Impact of selective iron and/or iodine interventions on iron and iodine status of adolescents

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The impact of iron and iodised salt supplementation and iron with iodised salt supplementation for a period of six months was studied in relation to non-supplemented controls, on selected indicators of iron and iodine status among goitrous and non goitrous adolescents. A significant reduction in total goitre rate (TGR) and visible goitre rate (VGR) was observed in the group given iodised salt alone or with iron supplements. No change was observed in TGR in the group receiving iron supplements though VGR decreased. An increase in urinary iodine excretion (UIE) was observed among goitrous and non goitrous subjects receiving iodised salt alone or iron supplements alone. The goitrous control subjects in contrast showed a significant decrease in their UIE (-10.9 mcg/dL $p < 0.05$). Iodised salt supplementation caused an increase in T4 (thyroxine) in goitrous and non goitrous subjects and a decrease in TSH (thyroid stimulating hormone) in goitrous subjects. However, iron supplementation had an adverse effect on T3 (triidothyronine) and T4 in non goitrous subjects. Dual supplementation caused a significant decline in T3 (among goitrous subjects) and T4 concentrations (among non goitrous subjects). Haemoglobin (Hb) and serum ferritin (sf) concentrations improved with iodised salt among both the goitrous and non goitrous subjects, but for goitrous subjects, not with iron alone. This study suggests that if a subject is both iron and iodine deficient, iodine deficiency may be corrected in part by iron or iodine supplementation, although their co-administration may not be synergistic. The metabolic relationship between iron and iodine deficiency needs further investigation. However, goitre prevalence is clearly ameliorated with combined micronutrient supplementation to a greater extent than with iodised salt alone and not at all with iron alone.

Key words: Goitre, iodine deficiency, iron deficiency, micronutrient supplements, urinary iodine excretion, triidothyronine, thyroxine, TSH, adolescents

Introduction

Iron and iodine are two minerals which are required in milligram and microgram quantities, respectively, in daily diets for human well-being. In such minute quantities they are essential as constituents of enzymes and proteins, for normal processes of growth, development, maintenance and resistance to infection. Thus iodine deficiency does not result in just a goitre nor iron deficiency in just nutritional anaemia. Recent studies reveal adverse consequences of milder deficiency states and more fundamental roles for these micronutrients in growth, development and immunity than was formerly believed, thus underscoring the need for prevention and treatment of micronutrient malnutrition[1]. The impact of iron and iodised salt supplementation and iron with iodised salt supplementation was studied on selected indicators of iron and iodine status among goitrous and non goitrous subjects.

Subjects and methods

The study fulfilled the ethical principles of the Helsinki declaration and informed consent was obtained. The subjects ie. two hundred and twenty eight viz 119 goitrous and 109 non-goitrous were between 12-16 year old school going adolescents, who were selected on their willingness to participate in the study. They were selected out of 700 adolescents studying at a municipal school at Kandivli, Mumbai, and were screened for presence of goitre by an endocrinologist. Grading of goitre was based on WHO-ICCIDD classification[2].

A random casual urine sample was collected from each subject in a wide mouthed polyethylene bottles to which toluene was added as a preservative. Urinary iodine excretion (UIE) was estimated by ceric-arsenite method[3].

A 5 ml venous blood sample was drawn from each subject. 20 µl was transferred to filter paper with a Sahli type pipette and these samples were dried and stored for haemoglobin estimation. Iron status was assessed by estimating the haemoglobin by the cyanmethemoglobin method[4] using a Span diagnostic kit. Serum was separated from the remaining blood and the samples were then frozen until analysed. T3 and T4 were estimated by radio immunoassay (RIA) while serum ferritin and thyroid stimulating hormone (TSH) were estimated by the immunoradiometric assay (IRMA) technique using kits obtained from Diagnostic Products Corporation, USA.

Experimental design

A pre-post experimental control design was used. The goitrous and non-goitrous subjects were assigned to the 3 experimental groups and one control group on the basis of their goitre grade. This study thus consisted of a minimum of fifteen adolescents (irrespective of gender) assigned to each treatment group. An attempt was, however, made to include more than 15 because of anticipated drop-out from the study. The number of subjects suffering from grade 2 and 3 goitre were limited because of absence of visible goitre. All subjects were dewormed before starting supplementation and were given one multivitamin tablet per day, during the course of the study. The experimental groups were as follows:

Group A. Iodised Salt (IS) Supplementation Group: This

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group received TATA's brand iodised salt (15 ppm iodine) for home consumption for six months. The amount of salt distributed depended on number of family members.

Group B. Iron Supplementation Group: 60 mg iron tablet was given daily for a period of 90 days.

Group C. Both Iron and Iodised Salt Supplementation Group: 60 mg iron tablet was given for a period of three months and also iodised salt distributed for home consumption for a period of six months.

Group D. Control Group: This group did not receive any iodised salt nor iron tablets.

All biochemical tests and clinical examination of thyroid gland was carried out for each and every subject before and after supplementation. The SPSS package was used for statistical analysis. The effect of selective iron and/or iodine interventions on goitrous and non goitrous subjects was compared separately.

Results

Table 1 shows the goitre prevalence in various treatment groups and control group before and after supplementation. A significant reduction in total goitre rate (TGR) and decrease in visible goitre rate (VGR) was observed in the group given iodised salt (IS) alone ($p<0.02$)[a] or with iron supplements ($p<0.02$)[b] after six months of intervention. The group which received iron supplements did not show any change in TGR, even though VGR showed a significant decrease. TGR in the controls after six months was slightly lower (32%) compared to 35.8% earlier, but the difference was not significant. The solitary case of visible goitre seen in the control group before supplementation showed a decline in goitre from grade 2 to grade 1b. Similar observations were also made in the group given both iron tablets and iodised salt. All 3 subjects receiving iodised salt and iron tablets showed a decline in goitre grade from 2 to 1b.

Table 1. Goitre prevalence among adolescents in different treatment groups. (% surveyed)

Goitre grade		Treatment groups			
		Iodised salt (n = 78)	Iron (n = 44)	Iron + iodised salt (n = 39)	Control (n = 67)
0	B	42.3	47.7	30.8	64.2
	A	66.7	47.5	52.9	68.0
1a	B	38.5	31.8	41.0	22.4
	A	24.2	35.0	29.4	32.0
1b	B	11.5	11.4	20.5	11.9
	A	4.5	12.5	17.6	--
2+3	B	7.7	9.1	7.7	1.5
	A	4.5	5.0	--	--
TGR	B	57.7	52.3	69.2	35.8
(1+2+3)	A	33.2	52.5	47.0	32.0
Change		-24.5	0	-22.2	-3.8
VGR	B	7.7	9.1	7.7	1 5
(2+3)	A	4.5	5.0	--	--
Change		-3.2	-4.1	-7.7	-1.5

B = Before supplementation; A = After supplementation
TGR is total goitre rate; VGR is visible goitre rate
Significance is given by [a] ($P<0.02$), [b] ($P<0.02$)

A highly significant increase in urinary iodine excretion (UIE) in both goitrous and non goitrous subjects given either iodised salt or iron tablets was observed as compared to those given both iodised salt and iron supplements or controls (Table 2). The increase in urinary iodine excretion in case of subjects given both iron and iodised salt together was not significant. The goitrous control subjects in contrast showed a significant decrease in their urinary iodine excretion over 6 months.

T3 concentrations (Table 3) after 6 months of supplementation with iodised salt in both goitrous and non goitrous subjects did not change significantly. A decrease in T3 concentrations after iron supplementation was noted. In the case of non goitrous subjects ($p<0.009$). The goitrous subjects given iron and iodised salt together also showed a significant decrease in their T3 concentrations ($p<0.002$).

Table 2. Effect of selective supplementation on UIE (urinary iodine excretion) (mcg/dL) among goitrous and non goitrous adolescents (mean ± SD).

Treatment Groups	Goitrous			Non-goitrous		
	Before	After	Change	Before	After	Change
Iodised salt	8.9±4.7	16.0±7.3 n=28a	+7.6***	5.6±2.0	13.4±8.6 n= 16a	+7.8***
Iron	8.0±4.5	13.1±6.1 n=163	+5.0***	4.5±2.9	14.5±3.6 n=9a	+10.0***
Iron & iodised salt	13.7±7.0	17.7±7.7 n=13a	+4.0	14.6±5.6	18.7±6.6 n=5a	+4.1
Control	16.8±4.4	5.8±8.3 n=4a	-10.9*	15.4±18.3	18.3±3.9 n=4a	+2.98

[a] number of subjects who completed the study significant change in values after intervention. * $P<0.01$ *** $p < 0.001$

Table 3. Effect of selective supplementation on T3 (ng/dL) among goitrous and non goitrous adolescents (means ± SD)

Treatment groups	Goitrous			Non-goitrous		
	Before	After	Change	Before	After	Change
Iodised salt	166.0±71	196.0±49 n=29[a]	+30	158.0±64	214±53.0 n=14[a]	+55
Iron	204.0±59	178.0±50 n=18[a]	-26	231.0±36	185.0+37 n=11[a]	-46[c]
Iron & iodised salt	233.0±40	185.0±40 n=13[a]	-48[b]	220.0±15	192.0±17 n=4[a]	-28
Control	172.0±53	172.0±23 n=11[a]	0	235.0±65	196.0±55 n=8[a]	-39

[a] number of subjects who completed the study
[b] significant $p < 0.002$; [c] significant $p < 0.009$

A significant increase in T4 concentrations (Table 4) in subjects given iodised salt (goitrous or non goitrous) was noted. Iron supplementation however showed a reverse trend ie, a significant decrease in T4 concentrations in the case of goitrous subjects. Even when iron and iodised salt were given together, a decrease in T4 concentrations was noted which was significant in case of non goitrous subjects. The control subjects did not show any significant change in their T4 concentrations.

Table 4. Effect of selective supplementation on T4 (μg/dL) among goitrous and non goitrous adolescents. (means ± SD)

Treatment groups	Goitrous			Non-goitrous		
	Before	After	Change	Before	After	Change
Iodised salt	8.1±3.3	10.3±3.3 n=28[a]	+2.2[c]	7.9±3.3	11 2±2 4 n=15[a]	+3.2[d]
Iron	9.1±2.1	7.2±2.8 n=18[a]	-1.8[d]	7.7±1 7	8.1±2.3 n=10[a]	+0.3
Iron & iodised salt	10 1±1.9	9.9±2 8 n=13[a]	-0.2	11 7±2 3	8.4±1.9 n=5[a]	-3.3[b]
Control	10.1 ±3.9	8.1±2.2 n=11[a]	-2.0	10.9±3.8	8.8±3.3 n=8[a]	-2.1

[a] number of subjects who completed the study
[b] $p < 0.05$; [c] $p < 0.01$; [d] $p < 0.001$

No significant change in TSH concentrations among non-goitrous (Table 5) in any of the treatment groups or control group was observed. The goitrous subjects given iodised salt showed a significant decrease in their TSH values after supplementation.

A significant increase in T4 concentrations (Table 4) in subjects given iodised salt (goitrous or non goitrous) was noted. Iron supplementation however showed a reverse trend ie. significant decrease in T4 concentrations in the case of goitrous subjects. Even when iron and iodised salt was given together, a decrease in T4 concentrations was noted which was significant in the case of non goitrous subjects. The control subjects did not show any significant change in their T4 concentrations

Significant change in Hb concentrations for goitrous and non goitrous subjects (+2.2g/dL and +2.8g/dL respectively) were observed with six months of use of iodised salt, while the subjects given iron supplements or both iodised salt and iron supplements did not show any significant change in their Hb (Table 6).

Table 5. Effect of selective supplementation on TSH (mIU/mL) among goitrous and non goitrous adolescents (means ± SD)

Treatment	Goitrous			Non-goitrous		
groups	Before	After	Change	Before	After	Change
Iodised salt	1.9±1.2	1.3±0.9 n=29[a]	-0.6[b]	2.1±1.0	1.6±1.2 n=10[a]	-0.4
Iron	2.0±0.9	2.1±1.4 n=18[a]	+0.05	1.8±1.4	1.4±0.6 n=9[a]	-0.4
Iron & iodised salt	1.7±0 7	1.7±1.3 n=13[a]	+0.05	1.4±0.3	1.7±1.2 n=4[a]	+0.3
Control	2.6±0.9	1.8±0.8 n=12[a]	-0.8	1.8±1.1	1.9±0.9 n=8[a]	+0.1

[a] number of subjects who completed the study
[b] p = 0.061

Table 6. Effect of selective supplementation on Hb (g/dL) among goitrous and non goitrous adolescents (means±SD)

Treatment	Goitrous			Non-goitrous		
groups	Before	After	Change	Before	After	Change
Iodised Salt	9.8±2.2	12.0±2.2 n=23[a]	+2.2[b]	9.6±2.6	12.4±2.1 n=11[a]	2.8[c]
Iron	11.2±1.9	11.4±2.0 n=12[a]	+0.2	10.3±1.3	11.6±2.5 n=16[a]	+1.3
Iron & iodised salt	9.7±4.5	11.8±2.0 n=16[a]	+2.1	9.2±3.5	11.3_3.1 n=9[a]	+2.1
Control	13.2±1.8	11.4±2.5 n=10[a]	-1.9	12.8±2.6	11.9±1.3 n=5[a]	-0.9

[a] number of subjects who completed the study
[b] p = 0.003; [c] p = 0.013

A significant increase in serum ferritin concentrations in non goitrous subjects was observed among both experimental and controls (Table 7). The goitrous subjects also showed an increase in ferritin only in the iodised salt supplemented group.

Table 7. Effect of selective supplementation on ferritin (ng/ml} among goitrous and non goitrous adolescents (means ± SD)

Treatment	Goitrous			Non-goitrous		
groups	Before	After	Change	Before	After	Change
Iodised Salt	21.1±13.8	59.3±51.9 n=9[a]	+38.2[b]	8.3±9.6	82.6+59.1 n=8[a]	+74.4[c]
Iron	57.7±61.0	60 3±36.9 n=7[a]	+2.6	54.0±29.6	90.1±44.4 n=7[a]	+36.4[d]
Iron & iodised salt	45.7±48.7	108.3±18.0 n=15[a]	+62.5	17.0+9.3	116.6±88.5 n=7[a]	+99.5[b]
Control	56.2±32.3	38.0±30.5 n=11[a]	-18.2	24.8±23.9	63.5±39.5	+38.7[b]

[a] number of subjects who completed the study
[b] p< 05; [c]p <.01; [d]p<0.008

Discussion

It has been demonstrated in many studies that goitre prevalence decreases and urinary iodine excretion increases with iodine prophylaxis (use of iodised salt)[5,6,7]. Sooch *et al*[5] in their classic Kangra valley study reported a decline in goitre prevalence from 38% to 19% and 15% in zones using salt fortified with potassium iodide and potassium iodate respectively. Six years later (1968) prevalence of goitre further decreased to 8.5% and 9.1% respectively. A decrease in goitre prevalence from 60% to 16.3% in a group using iodinated salt for 4 years compared to a group using non-iodinated salt has been reported[7]. Kavishe and Maletnlemae reported gross and visible goitre prevalence of 95.2% and 60.3% before distribution of iodised salt[8]. They observed a clear cut decrease in goitre prevalence after 6 months and 12 months of distribution of iodised salt. The VGR after 6 months and 12 months of iodine supplementation had fallen to 30.4% and 6.0% respectively[8]. A significant reduction in goitre rate was also observed in this study after six months of iodised salt use, alone or along with an iron supplement. Iron supplementation alone did not appear to have any significant effect on total goitre rate.

An increase in urinary iodine excretion has been reported on use of iodised salt[6,7,9,10]. Significant increase in urinary iodine excretion was noted in subjects receiving iodised salt. It was interesting to note that even though iron supplementation did not show any significant effect on goitre prevalence, it showed a significant increase in the urinary iodine excretion, a trend also observed with iodised salt supplementation,. The magnitude of increase in urinary iodine excretion was not significant when both iron and iodised salt were given together.

The increase in T4 concentrations and decrease in TSH concentrations with iodised salt use was expected[11,12]. Iron supplementation appears to have an adverse effect on T3 and T4. The decrease in T3 or T4 with iron or iodised salt is of concern. Among various consequences of iron deficiency, is poor thermo-regulation probably because both thyroid hormone metabolism and catecholamine metabolism are altered in iron deficiency. Beard *et al*[13] observed significantly lower concentrations of plasma T3, T4 and TSH in anaemic women as compared to controls. After supplementation with iron, there was a 12% rise in plasma T3 concentrations which was still significantly lower than controls. Plasma TSH concentrations were not significantly different after supplementation. Anaemia per se is a significant factor in thyroid hormone function. After iron supplementation and correction of anaemia thermogenic performance is improved[14].

In the present study, iodised salt supplementation resulted in improved T4 concentrations, but iron supplementation had negative effects on T3 or T4 concentrations. As observed by Beard[14], TSH values did not change. The iron supplementation did not show any beneficial effect on the iron status of the subjects.

Iron supplementation given alone or with iodised salt did not have any significant effect on haemoglobin concentrations. In contrast iodised salt used for 6 months significantly raised the haemoglobin concentrations among both goitrous and non goitrous subjects. The beneficial effects of iodine in the group given iodised salt alone or along with iron on iron status may be attributed to better utilisation of iron.

This suggests that iodised salt/ iodine use played a role in mobilisation of iron stores. It is however, difficult to explain the increase in the iron stores, as reflected by serum ferritin concentrations by use of iodised salt in both goitrous and non goitrous subjects. It has been reported that serum ferritin is not a good indicator of short term improvements in iron stores. Iron supplementation has been associated with modest increases in serum ferritin[15].

Hence, the deficiencies of the various nutrients cannot be considered in isolation[15] and effects of minerals when supplemented alone or in combination with one another should be studied. If a person's diet is marginal in one nutrient, then it could marginal in another nutrient as well[17].

Conclusion

Iodised salt supplementation improved both iodine and iron status of the adolescents (goitrous and non goitrous) as indicated by (i) a significant decline in total goitre rate (ii) a significant rise in urinary iodine excretion (iii) increase in circulating thyroid hormones (T3 or T4) (iv) Significant increments in Hb and serum ferritin values. Contrary to these observations, iron supplement when given alone, caused no change in total goitre rate nor an improvement in thyroid hormone status (although urinary iodine excretion increased), while serum ferritin rose only among the non goitrous subjects. In comparison combined iodised salt and iron supplementation caused no significant favourable changes in iron

or iodine status indicators ie. UIE, T3, T4 or Hb. Higher post serum ferritin values were however observed among both the goitrous and non goitrous subjects.

The present study indicates that, if a subject is both iron and iodine deficient, iodine deficiency should be corrected before giving iron supplementation as otherwise the iodine status may be adversely affected. Iodine favourably improves iodine and iron status among goitrous and non goitrous subjects. An interrelationship between iron and iodine utilisations does exist, but the mechanisms are not clear. Use of iodised salt should be mandatory among people with combined iron and iodine deficiencies.

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選擇性的補充鐵和／或碘對青少年鐵碘營養狀況的影響

摘要

作者選擇了甲狀腺腫和非甲狀腺腫的青少年爲對象，研究補充鐵或碘鹽和鐵加碘鹽 6 個月後對鐵和碘營養狀況的影響。他們觀察到補充碘鹽或鐵加碘鹽後，甲狀腺腫總發病率（ TGR ）和可見甲狀腺腫發病率（ VGR ）均明顯下降。補充鐵雖然 VGR 減少，但 TGR 沒有改變。補充碘鹽或鐵的甲狀腺腫和非甲狀腺對象可見尿碘排出（ UIE ）增加。甲狀腺腫的對照顯示尿碘排出顯著減少（－10.9 Mcg/dL $p < 0.05$ ）。碘鹽的補充可引起 T_3 和 T_4 濃度增加和甲狀腺刺激素（ TSH ）濃度下降。補充鐵加碘鹽可引起甲狀腺腫病人 T_3 濃度和非甲狀腺腫對象 T_4 濃度明顯減少。補充碘鹽的甲狀腺腫和非甲狀腺腫對象，其血紅蛋白和血清鐵蛋白得到改善，補充鐵或鐵加碘鹽的對象，血紅蛋白濃度增加，但增加並不顯著。僅補充碘鹽的甲狀腺腫對象在補充後期顯示血清鐵蛋白明顯增加。該研究的結果顯示如果對象是鐵和碘同時缺乏，碘的缺乏在補充鐵之前應得到改善，否則碘的營養狀況也許會得到相反的影響。

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