

## Short communication

### Low dose oral iodized oil for control of iodine deficiency in children

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In areas where iodized salt is not available, oral iodized oil is often used to correct I deficiency despite a lack of consensus on the optimal dose or duration of effect, particularly in children, a main target group. Annual doses ranging from 400 to 1000 mg have been advocated for school-age children. Because lower doses of iodized oil have been shown to be effective in treating I deficiency in adults, the aim of this study was to evaluate the efficacy and safety of a low dose of oral iodized oil in goitrous I-deficient children. Goitrous children ( $n$  104, mean age 8.4 years, range 6–12 years, 47% female) received 0.4 ml oral iodized poppyseed-oil containing 200 mg I. Baseline measurements included I in spot urines (UI), serum thyroxine ( $T_4$ ), whole blood thyroid-stimulating hormone (TSH), and thyroid-gland volume using ultrasound. At 1, 5, 10, 15, 30 and 50 weeks post-intervention, UI, TSH and  $T_4$  were measured. At 10, 15, 30 and 50 weeks, thyroid-gland volume was remeasured. At 30 and 50 weeks the mean percentage change in thyroid volume from baseline was –35% and –41% respectively. The goitre rate fell to 38% at 30 weeks and 17% at 50 weeks. No child showed signs of I-induced hypo- or hyperthyroidism. UI remained significantly increased above baseline for the entire year ( $P < 0.001$ ); the median UI at 50 weeks was 97  $\mu\text{g/l}$ , at the World Health Organization cut-off value (100  $\mu\text{g/l}$ ) for I-deficiency disorders risk. In this group of goitrous children, an oral dose of 200 mg I as Lipiodol (Guerbet, Roissy CdG Cedex, France) was safe and effective for treating goitre and maintaining normal I status for at least 1 year.

#### Iodine: Goitre

In western and central Africa it is estimated that 250 million people are at risk for I-deficiency disorders (IDD) and 50 million have goitre (Bailey & Clugston, 1990). A goal of the World Health Organization is global elimination of IDD by the year 2000 through iodine supplementation (World Health Organization, United Nations International Children's Emergency Fund and International Committee on Control of Iodine Deficiency Disorders, 1994). In areas where iodized salt is not available, oral iodized oil is often used to correct I deficiency despite a lack of consensus on the optimal dose or duration of effect, particularly in children, a main target group. Annual doses ranging from 400 to 1000 mg have been advocated for school-age children (Bautista *et al.* 1982; Eltom *et al.* 1985; Benmiloud *et al.* 1994; Furnée *et al.* 1995). The manufacturer of Lipiodol (Guerbet, Roissy CdG Cedex, France), the most widely used oral iodized oil, recommends 600 mg/year for

6–15-year-old children (Lipiodol Scientifique: International Division, 1998). Because of the potential adverse effects of acute high doses of I in I-deficient populations (DeLange, 1998), it is important to give the lowest effective dose. Low doses of iodized oil (118 mg I) have been shown to be effective in correcting I deficiency for 1 year in adults (Tonglet *et al.* 1992). The aim of this study was therefore to evaluate the efficacy of a low dose of oral iodized oil in goitrous, I-deficient children.

#### Materials and methods

The study was done in two villages in the Danané Health District, a mountainous region in the western Côte d'Ivoire. In this area of severe I deficiency, median urinary I excretion in children is 27  $\mu\text{g/l}$  and 45–55% of school-age children are goitrous (Latapie *et al.* 1981; Zimmermann

*et al.* 2000). The study was approved by the Ethical Review Board of the University Hospital of Zürich, Switzerland, the National Institute of Public Health and the Ministry of Research of the Côte d'Ivoire. Informed consent was obtained from the chiefs of the two villages and the families of the individual children.

All children aged 6–12 years ( $n$  419) in the villages were screened for goitre and all goitrous children were then invited to join the intervention study. We enrolled 109 children (mean age 8.4 years, range 6–12 years, 47 % female) and 104 children completed the study to 1 year. Baseline measurements before administration of iodized oil included I in spot urines (UI), serum thyroxine ( $T_4$ ), whole blood thyroid-stimulating hormone (TSH), and thyroid-gland volume using ultrasound (Aloka SSD-500, Mure, Japan). Each child then received 0.4 ml oral iodized poppy-seed-oil (Lipiodol, Guerbet) containing 200 mg I. At 1, 5, 10, 15, 30 and 50 weeks post-intervention, UI, TSH and  $T_4$  were measured. At 10, 15, 30 and 50 weeks, thyroid-gland volume was remeasured. To avoid interobserver variability, all ultrasound measurements were performed by a single investigator (M. Z.). At 10, 15, 30 and 50 weeks height and weight were remeasured to account for the potential effect of growth on thyroid volume.

In countries with a high prevalence of child growth retardation, thyroid volume is considered to be more directly a function of total body surface area than of age. Therefore, body surface area was calculated from weight and height measurements taken with each ultrasound measurement, and current WHO/International Committee on Control of Iodine Deficiency Disorders upper normal limits for thyroid volume in children aged 6–12 years according to sex, age and body surface area were used to define the presence or absence of goitre (World Health Organization/International Committee on Control of Iodine Deficiency Disorders, 1997).

Portions of blood and urine samples were frozen at  $-20^\circ\text{C}$  until analysis. UI was measured using a modification of the Sandell–Kolthoff reaction (Pino *et al.* 1996). Dried blood spots on filter paper were analysed for whole blood TSH and serum  $T_4$  using immunoassay (Torresani & Scherz, 1986).

Normal reference values are: UI 50–250  $\mu\text{g/l}$ ; whole blood TSH  $< 3.5$  mU/l; serum  $T_4$ , 65–165 nmol/l. Normally distributed data were expressed as means and standard deviations and were compared by Student's  $t$  test. Variables not normally distributed (UI, TSH) were expressed as medians (95 % CI) and were compared by Mann-Whitney tests.

## Results and Discussion

At 30 and 50 weeks the mean percentage changes in thyroid volume from baseline were  $-35$  % and  $-41$  % respectively (see Table 1). The goitre rate fell to 38 % at 30 weeks and 17 % at 50 weeks. UI remained significantly increased above baseline for the entire year ( $P < 0.001$ ); the median UI at 50 weeks was 97  $\mu\text{g/l}$ , at the WHO cut-off value (100  $\mu\text{g/l}$ ) for IDD risk. Baseline and follow-up median TSH and mean serum  $T_4$  were within the normal range in both groups. Although there was a small transient increase in mean TSH at 1 week after I, values at 5, 10, and 15 weeks were reduced significantly ( $P < 0.05$ ) compared with baseline. No child showed signs of I-induced hypo- or hyperthyroidism.

Previous studies of oral iodized oil in children have generally given doses  $>2$ -fold higher than the 200 mg I used in this study. Based on studies in Bolivian children, Bautista *et al.* (1982) recommended annual doses of 700–1000 mg oral I. In a study by Benmiloud *et al.* (1994) comparing different doses of oral iodized oil in I-deficient Algerian children aged 6–11 years, oral I doses of 480 and 960 mg were effective at maintaining adequate UI excretion ( $>50$   $\mu\text{g/l}$ ) for 1 year. An oral dose of 240 mg I maintained urinary excretion  $>50$   $\mu\text{g/l}$  for at least 6 months, but there was no significant decrease in mean thyroid volume after treatment (Benmiloud *et al.* 1994). In I-deficient schoolchildren in the Sudan, an oral dose of 400 mg I significantly decreased goitre prevalence and maintained adequate UI excretion for 1 year (Eltom *et al.* 1985). In I-deficient 8–10-year-old Malawian children, a single 490 mg dose of I as oral iodized oil (Lipiodol, Guerbet) maintained adequate UI excretion ( $>50$   $\mu\text{g/l}$ ) for only 14 weeks, whereas an oral dose of 675 mg I as

**Table 1.** Changes in thyroid size, goitre prevalence, urinary iodine, thyroid-stimulating hormone (TSH) and thyroxine ( $T_4$ ) in goitrous children after receiving 200 mg oral iodine

(Mean values and standard deviations or medians and 95 % confidence intervals for 104 children)

Time after oral iodine	Thyroid volume (ml)		Change in thyroid volume from baseline (%)†		Prevalence of goitre (%)	Urinary iodine ( $\mu\text{g/l}$ )		TSH (mU/l)		$T_4$ (nmol/l)	
	Mean	SD	Mean	SD		Median	95 % CI	Median	95 % CI	Mean	SD
Baseline	8.3	2.0			100	28	29, 46	1.0	0.9, 1.4	121	26
1 week						1100***	1192, 2015	1.6	1.4, 2.2	123	25
5 weeks						324***	302, 412	0.6*	0.5, 0.7	107	21
10 weeks	6.5***	2.1	-21	18	64	171***	169, 252	0.7*	0.6, 0.9	105	25
15 weeks	5.6***	1.8	-31	16	47	178***	167, 244	0.6*	0.5, 0.9	109	20
30 weeks	5.4***	1.7	-35	15	38	135***	122, 163	0.8	0.7, 1.1	133	30
50 weeks	4.9***	1.6	-41	13	17	96***	87, 118	0.8	0.7, 1.2	132	34

Mean or median values were significantly different from values at baseline, \* $P < 0.05$ , \*\*\* $P < 0.001$ .

† To reduce the effects of variability among individuals, percentage change in thyroid volume from baseline was calculated for each child before deriving means. Thyroid volume was not measured at 1 and 5 weeks.

triacylglycerol esters of iodized fatty acids (Oriodol, Guerbet) maintained adequate UI excretion for 1 year (Furnée *et al.* 1995). Varying conditions in these studies (age and number of subjects, severity of I deficiency, location, ultrasound *v.* palpation for goitre grading) make it difficult to compare results.

Because of the potential adverse effects of acute doses of I in I-deficient populations, it is important to give the lowest effective dose. The most common serious complication observed in areas of endemic goitre during introduction of I is a transient increase in I-induced hyperthyroidism, which affects mainly older adults and those with nodular goitres (DeLange, 1998; Stanbury *et al.*, 1998). In previous studies in I-deficient children using higher doses of oral iodized oil, side effects have been reported in up to 4% of children (Eltom *et al.* 1985; Benmiloud *et al.* 1994). In the present study, no child showed signs of I-induced hypo- or hyperthyroidism. This difference may be due to the use of a lower dose of I in a study population of children with small-to-moderately-sized, non-nodular goitres.

In this area of the Côte d'Ivoire, nearly half of school-age children suffer from goitre. Severe I deficiency is compounded by high intakes of cassava and elevated urinary thiocyanate (SCN) excretion; median UI : SCN ratio in urine is  $< 2 \mu\text{g}/\text{mg}$ , indicating increased risk for exacerbation of goitre by thiocyanate (Bourdoux *et al.* 1978). Other nutritional factors which may impair thyroid metabolism are common: the children are severely Se deficient (mean serum Se  $< 15 \mu\text{g}/\text{l}$ ) and 27% suffer from Fe-deficiency anemia (Zimmermann *et al.* 2000). Despite these unfavorable conditions, a low oral dose of 200 mg I was safe and effective for treating goitre and maintaining normal I status for at least 1 year.

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