

Evaluation of the impact of an iodine supplementation programme on severely iodine-deficient schoolchildren with hypothyroidism

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Abstract

Background: Northern rural areas of Tehran have been shown to have severe iodine deficiency in our previous studies. In 1989 the inhabitants of these villages received an injection of iodised oil, followed by iodised salt distribution in 1993. The aim of the present study was to evaluate the effect of the iodine supplementation on iodine-deficient schoolchildren with hypothyroidism in these villages.

Methods: In total, 571 students aged 6–14 years were studied. Goitre was graded according to the World Health Organization classification. Serum concentrations of thyroid hormones (thyroxine (T₄) and triiodothyronine (T₃)) and thyroid-stimulating hormone (TSH) were determined using commercial kits, and urinary iodine was measured using a digestion method. The results were compared with data from our previous study in 1989.

Results: Total goitre rate decreased by 42% in 1999 compared with that in 1989. A significant decrease in Grade 2 goitre concomitant with an increase in Grade 1 goitre was seen ($P < 0.001$). Values of the variables studied before (1989) and 10 years after iodine supplementation (1999) were: median urinary iodine excretion, 2.0 vs. 19.0 $\mu\text{g dl}^{-1}$ ($P < 0.001$); T₄, 6.5 \pm 2.0 vs. 8.4 \pm 1.6 $\mu\text{g dl}^{-1}$ ($P < 0.001$); T₃, 177 \pm 38.0 vs. 145 \pm 29.0 ng dl^{-1} ($P < 0.001$); TSH, 10.8 \pm 15.1 vs. 1.8 \pm 0.8 $\mu\text{U ml}^{-1}$ ($P < 0.001$). No correlation was found between thyroid hormones and TSH on the one hand, and goitre and urinary iodine, on the other. Serum T₄, T₃ and TSH concentrations were within normal ranges in all schoolchildren in 1999.

Conclusion: This study showed that euthyroidism induced by administration of iodised oil in iodine-deficient schoolchildren with hypothyroidism is sustained following the consumption of iodised salt.

Keywords

Iodine deficiency disorders
Iodised oil
Iodised salt
Schoolchildren

Iodine deficiency is one of the most important causes of mental impairment and has serious consequences on physical development¹. The most notable clinical sign of iodine deficiency is goitre. Universal salt iodisation is the mainstay of prevention of iodine deficiency. However, administration of iodised oil is recommended for prevention in severe endemic areas where iodised salt is not available, as well as for treatment in areas with hypothyroidism due to severe iodine deficiency². It has been shown that iodised oil treatment may improve mental and psychometric performance in school-aged children.

Iodine deficiency disorders (IDD) are one of the main public health issues in Iran³. Northern rural areas of Tehran have been known as areas of severe iodine deficiency^{4,5}. These villages are situated in a mountainous

region, at an altitude of approximately 2000 m above sea level, about 35 km to the north of Tehran. In 1989, the whole population of these villages received an injection of iodised oil. Increases in serum concentrations of the thyroid hormones thyroxine (T₄) and triiodothyronine (T₃), and in urinary iodine, and decreases in serum concentrations of thyroid-stimulating hormone (TSH), were observed and reported^{6,7}. Iodised salt distribution as the main strategy of the national plan for IDD control was initiated in 1989⁸. In northern rural areas of Tehran, however, iodised salt consumption started in 1993 and is ongoing.

The present study was carried out in 1999 to evaluate the impact of the iodine supplementation programme on indicators of iodine deficiency in the above-mentioned villages, 10 years after iodine supplementation.

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Materials and methods

Baseline data

In 1989 the total population of northern rural areas of Tehran, namely Kiga, Keshar, Randan, Sangan and Zagoon, who were known to be iodine-deficient^{4,5}, were injected with 480 mg iodised oil (Lipiodol®). Before receiving the iodised oil injection, all pupils aged 6–14 years in Kiga ($n = 192$), Keshar ($n = 149$), Randan ($n = 54$), Sangan ($n = 30$) and Zagoon ($n = 20$) villages were studied in order to determine goitre prevalence, concentrations of thyroid hormones and TSH, as well as urinary iodine excretion.

The 1999 study

In this study, performed 10 years after administration of the iodised oil injection and 6 years after the initiation of iodised salt consumption, all schoolchildren aged 6–14 years in the five villages were examined clinically and for biochemical status indicators.

Clinical examination

Goitre size was examined by palpation by an endocrinologist and classified as Grades 0, 1 and 2⁹. A venous blood sample was obtained from each child; serum was separated and stored at -20°C until analysis. Urine samples were collected randomly from the subjects. Casual samples taken from each child were stored in a clean container at -20°C until analysis. All urine samples were transported promptly and analysed in the urinary iodine laboratory at the Endocrine Research Center in Tehran.

Laboratory measurements

The acid digestion method was employed for analysis of urinary iodine¹⁰. Serum concentrations of T_4 , T_3 and TSH, and T_3 resin uptake, were determined with commercial kits from Fenzia, Finland. Free T_4 index (FT_4I) was calculated¹¹. Reference ranges for euthyroid subjects were: T_4 , $4.5\text{--}12.5\ \mu\text{g dl}^{-1}$; T_3 , $80\text{--}210\ \text{ng dl}^{-1}$; TSH, $<0.3\text{--}4.5\ \mu\text{U ml}^{-1}$.

Data analysis

All variables such as goitre size, urinary iodine excretion, serum TSH and thyroid hormone concentrations were determined in each age group in all villages. These data were compared with similar data in 1989 (before intervention) in all villages. Student's *t*-test was employed for quantitative variables and the Chi-square test for goitre size results. *P*-values below 0.05 were considered significant. Correlation among variables was assessed by the Spearman test. This study was approved by the University Human Research Review Committee.

Results

Total goitre rate decreased by 42% in 1999, as compared with that in 1989 (Table 1). A significant decrease in Grade 2 goitre was observed: from 94 to 14% in Kiga, from 66 to 9.4% in Keshar and from 82 to 9.7% in Randan ($P < 0.001$) (Fig. 1). Sixty per cent of schoolchildren aged below 10 years and 30% of students above 10 years did not have goitre. Grade 2 goitre rates in schoolchildren above and below 10 years of age were 3 and 19%, respectively. For Grade 1 goitre the corresponding values were 37 and 50%.

Table 2 indicates the median urinary iodine in four villages in 1989 and 1999. In 1989 all villages had median urinary iodine concentration below $2\ \mu\text{g dl}^{-1}$, while in 1999, the median concentration of urinary iodine in all

Table 1 Total goitre rate in schoolchildren of five villages in northern rural areas of Tehran, before (1989) and 10 years after iodine supplementation (1999)

Village	1989	1999		
		All students	11–16 years old	6–10 years old
Kiga	100	64	71	58
Keshar	99	52	53	51
Sangan	99	52	56	50
Randan	100	61	79	42
Zagoon	100	54	67	41
Total	99	57	72	41

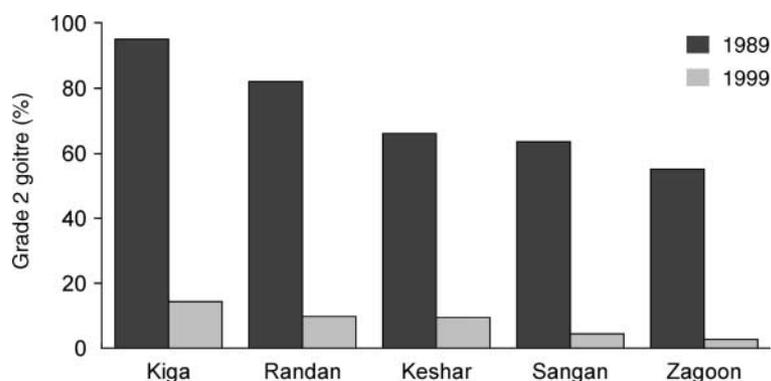


Fig. 1 Prevalence of Grade 2 goitre in schoolchildren of five villages in northern rural areas of Tehran, before (1989) and 10 years after iodine supplementation (1999). The changes in goitre prevalence and severity were statistically significant in all villages at $P < 0.001$

Table 2 Median urinary iodine concentration in schoolchildren of four villages in northern rural areas of Tehran, before (1989) and 10 years after iodine supplementation (1999)

Village	Urinary iodine excretion ($\mu\text{g dl}^{-1}$)	
	1989	1999
Kiga	1.9 (49)†	20.1* (61)
Keshar	1.8 (15)	20.1* (135)
Randan	1.2 (25)	17.3* (28)
Zagoon	1.8 (22)	20.1* (89)

* $P < 0.001$, as compared with 1989.

† The number of subjects is given in parentheses.

villages was above $17 \mu\text{g dl}^{-1}$ ($P < 0.001$). In 1999, 96% of subjects had values above $10 \mu\text{g dl}^{-1}$ with none below $5 \mu\text{g dl}^{-1}$.

Table 3 compares mean hormone levels in 1989 and 1999 in each village. In 1989 many of the schoolchildren had hypothyroidism. Forty per cent of the schoolchildren in Kiga and 24% of those in Keshar had serum TSH levels above $10 \mu\text{U ml}^{-1}$. TSH values between 5 and $10 \mu\text{U ml}^{-1}$ were observed in 30% of children in Kiga and 22% of children in Randan.

Serum T_4 , T_3 and TSH concentrations, FT_4I and resin T_3 uptake level were normal in all schoolchildren in 1999. No correlation was established between thyroid hormones, urinary iodine and grades of goitre.

Discussion

This study demonstrates that iodine prophylaxis restored euthyroidism in those subjects who had hypothyroidism, and prevented the consequences of iodine deficiency in the rest.

In subjects with goitre and iodine deficiency, iodine supplementation results in elevated thyroid iodine concentration¹² as well as a decrease in goitre prevalence and severity^{13–15}. The effects of iodine supplementation on the thyroid status of subjects with hypothyroidism and endemic goitre have also been reported. Percutaneous application of iodine to iodine-deficient newborns resulted in rapid disappearance of goitre and normalised serum T_4 and TSH levels within 5 days¹⁶. Iodised oil injection in children with endemic cretinism in Zaire resulted in decreased TSH and increased T_4 concentrations¹⁷. Greater changes were observed in children below 4 years of age, however, who attained normal TSH and T_4 levels 5 months following injection. In 14 children aged 4 to 14 years, only a partial response was seen. Administration of iodised oil did not reverse thyroid hormone deficiency in adolescents and adults with endemic myxoedematous cretinism in western China¹⁸. We have reported, both in boys⁶ and girls⁷ residing in Kiga, that the injection of iodised oil restores euthyroidism within 4 months of injection, perhaps due to the lesser severity of the lesion, since all children in Kiga had goitrous hypothyroidism and none had atrophic gland.

Iodised salt supplementation is the method of choice for prevention of IDD⁹. Therefore, in the present study, 4 years following iodised oil administration, while its effect was diminishing, distribution and consumption of iodised salt was applied, which had a complementary effect in the control of iodine deficiency. The decrease in goitre prevalence was appreciable 10 years after iodine prophylaxis and both the prevalence and severity of goitre decreased. Similar results have been obtained in other countries^{19–23}. However, more than a third of children

Table 3 Serum concentrations of thyroxine (T_4), triiodothyronine (T_3) and thyroid-stimulating hormone (TSH), T_3 resin uptake (RT_3Up) and free T_4 index (FT_4I) in schoolchildren of five villages in northern rural areas of Tehran, before (1989) and 10 years after iodine supplementation (1999)

Village	Serum concentration				
	T_4 ($\mu\text{g dl}^{-1}$)	T_3 (ng dl^{-1})	TSH ($\mu\text{U ml}^{-1}$)	RT_3Up (%)	FT_4I
Kiga					
1989 ($n = 95$)	5.1 ± 2.0	162 ± 38	19.7 ± 29.7	28.0 ± 1.7	1.4 ± 0.6
1999 ($n = 66$)	$8.8 \pm 1.8^*$	$149 \pm 27^\dagger$	$1.9 \pm 0.7^*$	27.0 ± 1.9	2.4 ± 0.6
Keshar					
1989 ($n = 103$)	8.4 ± 2.1	179 ± 39	3.3 ± 4.2	27.0 ± 2.1	2.3 ± 0.6
1999 ($n = 138$)	8.9 ± 1.7	$152 \pm 31^\dagger$	$1.7 \pm 8.8^*$	27.0 ± 2.7	2.4 ± 0.5
Sangan					
1989 ($n = 84$)	8.1 ± 2.2	136 ± 24	3.4 ± 6.7	28.0 ± 3.0	2.3 ± 0.6
1999 ($n = 87$)	7.6 ± 1.4	140 ± 30	$1.9 \pm 1.3^*$	26.5 ± 1.7	2.0 ± 0.4
Randan					
1989 ($n = 54$)	6.0 ± 1.8	189 ± 37	9.4 ± 11.6	25.0 ± 2.0	1.5 ± 0.5
1999 ($n = 28$)	$7.6 \pm 1.4^*$	$134 \pm 20^*$	$1.7 \pm 0.8^*$	27.0 ± 1.3	2.0 ± 0.5
Zagoon					
1989 ($n = 20$)	7.5 ± 1.6	168 ± 30	3.5 ± 0.9	27.0 ± 2.0	2.0 ± 0.5
1999 ($n = 99$)	$9.0 \pm 2.0^\dagger$	158 ± 23	$1.5 \pm 0.8^*$	27.0 ± 1.8	2.8 ± 0.6
Total					
1989 ($n = 356$)	6.5 ± 2.0	177 ± 38	10.8 ± 15.1	26.0 ± 2.3	1.9 ± 0.6
1999 ($n = 418$)	$8.4 \pm 1.6^*$	$145 \pm 29^*$	$1.8 \pm 0.8^*$	27.0 ± 1.8	2.2 ± 0.5

* $P < 0.001$; † $P < 0.05$; as compared with 1989.

aged 6–10 years still had goitre. It has been shown that thyroid size in children exposed to iodine deficiency in the first years of life might fail to regress completely following the consumption of iodised salt²⁴. However, palpation of the thyroid is not a precise method for the estimation of thyroid size; therefore, some of the findings might be due to the inaccuracy of the palpation method.

Median urinary iodine of 17.3–20.1 $\mu\text{g dl}^{-1}$ in the villages studied shows adequate iodine intake⁹ and the propriety of the 40 ppm iodised salt programme in Iran, as shown in our previous report⁸. Iodine supplementation has been recognised to increase the incidence of hyperthyroidism in iodine-deficient areas^{25,26}. Increases in T_4 and T_3 and decreases in TSH were observed in Kiga in the first year after iodised oil administration⁷. Thyroid function returned to normal, however, within a year and has remained so after 10 years. No untoward effects have occurred with respect to possible hyperthyroidism. It has to be taken into consideration, however, that the population studied was young schoolchildren and 10 years has passed since the initiation of iodine supplementation. Iodine-induced thyrotoxicosis is seen mainly in adults, and in particular the elderly, usually one to two years following intervention²⁶.

In conclusion, this study demonstrates that in children and adolescents with depressed thyroid function due to iodine deficiency, who had restoration of euthyroidism after iodised oil supplementation, normal thyroid function is sustained following consumption of iodised salt. Many children and adolescents residing in iodine-deficient regions may have decreased thyroid function resulting from moderate to severe iodine deficiency that is not grave enough to cause progressive degeneration and atrophy of thyroid tissue. Iodised oil administration appears to be the treatment of choice for these individuals, followed by supplementary iodised salt intake.

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