Original article

Thyroid responses to varying doses of oral iodized oil in school children in Awassa, Ethiopia

Cherinet Abuye, Gonfa Ayana, Melaku Umeta, Hana Neka Tibeb, Bantirgu Hailemariam

Abstract: A longitudinal study was conducted during 1994 - 1996 among elementary school children aged 6-14 years in Awassa, South Ethiopia. The aim of the study was to compare the efficacy of varying doses of oral iodized oil (200mg and 400mg) on thyroid function. The study included clinical examination of goitre, biochemical tests for thyroid function, and assessment of nutritional status of the children. A total of 110 children were randomly selected from six elementary schools and randomly assigned into high or 400mg (n=53) and low or 200 mg (n=57) dose groups for administration. After 13 months of intervention 42% goitre reduction was noted in the 200mg group while 49% regress of goitre was observed in the 400mg group. The difference was not statistically significant ($p>0.05$). There were no significant differences ($p>0.05$) in serum concentrations of T3, T4 and TSH between the two dose groups before or after administration. These clearly indicate that the two graded doses of oral iodized oil have the same effect on thyroid function and goitre reduction. [*Ethiop. J. Health Dev.* 2000;14(1):49-55]

Introduction

Goitre is a nutritional disease of public health significance in many parts of Ethiopia (1,2,3). A thyroid gland whose lateral lobes have a volume greater than the terminal phalanges of the thumbs of the person examined is considered goitrous (4). Under normal iodine intake, the thyroid gland should have the minimum size compatible with euthyroidism. An area is arbitrarily defined as endemic with respect to goitre if more than 10% of the population or of the children aged 6-12 years are found to be goitrous (4). To Iodine Deficiency Disorders combat the problem of (IDD), two main strategies have been adopted, namely, salt iodation and iodized oil capsule distribution (5). IDD control and eradication programmes by means of salt iodation and distribution was started in Ethiopia in 1989 and interrupted after three years of operation. High goitre endemic areas of the country were given priority in the distribution of iodated salt except some which were not covered due to capacity and inaccessibility.

Awassa Town, in Sidama Awraja, where this study was conducted, had a high prevalence of goitre among elementary school children (3). Awassa, which is about 285 km south of the capital city of Ethiopia, was not included in the distribution of iodated salt during this study period. As a result, oral iodized oil distribution was effected in this area.

Oral iodized oil on the treatment of IDD has been given importance when communities are inaccessible for distribution of iodated salt (5).

Several studies (6,7,8,9) indicated that oral iodized oil is effective in treatment of iodine deficiency problems. However, there are discrepancies in recommendation regarding what dose to use for the treatment of goitre and other IDD problems (7,8,9). Hence, the present study was designed to investigate the effect of varying doses of oral iodized oil on thyroid function and nutritional status of elementary school children.

Methods

A longitudinal study was conducted during the IDD control programme at Awassa, 285

Ethiopian Health and Nutrition Research Institute, P.O.Box 5654, Addis Ababa, Ethiopia, Fax: 251-1-754744, E-mail: EHNRI@telecon.net.et

km South of Addis Ababa, the capital city of Ethiopia, from 1994 to 1996. The study subjects were elementary school children aged six to fourteen years. It was intended to assess the effect of two varying doses of oral iodized oil capsules on nutritional status and thyroid function. All elementary schools (six) at Awassa Town were included in this study. After conducting clinical examination for goitre, 1500 children were selected by stratified systematic random sampling method. Of these 1500, only 154 were selected again by systematic random sampling method for this study. Because of missing (28%) children in any one of sample collection period, only 110 of the children participated in the clinical examination throughout the study. The age and sex of those children enrolled in the study were recorded, blood samples were collected, anthropometric measurements were taken from 120 children who were 6-10 years of age only, and thyroid gland size was graded by two experienced examiners following the method recommended by WHO/PAHO (5). Then, the children were assigned into two groups by random allocation. These were evenly distributed by sex. The first group was given 200mg of the oral iodized oil (Lipiodal ultra fluid obtained from Gerbert Lab, France, an organic compound consisting of iodized ethyl esters of fatty acids of poppy seed oil); the second group received 400mg of the same iodized oil. Blood samples collection was done one month after the initial administration of the iodized oil and again six and 13 months after initial administration while clinical examination for goitre was repeated 13 and 30 months after the initial administration of iodized oil. Anthropometric measurements were taken 13 months after the administration.

Blood samples were collected using sterile vacutainers and the sera separated within less than one hour. The serum was separated and stored at -20°c in the health institute until completion of the fieldwork. These were then transported to the Ethiopian Health and Nutrition Research Institute (EHNRI) where they were kept at -20°c awaiting analysis. All samples were assayed for triiodothyronine (T3), thyroxine, (T4) and thyroid stimulating hormone (TSH). The thyroid hormones T3 and T4, and the TSH were measured by ELISA based immunological technique. Specifically T4 was determined by simple ELISA competition principle where as T3 and TSH were analyzed by ELISA competition and one-step sandwich assay respectively, both using streptavidin coated solid phase system. The analysis was done on the ES 300 fully automated immuno-analyzer system using appropriate reagent kits from Boehringer Mannheim GMBH, Germany. Normal ranges of the thyroid hormones are given in Boehringer Mannhein reagent kit as follows: T3 0.8-1.8 ng/ml, T4 4.5-11.7 μg/dl, TSH 0.23-3.8 μu/ml.

Procedures followed for anthropometric measurements are as described by the United Nations (1986) in measuring weight and height. Weight was measured to the nearest 100g using a bathroom scale that was calibrated with a known weight at the start of the work and at regular intervals throughout the day. Before weighing each child, the scale was set at zero on a flat surface; then the lightly dressed child was made to stand on the scale and weight was recorded. Two readings were taken for each child to arrive at an average weight for that child. Height was measured to the nearest 0.5cm using a graduated height stick with a movable headpiece. The school children were made to stand barefooted on the flat board with hands hanging loosely at the sides, with feet parallel, and then, the child's height was taken. Two readings for each child were made to obtain the average height of that child. The anthropometric indicators of height-for-age (HA), weight-for-height (WH) and weight-for-age (WA) were used to classify the study children into categories of nutritional status. A WH score of 2.00 or -2.00 means that the child is 2 SD above or below the median weight-for-height, respectively, while HA refers to the Z-score for height-for-age.

Statistics: By the use of the anthro package developed by the National Center for Health Statistics (NCHS), standard deviation scores

(Z-Scores) were generated.

Comparison of the nutritional status of the children in the two dose groups (200mg and 400mg) of oral iodized oil was done using Péarsons Chi square test while differences between hormonal concentrations of the two dose groups were compared using group t-test.

Results

Mean age of the 200mg group of children was 9.6 ± 1.9 while the 400mg group was 9.4 ± 1.9 and, statistically, they were not significantly different ($p > 0.05$) from each other (Table 1). The sex ratio was similar in the two dose groups before intervention and the total goitre rates (TGR%) were 64.9% and 69.8% in 200mg and 400mg dose groups, respectively, while, visible goitre rates (VGR%) were 28.1% and 28.3% for the same dose groups, respectively. Thyroid function tests (T3, T4, and TSH) of the two groups at base-line were also indicated in Table 1. The two dose group are not significantly different statisfically.

Table 1: **Study base-line characteristics of the study subjects in the two groups, Awassa, 1995.**

	200mg	400mg	P-value
Age	9.60±1.9	0.40±1.9	NS
Goitre rate			
TGR	64.9%	69.8%	NS
VGR	28.1%	28.3%	NS
Thyroid tests			
T3	1.40±0.29	1.36±0.30	NS
T4	9.60±2.17	9.54±2.35	NS
TSH	3.70±2.69	3.69±2.12	NS

NS = not significant
TGR = Total goiter rate
VGR = Visible goitre rate

The effect of oral doses of iodized oil on prevalence of goitre is shown in Table 2. Forty-two per cent goitre reduction in the 200mg oral dose group and 49% reduction in the 400mg-dose group were found 13 months after intervention. However, the difference in reduction between the two dose groups did not reach the level of significance. Thirty months after intervention, further reduction in goitre size was noted only in four subjects of the 200mg group while, in the 400mg-dose group, a decrease in goitre size was noted on two children.

Table 2: **Effect of oral doses of iodized oil on goitre rate, Awassa, 1995.**

Dose		13 months after	30 months after
200mg			
(n=57)	decrease to normal	15(26.3)	17(29.8)
	total decrease	24(42.1)	28(41.9)
	Same	30(52.6)	26(45.6)
	increase	3(5.3)	3(5.3)
400mg			
(n=53)	decrease to normal	14(26.4)	11(20.8)
	total decrease	26(49.1)	25(47.2)
	same	26(49.1)	24(45.3)
	increase	1(1.9)	4(7.6)

Table 3 shows biochemical results of the thyroid function tests of the two dose groups. The T3 concentration was not significantly ($p > 0.05$) different between the two dose groups before and after intervention. This had the same trend in both male and female groups. Similarly, both T4 and TSH hormones were not significantly different ($p > 0.05$) between the two dose groups before and in subsequent months of follow-up after administration. However, the T3 concentrations decreased slightly during the first and 6th months after administration followed by an increase after 13 months from

Table 3: **Effect of 200mg and 400mg oral iodized oil on thyroid functions, Awassa, 1995.**

sex	Dose	(V)	Before intervention Mean ± SD (n)	t-test p-value	One month after intervention Mean ± SD (n)	t-test p-value
Male	200mg	T3	1.45 ± 0.025 (37)		1.25 ± 0.21 (32)	
	400mg	T3	1.39 ± 0.27 (41)	0.28	1.28 ± 0.27 (38)	0.68
	200mg	T4	9.55 ± 1.83 (37)		10.10 ± 2.06 (32)	
	400mg	T4	9.98 ± 1.95 (41)	0.32	9.83 ± 1.92 (38)	0.57
	200mg	TSH	4.08 ± 4.04 (37)		2.32 ± 1.56 (32)	
	400mg	TSH	3.45 ± 2.25	0.30	2.06 ± 0.99	0.40
Female	200mg	T3	1.34 ± 0.33 (35)		1.31 ± 0.24 (30)	
	400mg	T3	1.33 ± 0.32 (41)	0.94	1.23 ± 0.29 (37)	0.28
	200mg	T4	9.64 ± 2.50 (35)		9.72 ± 2.27 (30)	
	400mg	T4	9.09 ± 2.74 (41)	0.34	9.17 ± 2.22 (37)	0.33
	200mg	TSH	3.31 ± 2.34 (35)		2.20 ± 1.34 (30)	
	400mg	TSH	3.92 ± 1.99 (41)	0.21	1.97 ± 0.95 (37)	0.43

(Table 3 continued)

sex	Dose	(V)	7 month after interven. Mean ± SD (n)	t-test p-value	13 month after interven. Mean ± SD (n)	t-test p-value
Male	200mg	T3	1.36 ± 0.17 (23)		1.90 ± 0.29 (21)	
	400mg	T3	1.26 ± 0.21 (25)	0.09	2.09 ± 0.45 (25)	0.10
	200mg	T4	9.21 ± 1.07 (23)		8.99 ± 1.42 (21)	
	400mg	T4	8.92 ± 1.76 (25)	0.50	9.72 ± 2.02 (25)	0.17
	200mg	TSH	2.79 ± 1.52 (23)		2.18 ± 0.94 (21)	
	400mg	TSH	2.62 ± 1.20	0.67	2.09 ± 1.03	0.76
Female	200mg	T3 (16)	1.32 ± 0.23	(24)	1.92 ± 0.52	
	400mg	T3	1.36 ± 0.25 (19)	0.66	2.21 ± 0.52 (28)	0.51
	200mg	T4	9.10 ± 1.63 (16)		9.05 ± 2.04 (24)	
	400mg	T4	9.34 ± 4.74 (20)	0.85	9.13 ± 2.08 (28)	0.90
	200mg	TSH	2.43 ± 1.44 (16)		2.38 ± 1.32 (24)	
	400mg	TSH	2.28 ± 0.94 (20)	0.90	1.88 ± 0.92 (27)	0.12

Table 4: **The effect of two varying doses of iodized oil on the nutritional status of school children, Awassa, 1995**

	200mg (n=60)	400mg (n=60)	X^2	df	p-value
Before intervention					
% WA					
< -2.00 SD	3.3	3.3			
> -2.00 SD	44.2	49.2	0.02	1	0.88
% HA					
< -2.00 SD	5.0	5.0			
> -2.00 SD	41.7	48.3	0.6	1	0.81
% WH					
< -2.00 SD	0.8	0.8			
> -2.00 SD	46.7	51.7	0.01	1	0.94
13 months after intervention					
% WA					
< -2.00 SD	5.8	2.5			
> -2.00 SD	39.2	52.7	2.73	1	0.10
% HA					
< -2.00 SD	5.0	5.0			
> -2.00 SD	39.2	50.0	0.46	1	0.50
% WH					
< -2.00 SD	5.0	3.3			
> -2.00 SD	40.8	50.8	0.87	1	0.35

the initial value of 1.45 and 1.39 to 1.90 and 2.09 ng/ml in 200mg and 400mg dose groups of male, respectively. In females of the 200mg and 400mg groups it increased from 1.34 and 1.33 to 1.92 and 2.21 after thirteen months and, thereafter, remained constant. The T4 concentrations, however, remained within the normal range in the two dose groups of male and female before the administration and throughout the follow-up periods.

In Table 4 the nutritional status of the two dose groups of children (200mg and 400mg) are presented. The nutritional status of the children, was categorized as, above -2.00 SD normal nutritional status groups while, below -2.00 SD are malnourished. Before supplementation, 5.0% stunting was shown for both 200mg and 400mg while, wasting was 0.8% for the same dose groups. Nutritional status of the children before intervention was compared with nutritional status after intervention. In the 200mg as well as the 400mg groups, both weight and height of the children were significantly ($p<0.0001$) increased 13 months after intervention when compared with that of before intervention (data not Shown). However, there was no difference in effect of the two doses on nutritional status of the children.

Discussion

Endemic goitre blankets wider areas of Ethiopia where its occurrence has been characterized as iodine deficiency and other factors (1,2,3). Choice of oral iodized oil, in intervention and correction of iodine deficiency, is important where there are difficulties in achieving salt iodation, reaching isolated communities, and where iodine deficiency is so severe that immediate action is required.

This study showed the high rate of reduction in the prevalence of endemic goitre 13 months after administration of oral iodized oil in the two dose groups. The reduction was characterized by either complete regression of the thyroid swelling to the normal state or by reduction in size of the gland. The rate of reduction of the thyroid gland to the normal

state (grade 0) or reduction in size was similar in the two dose groups 13 months after intervention. This clearly confirms that 200mg oral iodized oil is as effective as 400mg in goitre reduction. Similarly, the effectiveness of 200mg oral iodized oil on urinary iodine excretion was reported by study (10) previously reported in Ethiopia. Studies (8,9,11) conducted elsewhere in the other parts of the world also indicated a definite reduction in goitre prevalence after administration of oral iodized oil. However, these studies vary in results of how long the given dose could work in the body and optimal dose that should be recommended. Furthermore, the effectiveness of the low dose (like 200mg) was not considered (7).

The situation after 30 months of administration of two graded doses showed increase in goitre prevalence in some subjects of the study. This may suggest that re-administration of iodized oil could be done not on two-year bases but 13 months after initial administration. This is in line with studies done in other parts of the world (12).

Thyroid hormones (T3 and T4) and TSH serum concentrations were similar for the two dose groups both before and after intervention. The concentrations of these parameters remain within the normal value ranges throughout the follow-up periods except T3 which became above the normal value range 13 months after administration for the two dose groups. Thyroid stimulating hormone is fast responding to the treatment than any other hormones involved in thyroid metabolism in this study. Before intervention, the mean thyroid stimulating hormone concentration was above the normal value range for the 200mg-dose group while for the 400mg it was in the upper limit. At the first month of administration, however, it was reduced one half to one third and remained constant within the normal value range up to 13 months of intervention for the 200mg-dose group. A similar trend was also observed for the 400mg-dose group.

The nutritional status of the two dose groups before and after intervention was compared (Table 4). It was assumed to investigate the difference in effect of the two doses on the nutritional status after intervention. Thyroid hormones are meant to regulate metabolism in the body. When there is shortage of the thyroid hormones in the body due to iodine deficiency the metabolism in the body is affected. The Chi-square value indicated that the base-line information about the nutritional status was similar for the two dose groups. Similarly, the two doses have no difference in effect of the nutritional status of the children. Children of the two dose groups were more wasted after intervention when compared with base-line information for reasons which were not known. It was confirmed that the two graded doses of oral iodized oil had the same effect on goitre treatment, normal bio-formation of the thyroid hormones, and nutritional status of the children for at least 13 months. Salt iodation programme is now interrupted in Ethiopia. There are very many pocket areas where high prevalence of goitre is reported (1,2,3,13). In conditions like this, oral iodized oil could be a better alternative to tackle the problems of goitre in high endemic areas of the country.

Besides, proving the efficacy of the two doses on goitre treatment and thyroid function, the present study also confirms the hypothesis that a 200mg oral iodized oil is as effective as a 400mg oral iodized oil in goitre prophylaxis and hormonal function of the thyroid gland. In addition to this, the use of 200mg oral iodized oil is cheaper than the 400mg dose. Hence, it is recommended that 200mg oral iodized oil be given at least every 13 months for the correction of the thyroid function and control of iodine deficiency in school children.

Acknowledgement

This work was financially supported by the United Nations Children fund (UNICEF).

References

1. Hofvander Y. Endemic goitre among children in the Ethiopian highlands. Ethiopia Med J. 1970;8:179-184.

2. W-Gebriel Z, Demeke T, West CE and Vander Haar F. Goitre in Ethiopia. British

Journal of Nutr. 1993;69:257-68.
3. Tibeb HN, Abuye C, Gebre P and Hailegiorgis B. Pattern of goitre in Sidama awraja in Ethiopia and its relation to piped water supply. East African Medical Journal. March 1993;70(3).
4. Delange F, Bastani S, Benmiloud M, DeMaeyer E, Isayama MG, Koutras D, Muzzo S, Niepomniszcze H, Pandov CS, Riccabona G. Definition of endemic goitre and cretinism, Classification of goitre size and severity of endemia, and survey technique. In: Dunn, JT., Pretell, EA., Daza, CH., Yiteri, FE., eds. To wards the eradication of endemic goitre, cretinism and iodine deficiency. Scientific Publication. No. 502. Washington DC. PAHO/WHO, 1986;373-6
5. Hetzel BS. The prevention and control of iodine deficiency disorders. United Nations Administration Committee on Coordination / Sub-Committee on Nutrition. Nutrition Policy Discussion paper March 1988;No.3.
6. Bautista A, Barker PA, Dunn JT, Sanchez M, Kaiser DL. The effect of oral iodized oil on intelligence, thyroid status and in school age children. from an area of an endemic goitre. Am J Clin Nutr. 1982;35:127-34.
7. Ermans AM, Tanglet R, Tshilembi MM, Bourdoiux P. Control of iodine deficiency through yearly oral administration of small amount of iodized oil. IDD Newsletter 1990;6:No.1.
8. Tai MA. The effect of oral iodized oil on prevention and treatment of endemic goitre. Chine Med J. 1981;61:533.
9. Eltom M, Karlsson FA, Kamal AM, Bostrom H, Dahlberg PA. The effect of oral iodized oil in the treatment and prophylaxis of endemic goitre. J Clin Endocrinol Metab 1985;60:1112-7.
10. Cherinet A, Bantirgu H, Hana NT, Kelbessa U, Haile G. The effect of varying doses of oral iodized oil in the prophylaxis of endemic goitre in elementary school children. Ethiop Med J 1995;33.
11. Boudida A, Bachtazi H, Benmiloud M. Experience with oral iodized oil in Algeria. IDD Newsletter 1985;1:18.
12. Thilly CH, Delange F, Goldstein-Golaire J, Ermans AM. Endemic goitre prevention by iodized oil. A reassessment. J Clin Endocrinol Metab. 1973;36:1196-204.
13. Aberra B, Bantirgu H, Cherinet A. Report on the IDD base line survey conducted prior to the distribution of iodated salt. Ethiopian Nutrition Institute (ENI) (1987/88).