Iodized Salt Consumption Maintains Euthyroidism in Iodine-Deficient Hypothyroid Subjects

Parvin Mirmiran, Rambod Hajipour and Fereidoun Azizi

Endocrine Research Center, Shaheed Beheshti University of Medical Sciences, Teheran, I.R. Iran

Received for publication: August 27, 2002

Abstract: Following previous reports of impaired physical and intellectual growth, hearing deficit, hypothyroidism, and hyperendemic goiter in Kiga, and the administration of iodized oil injection, this study was conducted to evaluate whether or not the effect of the injection could be sustained by iodized salt supplementation. In 1989, one mL of iodized oil solution containing 480 mg of iodine was injected in 198 schoolchildren aged 8 to 14 years. Four years later, in 1993, iodized salt consumption was begun and has since been continued. Serum thyroid hormones, RT₃ uptake and thyroid-stimulating hormone (TSH) were measured before, and three, four, and six years after intervention (1989, 1992, 1993, and 1995). Assessment of urinary iodine was performed by the Foss method at the same intervals mentioned above. Prior to the injection, 94% had grade 2 goiters; four years after injection, 26% and 41% had grades 2 and 1 respectively, and 30% had no goiter (p < 0.001). Two years after the introduction of iodized salt consumption, 5 and 39% had grades 2 and 1 goiter, and 56% were not goiterous. Urinary iodine was 11.4 ± 19.8 µg/L before intervention, and was increased to 93 ± 66 and 92 ± 34 µg/L, three and four years, respectively, after intervention. Two years after iodized salt consumption it was 161 ± 34 µg/L. Mean serum T₄ was 5.0 ± 2.0, 9.6 ± 2.0, 9.6 ± 2.0 and 9.2 ± 1.5 µg/dL; serum TSH was 20.3 ± 22.8, 2.1 ± 1.9, 2.5 ± 1.6 and 2.9 ± 1.7 mU/L; before and three, four, and six years after the beginning of the study. All children were euthyroid after three, four, and six years of study. Findings show the benefits of iodized oil administration in decreasing goiter size and in reversing abnormal thyroid function. These effects are sustained by iodized salt consumption in schoolchildren who had been previously hypothyroid due to iodine deficiency.

Key words: Iodized salt, hypothyroidism, iodine deficiency disorders

Introduction

Consumption of iodized salt is the main strategy to prevent iodine deficiency disorders (IDD) [1]. The administration of iodized oil has been known to improve IDD in patients who live in severely iodine-deficient regions [2–4] as well as to prevent IDD in fetus, neonates, and children. In Iran, a survey of IDD showed endemic goiter in all provinces [5], with universal salt iodization being implemented during the last decade [6]. However, in the beginning of the IDD control program, iodized oil administration was used for control of IDD in endemic regions.

The schoolchildren of Kiga village were the first group to receive iodized oil injections in Iran. Before the inter-
vention, 94% had grade 2 goiters, and 39% and 70% had low serum T4 and high serum thyroid-stimulating hormone (TSH), respectively. Growth retardation, abnormal neurologic signs, hearing deficits, and impairment of intellectual and psychomotor development were observed in the majority of schoolchildren of Kiga [7]. We previously reported that injection of iodized oil induced euthyroidism up to one year after intervention in hypothyroid schoolchildren of Kiga [8, 9]. Four years after the use of iodized oil, iodized salt was distributed in this village. In this paper, we report changes in goiter prevalence, urinary iodine, and serum hormone levels two years after initiation of iodized salt consumption in the schoolchildren of Kiga.

Materials and Methods

This study was carried out in the school of Kiga village located in a mountainous region 35 km northwest of Tehran. Schoolchildren were extensively studied during 1987–1989. Endemic goiter, hypothyroidism, and impairment of physical and intellectual development were found and have been reported elsewhere [7].

One mL iodized oil solution (Lipiodol, Guerbet Co., France) containing 480 mg of iodine was injected intramuscularly in schoolchildren in 1989. In 1993, the iodized salt program reached Kiga village, and iodized salt was the only salt available for household use from that time forward. The iodide content of salt is 40 ± 5 parts per million (ppm) in Tehran province, where Kiga is situated. One hundred ninety-eight schoolchildren, 98 girls and 100 boys aged 6 to 14 years, were assessed before, and one, two, three, four, and six years after the intervention. The results of studies before, three, and four years after iodized oil injection and two years after the initiation of iodized salt consumption are presented in this paper.

Clinical variables

An endocrinologist examined schoolchildren for symptoms and signs of thyroid dysfunction. Goiter was graded according to criteria established by the World Health Organization [1]. Venous blood samples were collected between the hours of 9:00 a.m. and 12:00 p.m. Samples were transferred to the hormone laboratory and centrifuged, and sera were separated and stored at −20°C until analysis.

Biomedical Evaluation

Serum concentrations of T4, T3, TSH, (IRMA), were determined by kits from Amersham Corp., England, and RT3U by kits from Diagnostic Products Corp., Los Angeles, CA, USA. Interassay and intra-assay coefficients of variation were 10% and 12% respectively. Urine samples were collected before and three, four, and six years after the intervention and iodine content was measured by the Foss method [10]. Reference ranges of serum parameters for euthyroid young subjects are, for T4: 4.5–12.5 µg/dL (56–167 nmol/L); T3: 75–175 ng/mL (1.2–3.1 nmol/L); TSH: 0.3–5.0 mU/L and RT3U: 25–35%.

The study was approved by the appropriate human research review committee.

Statistical Analysis

Differences between mean values for quantitative variables were evaluated with Student’s paired and unpaired t-test. Differences in the proportions of goiter sizes were analyzed by the chi-square test.

Results

Prevalence of goiter

The prevalence and severity of goiter decreased after iodized oil injection in girls and boys. The differences in both prevalence and severity between genders were not statistically significant. Before intervention, 94% of schoolchildren had grade 2 and 6% had grade 1b goiters. Three years after intervention, 44 and 32% had grades 2 and 1, respectively. Four years after iodized oil injection, 29% of pupils had grade 2, 41% had grade 1, and 30% had no thyroid enlargement. The difference was statistically significant (p < 0.001). Two years after iodized salt consumption was begun, 5% had grade 2, 39% grade 1, and 56% had no goiter (Figure 1). The difference between three and six years post-intervention was significant at p < 0.001.

Serum TSH concentration

Prior to the injection of iodized oil, mean serum TSH was 20.6 ± 25.7 in boys and 19.9 ± 20.1 mU/L in girls. Forty-six percent of the schoolchildren had a serum TSH > 5 mU/L and serum T4 < 4.5 µg/dL. The TSH concentration decreased to normal range in all schoolchildren one year after the injection. Mean serum TSH was significantly decreased three and four years after injection. Mean serum TSH was in the normal range two years following iodized salt consumption (Table I). Only one child had serum TSH > 8 mU/L.
Serum T4 concentration

Mean serum T4 was 5.4 ± 2.0 in boys and 4.5 ± 2.1 µg/dL in girls prior to the intervention. Serum T4 concentration increased to the normal range in all pupils four months after injection. Mean serum T4 was in the normal range three and four years after iodized oil injection and two years after iodized salt consumption (Table I). None of the children had T4 < 4.5 µg/dL, six years after intervention.

Serum T3 concentration

Prior to iodized oil injection, mean T3 value was 168 ± 40 in boys and 167 ± 47 ng/dL in girls. Mean serum T3 concentration did not change significantly three and four years after iodized oil injection and two years after iodized salt consumption, respectively. Three, four, and six years after intervention, there were no cases with elevated T4 and/or T3 and suppressed serum TSH.

T3 to T4 ratio

The T3 to T4 ratio was high in most subjects prior to the intervention and decreased to the normal range within four years after the injection. The fall in T3/T4 ratio occurred in both groups of the schoolchildren with high and normal serum TSH. Mean T3/T4 ratio was 33.4, 15.7, 15.6, and 17.3 before, three and four years after iodized oil injection, and two years following iodized salt consumption, respectively.

Urinary iodine level

Mean urinary iodine was 11.4 ± 19.8 before intervention and 93 ± 66 and 92 ± 34 µg/L, three and four years after iodized oil injection, respectively (p < 0.001 when the “before” value was compared to that of three and four years after). There was no significant difference between urinary iodine three and four years after intervention. Two years after iodized salt consumption, mean urinary iodine was 161 ± 34 µg/L and 89% of schoolchildren had urinary iodine above 100 µg/L; only one had a value of below 50 µg/L.

There was significant increase in urinary iodine when values at six years were compared to those of three and four years after intervention (p < 0.001).

Discussion

We have evaluated the effects of iodized oil administration followed by iodized salt consumption on goiter size, thyroid function, and urinary iodine concentration in the schoolchildren of Kiga village. The major finding of this study is that the injection of iodized oil reversed thyroid function in all hypothyroid schoolchildren, and this effect was sustained by consumption of iodized salt, when the effects of iodized oil had been washed out.
Our previous report demonstrated that severe physical and mental growth disorders and visible goiter had been present in a great majority of the schoolchildren of Kiga [7]. The prevalence of grade 2 goiter decreased to one-half, three years after intervention. These findings are in accordance with previous reports [2–4]. With iodized salt supplementation, there was further decrease in both prevalence and severity of goiter, which is also in accordance with other reports [11]. According to the World Health Organization/International Council for the Control of Iodine Deficiency Disorders (WHO)/ICCIDD, palpation of the thyroid is particularly useful in assessing goiter prevalence, but much less in determining impact of salt iodization [12]. However, due to the high prevalence of severe goiter in schoolchildren of Kiga, significant changes were observed in this study. It is obvious that increase in urinary iodine excretion is a much more reliable index of effectiveness of iodine supplementation.

Low serum T4 and elevated serum TSH were indicative of defects in thyroid hormone synthesis due to iodine deficiency before intervention. These findings are similar to the reports of hormone concentration in children residing in severe iodine-deficient regions [13, 14]. In more severely iodine-deficient regions [15, 16], low serum T3 and elevated TSH existed in the majority of individuals. Remarkably low urinary iodine was further evidence of severe iodine deficiency in the schoolchildren of Kiga.

Increase in serum T4 and decrease in TSH are similar to reports of other published experiences following iodized oil supplementation [4, 11]. In a study in Zaire, all the children under the age of 4 became euthyroid, but only in two children aged 4 to 14 years did the serum TSH decrease to normal levels [17]. Iodized oil injection did not increase thyroid hormones remarkably in Chinese cretins, and only one of 28 individuals reached a normal TSH level [16]. In our study, euthyroidism was attained in all the schoolchildren, even in those with severe hypothyroidism and very high serum TSH levels before iodized oil injection. This difference could be due to a milder intensity of the disease in Kiga children than in the population studied in China and Zaire. The schoolchildren of Kiga had large goiters, while the hypothyroid cretins in China and Zaire did not have goiter and carried damaged and atrophic thyroids, probably due to both iodine and selenium deficiencies.

The thyroid gland produces T3 more than T4 selectively when it encounters a relatively severe iodine-deficient condition. Serum T3 to T4 ratio was very high before the injection, but it decreased remarkably and reached normal values after the intervention. All these changes were sustained four years after injection of iodized oil and two years after iodized salt supplementation. It is well established that normal urinary excretion of iodide may last three or four years, and in a very rare cases up to five years, following 480 mg iodized oil injection [18]. In fact, four years after iodized oil injection, mean urinary iodine had declined to 92 µg/L, and two years after iodized salt consumption it increased to 161 µg/L. Therefore sustained euthyroidism in the last two years of this study was due to iodized salt supplementation.

We reported that serum T3 and T4 increased in 12 of 96 girls four months after the injection in Kiga, and three individuals had serum T3 above normal limits [9]. Rare cases of hyperthyroidism have been mentioned in several previous reports [18–20]; however, hyperthyroidism did not occur after iodized oil injection in other reports [17, 21]. Hypothyroidism due to pharmacological doses of iodine may be seen in some disorders [22, 23] and has been reported in a few subjects after iodized oil injection as a temporary increase of serum TSH [24–26]. Hypothyroidism did not occur in the schoolchildren of Kiga village after the injection. The transient elevation of serum T4 and T3 subsided after the first year of iodized oil injection and, following iodized salt supplementation, none of the children had evidence of clinical or biochemical hyperthyroidism.

In conclusion, the present study confirms that iodized oil injection reduces the prevalence and the size of goiter and restores euthyroidism. Iodized salt consumption sustains normal thyroid function in schoolchildren who were previously hypothyroid due to severe iodine deficiency.

Acknowledgement

The authors would like to thank Dr. Masoud Kimiagar, Mrs. M.T. Nafarabdi, and Mrs. F. Jazayeri for their valuable help in conducting this study.

References


Professor Fereidoun Azizi
Endocrine Research Center
P.O.Box 19395-4763
Tehran
I.R. Iran
Phone +98 21 2409309
Fax +98 21 2402463
E-mail: azizi@erc-iran.com