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Treatment of goitrous hypothyroidism with iodized oil supplementation in an area of iodine deficiency

F. Azizi, M. Kimiagar, A. Ghazi, M. Nafarabadi, J. Behjati, F. Esfahanian

Endocrine Research Center and the Institute of Nutrition, Shaheed Beheshti, University of Medical Sciences, Tehran, I.R. Iran

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Summary: In order to investigate the effect of iodized oil administration on the thyroid status of male hypothyroid children and adolescents residing in an area of iodine deficiency, 32 apparently normal school boys with increased serum TSH, aged 7 to 15 years, were given a single intramuscular injection of 480 mg iodized oil. Four months after injection, serum T4 increased from 60 ± 23 to 118 ± 24 nmol/l and serum TSH decreased from 39 ± 33 to 2.5 ± 1.2 mU/l. Serum T4 remained unchanged while a further decline in TSH to 1.3 ± 0.9 and 1.4 ± 1.3 mU/l was observed 7 and 12 months after injection, respectively. There was a small but significant reduction in serum T3, FT3I as well as in the prevalence and severity of goiter 1 year following iodine treatment. Neither the age of the subject nor the severity of hypothyroidism affected the thyroid response to iodine treatment.

It is concluded that iodized oil injection is an effective and convenient treatment for goitrous hypothyroid youngsters in iodine-deficient areas.

Introduction

Iodine supplementation with oral or intramuscular iodized oil has been employed to provide long-lasting supply of iodine in people residing in areas of severe iodine deficiency. Iodized oil reduces goiter size (Buttlfield and Hetzel, 1969; Thilly et al., 1973), improves mental and psychomotor performance in school children (Bautista et al., 1982; Fierro-Benitez et al., 1986) and prevents undesirable peri- and postnatal complications of iodine deficiency (Thilly et al., 1978). Iodized oil injection has been shown to be effective in restoring normal thyroid function in children with cretinism up to 4 years of age, but only partially beneficial in older children (Vanderpas et al., 1986). It has also failed to reverse hypothyroidism in adolescent and adults with endemic myxedematous cretinism (Boyages et al., 1990).

The present study reports the outcomes of iodized oil administration to boys with thyroid hormone deficiency in a hyperendemic region in Iran (Azizi et al., 1990).

Subjects and methods

Thirty-two apparently normal school boys, aged 7 to 15 years, with elevated serum TSH values were studied in Kiga, a village 35 km to the northwest of the City of Tehran, a known severe iodine-deficient area (Azizi et al., 1994).

Protocol

Each subject was clinically examined for thyroid status, goiter being graded according to WHO classification (Delange, 1974) before receiving one ml of iodized oil (Lipiodol) containing 480 mg iodine intramuscularly. Subjects were reassessed at 4,

Table 1 The effect of iodized oil injection on different grades of goiters in 32 hypothyroid boys with iodine deficiency after one year

Iodized oil injection	Grades of Goiter 0	1A	1B	2	3
Before	0	0	4	16	12
After	1	1	10	19	1

7, and 12 months following the injection when blood samples were drawn, centrifuged and sera stored at −20 °C until the time of analysis. Two boys showing elevated serum T4 values one year after the injection of iodized oil, were administered 400 μg TRH intravenously and serum for TSH determination was obtained before and 15, 30, 45, and 60 minutes following TRH administration.

This study was approved by the appropriate Human Research Review Committee, and informed consent was obtained, in writing when possible, from parents.

Hormonal assays

Serum T4, T3, and TSH concentrations were determined by radioimmunoassay using commercial kits (Diagnostic Products Corp. Los Angeles, Ca, USA). Free T4 index (FT4I) and free T3 index (FT3I) were then calculated (Sawin et al., 1978). Interassay and intrassay coefficient of variation were less than 12 and 10%, respectively. Reference ranges of serum parameters for euthyroid young subjects are: T4: 56−167 nmol/l, T3: 1.2−3.1 nmol/l, TSH: <0.3−5.0 mU/l and resin T3 uptake: 25−35%.

Statistics

The student's paired and unpaired t tests were employed for the detection of differences between mean values for parametric variables. Simple linear regression analysis was used for the study of the effects of variables or intervention outcome.

Results

Grades of goiter

Table 1 shows the effect of iodized oil administration on the grades of goiter. Before injection, all boys exhibited goiter grades of 1b or larger, with 12 (37%) having large goiters (grade 3). One year following iodine supplementation the goiter size diminished appreciably, with only one boy having grade 3 goiter, clearly demonstrating a shift to lower grades.

Thyroid function

Clinical findings proved not to be helpful in the diagnosis of hypothyroidism and were unable to predict the biochemical alterations. As shown in Table 2, prior to iodized oil administration the mean serum T4 and FT4I values were on the low borderline while T3 and FT3I could be classified as on the high borderline of normal range. Serum TSH was distinctly elevated before treatment. Four months after the injection, serum T4 rose while TSH decreased in all subjects. The fall in serum T3 was most probably due to binding alteration in TBG, as FT3I had remained unchanged. However, one year following treatment, a significant reduction occurred both for T3 and FT3I compared to pre-treatment values (Table 2). Serum TSH decreased further by 7 and 12 months following the iodine injection while serum T4 was unaltered. In 2 boys who had increased serum T4 of more than 167 nmol/l at the end of the 12-month period, TSH response to TRH was normal with increments of 14 and 13 mU/l. Changes in serum T4, T3, and TSH levels were not age-dependent.

Grades of hypothyroidism

Seventeen boys had serum TSH concentration above 10 mU/l and 15 showed TSH levels between 5 and 10 mU/l. Figure 1 demonstrates the effect of iodized oil treatment on thyroid function in subjects with baseline TSH of above 10 mU/l. Four months following injection, serum T4 surpassed 84 nmol/l while serum TSH fell below 5.5 mU/l in all subjects. Serum T3 decreased in 11, increased in 3 and changed less than 0.15 nmol/l in 4 boys. Table 3 compares T4, T3 and TSH levels before, 4 and 7 months after iodine injection in 2 groups of boys with above 10, and between 5−10 mU/l TSH levels. Pre-treatment T4 was significantly lower in the group with higher TSH, but there was no difference in serum T3 between the two groups. Serum T4 increased in both groups following iodized oil injection. The increment between pre- und post-treatment, however, was significantly larger in the group with TSH > 10, as compared to those with TSH of 5−10 mU/l (75 ± 21 vs 39 ± 22 nmol/l, $P < 0.001$). Mean TSH concentration retracted to normal values four months after the injection in both groups. Nevertheless, TSH was slightly but significantly higher in the group with pre-treatment TSH of > 10 mU/l. This difference in TSH levels disappeared at 7 and 12 months following treatment. A negative correlation between TSH and FT4I ($r = -0.5655$, $P < 0.01$) was found.

Table 2 Serum T4, T3, TSH and thyroid indices in 32 hypothyroid boys with Iodine deficiency before and after iodized oil treatment

Iodized oil treatment	Serum T4 (nmol/l)	FT4I	Serum T3 (nmol/l)	FT3I	TSH (mU/l)
Before	60 ± 23	17 ± 6	2.6 ± 0.7	0.7 ± 0.18	38 ± 33
4 months	118 ± 24*	36 ± 9*	2.3 ± 0.5$^+$	0.7 ± 0.18	2.5 ± 1.2*
7 months	118 ± 26*	35 ± 6*	2.4 ± 0.4$^+$	0.7 ± 0.11	1.3 ± 0.9*
12 months	125 ± 39*	37 ± 14*	2.0 ± 0.4*	0.6 ± 0.12$^+$	1.4 ± 1.3*

* $P < 0.001$, and $^+$ <0.025, as compared to values before treatment

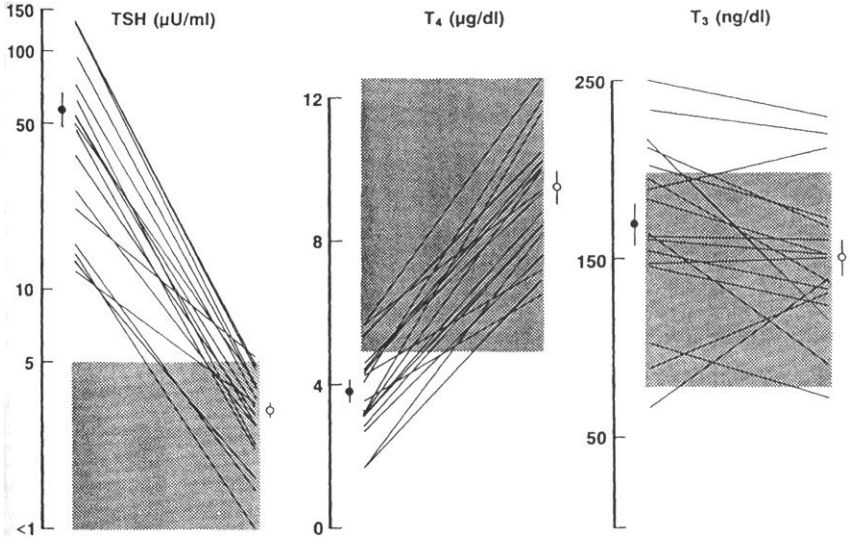

Fig. 1 Individual values and mean (± 1 SAM) levels (bars) of serum thyrotropin (TSH), thyroxine (T4), and Triiodothyronine (T3) in schoolboys with iodine deficient hypothyroidism (aged 7 to 15 years) before therapy (closed circles) and four months after the administration of iodized oil (open circles). The shaded areas represent the normal ranges in euthyroid children in Tehran.

Table 3 Biochemical parameters before and 4 and 7 months after iodized oil administration in two groups of boys

Groups (mU/l)	T4 (nmol/l) Pre*	4 mo.	7 mo.	T3 (nmol/l) Pre	4 mo.	7 mo.	TSH (mU/l) Pre	4 mo.	7 mo.
TSH > 10 (n = 17)	48 ± (15)$^+$	122 ± (24)	116 ± (23)	2.6 ± (0.8)	2.3 ± (0.6)	2.4 ± (0.4)	57 ± (42)	3.1 ± (1.3)	1.6 ± (0.9)
TSH 5–10 (n = 15)	76 ± (19)	114 ± (26)	108 ± (28)	2.7 ± (0.6)	2.3 ± (0.3)	2.3 ± (0.3)	7.2 ± (1.6)	1.9 ± (1.1)	1.0 ± (0.8)
P	<0.001	NS	NS	NS	NS	NS	<0.001	<0.01	NS

* Pre, 4 mo., and 7 mo., represent values before, 4 and 7 months after injection of iodized oil.
$^+$ Numbers in parenthesis represent SD

Discussion

The effect of iodine supplementation on thyroid function in male children and adolescents with depressed thyroid function due to iodine deficiency is reported here. The results reveal that iodized oil administration restores euthyroidism in all subjects at least up to one year following injection.

It has been shown that in euthyroid goitrous subjects with iodine deficiency, iodine supplementation results in an elevated thyroid iodine concentration (Leisner et al., 1985), as well as a decrease in goiter prevalence and severity (Buttlfield et al., 1969; Fierro-Benitez et al., 1986; Thilly et al., 1980; Philips et al., 1989). In the present study, iodized oil injection caused a decrease in severity of goiter with most of the large goiters subsiding.

The effects of iodine supplementation on thyroid status of hypothyroid subjects with endemic goiter have recently been reported. Cutaneous application of iodine to iodine-deficient newborns, having increased serum TSH and borderline low

serum T4 levels normalized both values (Heidemann et al., 1978). Iodized oil injection in children with endemic cretinism in Zaire resulted in decreased TSH and increased T4 concentrations in children (Vanderpas et al., 1986); however, greater changes were observed in children below four years of age who attained normal TSH and T4 five months following injection. In 14 children of 4 to 14 years of age only partial response was seen. Administration of iodized oil did not reverse thyroid hormone deficiency in adolescents and adults with endemic myxedematous cretinism in western China (Boyages et al., 1990). Restoration of euthyroidism in all subjects in the present study points to lesser severity of the lesion, as compared to previous studies. In fact, all our subjects had enlarged goiter of significant degree but none had atrophic gland.

The rise in serum T4 following injection of iodized oil in women aged 15–44 years have been reported in Zaire (Philips et al., 1989), however, no information on serum T3 and TSH was supplied. A mild increase in the incidence of hyperthyroidism has previously been described following implementation of iodinated salt programs (Connolly et al., 1970). Elevation of mean serum T3 in response to iodized injection was not observed in our subjects. Normal TSH response to TRH in two boys who had supra-normal serum T4 values indicates that thyroid autonomy had not occurred.

In conclusion, this study demonstrates that a single intramuscular injection of iodized oil in children and adolescents with depressed thyroid function due to iodine deficiency is capable of restoring euthyroidism. Many children and adolescents residing in iodine-deficient regions may have decreased thyroid function resulting from moderate to moderately severe iodine deficiency not grave enough to cause progressive degeneration and atrophy of thyroid tissue. Iodized oil injection appears to be the treatment of choice for these individuals. Current management of goitrous hypothyroidism in endemic areas consists of life-long thyroid hormone therapy which could be unsuccessful, at times, due to lack of compliance or undesirable side effects such as palpitation. Prolonged hormone therapy also reduces bone density (Ross et al., 1987). We, therefore, propose iodized oil treatment of youngsters with goiter, hypothyroidism and negative thyroid antibodies residing in areas of iodine deficiency.

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Dr. Feriedoun Azizi
Shaheed Beheshti University of Medical Sciences
P.O. Box 19395-4763
Tehran, I.R. Iran