

IODINE SUPPLEMENTATION IN IODINE-DEFICIENT HYPOTHYROIDISM AND SUB-CLINICAL HYPOTHYROIDISM

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ABSTRACT

Objective: To see the effect of iodine supplementation in iodine-deficient hypothyroidism and sub-clinical hypothyroidism.

Design: This is a cross sectional prospective study.

Setting: Thyroid Clinic of Centre for Nuclear Medicine & Ultrasound, Khulna (CNMU, Khulna) run jointly by CNMU, Khulna and Medicine department of Khulna Medical College, Khulna for a period of 3 years from January 2001 to December 2003.

Subjects: Patients were selected from the Thyroid Clinic. Inclusion criteria were (1) presence of goitre, (2) normal or low T4 and high TSH level and (3) high two hours and 24 hours radioactive iodine uptake.

Main outcome variables: Percentage of euthyroidism with iodine supplementation in iodine-deficient hypothyroidism and sub-clinical hypothyroidism. Changes in goitre grade, thyroid volume, serum T4 & TSH.

Results: Out of fifty-seven patients, 42 (73.7%) resumed euthyroidism with iodine supplementation alone and 15 (26.3%) needed thyroid replacement along with iodine supplementation. Regarding the goitre grade and thyroid volume, out of 6 goitre grade 1B, two (33.3%) remained goitre 1B, three (50%) had grade 1A and one (16.7%) had goitre grade 0 respectively and out of 51 goitre grade 2, six (11.8%) remained grade 2, 32 (62.7%) had grade 1B and 13 (25.5%) had grade 1A goitre respectively with overall reduction of thyroid volume from 24.60 ± 6.07 ml to 16.86 ± 3.23 ml i.e., reduced by 31.5%. Regarding the biochemical status, mean T4 increased from 65.65 ± 27.32 to 89.59 ± 21.69 nmol/L & mean TSH decreased from 24.28 ± 15.90 mIU/L to 3.59 ± 1.24 mIU/L.

Conclusion: Iodine supplementation in iodine-deficient hypothyroidism and sub-clinical hypothyroidism reverses abnormal thyroid function as well as reduces the goitre size.

KEY WORDS: Iodine-deficient hypothyroidism, iodine-deficient sub-clinical hypothyroidism, iodine supplementation.

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INTRODUCTION

Hypothyroidism is a term used for deficient thyroid hormone secretion by the thyroid gland and is associated with lowering of metabolic activity, limiting physical and mental activity and it eventually leads to myxedemic coma with very high rate of mortality.¹ Sub-clinical hypothyroidism or mild hypothyroidism is also having subtle symptoms and mood alteration.² Early diagnosis and treatment of both hypothyroidism and sub-clinical hypothyroidism is emphasized to reduce morbidity and to improve the quality of life.

There are many causes of hypothyroidism and sub-clinical hypothyroidism of which iodine deficiency disorder (IDD) is one of them.³ As iodine deficiency is endemic in Bangladesh⁴, association of iodine deficiency with hypothy-

roidism and sub-clinical hypothyroidism should be sort out first. In IDD, therapeutic strategy is based on preventive measures.^{5,6} It has been shown that adequate iodine prophylaxis prevents endemic goitre as well as other forms of IDD.^{5,6} There are two preventive measures. Population measures for whole population such as universal salt iodization program and prescriptive measures such as iodized oil for target group.⁶ Compulsory iodization of table salt has been introduced in our country since 1995 under Iodine Deficiency Prevention Act of 1989 though non-iodized salt is still available in the market in a sporadic way⁷. There are the few reports of iodine supplementation in the form of iodized oil as parenteral route (intramuscular injection of lipiodol) followed by iodized salt distribution on iodine-deficient hypothyroidism.⁸⁻¹⁰ But so far, no report of iodine supplementation in the form of iodized oil as oral route (iodine capsule) is available. The aim of this study was to see the effect of iodine supplementation in the form of capsule on iodine-deficient hypothyroidism and sub-clinical hypothyroidism.

MATERIALS AND METHODS

The study was done prospectively in the "Thyroid Clinic" of Centre for Nuclear Medicine & Ultrasound, Khulna (CNMU, Khulna) run jointly by CNMU, Khulna and Medicine department of Khulna Medical College, Khulna during the period from January 2001 to December 2003. A total of 850 thyroid patients attended in the "Thyroid Clinic" during the studied period from which only 57 patients were included in the study. Inclusion criteria were (1) presence of goitre, (2) normal or low T4 and high TSH level and (3) high two hours and 24 hours radioactive iodine uptake (RAIU). Goitre was graded on clinical inspection and palpation on the basis of World Health Organization (WHO) and the Pan-American Health Organization criteria.⁶ Thyroid volume was measured in all cases using Toshiba ultrasound machine (Just vision 400) using 7.5 MHz linear probe. T4 was done in all cases using Ra-

dioimmunoassay (RIA) technique and TSH was also done in all cases using Immunoradiometric assay (IRMA) technique with kit supplied from China Atomic Energy Institute of Beijing. Normal range of T4 and TSH in our laboratory is 54 - 174 nmol/L and 0.3 - 5.0 mIU/L respectively. Patients having low T4 and high TSH were grouped as hypothyroidism and those having normal T4 and high TSH were grouped as sub-clinical hypothyroidism. RAIU tests were done with Oakfield thyroid uptake system. Normal range of two hours and 24 hours RAIU in our laboratory is 5-15% and 16-45% respectively. All patients were treated with iodine supplementation in the form of capsule. Two Iodine capsules (1 cap- each capsule was soft gelatin capsule contained iodized oil B.P. equivalent to 200 mg of iodine B.P.) were given stat and 2 capsules weekly for 2 weeks and then 2 capsules yearly as prophylaxis. All patients were followed up for 12 months. Follow up was done at 6 weeks, 3 months, 6 months, 9 months and one-year intervals. During follow up period, goitre assessments were done and thyroid volume, T4 and TSH were measured. If after 6 months, TSH remained same or high from baseline, thyroid replacement therapy i.e., L-Thyroxine were added. The results were analyzed using paired t test.

RESULTS

Total 57 patients were studied where 50 (87.7%) were female and 7 (12.3%) were male with female to male ratio 7.1:1 and age ranged from 10 years to 40 years with mean 21.1 ± 8.34 years. Age and sex distribution of studied patients is shown in Table-I. Pre treatment and post treatment status of studied patients was shown in Table-II. It was found from the study that out of 18 hypothyroidism cases, 6 resumed euthyroidism with iodine supplementation alone and 12 required thyroid replacement therapy and out of 39 sub-clinical hypothyroidism cases, 36 resumed euthyroidism with iodine supplementation alone and only 3 needed thyroid replacement therapy. It was also found

that goitre grade, overall thyroid volume, mean T4 and mean TSH changed significantly during the follow up period. Prior to iodine supplementation 6 (10.5%) had goitre grade 1B and 51 (89.5%) had goitre grade 2. After iodine supplementation it was found that out of 6 goitre grade 1B, 2 (33.3%) remained goitre 1B, 3 (50%) had grade 1A and 1 (16.7%) had goitre grade 0 respectively and out of 51 goitre grade 2, 6 (11.8%) remained grade 2, 32 (62.7%) had grade 1B and 13 (25.5%) had grade 1A. Goitre with overall reduction of thyroid volume by 31.5% ($p < 0.001$). Mean T4 increased from 65.65 ± 27.32 nmol/L to 89.59 ± 21.69 nmol/L ($p < 0.001$) and mean TSH decreased from 24.28 ± 15.90 mIU/L to 3.59 ± 1.24 mIU/L ($p < 0.001$) during the follow up period.

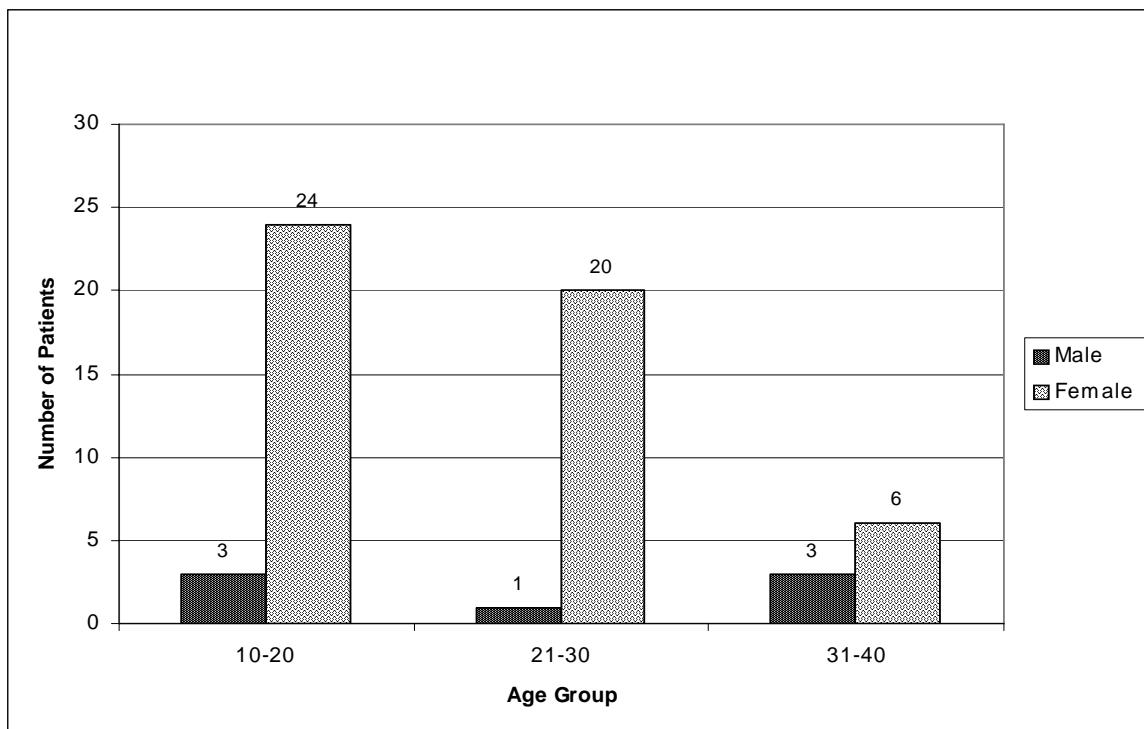
DISCUSSION

Hypothyroidism and sub-clinical hypothyroidism is usually treated with L-thyroxine or thyroid replacement therapy.^{3,11} But in iodine-deficient hypothyroidism and sub-clinical hypothyroidism, the treatment strategy should

rely on preventive measures.⁶ Thyroid replacement therapy should be given in irreversible hypothyroidism, but in reversible hypothyroidism treatment depends on etiology.¹² Iodine deficiency is one of the exogenous factors for reversible hypothyroidism.¹² In iodine deficiency, irreversible hypothyroidism may develop if the severity of hypothyroidism is enough to cause thyroid cell atrophy.^{9,12}

We conducted a prospective study to see the effects of iodine supplementation in the form of capsule in iodine-deficient hypothyroidism and sub-clinical hypothyroidism. There are few publications about the parenteral route (I/M) of iodized oil on IDD.⁸⁻¹⁰ But so far, no papers regarding the oral use of iodized oil on IDD have been published. From such realization we carried out this study to establish a criteria of using iodized oil as oral routine (capsule) in iodine deficient hypothyroidism and sub-clinical hypothyroidism and also to justify the acceptability of these practices. We prescribed 2 capsules (200 mg iodine B.P. each) stat followed by 2 capsules weekly for 2 weeks and thereafter 2 capsules yearly as prophylaxis. We have

Table-I: Age and sex distribution of studied patients



found that goitre grades and thyroid volumes were reduced after iodine supplementation. Out of 6 grade 1B goitre, 2(33.3%) remained grade 1B, 3(50%) became grade 1A and 1(16.7%) became grade 0 respectively and out of 51 grade 2 goitre, 6(11.8%) remained grade 2, 32 (62.7%) became grade 1B and 13(25.5%) became grade 1A goitre respectively with overall reduction of thyroid volume from 24.60 ± 6.07 ml to 16.86 ± 3.23 ml. The normal thyroid volume is 13.6 ± 6.2 ml.¹³ There was significant reduction of goitre size and thyroid volume with $p < 0.001$ in our study. Mirmiran et al showed 94% grade 2 goitre were reduced to 26% grade 2, 41% grade 1 and 30% no goitre.¹⁰ In our study, it was also found that mean T4 and mean TSH were significantly changed before and after iodine supplementation i.e., T4 from 65.65 ± 27.32 to 89.59 ± 21.65 nmol/L ($p < 0.001$) and TSH from 24.28 ± 15.90 (excluding the value > 60 mIU/L) to 3.59 ± 1.24 mIU/L ($p < 0.001$) that is also supported by other reports.⁸⁻¹⁰ During follow up period we didn't do RAIU as RAIU test is invalidated after iodine supplementation as iodine capsule or any

iodine containing medication interferes RAIU test.¹⁴ We have found that 73.7% (42/57) cases resumed euthyroidism by iodine supplementation alone and in 26.3% (15/57) cases thyroxine was needed to resume euthyroidism. In some reports of iodine supplementation in the form of intramuscular injection, cent percentage resumed euthyroidism in course of time.⁸⁻¹⁰ But in our study, duration of follow up period was 12 months and after 6 months of iodine supplementation, if TSH remained same or was elevated, we added thyroxine. Euthyroidism resumed in our study within 5.3 ± 2.3 months. Thyroxine need in some cases might be due to iodine deficiency may be severe enough to cause thyroid cell atrophy and thus causing some irreversible damage or the other reason might be that the dose of iodine supplementation given was in sub optimal dose. The exact dose of iodine in iodine-deficient hypothyroidism and sub-clinical hypothyroidism is not yet established. Even daily requirement of iodine is unknown.¹⁵ Highest Federal standard (RDA or DV) recommended daily requirement as 150 microgram/day.¹⁵ In an io-

Table-II: Pre treatment and post treatment status of studied patients

<i>Pre Treatment Status</i>		<i>Post Treatment Status</i>	
Goitre grade:		Goitre grade	
Grade 1B	- 6	Grade 0	-1
		Grade 1A	-3
		Grade 1B	-2
Grade 2	- 51	Grade 1A	-13
		Grade 1B	-32
		Grade 2	- 6
Mean thyroid volume	- 24.60 ± 6.07 ml	Mean thyroid volume	- 16.86 ± 3.23 ml
Mean T4	- 65.65 ± 27.32 nmol/L	Mean T4	- 89.59 ± 21.65 nmol/L
Mean TSH	- 24.28 ± 15.90 mIU/L	Mean TSH	- 3.59 ± 1.24
RAIU:			
Mean 2 hours	- $24.59 \pm 9.65\%$	Euthyroidism	Euthyroidism
Mean 24 hours	- $51.35 \pm 11.39\%$	with I-cap only	with I-cap + Thyroxine
Response of treatment			
Hypothyroidism	-18	6	12
Sub-clinical hypothyroidism	-39	36	3

dine endemic area, generally 0.5 ml (240 mg iodine) iodized oil (lipiodol injection) is given for children and 1 ml (480 mg iodine) for older subjects.⁶ The exact dose of iodine in the form of capsule has not yet been explored. Iodine-induced thyrotoxicosis is a potential side effect⁶. In our study group, no such side effects was observed. So far, iodine supplementation in the form of capsule has not yet been done. More studies of iodine supplementation in the form of capsule are needed to estimate the dose and the duration of cure. This form of treatment definitely benefits the patient by reducing cost and sufferings. This preliminary study only reflects our initial experiences. Further studies are needed to estimate the dose and duration of cure.

CONCLUSION

Iodine supplementation in iodine-deficient hypothyroidism and sub-clinical hypothyroidism reverses abnormal thyroid function as well as reduces goitre size and thus before prescribing lifelong thyroid replacement therapy in hypothyroidism and sub-clinical hypothyroidism, association of iodine deficiency should be sorted out first. This will reduce treatment cost and patients sufferings.

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