Efficacy of oral iodised oil is associated with anthropometric status in severely iodine-deficient schoolchildren in rural Malawi

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The effect of anthropometric status on the efficacy of an oral supplement of iodised oil (1 ml Lipiodol Ultrafluide, 490 mg I; Laboratoire Guerbet, Aulnay-sous-Bois, France) was examined in 8–10-year-old schoolchildren (*n* 197) of Ntcheu, a severely I-deficient district of Malawi. The study was a controlled trial using the I concentration of casual urine samples to monitor the I status. The median urinary I concentration increased from 0·15 μmol/l at baseline (51·3 % of children < 0·16 μmol/l, 89·7 % < 0·40 μmol/l, 95·7 % 0·79 μmol/l) to 0·32 μmol/l at 40 weeks (29·1 % of the children < 0·16 μmol/l, 71·0 % < 0·40 μmol/l, 96·1 % < 0·79 μmol/l) while the total goitre prevalence fell from 63 % to 21 %. Variables of efficacy were estimated from a hyperbolic function describing the longitudinal pattern of urinary I excretion after the dose. The I retention and I elimination rate, and the periods of protection from mild (< 0·79 μmol/l) or moderate (< 0·40 μmol/l) I deficiency were obtained for groups of children with differing anthropometric status at baseline. Initial height-for-age and mid upper-arm circumference were not significantly related to efficacy. However, both the I retention and I elimination rate were reduced in children with lower initial weight-for-height. Children with lower skinfold thickness at baseline also had reduced I retention, which resulted in shorter protection periods from recurrent moderate and mild I deficiency. The efficacy of the oral iodised-oil supplement was not related to changes in anthropometric status during follow-up, nor was it related to the consumption of a food supplement of 1610 kJ immediately before the iodised-oil dose. Very low (< 0·16 μmol/l) urinary I concentration, and the presence of goitre at baseline were both associated with higher I retention and elimination rate. Children with goitre at baseline were found to have a prolonged duration of protection against recurrent moderate I deficiency. We conclude that in apparently healthy schoolchildren in I-deficient areas, general anthropometric status has a little influence on the efficacy of oral iodised oil for correcting I deficiency.

Iodine deficiency: Oral iodised oil: Urinary iodine excretion

Iodised salt is the most cost-effective programme option for the supply of I to large populations but in cases of immediate need or ineffective entry of iodised salt into remote, I-deficient areas, supplementation with iodised oil is the main alternative. Oral administration of iodised oil has economic and practical advantages over injection. However, large variations in efficacy after oral iodised oil have been reported (Watanabe *et al*. 1974; Bautista *et al*. 1982; Eltom *et al*. 1985; Benmiloud *et al*. 1994; Elnagar *et al*. 1995; Kywe-Thein, Tin-Tin-OO, Khin-Maung-Niang, J Wrench and IH Buttfield, unpublished results) which may be due to factors associated with the host, the environment and the preparation. Host factors include age and sex and the physiological needs of growth, pregnancy and lactation, and possibly nutritional status. To study the impact of the energy balance a carbohydrate-rich drink was provided to a subgroup of children. The aim of the present study was to evaluate the effect of anthropometric status and energy balance in schoolchildren on I retention and elimination rate, and duration of protection after an oral dose of iodised oil. Understanding the factors that influence the efficacy of oral iodised oil should contribute to improved procedures for protecting populations against I deficiency.

Materials and methods

Subjects

Subjects in this study were schoolchildren aged 8, 9, and 10 years attending four primary schools in Ntcheu District,

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Malawi. Approval of the Human Ethics Committee of Wageningen Agricultural University as well as the Netherlands Foundation for Scientific Research was obtained prior to the onset of the study. After approval by the Ethics Committee of the National Council for Medical Research in Malawi, the National Health authorities selected the schools on the basis of having a sufficient number of pupils and their easy access from the main trunk road connecting the three regions of the country.

In Ntcheu District, which is mountainous, the majority of inhabitants have an income from farming and more than 90 % of the people suffer from I deficiency of which approximately 50 % can be classified as severely I deficient.

The ages of the children were obtained from the school records, and double-checked by questionning parents or guardians, and with records of the under-five clinics. In case of doubt the child was either asked to grasp an ear with the arm fully over the head to rule out younger children or checked for signs of puberty in case of older children. Informed consent was obtained from the parents or guardians for each participating child. As only apparently healthy children were considered eligible, all pupils were examined by a medical assistant from Ntcheu District Hospital. Those with a significantly enlarged liver or spleen, indicative of disease which may interfere with fat or protein metabolism, or with a mid upper-arm circumference below 15·5 cm, indicative of protein–energy malnutrition, were excluded from the study (*n* 16). Stool samples were examined by a microscope for intestinal parasites and infected children received appropriate anti-parasitic treatment 2 weeks prior to inclusion in the study.

Study design

Data for this report were obtained as part of a series of studies, carried out during February–December 1991 in Malawian schoolchildren, on factors that may influence the efficacy of oral iodised oil (Furnée *et al.* 1995). A total group of children (*n* 237), selected from the school registry, participated in the present study. A subgroup of thirtyfive children was randomly divided, by age and sex group to receive 1 ml of neutral poppy-seed oil as placebo at entry into the study and 1 ml oral iodised oil after 44 weeks follow-up. The remaining group of pupils (*n* 202) received 1 ml Lipiodol Ultrafluide orally (490 g I/l, Laboratoire Guerbet, Aulnay-sous-Bois, France) by use of a glass dispenser (Englass Dispensing Devices, The English Glass Co. Ltd., Leics., UK). Within this group a subgroup (*n* 37) of children was randomly selected, by drawing numbers, to consume a carbohydrate-rich drink (Fantomalt, 100 g in 100 ml water, 1610 kJ; Nutricia, Zoetermeer, The Netherlands) 15–30 min prior to swallowing the iodised-oil supplement. Power calculation using the standard deviation associated with mean urinary I excretion in three casual urine samples collected on three consecutive days, a confidence level of 95 %, a precision level of 5 %, and a sample size selection of 90 % was used to establish the sizes of both subgroups.

Urinary I excretion was estimated from the average concentration of I in three casual urine samples collected on three consecutive days. The I : creatinine ratio in casual urine samples was not used because prior research showed a significant correlation between this ratio and the creatinine concentration and was therefore not suitable (Furnée *et al.* 1994). It was not possible to collect 24 h samples. The urine samples were obtained in the morning at school under supervision of field assistants. The initial I status of each subject was assessed from urine collected on the two consecutive days prior to the day of iodised oil administration. During the 4th, 8th, 20th, 40th and 44th week after supplementation, urine was obtained on three consecutive days. The average I concentration at each time point was used for data analysis.

The size of the thyroid gland was graded by palpation as recommended by the World Health Organization (Delange *et al.* 1986). Goitre grading of all children was done by the same medical assistant from Ntcheu District Hospital before and 40 weeks after oral oil administration. This person was not informed of the allocation of children to the various treatment schedules. Cross checks were done by one of the authors (C.A.F.) who had no direct access to the treatment schedules or previous results. In case of doubt the lowest goitre grade was recorded.

Anthropometry

Body weight, standing height, mid upper-arm circumference, and biceps, triceps, subscapular and suprailiac, skinfold thicknesses were measured as described by Jelliffe & Jelliffe (1989). The same person took all anthropometric measurements throughout the study. Body weight with minimum clothing and no shoes on was read to the nearest 0·1 kg in duplicate, from one digital electronic scale, which was periodically checked for its accuracy by calibration weightings. Heights were measured to the nearest 0·1 cm in duplicate by a Microtoise (steel measuring tape; Stanley Tools, Ashton-Under-Lyne, Lancs., UK), using a portable hardwood board with foot board (90°) to support the standing body position. Mid upper-left-arm circumference was taken to 0·1 cm halfway between the acromion process of the scapula and the olecranon process of the ulna in triplicate using a flexible tape. The four skinfold thickness measurements were taken in triplicate to 0·2 mm on the left side of the body with a Harpenden calliper (Holtain Ltd, Crymmych, Wales, UK) set at zero before each measuring session. Only one weighing scale, one Microtoise, one flexible tape and one calliper were used for taking the anthropometric measurements. Calibration and adjustment at regular time intervals monitored the technical performance of the measurement equipment. The measurement precision (e.g. CV between duplicate readings < 5 % for weight, height and arm circumference and < 10 % for each skinfold thickness) and accuracy (e.g. CV between readings by observer and supervisor < 10 % for weight, height and arm circumference, and < 10 % for skinfolds thicknesses) were found satisfactory at each round.

Urine analysis

Urine samples, preserved with thymol, were sent to the Department of Human and Animal Physiology of Wageningen Agricultural University, The Netherlands, where they

were stored at −20°C before laboratory analysis. I was assayed after alkaline digestion by using the Sandell–Kolthoff reaction (Sandell & Kolthoff, 1937; Benotti *et al*. 1965; Moxon & Dixon, 1980) adapted for use with a micro-titre plate reader (Thermomax; Molecular Devices Corp., Palo Alto, CA, USA) coupled to a personal computer equipped with special software (Softmax; Molecular Devices Corp.). Samples were assayed in duplicate and when measurements differed by $> 10\,\%$ from their mean, the duplicate analysis was repeated. The average of duplicate measurements was used in data analysis. The smallest detectable concentration was 0·04 μmol/l and precision was ⩽0·012 μmol/l. The laboratory participated in the sample exchange and quality control programme from the Center for Disease Control and Prevention, Atlanta, GA, USA. The mean recoveries of added iodate and iodide were 100 (range 95–105) and 97 (range 92–100) % respectively. The assay method was confirmed to be insensitive to interference by thiocyanate.

Statistical analysis

Only the data of children from whom urine samples were obtained at least at four time points during follow-up were included in the analysis. Thus, the results in this report are based on 197 I-supplemented children (thirty-five of whom consumed a food supplement), and another thirty-three whom received a placebo (poppy-seed oil).

Z-scores for height-for-age and weight-for-height were calculated using National Committee on Health Statistics reference data (World Health Organization, 1983). Children were grouped on the basis of their anthropometric data at baseline into one of three classes as follows: group means and standard deviations were obtained and the child's anthropometric index was classified as either 'high' (value above mean + 1 SD); 'medium' (value between mean + 1 SD and mean − 1 SD); or 'low' (value below mean − 1 SD). To study the effect of a change in anthropometric status, a repeated measurement obtained 8 weeks after supplementation was subtracted from the baseline result and the difference between the measurements was classified as described earlier.

The time pattern of urinary I responses to oral iodised-oil supplementation can most efficiently be described by a hyperbolic function (Furnée *et al*. 1995). This model, which reflects the mutual effects of all physiological mechanisms involved in I retention and elimination, allows the estimation of an I retention and elimination rate associated with a particular group characteristic, dose or procedure. In the present study, the association of the urinary I patterns with anthropometric status indices was analysed by the equation:

$$I_{(T,x)} = (\alpha_0 + \alpha_{1,2}.x)\ T^{-(\beta_0 + \beta_{1,2}.x)},$$

where I is the urinary I concentration (μmol/l); T is the time point (weeks) after oral dosing; x is the anthropometric status class (dummy variable) under consideration; α is the I retention capacity for subjects with a anthropometric status index classified in the 'medium' (α_0), 'low' (α_1) or 'high' (α_2) group respectively; β is the I elimination rate for subjects with a anthropometric status index classified in the 'medium' (β_0), 'low' (β_1) or 'high' (β_2) groups.

In a similar fashion, the model was used for evaluating the urinary I patterns for the presence (α_1, β_1) or absence (α_0, β_0) at baseline of goitre, urinary I ⩾ or < 0·16 μmol/l and consumption or not of a food supplement.

The variables of the hyperbolic functions were computed by maximum likelihood (Kleinbaum *et al*. 1988). Asymptotic Student's t values were used to test the significance of differences between the variables α_0, $(\alpha_0+\alpha_1)$ and $(\alpha_0+\alpha_2)$; and β_0, $(\beta_0+\beta_1)$ and $(\beta_0+\beta_2)$ respectively. The goodness of fit (adjusted R^2) was obtained from the correlation coefficient of the model.

The estimated I retention and elimination rate for a given group were used to calculate the time duration T* that the urinary I concentration in the group remained above I*, the level indicative for I deficiency. I* was evaluated at 0·79 and 0·40 μmol/l, suggested as cut-off levels for mild or moderate deficiency respectively (World Health Organization/United Nations International Children's Emergency Fund/International Council for Control of Iodine Deficiency Disorders, 1994).

Results

General anthropometric status and I indices before and at 40 weeks after oral supplementation with either iodised oil or neutral poppy-seed oil are shown in Table 1. For all pupils combined, the initial median urinary iodine concentration was 0·15 μmol/l, indicating that the population in the area was severely I deficient (World Health Organization/United Nations International Children's Emergency Fund/International Council for Control of Iodine Deficiency Disorders, 1994). The total goitre prevalence of all children at baseline was 62·5 %. Anthropometric indices weight-for-height and height-for-age demonstrated a sizeable linear growth deficit, or stunting, while body proportions in the children were relatively well preserved.

General anthropometric status indices of the study and placebo groups were comparable before the study as well as at completion. During the study period, mean body weight and mean height (5·1 % and 2·6 % respectively) increased and mid upper-arm circumference remained stable, while skinfold thickness decreased in both the study ($P < 0{\cdot}001$) and placebo groups. Both the study group and the placebo group remained comparable with regard to the nutritional variables under study. The median urinary I concentration of the study group was elevated ⩾ 0·16 μmol/l throughout 40 weeks of follow-up but in the placebo group, urinary I remained low as at baseline. A reduction of total goitre to one-third of initial was observed in the group of children that had received oral iodised oil while the baseline prevalence of 60 % goitre in the placebo group persisted during the 40 weeks.

For the total group of 197 children receiving oral iodised oil, irrespective of anthropometric status, the I retention α was 1·37 μmol/l and elimination rate β was 0·48 μmol/l per week, which resulted in a period of protection against recurring severe to moderate I deficiency (< 0·40 μmol/l) of 13·7 weeks.

The variables (retention ($\alpha_{1,2}$) and elimination rate ($\beta_{1,2}$)

Table 1. General anthropometric and iodine status of 8–10-year-old schoolchildren from Ntcheu, Malawi, before and 40 weeks after receiving either oral iodised oil* or neutral poppy-seed oil

(Mean values and standard deviations)

	Iodised oil (*n* 197)				Poppy-seed oil (*n* 33)			
	Baseline		40 weeks		Baseline		40 weeks	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Body weight (kg)	25·3	3·6	26·7	4·0	25·2	3·9	26·1	3·3
Height (cm)	126·2	7·1	129·6	7·2	127·2	6·4	130·1	6·5
Height-for-age (Z-score)	–1·4	1·1	–1·7	0·9	–1·5	1·0	–1·6	1·0
Weight-for-height (Z-score)	–0·2	0·7	–0·2	0·9	–0·2	1·0	–0·2	1·0
MUAC (cm)	18·2	1·4	18·1	2·8	18·1	1·0	8·1	1·1
Sum of skinfold thicknesses† (mm)	20·8	7·5	18·6	4·4	19·8	3·5	18·3	3·2
Urinary iodine (mmol/l)‡	0·15 (0·11, 0·23)		0·32 (0·16, 0·54)		0·19 (0·10, 0·54)		0·16 (0·07, 0·30)	
$<$ 0·79 mol/l (%)	95·7		96·1		94·3		95·3	
$<$ 0·40 mol/l (%)	89·7		71·0		91·1		92·0	
$<$ 0·16 mol/l (%)	51·3		29·1		51·7		53·1	
Total goitre (%)	62·9		20·8		60·0		65·7	

MUAC, mid upper-arm circumference.
* Oral iodised oil: 1 ml Lipiodol Ultrafluide (490 mg I; Laboratoire Guerbet, Aulnay-sous-Bois, France).
† Biceps, triceps, subscapular and suprailiac sites.
‡ Median values with 25th and 75th percentiles in parentheses.

which are used to calculate the duration of effectiveness ($T_{1,2}$) for groups of children with different initial anthropometric status are given in Table 2. The indicators height-for-age and mid upper-arm circumference did not reveal a consistent association with either I retention or elimination and hence duration of effectiveness. Subjects with high weight-for-height, however, demonstrate an increase in both the I retention and elimination rate which result in a difference in the duration of effectiveness of oral iodised oil (high ($T_2 = 21{\cdot}3$ weeks) *v.* low ($T_1 = 14{\cdot}6$ weeks), $P < 0{\cdot}01$). For children with low initial weight-for-height, the periods T* of protection against recurring mild or moderate I deficiency were 1·8 and 6·7 weeks shorter than for children with high weight-for-height but this difference is not statistically significant ($P = 0{\cdot}081$).

Pupils with low skinfold thicknesses showed a reduction in I retention ($P < 0{\cdot}05$) compared with their peers while the elimination rate did not differ. The periods of protection

Table 2. Variables of efficacy of oral iodised oil and initial anthropometric status of 8–10-year-old schoolchildren (*n* 197) in Ntcheu, Malawi†

Initial nutritional status classification‡	Height-for-age (Z-score)	Weight-for-height (Z-score)	Mid upper-arm circumference (cm)	Skinfold thickness (mm)
Retention (μmol/l urine)				
Low (α_1)	1·04	–0·01	6·90*	1·93*
Medium (α_0)	1·27*	0·93*	7·22*	2·71*
High (α_2)	1·23	3·36*	6·92*	2·69*
Elimination rate (μmol/l urine per week)				
Low (β_1)	–0·14	0·07	2·15*	0·57
Medium (β_0)	–0·03	0·35*	2·25*	0·58*
High (β_2)	–0·02	0·77*	2·16*	0·57
Goodness of fit (R^2)	0·15	0·17	0·17	0·18
Protection periods (weeks)§				
Low (T_1)				
Mild	4·6	3·7	4·0	3·1
Moderate	17·4	14·6	15·2	13·0
High (T_2)				
Mild	2·9	5·5	3·7	5·6
Moderate	13·3	21·3	16·9	20·6
High minus low ($T_2 - T_1$)				
Mild	–1·7	1·8	–0·3	2·5
Moderate	–4·11	6·7	1·7	7·6
P-value				
Mild	0·196	0·207	0·752	0·018
Moderate	0·162	0·081	0·572	0·018

Values were significantly different from zero (Student's *t* test): *$P < 0{\cdot}05$.
† Subjects received 1 ml Lipiodol Ultrafluide orally (490 mg I; Laboratoire Guerbet, Aulnay-sous-Bois, France). For details of circulation of variables of efficacy see pp. 347–348.
‡ Low, measurement < -1 SD; high, measurement $> +1$ SD; medium, measurement $\geqslant -1$ SD, $\leqslant +1$ SD).
§ At 0·79 (mild I deficiency) and 0·40 μmol I/l urine (moderate I deficiency).

Table 3. Variables of efficacy of oral iodised oil and initial urinary iodine excretion, goitre and food supplementation of 8–10-year-old schoolchildren (*n* 197) in Ntcheu, Malawi†

	Initial urinary iodine (μmol/l)		Goitre		Food supplement‡	
	< 0·16	⩾ 0·16	Present	Absent	Given	Not given
n	101	96	124	73	35	162
Retention (μmol/l urine)	1.47*	0.91*	1.64*	1.72*	2.09*	1.52*
Elimination rate (μmol/l urine per week)	0.48*	0.40*	0.61*	0.46*	0.62*	0.51*
Goodness of fit (R^2)	0.14		0.20		0.17	
Protection periods (weeks)§						
Mild	3.6	1.4	5.4	3.3	0.7	4.9
Moderate	15.7	8.5	25.4	10.6	14.8	15.6
Difference						
Mild	2.2		2.1		−1.3	
Moderate	7.2		14.7		−0.8	
P value						
Mild	0.236		0.326		0.378	
Moderate	0.115		0.025		0.750	

Values were significantly different from zero (Student's *t* test): *$P = 0.05$.
† Subjects received 1 ml Lipiodol Ultrafluide orally (490 mg I; Laboratoire Guerbet, Aulnay-sous-Bois, France). For details of circulation of variables of efficacy see pp. 346–347.
‡ Fantomalt (100 g + 100 ml water (1610 kJ); Nutricia, Zoetermeer, The Netherlands).
§ At 0·79 (mild I deficiency) and 0·40 μmol I/l urine (moderate I deficiency).

against recurring mild or moderate I deficiency were shorter ($P < 0.05$) by 2·5 and 7·6 weeks respectively, for children with lower initial skinfold thicknesses.

Although children with severely deficient initial urinary I concentrations had a higher I retention and elimination rate (both $P < 0.01$), urinary I classification at baseline was not significantly associated with the duration of protection (Table 3). I retention ($P = 0.05$) and elimination rate ($P < 0.001$) were significantly greater in children with goitre at baseline and the protection periods against recurring mild or moderate I deficiency were 2·1 and 14·7 weeks ($P < 0.05$) longer compared with children without goitre. Consumption of a food supplement prior to dosing with oral iodised oil was found to have no effect on the efficacy.

Changes in weight, height-for-age, weight-for-height or skinfold thickness during the first 8 weeks of follow-up did not affect the parameters of efficacy (results not shown). Children whose mid upper-arm circumference decreased in the first 2 months after the dose were, however, found to have lower I retention and elimination rate compared with those with stable and increased mid upper-arm measurements, but these differences were not significant. The reduced duration of protection in these children (−2·0 and −6·0 weeks respectively) was significant ($P < 0.05$).

The various estimates for goodness of fit indicated that 15–20 % of the variation in urinary I concentrations among children was statistically explained by the variables under study.

Discussion

Although the use of oral iodised-oil supplements in schoolchildren was pioneered in the early 1970s (Watanabe *et al.* 1974) and found useful in correcting I deficiency, only limited information had been collected at the time of this study about factors that may determine the efficacy. In a study in severely deficient schoolchildren (Bautista *et al.* 1982) from Bolivia, an oral dose of 475 mg I as iodised oil failed to secure adequate urinary I levels at 6-months follow-up. From 24 h urine collected in the first week after an iodised-oil supplement containing 470 mg I was given to mildly deficient male adults, it was observed that half of the I dose was lost from the body in the first 2 d after oral supplementation which compared unfavourably to injection (W Lianfang, S Maoyi, W Shenling and Z Zougying, unpublished results). Eltom *et al.* (1985), however, showed that a single oral iodised oil dose of 400 mg I raised mean urinary I levels above 100 μg/g creatinine for ⩾ 2 years in mildly deficient schoolchildren from rural Darfur, Sudan. A review (Dunn, 1987) of ten studies in various age and sex groups with doses ranging between 240 and 960 mg I from different iodised vegetable oils suggested that the observed periods of protection after oral dosing were roughly related to the severity of initial I deficiency.

Correction of I deficiency has priority in countries where I deficiency disorders in the population are acknowledged as a serious obstacle to development efforts. Malawi in the Rift Valley of East Africa is among the countries of the world that are most severely affected and Ntcheu District, Central Region, is a very severely deficient area in the country. Because the implementation of universal salt iodination encountered delay in providing relief, iodised oil was used as a temporary alternative measure for the most affected population groups. In special campaigns during the 1980s, the Ministry of Health administered more than 65 000 parenteral doses of iodised oil to goitrous persons. Concerns about issues such as costs, inequity, potential hazards and long-term durability of this strategy were at the basis of the present study. Children of primary school age who are more sensitive to I deficiency and its correction were easily accessible in Ntcheu district for a study of factors that may influence the efficacy of oral iodised oil under conditions characteristic of Malawi.

Following the urinary I excretion patterns after a supplement has proved useful for assessing the efficacy of iodised oil in correcting I deficiency. Large variations in urinary I

among individuals after an oral supplement (Watanabe *et al*. 1974; Bautista *et al*. 1982; Eltom *et al*. 1985; Benmiloud *et al*. 1994; Elnagar *et al*. 1995; Kywe-Thein, Tin-Tin-OO, Khin-Maung-Niang, J Wrench and IH Buttfield, unpublished results) have made definitive recommendations about the optimal dose, procedure and preparation more difficult, however. For definition of the temporal I status, the median concentration of a population is sufficiently reliable (World Health Organization/United Nations International Children's Emergency Fund/International Council for Control of Iodine Deficiency Disorders, 1994). If cross-sectional analysis is applied to define the point of time at which deficiency re-occurs in intervention studies, timing of urine sampling at follow-up becomes more critical for precision. Thus, a model that describes the longitudinal urinary I pattern is preferable. Because such a model allows the input of observations collected at any given point in time, timing of urine sample collection in individuals becomes less critical. For estimating the period that urinary I remains elevated, a model also requires only a limited number of urine samples during follow-up. In our studies of oral iodised oil supplementation of schoolchildren in Malawi (Furnée *et al*. 1995), a hyperbolic function was found to best describe the pattern of I excretion over time. In the present report, the model was applied to assess the effect of general and I anthropometric status on the efficacy of 490 mg I given as iodised ethyl esters of poppy-seed oil. Description of nutritional and I status at baseline and 40 weeks after supplementation confirmed that the children were from a severely I-deficient area and that the single oral iodised-oil dose was effective in increasing the median urinary I concentration and reducing goitre.

Anthropometric status of school-aged children is most conveniently described by anthropometric data that reflect previous linear growth and current body leanness and fatness (Jelliffe & Jelliffe, 1989). Neither height-for-age, an index for previous growth stunting, nor mid upper-arm circumference, indicative of muscle mass, were found to be related to the efficacy of oral iodised oil. In contrast, both weight-for-height, an index of body leanness–fatness, and skinfold thickness which assesses the size of the body fat stores more directly were related to the I retention, elimination rate and duration of effect. For weight-for-height, the quantitative effect was stepwise and in children with lower initial weight-for-height, both the I retention and elimination rate were found to be rather ambiguous.

Since the effect of skinfold thickness showed that I retention in the leaner children was reduced as compared to other children while the I elimination rate at all skinfold thickness levels were comparable, we conclude that low body-fat reserves were associated with a diminished efficacy of oral iodised oil in thin children.

It is important to point out that anthropometric measurements are not very precise measurements and that they are prone to considerable unintended measurement errors. Although we have done the utmost to limit the measurement errors characteristic of anthropometry we need to point out the limitations of our anthropometric measurements, especially with regard to their effect on the outcomes of calculating other indirect body composition indices. Indirect indices, such as arm-fat area and arm-muscle area by themselves or in relation to other anthropometric indices such as height, may in theory provide a more detailed description of body composition. These indirect indices, if error free, would greatly contribute to a more detailed investigation into the role of body composition in I retention and elimination. However, in our experience of measuring schoolchildren both in the Netherlands and in Malawi, the calculation of indirect anthropometric indices from the actual anthropometric measurements often results in an accumulation of respective measurement errors. In this case the correlation of indirect indices of the body composition with explanatory variables may become a matter of chance. For this reason we have chosen to work with the actual anthropometric measurements weight, height, mid-upper arm circumference, and four skinfold thicknesses.

So far, no direct information has been published about possible storage sites of I other than the thyroid after oral iodised-oil administration in human subjects. Reichel & Seer (1970) studied the absorption of Lipiodol (Laboratoire Guerbet) in the lymph of cats using X-ray photography, concluding that the uptake and metabolism of iodised oil from the gut was analogous to that of other dietary fats. An increase in I concentration of body fat has been demonstrated in rabbits, rats and mice after oral iodised oil and iodofat, a preparation of sodium salts of iodised fatty acids (Van der Heiden *et al*. 1989; W Lianfang, S Maoyi, W Shenling and Z Zougying, unpublished results). The results of our present study suggest that in human subjects, iodised oil may also be stored by body fat since the children with a lower amount of subcutaneous adipose tissue ('low' sum-of-skinfold-thicknesses) demonstrate reduced I retention and a reduced duration of protection after oral iodised-oil administration. Although the importance of the adipose tissue as a storage site for iodised fatty acids may be limited compared to the thyroid gland itself, it may play an important role in prolonging the presence of I in the body since I uptake by the thyroid gland, after giving a large dose of I, is not unlimited. In our study the initial skinfold thickness did not seem to have an effect on the elimination rate of the I after oral dosing. Further research, using larger groups of subjects or more sensitive indicators, may provide more insight in the elimination process of excess I after oral iodised-oil administration.

Initial I status as indicated by goitre or very low urinary I concentration was related to I retention, elimination rate and duration of protection. An increase in I retention by goitrous subjects may be due to the greater thyroidal I clearance rate which occurs when the thyroid gland is enlarged to compensate for I deficiency (Koutras, 1986; Ingbar, 1989). In addition, a significant increase in I elimination rate was observed in goitrous children. Because no side-effects of the I dose became apparent during the study, it is postulated that the increased elimination rate may be associated with an adjustment by the thyroid gland to its higher I content.

A food supplement consumed 15–30 min prior to supplementation with oral iodised oil did not influence the variables of efficacy. Because the iodised oil dose was supplied in the form of a vegetable oil, it was thought that the rapid renal I excretion observed in previous studies may have been due in part to rapid lipolysis and β-oxidation of newly

absorbed fat when subjects were catabolic. The lack of effect of a 1610 kJ supplement suggests that the metabolic state of children at dosing was of no significance to the efficacy or that, contrary to expectations, other children also arrived at school in an anabolic state.

The period of protection against recurrent I deficiency in this study was very short in comparison to other studies in schoolchildren (Watanabe *et al*. 1974; Eltom *et al*. 1985; Benmiloud *et al*. 1994) who were supplemented with oral Lipiodol Ultrafluide (Laboratoire Guerbet). In schoolchildren from a mildly I-deficient area in Sudan (Eltom *et al*. 1985), an oral dose of 400 mg I was shown to provide protection for at least 1 year. A recent study in Algerian schoolchildren with moderate I deficiency (Benmiloud *et al*. 1994) reported that 480 mg I provided an interval of about 6 months before return of median urinary I levels below 0·79 μmol/l, whereas in the severely I-deficient children from Malawi protection from the same dose lasted only 3 months. Because goitrogenic factors may have played a role, analyses of thiocyanate were performed in remaining urine samples of seventy-nine children after the fieldwork was completed. The results indicated normal thiocyanate levels (34·2 (SD 27·3), range 2·6–166·4 μmol/l) which rule out the possibility that cassava consumption might have been the cause for the diminished protection period in this study. Initial body weight and height, and growth performance during follow-up in the Malawian children were similar to those from Algeria, indicating that different general anthropometric status did not provide a likely cause for the observed differences.

Results of this present study suggest that the size of the body fat depot, as measured by the sum of skinfold thicknesses, may have some influence on the efficacy of oral supplementation with iodised oil. In efforts to increase the effectiveness of I-deficiency-disorder programmes, it may be worthwhile considering this finding when planning prophylaxis with iodised oil. In countries where the anthropometric status of the people is poor and fluctuates with the seasons, oral iodised oil should preferably be given when anthropometric status is at its best.

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