Original Article

Effect of iodized oil supplementation on thyroid hormone levels and mental performance among *Orang Asli* schoolchildren and pregnant mothers in an endemic goitre area in Peninsular Malaysia

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Although endemic goitre is no longer a major public health problem in Malaysia, iodine deficiency still remains a significant problem in a few remote settlements. The aim of this study was to determine the effectiveness of iodized oil intervention in the prevention of endemic goitre among the indigenous people in Malaysia. A pretest and post-test controlled trial was conducted among primary schoolchildren and pregnant mothers in Lasah, Sungai Siput and Perak. Legap Post and Yum Post were selected as the intervention areas, while Perwor Post and Poi Post were taken as controls. The variables studied included thyroid hormone concentrations, thyroid volume, urinary iodine excretions and mental performance. A baseline and two follow-up visits were conducted in both intervention and control areas. Intervention subjects were given iodized oil in the form of capsules which were taken orally (Laboratoire Guerbet, Paris, France). There was a significant increase in serum thyroxine hormone (T4) concentrations ($P < 0.0001$) and a significant decrease in thyroid stimulating hormone (TSH) concentrations ($P < 0.05$) in the schoolchildren following the intervention, however, pregnant mothers did not show any significant changes in T4 and TSH concentrations. Thyroid size was significantly reduced in both groups ($P < 0.05$). Urinary iodine excretions showed a significant increase in both groups following the intervention ($P < 0.01$). However, mental performance in schoolchildren was not affected. In conclusion, iodized oil (oral) is effective in reducing thyroid size, as well as improving the supply of iodine among schoolchildren and pregnant mothers in endemic goitre areas; however, its long-term effects need to be monitored closely. This method can be considered as an alternative while awaiting national coverage for the salt iodization program.

Key words: goitre, iodized oil, Malaysia, mental performance, *Orang Asli*, pregnant women, schoolchildren, thyroid hormones.

Introduction

The prevention of iodine deficiency disorders (IDD) worldwide by 2000 will benefit more than 20 million people in endemic areas.[1] Apart from salt, iodized oil is considered as the best alternative method, especially in the most remote areas of developing countries. Iodized oil (Lipiodol) is an organic compound consisting of iodized ethyl ester in poppy seed oil. It can be administered either orally (via oil capsules or dispenser) or by intramuscular injection. Both oil capsules and injectable form contain 480 mg iodine per mL (37% of iodine by weight), while in oil dispenser it contains 540 mg iodine per mL (Andre Guerbet Laboratories, Paris, France). One mL of this iodized oil contains 30 times the quantity of iodine inside the body. A single dose of iodized oil is able to supply iodine to individuals for a period of one year. Doses in the range of 0.2 mL to 5 mL were used in many studies and goitre intervention programs.[2–4]

In severely iodine-deficient areas, abnormalities of thyroid function was found in pregnant women and their newborn babies.[5] In several observational studies, schoolchildren living in iodine-deficient areas were found to have poorer levels of IQ, cognitive and motor function than schoolchildren living in iodine-sufficient areas.[6–13] The most current studies showed that a single dose of iodized oil given to individuals in populations affected by endemic goitre has reduced the prevalence of the disease, corrected iodine deficiency and normalized the thyroid function. A study in Equador showed that the supplementation of iodized oil by injection to villagers in endemic goitre areas reduced the prevalence of the disease in the following months.[14–16] The reduction was observed in all goitre grades. However, there was a gradual increase in the reappearance of cases. It was

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faster in children, women in the reproductive age, and those who had small goitres. It was slower and less significant in men more than 45 years old, and among those who have had a large goitre, for instance grade 2 and grade 3. In many studies, low thyroid hormone concentrations, high thyrotropin concentrations and low iodine content in the thyroid gland were found before the injection, but became normal in the following months after injection.[14–19] In Zaire, the signs of iodine deficiency persisted in some individuals despite normal thyroid hormone concentrations.[16,19] However, injections under field conditions in developing countries have disadvantages, particularly the potential risk of communicable diseases such as hepatitis and HIV, and dependence on trained manpower. Due to the extra costs and health risks associated with dosing parenterally, oral dosing of iodized oil is increasingly being used in iodine deficiency control programs.[20] Its administration requires less technical training, fewer instruments and less time. In addition, certain hazards are avoided such as infections and improper disposal of needles. In such areas, oral iodized oil could be administered by a responsible person who would not need to be technically trained. A single dose of oral iodized oil is able to supply iodine to individuals for a period of one year.

Oral administration of iodized oil before or during the first trimester of pregnancy normalizes thyroid function in newborn babies and mothers, increases placental and birthweight and reduces the prevalence of iodine deficiency disorders.[21] The study on the effect of iodized oil among cretins showed that there was an increase in psychomotor development among these children following iodized oil intervention.[2–4]

The *Orang Asli* are indigenous people from the Senoi tribe (Temiar ethnic group) who had already settled in government gazetted remote rural areas along the Titiwangsa Dividing Range for more than 20 years. They are mainly farmers and hunter–gatherers (depending on the season). Compared to the Malays who inhabited rural or semi-urban areas, they are still disadvantaged in socioeconomy, education, health and nutritional status. It was found in an earlier study that the *Orang Asli* in remote rural areas are suffering from IDD.[22]

Therefore, the aim of this study was to determine the effect of an iodized oil intervention program (Lipiodol) on thyroid hormone levels and mental performance among *Orang Asli* schoolchildren and pregnant mothers in Lasah, Sungai Siput and Perak.

Subjects and methods

Population and sample

The study was approved by the Universiti Kebangsaan Malaysia research ethical committee. Almost all eligible schoolchildren and pregnant women in the treatment areas participated. All the subjects and parents of the schoolchildren gave written informed consent. The *Orang Asli* at Legap Post and Yum Post were selected as the treatment group. All the villagers in these areas were given oral iodized oil in the form of oil capsules. The *Orang Asli* at Perwor Post and Poi Post were chosen as controls and they were not given any intervention. During each visit, villagers who attended our clinic were assessed. Sixty schoolchildren and 13 pregnant mothers were examined at the baseline. During the first visit, a total of 60 schoolchildren and 19 pregnant mothers were examined (6 months of iodized oil supplementation), and 60 schoolchildren and 14 pregnant mothers were examined during the second follow-up visit (12 months of iodized oil supplementation). In the control group, a total of 105 schoolchildren and 18 pregnant mothers were examined at the baseline, 116 schoolchildren and 18 pregnant mothers during the first follow-up visit and 101 schoolchildren and 11 pregnant mothers during the second follow-up visit (Table 1).

Background of study area

The selection of the study areas was done after pre-surveys were conducted in several *Orang Asli* settlements in remote rural areas. Only areas with moderate to severe endemia of IDD were selected.

Intervention areas

Legap Post and Yum Post were selected as the intervention areas by purposive sampling. All the individuals in the two villages were selected as samples. Areas selected for control, namely Perwor Post and Poi Post, were also purposely selected as these areas were inhabited by a similar tribe with similar IDD endemicity (Fig. 1).

Intervention method

A pretest and post-test controlled trial was used in the study (Fig. 2). The intervention group were given a single dose of

Table 1. Study sample

Group	Location	Visits	Subjects	
			School-children	Pregnant mothers
Intervention	[Legap Post	Baseline	60	13
	and Yum Post]	1	60	19
		2	60	14
Control	[Perwor Post	Baseline	105	18
	and Poi Post]	1	116	18
		2	101	11

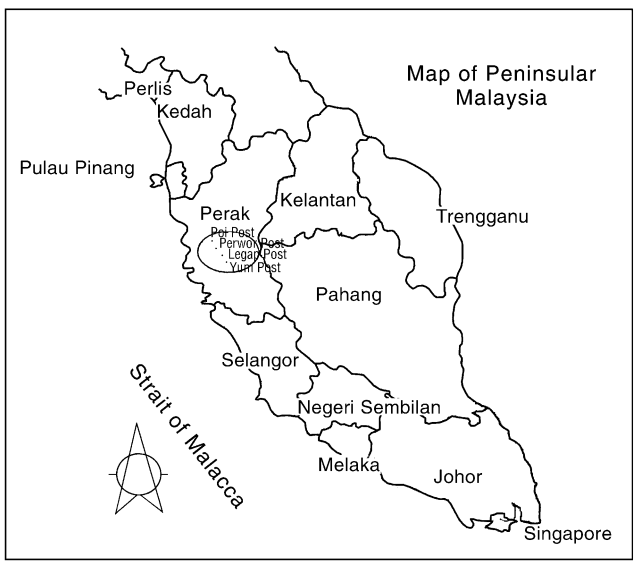

Figure 1. Study areas.

iodized oil orally (Lipiodol; Laboratoire Guerbert, Paris, France) in the form of capsules after the baseline data had been collected. The medication given was based on the dose recommended by the manufacturer (Laboratoire Guerbert, Paris, Table 2). A total of three visits were made in both treatment and control groups of six months apart. Those suffering from cardiovascular diseases such as congestive heart failure or arrythmias were excluded from the study. Five to 10 mL of blood were taken for biochemical analysis. Urine samples were also collected to determine the iodine concentration.

Biochemical test

The blood samples were centrifuged at 3000 *g* for 5 min at room temperature. The serum were subsequently separated from the blood cells and kept in a freezer at –20°C. The frozen serum were then sent to the endocrine lab in the Department of Medicine, Medical Faculty, UKM for analysis. Serum thyroxine hormone (T4) and thyroid stimulating hormone (TSH) concentrations were determined. Free serum thyroxine (normal range: 10–23 pmol/L) and thyroid stimulating hormone (normal range: 0.3–4.0 mLU/L) were measured using ELISA method (enzyme-linked immunosorbent assay). Urinary iodine excretions (in random samples) were measured by using alkaline ashing method (Hu Ashing) based on the Sandell-Kolthoff reaction.[23,24]

Clinical examination

Blood pressure was measured using a digital blood pressure/pulse monitor set (model HEM-400C; Omron, Tokyo, Japan). Thyroid volume was determined using portable ultrasound (Toshiba Sonolayer–Model SAL-32B; Toshiba, Tokyo, Japan) with a 5.0 Megahertz transducer on subjects lying supine, as described elsewhere.[25,26]

Mental performance evaluation

Mental performance was assessed in schoolchildren in both groups using TONI-2 (Test of Non-Verbal Intelligence — 2nd Edition), a language-free cognitive ability measurement tool for solving abstract/diagrammatic problems. It has a format that can minimize motor and cultural factors. There are two similar types of TONI-2, namely form A and form B, each of which contains 55 questions that were arranged according to difficulty levels. Both forms were used alternately to prevent subjects from memorizing and learning from the repeated questions. Mental performance was stated in the forms of percentile and quotient. As for the percentile, the median score was taken as the cut-off point in which the results obtained were shown as the number of subjects who scored above the median score. In the quotient, scores were divided into subscores as follows : > 130 (superior), 121–130 (good), 111–120 (above average), 90–110 (average), 80–89 (below average), 70–79 (poor) and < 70 (very poor), in which the number of subjects were determined in every range

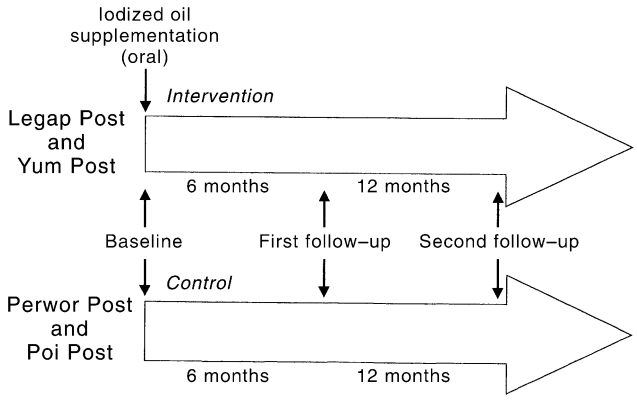

Figure 2. Iodized oil (oral) intervention design.

Statistical analysis

Statistical analysis were done using SAS package (System for Elementary Statistical Analysis, SAS Institute Inc., Cary, NC, USA). All values were given as mean ± SD unless otherwise noted. For statistical evaluation, analysis of variance (ANOVA), Student's *t*-test and χ^2 test were used to observe the difference between groups and variables. Correlation was used to observe the relationship between variables, while multiple regression using 'enter' and 'backward' method was used to observe the treatment effect on the outcomes. The probability of 0.05 or less was considered significant.

Results

1. Baseline demographic characteristics

The baseline demographic characteristics of the treatment and control groups are shown in Table 3. Both groups were comparable in most characteristics, as shown in Table 3. There was a significant difference in TSH and thyroid volume between the treatment group and control group. There is a possibility that the control group had more individuals with severe IDD.

2. Free thyroxine hormone (T4) and thyroid stimulating hormone (TSH) concentrations among schoolchildren and pregnant mothers following iodized oil supplementation

In schoolchildren, there was an increase in free T4 concentrations in both treatment and control groups after 12 months of supplementation ($P < 0.0001$), with a more pronounced effect in the treatment group (Table 4). The TSH concentrations showed a significant reduction in the treatment group after 12 months of supplementation ($P < 0.05$) while no significant difference was observed in the control group. In pregnant mothers, no significant difference was observed in T4 and TSH concentrations in both treatment and control groups following iodized oil supplementation (Table 4). This might be due to an insufficient dose having been received, following the increased requirement of iodine during pregnancy.

3. Thyroid volume among schoolchildren and pregnant mothers following iodized oil supplementation

In schoolchildren, there was a reduction in the thyroid volume in both treatment and control groups after six months of

Table 2. The dosage of iodized oil* trial

Subjects	Number of capsules per year
Baby/infant (0–1 year old)	1
Children (1–5 years old) and pregnant mothers	2
Children (6–15 years old), women of reproductive age and men (16–45 years old)	3

*Laboratoire Guerbet, Paris, France.

Table 3. Baseline demographic characteristics of the schoolchildren and pregnant mothers

Baseline demographic characteristics	Schoolchildren		Pregnant mothers	
	Legap Post & Yum Post (treatment group) *n* = 60	Perwor Post & Poi Post (control group) *n* = 105	Legap Post & Yum Post (treatment group) *n* = 13	Perwor Post & Poi Post (control group) *n* = 18
Proportion				
Male	31	59	—	—
Female	29	46	13	18
Age (year)	11.62 ± 2.62	11.16 ± 2.64	26.62 ± 8.33	25.50 ± 6.86
Weight (kg)	29.97 ± 9.93	27.80 ± 10.02	44.43 ± 3.93*	55.50 ± 4.77
Height (cm)	133.04 ± 13.28	130.11 ± 16.08	143.38 ± 3.49*	149.01 ± 6.21
Thyroid hormone levels				
Free T4 (pmol/L)	20.97 ± 6.08	22.56 ± 7.80	14.14 ± 4.46	14.84 ± 4.40
TSH (mIU/L)	1.53 ± 0.64*	2.42 ± 0.95	2.05 ± 1.43	2.56 ± 1.70
Thyroid volume (ml)	18.93 ± 6.64*	23.60 ± 10.45	35.65 ± 7.67	34.41 ± 10.58
Urinary iodine levels (µg/dL)	1.61 ± 1.08	1.50 ± 0.96	1.07 ± 0.43*	2.11 ± 1.42
Arterial blood pressure (mmHg)				
Systolic	110 ± 8*	105 ± 7	107 ± 12	111 ± 13
Diastolic	61 ± 9*	70 ± 6	66 ± 6	69 ± 13
Pulse rate (min^{-1})	84 ± 19*	74 ± 6	96 ± 17	103 ± 22
Mental performance				
Raw score (score/55)	8.83 ± 5.43	9.53 ± 5.02	—	—
Quotient (%)				
>130 (Superior)	0	0	—	—
121–130 (Good)	0	0	—	—
111–120 (Above average)	0	0	—	—
90–110 (Average)	6.8	18.4	—	—
80–89 (Below average)	17.0	24.3	—	—
70–79 (Poor)	23.7	18.4	—	—
< 70 (Very poor)	52.5	38.8	—	—
Percentile (%)	40.7	54.4	—	—

Datas are mean ± SD values; *Significant difference between the treatment and control groups: $P < 0.05$; *n*, number of subjects; –, indicate data not relevant.

supplementation ($P < 0.05$) (Fig. 3). In pregnant mothers, both treatment and control groups showed a significant reduction in thyroid volume following iodized oil supplementation, with a more pronounced effect in the treatment group ($P < 0.0001$ *vs* $P < 0.05$) (Fig. 4). Contamination to control groups cannot be excluded as the reason for the reduction of thyroid volume among the controls.

4. Urinary iodine excretions among schoolchildren and pregnant mothers following iodized oil supplementation

There was a significant increase in urinary iodine excretions in both treatment and control groups following iodized oil supplementation ($P < 0.01$), with a marked increase in the treatment group in schoolchildren as well as in pregnant mothers (Fig. 4). Urinary iodine excretions were also higher in the treatment group as compared to the controls after 6 months and 12 months of supplementation ($P < 0.05$).

5. Mental performance among schoolchildren following iodized oil supplementation

(i) Percentile In terms of percentile, it was found that the treatment group showed a significant increase in the proportion of subjects who scored above three percentile after 12 months of supplementation ($P < 0.0001$), while the control group showed an increase after the first six months ($P < 0.01$;

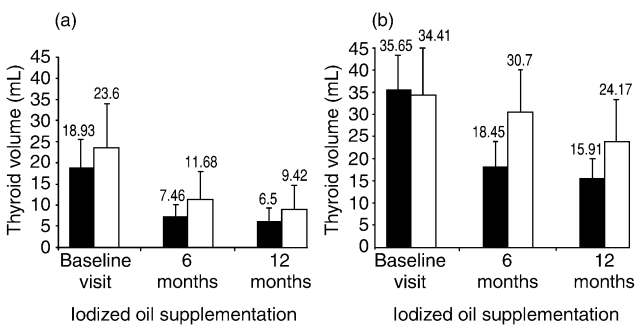

Figure 3. (a) Thyroid volume among schoolchildren following iodized oil supplementation compared between (■) treatment and (□) control. (b) Thyroid volume among pregnant mothers following iodized oil supplementation compared between (■) treatment and (□) control.

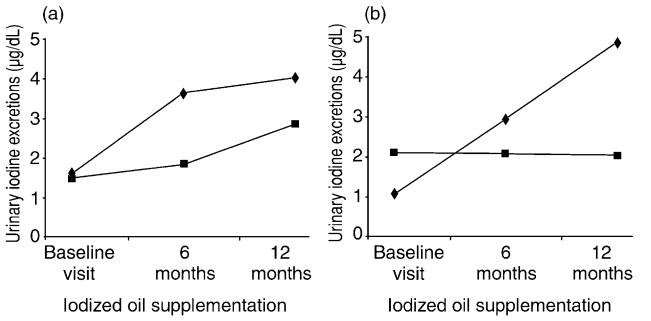

Figure 4. (a) Urinary iodine excretions among schoolchildren following iodized oil supplementation compared between (♦) treatment and (■) control. (b) Urinary iodine excretions among pregnant mothers following iodized oil supplementation compared between (♦) treatment and (■) control.

Table 4. Thyroxine hormone (T4) and thyroid stimulating hormone (TSH) concentrations among schoolchildren and pregnant mothers following iodized oil supplementation

Iodized oil supplementation	Schoolchildren				Pregnant mothers			
	T4 (pmol/L)		TSH (mLU/L)		T4 (pmol/L)		TSH (mLU/L)	
	Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control
Baseline visit	20.97 ± 6.08[a]	22.56 ± 7.80[a]	1.53 ± 0.64[x]	2.42 ± 0.95	14.14 ± 4.46	14.84 ± 4.40	2.05 ± 1.43	2.56 ± 1.70
	60	103	60	104	4	17	4	17
6 months	20.82 ± 5.59[b]	20.31 ± 7.86[b]	1.33 ± 0.52[x]	2.54 ± 1.27	18.37 ± 6.82[x]	14.11 ± 4.06	2.03 ± 0.96[x]	2.93 ± 1.39
	60	115	60	115	19	18	19	18
12 months	51.64 ± 9.49[x]	31.49 ± 12.86	1.29 ± 0.50[x]	2.42 ± 2.13	20.70 ± 13.47	18.76 ± 9.03	2.58 ± 0.84	2.06 ± 1.45
	56	91	56	96	14	11	14	11
Statistical test	ANOVA	ANOVA	ANOVA	ANOVA	ANOVA	ANOVA	ANOVA	ANOVA
	$F = 347.74$	$F = 37.23$	$F = 3.13$	*NS*	*NS*	*NS*	*NS*	*NS*
	$P < 0.0001$	$P < 0.0001$	$P < 0.05$					

[a]Significant difference between baseline visit and 12 months of iodized oil supplementation ($P < 0.05$); [b]Significant difference between 6 months and 12 months of iodized oil supplementation ($P < 0.05$); [x]significant difference between the treatment and control groups ($P < 0.05$); *NS*, not significant.

Table 5). The control group showed a more pronounced rise in the proportion of subjects who scored above three percentile compared to the treatment group ($P < 0.0001$). Thyroid stimulating hormone also affects mental performance in which there was a reduction in the percentile score with the increase of TSH (Table 6a, b). However, if the study were to continue, it is believed that the number of scored subjects of the treatment group would continue to increase while the control group showed vice versa.

(ii) Quotient In the treatment group, the best score achieved after 12 months of supplementation was the 'good' score (121–130), while the control group obtained the 'superior' score (>130; Table 7). During the first 6 months of supplementation, the control group had already reached the 'good' score (121–130), while the treatment group was still at the 'average' score level (90–110). In the treatment group, there was a significant increase in number of subjects in the 'average' score (90–110), the 'above average' score (111–120) and the 'good' score (121–130) following the supplementation, while in the control group, the increase in number of subjects was observed in the 'above average' score (111–120) and the 'superior' score (> 130). Although the control group generally showed better mental performance than the treatment group, there is an increasing trend of performance in the former group and a decreasing trend in the latter group.

Table 5. Mental performance (proportion of subjects obtaining above 3 percentile) among schoolchildren following iodized oil supplementation

Iodized oil supplementation	Proportion of subjects obtaining above 3 percentile		Statistical test
	Treatment	Control	χ^2
Baseline visit	40.7[b]	54.4[a]	3.234, *NS*
6 months	44.1[c]	78.2	23.059, $P < 0.0001$
12 months	75.0	68.0	0.883, *NS*
Statistical test (χ^2 trend)	$\chi^2 = 28.694$ $P < 0.0001$	$\chi^2 = 12.870$ $P < 0.01$	Overall (χ^2 trend) 7.299, $P < 0.05$

[a]Significant difference between baseline visit and 6 months of iodized oil supplementation ($P < 0.0001$); [b]Significant difference between baseline visit and 12 months of iodized oil supplementation ($P < 0.0001$); [c]Significant difference between 6 months and 12 months of iodized oil supplementation ($P < 0.0001$); *NS*, not significant.

6. Correction for baseline differences

In the baseline visit, the treatment group of the schoolchildren showed lower TSH concentrations compared to the controls ($P < 0.05$; Table 4). After controlling the initial TSH concentration, it was found that iodized oil intervention did not affect TSH concentrations at the end of intervention (Table 8). The treatment group also showed smaller thyroid volumes compared to the controls ($P < 0.01$) at the initial phase (Fig. 2). However, after controlling the initial thyroid volume, the intervention still has a significant effect in reducing the thyroid size during the final visit ($P < 0.001$; Table 9).

7. The prevalence of hyperthyroid following iodized oil supplementation

In schoolchildren, an increase in free T4 levels was noted in both the treatment and control groups following 12 months of iodized oil supplementation. The increase was more

Table 6. Multiple regression analysis using 'enter' and 'backward' method to observe the effect of iodized oil supplementation and other factors on final percentile among the schoolchildren

Independent variables/ constant	Regression coefficient (β)	*t*-value	*P*-value
Enter method			
Constant	15.69	0.54	0.5943
Initial percentile	0.23	0.99	0.3289
Sex	–6.93	–0.97	0.3349
Age	–0.38	–0.22	0.8265
Final body fat percentage	1.10	1.40	0.1685
Final T4 concentrations	–0.14	–0.50	0.6216
Final TSH concentrations	–6.34	–2.11	0.0404[1]
Iodized oil intervention	12.60	1.50	0.1405
Backward method			
Constant	8.04	0.69	0.4928
Final TSH concentrations	–7.65	–2.77	0.0079[2]
Iodized oil intervention	18.01	2.62	0.0116[1]

[1]β significant at $P < 0.05$; [2]β significant at $P < 0.01$; T4, thyroxine hormone; TSH, thyroid stimulating hormone.

dramatic in the treatment group, where all of the children studied showed free T4 levels exceeding the upper normal range during the final visit (Table 10). The pregnant mothers also showed the same pattern, in which both treatment and control groups showed an increase in free T4 levels with a more obvious effect in the treatment group.

Discussion

Until now, there is no known technology available to replace the leached iodine from the soil, therefore, it must be supplemented through the diet.[27] A national IDD program through universal salt iodization is possibly the best long-term solution to this problem in most endemic areas. In Malaysia,

Table 7. The prevalence of mental performance (quotient) among schoolchildren following iodized oil supplementation

Iodized oil supplementation Quotient score	< 70	70–79	80–89	90–110	111–120	121–130	> 130
Treatment							
Baseline visit	52.5[b]	23.7	17.0	6.8[b]	0	0	0
	(31)	(14)	(10)	(4)	(0)	(0)	(0)
6 months	50.8[x,c]	25.4	11.9[x]	11.9	0	0	0
	(30)	(15)	(7)	(7)	(0)	(0)	(0)
12 months	20.0	16.7	28.3	31.7	1.7	1.7	0
	(12)	(10)	(17)	(19)	(1)	(1)	(0)
Statistical test (χ^2 trend)	$\chi^2 = 16.552$ $P < 0.0001$	*NS*	*NS*	$\chi^2 = 14.716$ $P < 0.0001$	*NS*	*NS*	—
Control							
Baseline visit	38.8[a]	18.4	24.3	18.4	0	0	0
	(40)	(19)	(25)	(19)	(0)	(0)	(0)
6 months	16.4	25.4	28.2	28.2	0.9	0.9	0
	(18)	(28)	(31)	(31)	(1)	(1)	(0)
12 months	30.0	13.0	25.0	26.0	5.0	0	1.0
	(30)	(13)	(25)	(26)	(5)	(0)	(1)
Statistical test (χ^2 trend)	$\chi^2 = 10.754$ $P < 0.01$	*NS*	*NS*	*NS*	$\chi^2 = 7.663$ $P < 0.05$	*NS*	*NS*

Quotient: < 70 (very poor), 70–79 (poor), 80–89 (below average), 90–110 (average), 111–120 (above average), 121–130 (good) and > 130 (superior); [a] Significant difference between baseline visit and 6 months of iodized oil supplementation ($P < 0.01$); [b] Significant difference between baseline visit and 12 months of iodized oil supplementation ($P < 0.01$); [c] Significant difference between 6 months and 12 months of iodized oil supplementation ($P < 0.05$); [x] Significant difference between treatment and control groups ($P < 0.05$); *NS*, Not significant.

Table 8. Corrections for baseline differences in schoolchildren*

Independent variables/ constant	Regression coefficient (β)	*t*-value	*P*-value
Constant	0.01	0.01	0.9908
Initial TSH concentrations	0.34	1.49	0.1415
Iodized oil intervention	0.73	1.42	0.1609

TSH, thyroid stimulating hormone.*multiple regression analysis using 'enter' method to observe the effect of iodized oil intervention on thyroid stimulating hormone (TSH) concentrations when the initial TSH is controlled.

Table 9. Corrections for baseline differences in schoolchildren*

Independent variables/ constant	Regression coefficient (β)	*t*-value	*P*-value
Constant	–14.13	–2.34	0.0236[1]
Initial thyroid volume	0.13	1.12	0.2707
Iodized oil intervention	7.20	4.05	0.0002[2]

[1]β significant at $P < 0.05$; [2]β significant at $P < 0.001$. *multiple regression analysis using 'enter' method to observe the effect of iodized oil intervention on thyroid volume when the initial thyroid volume is controlled.

Table 10. The prevalence of hyperthyroid (free T4 > 23 pmol/L) among schoolchildren and pregnant mothers following iodized oil supplementation

Iodized oil supplementation Subjects	Schoolchildren				Pregnant mothers	
	Treatment		Control		Treatment	Control
Sex	Male	Female	Male	Female		
Baseline visit	29.0	31.0	30.5	43.2	0	5.9
n	9	9	18	19	0	1
6 months	25.0	28.1	26.3	27.6	21.1	0
n	7	9	15	16	4	0
12 months	100.0	100.0	77.6	66.7	35.7	18.2
n	27	29	38	28	5	2

n, number of subjects; T4, thyroxine hormone.

where IDD is considered not a public health problem, it may be beneficial to obtain moral and political support for other alternatives, such as the use of water iodization, oral or injection of iodized oil, or thyroxine as supplement for short-term measures. Iodized oil was chosen as the intervention tool in this study, because only one single dose is required to maintain its effect for about one year, and this helped to minimise the problem of compliance.

The study done by Thilly showed that there was a reduction in goitre prevalence following iodized oil injection, and it was concurrently accompanied by the reduction of TSH concentrations and normalization of serum T4 concentrations.[16] In the study of Ma Tai, the serum thyroxine concentrations remained normal without any marked changes in both groups treated either with oral or intramuscular iodized oil.[28] In our study, both treatment and control groups of the schoolchildren showed a significant increase in T4 concentrations after 12 months of supplementation. The increased T4 concentrations in the control group might be due to contamination. In pregnant mothers, T4 concentrations remained normal in both treatment and control groups throughout the intervention. No significant changes were also noted in TSH concentrations in both treatment and control groups following the intervention.

The iodized oil reaction is beneficial in terms of goitre prevention and was able to induce goitre to its normal size. In Equador, Fierro-Benitez reported that goitre problems no longer exist in children who were given iodized oil and in contrast to the control children, if there were small goitres, they would always disappear. Goitre size was also reduced in the adults given the iodized oil, and in many instances totally disappeared.[2] In the report of Watanabe, there was a marked decrease in goitre size in more than 70% of patients treated with iodized oil either through oral or intramuscular route, and the results of oral supplementation were equally as good as the intramuscular supplementation.[29] In this study, among the schoolchildren, there was a reduction in thyroid size more than double in the treatment group after 6 months of supplementation. After controlling of factors, such as the initial thyroid volume, age, final T4 concentrations, final TSH concentrations and final body fat percentage, it was found that iodized oil supplementation was still associated with thyroid size reduction in the treatment group. A significant reduction in thyroid size was also observed among pregnant mothers who received iodized oil.

In this study, among the schoolchildren, there was a significant increase in urinary iodine excretions following iodized oil supplementation. In the treatment group, the increase in urinary iodine excretions was twice its original values, which is still far lower than the urinary iodine excretions reported in the iodized oil supplementation study through intramuscular injection by Thilly.[16] In pregnant mothers, urinary iodine excretions increased linearly in the treatment group following the intervention, while the control group remained constant at approximately 2 µg/dL.

Iodine is essential for thyroid hormone synthesis and for organizing the activity of metabolic cells and growth, particularly of the brain, during early stages of the fetus and the early postnatal period. Iodine deficiency is known as the most important cause of reversible brain damage and mental defect in the world. It has been reported that iodine supplementation, as late as four to eight years, might have some effects on intelligence measures. Bautista had carefully observed the effect of oral iodized oil on mental performance, and he found that goitre size reduction was well correlated with the increase in urinary iodine excretions and intelligence measures in female subjects.[30] Dodge also made a similar conclusion from the study in Equador.[31] Tiwari observed the effect of continuous iodine deficiency on learning and motivation among 100 male schoolchildren who were matched for age, socioeconomic status and formal education, selected from severe iodine deficiency area (SID) and mild iodine deficiency area (MID).[12] The results showed that SID schoolchildren were slower compared to the MID schoolchildren, and in both groups, the learning rates in the test were better in younger children. Therefore, iodine deficiency can prevent millions of children from the SID group from achieving their full potential, even though education facilities have been provided.

In this study, iodized oil intervention has increased the mental performance of the treatment group, as shown by the proportion of subjects scoring above the median level. The increase in mental performance was found in both genders, and it was more pronounced in males. However, after controlling several factors such as the initial percentile, sex, age, final body fat percentage, final T4 and TSH concentrations, it was found that there was a significant increase in mental performance in the control group, rather than the treatment group. The marked increase of mental performance in the control group was shown during the second visit, and this might be due to genetic or environmental factors, such as contamination either from the treated subjects, or the control group might be more receptive to education compared to the treatment group. Multiple regression analysis also proved the existence of TSH influence on mental performance, in which the treatment group showed elevated concentrations of TSH compared to the control group. Low TSH concentrations in the control group were found to be associated with the increase of mental performance in this group. However, the association is only true for the schoolchildren; the pattern of the older children and adults are not known. The distribution of mental performance according to quotient score proved that the control group had better intelligence compared to the treatment group. However, there is a tendency of increment in the performance of the treatment group as compared to the control group. Iodized oil intervention for a period of one year did not increase mental performance of the schoolchildren, but the study needs to be prolonged to observe the effect in a long-term study.

Conclusion

In this study, oral iodized oil is considered an effective alternative method in reducing thyroid size, particularly in schoolchildren and pregnant mothers in endemic goitre areas. It increases T4 concentrations and decreases TSH concentrations in schoolchildren, but not in pregnant mothers, as this is probably due to insufficient doses received following the increase in iodine requirement during pregnancy. The iodized oil supplementation also increases urinary iodine excretions in both groups; paradoxically, it did not increase mental performance of the schoolchildren. It is suggested that pregnant mothers should be given a higher dose of oral iodized oil

to fulfill their increased requirement. There is also a need to have further study on mental performance of the schoolchildren to look at the possibility of this group being influenced by genetic or environmental factors, or that one group might be more receptive to education than are others.

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