed consent was also obtained from parents, who authorised their children to participate in the study. Due to the relatively small sample size, data from Sperlinga and Villadoro were collected together.

Thyroid volume and definition of goitre

Goitre prevalence was assessed by thyroid gland palpation, according to WHO criteria (20, 21). The same methodology had been used in previous epidemiological studies in 1977 (5) and in 1994 (6). These studies served as a comparison to detect changes with time in goitre prevalence over time by the palpation method.

In addition, a thyroid ultrasound scan was performed on all subjects using a portable instrument (Logiq q-100, General Electric, Fairfield, CN, USA) with a 7.5 MHz probe. Thyroid volume was calculated by the elliptical shape volume formula (antero-posterior diameter x lateral diameter x longitudinal diameter x 0.52) for each lobe and was expressed in ml (22). Ultrasound scans were performed by two different operators. The coefficient of variation between operators was 12.1%.

A thyroid volume greater than 2 SD for each age group was defined as a goitre. In detail, we utilised the thresholds described by Viti et al. (3), which were 7.9 ml for age 11, 8.1 ml for age 12, and 9.3 ml for ages 13 and 14.

Iodine urinary excretion

Morning urine samples were collected from 601 subjects. Of these, 94 were from the control area and 507 were from the endemic area. Samples were stored at ~80 C, and subsequently urinary iodine was measured by a simple quantitative method based on the Sandell-Kolthoff reaction (23). Results were expressed as μg of iodine per litre of urine.

Statistical analysis

Differences in goitre prevalence assessed by thyroid palpation and variations in different surveys were analysed by chi-square test. Differences in thyroid volume observed by ultrasound scan were evaluated by ANOVA multivariate analysis. The linear regression test was used to evaluate the correlation between age or body surface and thyroid volume obtained by the ultrasound scan.

A p-value <0.05 was considered as statistically significant. All statistical analyses were carried out with Microsoft Excel Software.

RESULTS

Inquiry on iodised salt

Information obtained in the endemic goitre centres revealed a well-diffused sale of iodised salt. Iodine content (as potassium iodate) was 30 mg/kg of salt in all packages examined. Iodised salt consumption was markedly increased, as compared to data recorded prior to 1996, with a mean annual consumption corresponding to 44% of total salt consumption (ranging from 28% in Maniace to 55% in Gagliano (Table 1). A significant decrease in goitre prevalence assessed by thyroid palpation

A significant decrease in goitre prevalence assessed by thyroid palpation was observed in all of the studied centres when compared to previous epidemiological surveys carried out in 1977 and in 1994. In the areas where a moderate iodine deficiency had been previously identi-
fied, goitre prevalence in schoolchildren was lower than 5% (3.0% in Bronte, 4.7% in Nicosia, and 4.9% in Gagliano). The persistence of a mild goitre endemic was observed in small rural centres (5.8% in Sperlinga/Villadoro and 11.4% in Maniaci) (Table 2).

In Table 2, we report the data relative to Bronte and Maniaci in 1977, 1994, and 2007. Goitre prevalence decreased by 67% and 61%, respectively, in 1994 compared to 1977. A further decrease of 75% and 57%, respectively, was observed in 2007 vs 1994, subsequent to the initiation of the campaign for iodised salt prophylaxis. Variations in goitre prevalence in the different surveys were statistically significant (p<0.01) in all centres of the endemic area.

Goitre prevalence assessed by thyroid ultrasound scan
Thyroid volume increased with age (r=0.263; p<0.0001) (Fig. 1) and with body surface (r=0.432; p<0.0001) (Fig. 2), with no significant difference between sexes. Mean thyroid volume in children from the endemic area was slightly greater than in children from the control area, but this increase was statistically significant only for the rural centres Sperlinga/Villadoro and Maniaci (p<0.05 and p<0.005, respectively) (Table 3).

Fig. 1 - Correlation between age and thyroid volume evaluated by ultrasound scan in schoolchildren.

In all centres of the endemic area, goitre prevalence in schoolchildren was greater than 5% (Table 3). Goitre prevalence assessed by thyroid ultrasound was greater than that assessed by thyroid palpation in all the towns studied.

A thyroid nodule smaller than 7 mm was noticed at ultrasonography in 11 schoolchildren (2%). Their families received instructions for an appropriate follow-up.

Iodine urinary excretion
Table 4 illustrates iodine urinary excretion in 1977, 1994, and 2007. A progressive increase in iodine urinary excretion can be observed in the endemic area. In the present study we observed a mean value above 100 μg/l in all the towns studied.

DISCUSSION
Iodine deficiency and related disorders still represent a worldwide concern in public health. An insufficient iodine dietary intake is responsible for goitre development and other disorders, including neuropsychological

Table 3 - Thyroid volume (ml) and goitre prevalence assessed by thyroid ultrasound scan in schoolchildren from a control area and an endemic goitre area, surveyed in 2007.

<table>
<thead>
<tr>
<th>Centre</th>
<th>No. of subjects</th>
<th>Thyroid volume (mean±SD)</th>
<th>Goitre (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catania</td>
<td>180</td>
<td>5.6±1.7</td>
<td>4.9</td>
</tr>
<tr>
<td>Area with moderate goitre endemic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronte</td>
<td>129</td>
<td>5.8±2.0</td>
<td>8.5</td>
</tr>
<tr>
<td>Nicosia</td>
<td>152</td>
<td>5.7±2.3</td>
<td>9.4</td>
</tr>
<tr>
<td>Gagliano</td>
<td>62</td>
<td>6.1±2.4</td>
<td>9.8</td>
</tr>
<tr>
<td>Area with severe goitre endemic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sperlinga/Villadoro</td>
<td>52</td>
<td>6.3±2.0</td>
<td>13.4</td>
</tr>
<tr>
<td>Maniaci</td>
<td>122</td>
<td>6.6±2.4**</td>
<td>14.0</td>
</tr>
</tbody>
</table>

*p<0.05 vs Catania; **p<0.005 vs Catania, Bronte, Nicosia.
Table 4 - Urinary iodine excretion in schoolchildren from a control area and an endemic goitre area, surveyed in 1977, 1994, and 2007 (μg/l).  

<table>
<thead>
<tr>
<th></th>
<th>1977 (mean±SD)</th>
<th>1994 (mean±SD)</th>
<th>2007 (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catania</td>
<td>113.8±8.4</td>
<td>223.9±15.1</td>
<td>187.7±94.3</td>
</tr>
<tr>
<td>Area with moderate goitre endemic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronte</td>
<td>43.2±4.9</td>
<td>129.3±16.6</td>
<td>192.0±417.2</td>
</tr>
<tr>
<td>Nicola</td>
<td>39.2±4.1</td>
<td></td>
<td>135.2±46.5</td>
</tr>
<tr>
<td>Gagliano</td>
<td>40.7±2.6</td>
<td></td>
<td>182.7±88.9</td>
</tr>
<tr>
<td>Area with severe goitre endemic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sperlinga/Villadoro</td>
<td>-</td>
<td>-</td>
<td>177.6±97.6</td>
</tr>
<tr>
<td>Maniace</td>
<td>18.9±4.1</td>
<td>68.2±12.6</td>
<td>160.8±79.5</td>
</tr>
</tbody>
</table>

Defects, starting from intrauterine life (24, 25). Today, iodine deficiency is mild-moderate in Italy, as well as in the majority of European countries, and its impact significantly affects thyroid volume and morphology; however, its effect on neuro-intellectual development is minimal. According to WHO, UNICEF, and ICCIDD recommendations, the assessment of endemic goitre relies on goitre prevalence in populations of schoolchildren aged 6-15 and on the measurement of urinary iodine excretion (26-28). In particular, goitre is defined as endemic if its prevalence is greater than 5% in schoolchildren examined by thyroid palpation or, better, by a thyroid ultrasound scan. Iodine deficiency is indicated by a urinary iodine excretion lower than 100 μg/l. In many countries, iodine prophylaxis has been introduced by appropriate legislation and campaigns and has been operative for decades, yielding excellent results. In many areas, including several Italian regions, the goitre endemia has improved spontaneously, thanks to the so-called "silent prophylaxis" (6, 17, 29, 30). In spite of this, goitre prevalence is still moderate in several areas of central and southern Italy (31, 32). This persistence of goitre is probably due to insufficient legislative measures adopted to implement the use of iodised salt. Only recently, adequate widespread campaigns to encourage the use of iodised salt have been promoted. In addition, in March 2005, a law was approved in Italy, that regulates the sale and consumption of iodised salt (19). In Sicily, prior to 1996, iodised salt consumption was lower than 1% of total salt consumption. Epidemiological studies on endemic goitre in Sicily, initiated in the 1970s, had demonstrated a high prevalence of endemic goitre and related disorders, in several areas of the island, that was associated with very low levels in urinary iodine excretion. These pilot surveys and subsequent studies conducted in this iodine-deficient area not only documented the goitre endemia but also detected several other disorders related to iodine deficiency. In fact, we found a high frequency of functional thyroid abnormalities and congenital hypothyroidism in newborns (33-35), including foci of endemic cretinism (36, 37), an increased frequency in thyroid nodules (38), including autonomously functioning thyroid nodules (39) and a higher prevalence of thyroid cancer compared to that in control areas, mainly due to an increased frequency in the more aggressive histotypes (follicular and anaplastic carcinomas) (40). Since those pilot studies, it has been observed that the severity of endemic goitre was not tightly correlated with the severity of iodine deficiency, probably due to the influence of other environmental factors, like thiocyanates and volcanic soil (5). Moreover, in the study carried out in 1994, a high goitre prevalence was still observed in the town of Bronte, in spite of urinary iodine excretion greater than 100 μg/l (6). The present work was aimed at evaluating the degree of iodised salt consumption, the expected reduction in endemic goitre prevalence, and the increase in urinary iodide excretion in this area of north-eastern Sicily after 10 years of adequate campaigns promoting the use of iodised salt. Market surveys confirmed a marked increase in iodised salt consumption, with an average use of 44% of total salt even if in the rural area of Maniace it was only 28%. Epidemiological studies in schoolchildren aged 11-14 years showed a marked decrease in goitre prevalence assessed by thyroid palpation when compared to goitre prevalence in previous studies. By this method, goitre prevalence was lower than 5%, except in rural areas (5.6% in Sperlinga/Villadoro and 11.4% in Maniace). However, thyroid ultrasound studies revealed a higher goitre prevalence than by the palpation method. All values from the endemic area were greater than 5%, and even the control area (the town of Catania) was close to the cut-off value for the definition of goitre endemia. Mean thyroid volume, as assessed by ultrasound scan and corrected for age and body surface, was significantly greater in the rural areas (Sperlinga/Villadoro and Maniace) than in the other centres. Despite these data on goitre prevalence and the significantly increased thyroid volume in the rural areas, no significant difference was found among these various centres in urinary iodine excretion, which was always above 100 μg/l. The percent decrease in goitre prevalence recorded in the period 1995-2007, following a sustained initiative for the implementation of the iodine prophylaxis, is similar to that observed in the period 1977-1994, attributable only to the "silent iodine prophylaxis". This observation is difficult to interpret. It may be speculated that the introduction of iodised salt is not able to fully reverse a thyroid enlargement in children previously exposed to iodine deficiency (41). In conclusion, our longitudinal studies (1977, 1994, and 2007) indicate a progressive reduction in goitre prevalence over a period of 30 years in the population of schoolchildren in a well-characterised endemic area in north-eastern Sicily. The decrease in goitre prevalence was associated with a significant increase in urinary iodine excretion, confirming the crucial role played by iodine deficiency in the aetiology of goitre endemias. However, after 30 years, despite considerable changes in alimentary habits and improved socio-economic conditions, which contributed to the silent iodine prophylaxis, and despite the increased use of iodised salt, which has led to an urinary iodine excretion of over 100 μg/l in the last decade, goitre prevalence assessed by thyroid ultrasound studies was still more than 5% in all centres of the endemic area ex-
amed, with higher peaks in rural localities. It may be speculated that iodine deficiency is the pre-eminent, but not the exclusive cause of goitre endemic in this area of north-eastern Sicily. Other aetiological factors may play an important role in the persistence of this endemic. Among ambient factors, thiocyanates may play a role, since we previously detected high urinary thiocyanate levels in Catania, Bronte, and Maniace, all centres situated in the territory of Mount Etna. In the other centres, more distant from the volcano, thiocyanate levels were lower (5). It is possible, therefore, that a correlation exists between the sulphate-rich volcanic soil and the elevated levels of thiocyanates in the populations of these centres. Genetic factors may also play a role in the development of endemic goitre (32, 42). This idea is supported by observations of goitre in family groups or in identical twins. Single genes may be important in this regard, like the thyroglobulin gene, the TSH receptor gene, or the NIS (Na/\textsuperscript{I-} symporter) gene. Although these observations are well known, it should be emphasised that all these variables should be considered when looking for possible causes of a goitre endemic. The presence of one of these factors, for instance high thiocyanates, might require a higher level of iodine supplementation in order to prevent endemic goitre. Of course, iodine prophylaxis remains the cornerstone for the prevention of goitre endemic and it has achieved excellent results worldwide so far. The use of iodised salt is the easiest method to increase iodine intake in Western countries, and it should be implemented more extensively in a region, like Sicily, where the risk of goitre is still present.

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REFERENCES


