Community trials with iron and iodine fortified salt (Double fortified salt)

G.N.V. Brahmam, K. Madhavan Nair, A. Laxmaiah, Ch. Gal Reddy, S. Ranganathan, M. Vishnuvardhana Rao, A. Nadamuni Naidu, K.Vijayaraghavan, B.Sivakumar, Kamala Krishnaswamy, J. Gowrinath Sastry, M. Mohan Ram, N. Pralhad Rao and Vinodini Reddy. National Institute of Nutrition, Indian Council of Medical Research, Jamai-Osmania (P.O), Hyderabad – 500 007, India.

Iron deficiency anaemia (IDA) and iodine deficiency disorders (IDD) co-existing in many parts of India, are two major micronutrient deficiency diseases of public health significance. The National Institute of Nutrition has successfully developed the technology of fortification of salt with iodine and iron (DFS). The laboratory studies have confirmed stability, bioavailability, and bio-effect. Two community-based trials with DFS were carried out for two years, one in a tribal community where IDA and IDD co-exist, followed by the other among children in residential schools. Both these studies revealed the feasibility of large-scale production, distribution and stability of DFS and its acceptability by the community. No untoward effects were observed on consumption of DFS, there by establishing its safety. The consumption of DFS had significant positive impact on iodine nutriture of the community. Although the results on the impact on haemoglobin (Hb) status were not uniform in all the age/sex groups, the DFS supplementation in the residential schools had significant impact in preventing the decline and improving the Hb levels.

1. INTRODUCTION

Iron deficiency anaemia (IDA) and iodine deficiency disorders (IDD) are two major micronutrient deficiencies of public health significance in the developing countries, including India [1]. The most important etiological factor responsible for this is dietary deficiency of iron and iodine respectively. Since these two deficiency disorders affect adversely the human resource, country specific programmes are being implemented in several parts of the World. In India, National Goitre Control programme (NGCP), and National Nutritional Anaemia Prophylaxis Programme (NNAPP) were initiated during 1962 and 1970 respectively for the prevention and control of these micronutrient deficiencies in the populations. Evaluation of NNAPP during 1985 revealed that the programme did not achieve the expected objectives, due to various operational and logistic problems [2]. Fortification of foods is now being considered as an effective and sustainable strategy for control of IDA. Based on the principles of fortification, common salt has been identified as the most appropriate vehicle for fortification in India.

The National Institute of Nutrition (NIN) had earlier developed the technology of fortification of salt with iron, which has undergone successful community trial [3]. Since the Government of India, in the year 1985, embarked on universal iodisation of salt and because of the fact that the IDA and IDD often co-exist in the community, the NIN developed a technology of double fortification of common salt with iron and iodine. The laboratory studies conducted with DFS indicated good stability and bioavailability of both iron and iodine [4]. Before it is recommended as a National programme, it is essential to assess the feasibility of large scale production and distribution of DFS, its acceptability and safety in the community, the stability of iron and iodine at consumer level and its impact on anaemia and iodine status. Therefore, two community-based studies were carried out.

2. METHODOLOGY

2.1. Study - I

This study was carried out in four randomly selected blocks of East Godavari district in the State of Andhra Pradesh where both IDA and IDD are widely prevalent. In each block, 15-20 contiguous villages were selected to cover a population of about 5000. Three blocks were randomly allocated to experimental areas, while the fourth area served as control. DFS, iron fortified salt (IFS) and iodised salt (IS) were provided respectively in the experimental areas, while in the control area, unfortified salt was consumed.

2.2. Study-II

Followed by study-I, a double blind randomized study was carried out in four residential schools (2 boys' and 2 girls') each having about 400 children, around Hyderabad. One boys' school and one girls' school were randomly allocated to experimental group where DFS was supplemented, while the rest served as control and received IS. The Scientific Advisory Committee of NIN approved experimentation in both the studies.

2.3. Production of Fortified salts

For the study-I, a private factory in Hyderabad and for the study-II Tamil Nadu Salt Corporation, Chennai, manufactured the fortified salts under the technical supervision of NIN. The DFS, IFS and IS were prepared by dry mixing (in batches) method [4,5], as per the formulae given in Table 1. A 'pre-mix' was made by adding the chemicals of fortification along with the stabilizer required for one tonne of fortified salt to 10 kg of common salt and mixed thoroughly. This was added to 990 kg of common salt in a ribbon blender and mixed thoroughly for ten minutes. Random samples of fortified salt were collected and tested for iodine/iron to ensure uniform mixing.

2.4. Distribution of Fortified Salt

In study-I, the salts were packed in 1-kg high-density polyethylene bags, with suitable markings and distributed to the households every month, at the rate of 0.5 kg per person per month. In case of study-II, the salts were packed in 50-kg high-density polyethylene bags with code numbers and transported periodically to kitchens of respective school hostels. The codes were broken only at the end of the study. In both the studies, the fortified salts were supplemented for a period of 24 months.

2.5. Investigations

Haemoglobin (Hb) was estimated by cyanmethaemoglobin method, from 20 µl of finger prick blood sample collected on Whattman No.1 filter paper [6]. In both the studies duplicate samples were collected from a sub-sample of individuals for quality control. Urinary iodine excretion levels were estimated by kinetic method on every fiftieth individual in study-I and on every tenth child in study-II [7,8]. Clinical examination for IDD and adverse effects, if any, on consumption of fortified salts were carried out on all the available individuals. In study-I, T_4 levels in blood samples collected on filter paper was measured by RIA (BRIT, Mumbai), on every thirtieth individual. The above investigations were carried out at baseline and at the end of 24 months of salt supplementation, covering children of 1-18 years, pregnant women and lactating mothers in study-I and 6-18 year children in study-II.

In addition, questionnaire on salt consumption pattern was administered every month on a sub-sample of households for obtaining information on the type of salt being used, its acceptability and side effects experienced, if any. Salt samples were also collected for the estimation of iodine/iron. Iodine levels in DFS were measured by volumetric method [9], while iodine in IS and iron levels in DFS and IFS were assessed by spot test [10].

2.6. Statistical analysis

In study-I, analysis of data on Hb values at various points was carried out on cross sectional basis, while in the study-II data on those subjects who were covered at both initial and final rounds only was considered. In the study-I, the impact on Hb status was assessed in DFS, IFS and control groups, and that of iodine status in DFS, IS and control groups. The difference between the initial and final median urinary iodine excretion levels with in a group was tested by median test. The

Table 1
Composition of fortified salts

Type of salt	Common Salt (g)	Sodium hexa meta phosphate (g)	$CaCO_3$ (mg)	$FeSO_4\,7H_2O$ (g)	KIO_3 (mg)
DFS	1000	10	-	5	67
IFS	1000	10	-	5	-
IS	1000	-	630	-	67

DFS: double fortified salt, IFS: iron fortified salt, IS: iodised salt difference in the prevalence of total goitre was tested by proportion t-test. The difference in the initial and final mean Hb level was tested by student t-Test. In the study-II, ANCOVA was carried out to test the changes in the Hb levels between DFS and IS groups after adjusting for differences in age, sex and initial Hb levels, and the significance was tested by F-test. Paired t-test was used to test the differences in the mean increments. In the study-II, children were categorized into those with no change ($\pm < 1$ g/dl), with increase ($+ \geq 1$ g/dl) and with decrease ($- \geq 1$g/dl), considering a change of 1 g/dl in the Hb as significant. The differences in the distributions in different groups were tested by Chi-square test.

3. RESULTS

3.1 Production and distribution of DFS

For the purpose of study-I, a total of 59 MT each of DFS and IFS and 62 MT of IS were manufactured and packed in 1 kg packs. The fortified salts were distributed to the households periodically @ 0.5 kg per head per month. In the study-II, 9 MT each of DFS and IS were manufactured and packed in 50 kg sacks in three batches. The salts were supplied to the schools once a month.

3.2. Acceptability and safety of fortified salt

All the families in the study-I accepted the fortified salt as cooking salt. Similarly, in study-II, the DFS and IS were well accepted in the residential schools. None of the beneficiaries complained of any side effects on consumption of the fortified salts.

3.3. Stability of iron and iodine

In study-I, about 95% of the DFS and IFS samples collected from consumer level had 800-1000 ppm of iron, while 91% of DFS samples and 98% of IS samples had ≥ 15 ppm of iodine.

In study-II, all the three batches of DFS supplied had 800-1000 ppm of iron. Samples from two batches of DFS had ≥ 15 ppm of iodine, while one batch had <15 ppm. All the IS samples had ≥ 15 ppm of iodine.

3.4. Urinary iodine excretion

In study-I, the median urinary iodine excretion levels (μg/L) increased significantly from 116 (n 104) to 155 (67) ($P<0.02$) in the DFS group, and from 59 (89) to 160 (92) ($P<0.01$) in IS group. In control area, there was no significant ($P> 0.05$) difference between the initial [101 (102)] and final [97 (54)] values. In study-II, the median urinary iodine excretion levels increased significantly ($P<0.001$) from 68 (91) to 108 (76) in the DFS group and from 70 (85) to 452 (75) in IS group.

3.5. Goitre prevalence and serum T_4 levels

There was a significant ($P<0.001$) reduction in the prevalence of total goitre in DFS (from 28.0 to 13.7%) and IS (25.8 to 16.1%) areas in study-I. In the control area it remained around 14 % after 12 months of supplementation. The mean T_4 levels were around initial levels (7.3-7.6 μg/dl) in DFS and IS area, while the levels decreased significantly ($P<0.001$) from 7.8 to 6.6 μg/dl in the control area.

3.6. Effect on haemoglobin levels

In the study-I, among the adolescent boys and lactating women, there was significant ($P <0.05$) rise in the mean Hb levels in DFS and IFS groups (Table 2). A significant rise in mean Hb levels was observed in 1-13 year age group, in all the areas including control area. The increase in mean Hb levels was maximum (1.5g/dl) in adolescent boys and least (0.3g/dl) in adolescent girls.

In the study-II, the initial mean Hb levels were comparable between DFS and IS groups among girls (12 g/dl), while among boys, they were significantly ($P<0.001$) higher in DFS group (12.6 g/dl) compared to IS group (11.7 g/dl). A marginal increase in the mean Hb levels in DFS (+0.19 g/dl) group, with a small decrease in IS (-0.06 g/dl) group was observed among boys at the end of 24 months. The mean Hb levels significantly ($P<0.001$) declined from the initial levels among the girls of DFS as well as IS groups. The magnitude of decrease was significantly ($P<0.001$) less in DFS group (-0.87 g/dl) compared to IS (-1.95 g/dl.).

The ANCOVA showed significant ($P<0.001$) differences in the mean increments in Hb levels between DFS and IS. Among the boys with initial Hb levels of 7-10 g/dl, DFS group showed a mean increment of 2.0 g/dl compared to 0.5 g/dl in IS (Table 3). In the group with initial Hb levels of 10-12 g/dl, there was a significant ($P<0.05$) increase in the mean Hb level (0.68 g/dl) in DFS group, while there was no significant change in IS group. Among those with initial Hb levels of ≥ 12 g/dl, the DFS group maintained the initial levels, while IS group registered a significant decline (-0.46 g/dl).

Among the girls with initial Hb levels of 7-10 and 10-12 g/dl, the initial levels were maintained in DFS group. On the other hand, in the IS group there was a significant decline (-0.78 and –1.62 g/dl respectively). Among those with initial Hb levels of ≥12 g/dl, both the DFS (-1.33 g/dl) and IS (-2.38 g/dl) groups showed significant decline from the initial levels. However, the magnitude of decline was significantly lower compared to IS group. A significantly higher proportion of the girls (χ^2_2 = 21.7, P<0.001) showed decrease (– ≥ 1g/dl) in Hb levels among IS (73.2%) compared to DFS (52.7%) group (Fig.1). Relatively higher proportion of the

Table 2

Initial and final mean±SD haemoglobin (g/dl) levels by age groups and type of salt supplemented in study-I

Group		1-5 years	6-13 years		14-17 years		Adult Women	
		M + F	M	F	M	F	Pregnant	Lactating
DFS	Initial	10.2[a] ±1.52 (233)	10.7[a] ±1.67 (133)	11.1[a] ±1.46 (145)	12.2[a] ±2.07 (18)	11.1[a] ±1.05 (15)	9.6[a] ±1.67 (15)	10.4[a] ±2.07 (47)
	Final	11.2[b] ±1.30 (360)	11.7[b] ±1.65 (116)	11.5[b] ±1.47 (116)	13.7[b] ±1.79 (18)	11.4[a] ±2.20 (19)	10.4[a] ±1.62 (25)	11.4[b] ±1.16 (35)
IFS	Initial	10.1[a] ±1.16 (334)	10.8[a] ±1.32 (92)	10.5[a] ±1.36 (131)	11.8[a] ±1.45 (19)	10.7[a] ±1.30 (32)	9.9[a] ±1.12 (30)	10.4[a] ±1.48 (68)
	Final	11.4[b] ±1.39 (511)	12.3[b] ±1.71 (101)	11.8[b] ±1.67 (150)	13.2[a] ±2.20 (9)	11.3[a] ±1.57 (30)	10.5[a] ±1.52 (14)	11.3[b] ±2.18 (43)
CONTROL	Initial	10.3[a] ±1.21 (243)	10.9[a] ±1.53 (148)	10.8[a] ±1.44 (193)	12.4[a] ±2.36 (22)	11.3[a] ±1.38 (24)	9.1[a] ±1.47 (14)	10.7[a] ±1.26 (32)
	Final	11.3[b] ±1.69 (369)	12.0[b] ±1.70 (113)	12.0[b] ±1.64 (148)	12.6[a] ±2.29 (8)	12.0[a] ±1.93 (24)	9.9[a] ±1.73 (14)	10.9[a] ±2.15 (26)

Figures in parentheses indicate numbers. M: male, F: female. DFS: double fortified salt, IFS: iron fortified salt. Initial and final figures in each group with different superscripts are significantly different at 5% level (Student t-test test).

Table 3

Mean change in haemoglobin (g/dl) levels of residential school children by sex, initial haemoglobin levels and type of salt supplemented in study-II

Sex group	Initial Hb level					
	7 - 10		10 - 12		≥ 12	
	DFS	IS	DFS	IS	DFS	IS
Boys	2.00 ±1.829 (4)	0.50 ±2.448 (16)	0.68* ±2.060 (50)	0.16 ±1.627 (73)	–0.05 ±1.631 (133)	–0.46* ±1.232 (64)
Girls	0.07 ±2.107 (27)	–0.78* ±1.953 (25)	–0.18 ±1.540 (75)	–1.62* ±1.417 (59)	–1.33** ±1.337 (159)	–2.38** ±1.757 (115)

Figures in parentheses indicate numbers. * p<0.05 and **p<0.001 by 't' test girls in DFS group (12.8%) showed an increase (+ ≥ 1g/dl) compared to IS group (4.5%). Among the boys, the proportion with increase in Hb levels was higher and that with decrease was lower (not significant) in DFS group compared to IS.

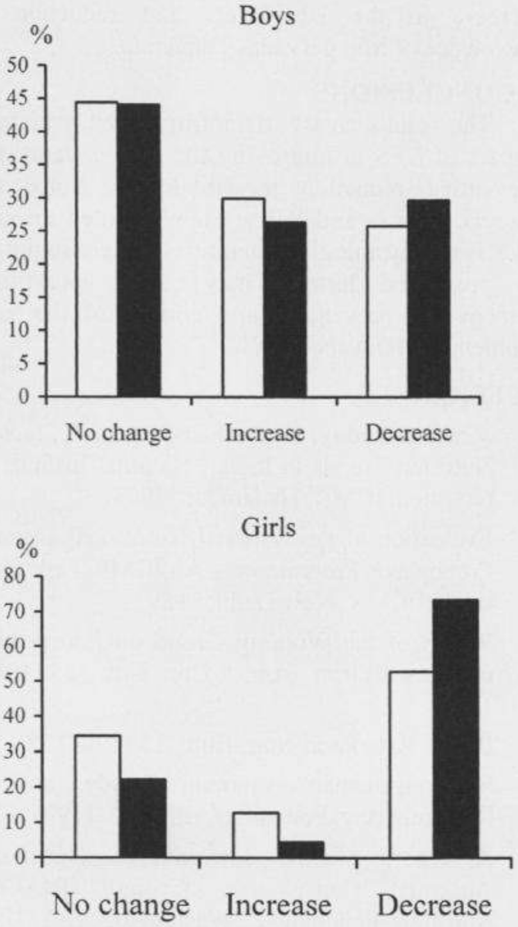

Fig. 1 Distribution (%) of boys and girls according to no change (± <1g/dl), increase (+ ≥1g/dl) and decrease (– ≥1g/dl) in Hb levels in DFS ☐ and IS ■ supplemented groups.

4. DISCUSSION

Adding nutrients to foods to prevent nutritional deficiencies has been successful in many developed countries. The iodisation of common salt is practiced in many countries, and has been very effective in reducing the prevalence of IDD. Though, the technology of iron fortification of salt was successfully developed in India, the same could not be translated into a national programme, because of Government of India adopting the strategy of universal iodisation of salt for strengthening the NGCP. With the technological success of double fortification of salt with both iron and iodine, controlling both IDD and IDA has become feasible.

4.1. Production and distribution of fortified salts

The production of DFS by the two factories, which were hitherto producing iodised salt, has confirmed the feasibility of large-scale production. The logistics of transportation and distribution in a remote tribal community within the State of Andhra Pradesh (study-I) and from one State to another (study-II) was possible.

4.2. Stability of DFS

A major factor that contributes to the positive impact of consumption of DFS on the iron and iodine status of the community is their stability in the salt. Unlike iron, which is quite stable, the stability of iodine is often affected by the presence of impurities in the salt and iron in DFS. A significant finding of this study was the use of refined salt and sodium hexa meta phosphate as a chelater of iron prevented the loss of iodine.

In both the studies adequate levels of iron (800-1000 ppm) were retained at the consumer level. An acceptable level of >15 ppm of iodine was achieved in 98% of the DFS samples at the household level, in study-I, while a large variation was observed in its levels in the study-II. This differential stability could be due to the use of less refined raw salt in one of the three batches of DFS produced as well as the bulk packing in 50 kg sacks, instead of 1 kg bags used in the case of study-I. Both these factors are crucial in maintaining the levels of iodine.

4.3. Acceptability of DFS

The study revealed regular consumption of fortified salts by the community. The DFS was very well accepted as a cooking salt, which was compatible with local food preparations. In both the studies, the average per capita intake of salt was about 7-9 g/day.

4.4. Safety of DFS

Daily consumption of sodium hexa meta phosphate (70-90 mg), a polyphosphate used at 1% level as stabilizer, may influence the calcium and phosphorous homeostasis. Experiments on animal model, rat, provided the convincing evidence of its safety [11]. No complaints were registered or any clinical signs of adverse effects were observed among the consumers during the period of supplementation in both the studies. This suggests that use of DFS, as a daily food component is safe.

4.5. Impact on iodine status

Both the studies provided the biochemical evidence of improvement in the iodine status, after consumption of DFS. This is further substantiated by a 50% reduction in the prevalence of total goitre on consumption of DFS or IS in the tribal areas. This is in accordance with the reported results on IDD prevalence after effective introduction of iodised salt [12]. This shows that DFS is as effective as IS in controlling the IDD.

4.6. Impact on haemoglobin status

The laboratory studies carried out earlier on the bioavailability of iron from DFS provided satisfactory results comparable to that of IFS. In view of this, the use of DFS as an additional source of iron over a period of 2 years is expected to improve the Hb levels in the vulnerable segments of population. In the study-I, increase in the Hb levels was observed in both the DFS and IFS groups in all the age groups, except in the 14-17 year females and pregnant women. Contrary to the expected results, increase in Hb levels was seen in 1-13 year age group in control area also. The reasons for unequivocal response in certain age groups and equivocal response in 1-13 year age group are not clear at present, and need to be examined carefully. The probable reasons could be some inherent practices of the community such as consumption of wild tubers in large quantities, and very high endemicity of malaria, in the areas studied.

The impact of DFS on Hb levels was more obvious in study-II, where the confounding factors observed in study-I were not operating. In case of boys, an increasing trend, though not of significant magnitude was seen. This could be due to higher initial mean Hb levels among the boys in DFS group. In the case of girls, daily consumption of DFS could significantly prevent decline in Hb levels compared to those who received IS. Relatively a higher proportion of children of DFS supplemented group either maintained initial Hb levels or registered an increase compared to those supplemented with IS. Further, the possibility of intestinal worm infestations adversely affecting Hb status was not explored in this study.

Within the DFS supplemented group those with initial Hb levels of 10-12 g/dl showed significant improvement in the Hb levels compared to those with more than 12 g/dl. There appears to be no additional benefit of DFS supplementation, when the initial Hb level is more than 12 g/dl. Similar results were reported with iron fortified salt in a multicentric study [3]. A community having very low Hb levels may need longer duration of DFS supplementation to register a significant increase in the Hb levels and reduction in prevalence of iron deficiency anaemia.

5. CONCLUSIONS

The results clearly demonstrate the beneficial impact of DFS in improving the iodine status and preventing reduction in Hb levels. Since the amount of iron and iodine supplemented through DFS is in physiological quantities, its consumption for prolonged duration may be an appropriate strategy for prevention and control of the twin problems of IDD and IDA.

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