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The Contribution of Iron Fortified Soy Sauce in the Decrease of Anemia Prevalence in China

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Abbreviations: DC: Disease Control and Prevention; ILSI: International Life Sciences Institute; IDA: Iron Deficiency Anemia; USI: Universal Salt Iodization

ABSTRACT

Objectives: To study the contribution of iron fortified soy sauce (IFSS) application in the decrease of anemia prevalence in China in the last decade. Methods: Contribution of IFSS is defined as the percentage of the reduction of anemia population by IFSS application to the total reduction of anemia population between 2004 and 2013 in China. Reduction by IFSS was calculated with total IFSS production and average consumption of soy sauce 8.9 g per day per person. It was adjusted with the ratio 40.0% of regular or constant IFSS consumers and the odds ratio of anemia prevalence between IFSS intervention groups and control groups as reported in RCT studies was used as effectiveness. Results: Total reduction of anemia population from year 2004 to 2013 was 128 million and the national anemia prevalence decreased from 20.1% to 9.7%. The reduction of anemia population by consumption of IFSS was 207.78 million, accounted for 23.8% of the total reduction of anemia population. It is concluded that in the past decade IFSS has contributed to more than one fifth of the total reduction of anemia prevalence. In addition, the results suggested that the working model of the IFSS project which focused on the promotion of IFSS application in the market with the government playing a leading role is efficient and sustainable.

Keywords: CIron Fortification; Soy Sauce; Anemia; Iron Deficiency; Nutrition

Introduction

Iron deficiency anemia (IDA) as a malnutrition disease causes fatigue, weakness and susceptibility to other diseases. In addition, decreased working performance and cognition development in IDA population have significant impact on quality of life and furthermore the national economic development [1]. The national nutrition surveys of China found that anemia prevalence remained unchanged during 1980s and 1990s, and the national average of anemia prevalence was 20.1% in 2002 [2]. Childbearing age women, children and elderly population were the main at-risk population. Food fortification with iron was recognized an efficient approach for IDA prevention and control with enough international experiences [3]. Chinese government has successfully put iodine deficiency under control through universal salt iodization (USI) since 1994 [4]. Since soy sauce is a traditional condiment in China with wide national coverage, it was considered as a suitable food vehicle for iron fortification. In addition, its consumption is less varied among years and provinces, and its dark brown color and salty taste could minimize the organoleptic changes from iron fortification. NaFeEDTA, a soluble and stable chelating iron fortificants which showed little impact on the taste and homogeneity (no precipitation) of soy sauce has been used in IFSS [5]. The increase of cost for manufacturing NaFeEDTA fortified soy sauce is less than 2% of the total cost which is acceptable for the manufacturers and market. Market price of IFSS is the same or 5% to 10% higher than that of the non-fortified soy sauce in most of the cases [6].

The Food Fortification Office, China Centre for Disease Control and Prevention (CDC) initiated iron fortified soy sauce (IFSS)

application project under the guidance of Ministry of Health and funded by Global Alliance of Improved Nutrition in 2003 after a series of efficacy and effectiveness studies supported by the International Life Sciences Institute (ILSI) and United Nations International Children's Emergency Fund (UNICEF). The project has continuously implemented for more than 13 years. IFSS has become an accepted type of soy sauce products in the market, although the total market share of IFSS is lower than expected [7]. In the randomized controlled IFSS intervention trial in anemic students, the efficacy was more than 90% for reduction of IDA students and in the large-scale population-based efficiency study, IDA reduction was also significant. However, there is lack of data on the contribution of IFSS application on anemia at national level. This study was aiming at the evaluation of the contribution of IFSS in the reduction of anemia prevalence in China at national level [8].

Methods

Change of IDA Prevalence and Population from 2004 to 2013

Data of anemia prevalence from national nutrition surveys in 2002 and 2010-2013 were retrieved and analyzed from CNKI and data library of China CDC. The number of anemia population was estimated from the prevalence of anemia and the total population in 2004 and 2013, respectively [9]. The reduction of anemia population was expressed as the difference between anemic population in 2004 and 2013.

Effect of IFSS on Anemia Prevalence

Based on the systematic overview and meta-analysis for the effect of IFSS on IDA [10], results in different age groups and intervention durations of IFSS application were analyzed in this study. The data of Odd ratio were used for the estimation of population recovered from anemia by consumption of IFSS. Published original research papers were retrieved by searching PubMed (1997 to June 2013), Cochrane Library (issue 2, 2013), Highwire (1997 to June 2013), WHO Library (WHOLIS), and China National Knowledge Infrastructure (CNKI) (1997 to 2013). As research on IFSS was initiated in 1997 in China, we searched all the databases after 1997 until December 2013.

Estimation of The Reduction of Anemia Population Due to IFSS Consumption

This study only considered the use of IFSS as the major factor, although the nutrition education activities of the project on iron and anemia knowledge could have impact on the reduction of anemia. The number of effective consumers of IFSS was estimated by the equation below:

$X_1=a\times Y/(b\times 365)$

X_1: number of IFSS effective consumer of IFSS.

Y: total IFSS production in last 10 years from 2004 to 2013.

a: IFSS effective population ratio, which is defined as the percentage of population who regularly and constantly consumed IFSS in the total IFSS consumers, including seldom or intermittent consumers. Questionnaire designed for IFSS consumption included: regular, constant, intermittent and occasional. The ratio of the regular plus the constant (IFSS effective) to the total is 40.0%, therefore, 40.0% was assumed as a [11]

b: Average soy sauce consumption of 8.9 g per person per day was obtained from the national nutrition survey in 2002. The value is considered unchanged since the total national soy sauce production including IFSS were stable at about 5 million MT during these years [12].

The number of reduced anemia population is estimated as below :

$(X_2/N_2)/(X_t/N_t)$ =Odds ratio

X_2: number of anemia consumers of IFSS, calculated by the equation in case other values are known.

N_2: number of no anemia consumers of IFSS, $N_1=X_1-X_2$

X_1: number of IFSS effective consumer of IFSS

X_t: total number of anemia population, 20.1%×1.29 millions

N_t: total number of no anemia population, (1-20.1%)×1.29 millions

Odds ratio: obtained from effective analysis of IFSS intervention groups and control group.

IFSS contribution= (X_2/reduced population from 2004 to 2013)×100%

The Contribution of IFSS Application to Anemia Control in China

The contribution is defined as a ratio of number of IFSS reduced anemic population with total number of reduced anemic population.

Result

Decrease of Anemia Rate and Population in 2004-2013

The average prevalence of anemia in 2004 and 2013 were 20.1% and 9.7%, respectively, which shows a remarkable decrease of anemia prevalence during the 10 years period. Because there were no national data for anemia prevalence in each year, it is not possible to obtain the annual changes of anemia (Table1).

Table 1: Reduction of anemic populations in 2004 and 2013 (millions).

Year	Estimated Anemia Prevalence	Total Population	Anemia Population	Reduced Anemia Population
2004?	20.10%	1,292	259	
2013	9.70%	1,354	131	128

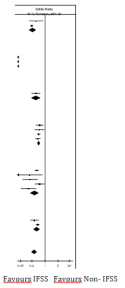
Note: The age range of population surveyed was from 3 years old more than 70 years old.

Effects of IFSS on Anemia Prevalence

Based on a published meta-analysis including 16 RCT studies, detailed studies on different age and duration groups was conducted [13-29]. Result in Tables 2 & 3 showed the odds ratio for duration between intervention groups was 0.27, but not linearly related with the intervention duration from 2 to 18 months and this also true for subgroups from 3 years old to more 55 years old. It was assumed that consumption of IFSS more than 2 months would have beneficial effect on anemia prevalence that would accounts for 27% of that in none IFSS consumption group. The concentration of iron in soy sauce from NaFeEDTA is 24-28 mg/100 ml according to national standard, which in most cases the concentration on the label, was 26 mg/100 ml.

Table 2: Effect of IFSS on anemia prevalence in different intervention duration.

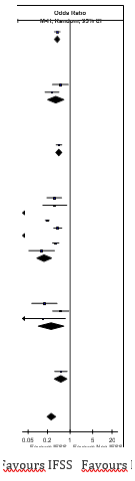
Study Group or Subgroup	Favours IFSS Events	Total	Favours Non-IFSS Events	Total	Weight	Odds Ratio MH, Random,95%CI	Year	
2.1.1 Duration of Observation: 2 Months								
He SL et al. [26]	8	68	27	95	5.20%	0.34 [0.14, 0.80]	2008	
Li LJ et al. [27]	265	2600	972	2648	8.70%	0.20 [0.17, 0.23]	2008	
Subtotal (95% CI)		2668		2743	14.00%	0.22 [0.14, 0.32]		
Total events	273		999					
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 1.46$, df = 1 (P = 0.23); $I^2 = 32\%$								
Test for overall effect: Z = 7.43 (P < 0.00001)								
2.1.2 Duration of Observation: 3 Months								
Huo JS et al. [12]	1	77	73	81	1.70%	0.00 [0.00, 0.01]	2001	
Sun J et al. [8]	2	82	73	81	2.60%	0.00 [0.00, 0.01]	2003	
Subtotal (95% CI)		159		162	4.40%	0.00 [0.00, 0.01]		
Total events	3		146					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.23$, df = 1 (P = 0.63); $I^2 = 0\%$								
Test for overall effect: Z = 9.51 (P < 0.00001)								
2.1.3 Duration of Observation: 4 Months								
Fang ZF et al. [25]	22	376	48	299	7.00%	0.32 [0.19, 0.55]	2008	
Subtotal (95% CI)		376		299	7.00%	0.32 [0.19, 0.55]		
Total events	22		48					
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.16 (P < 0.0001)								
2.1.4 Duration of Observation: 6 Months								
Wang SS, et al. [16]	58	184	69	147	7.50%	0.52 [0.33, 0.82]	2002	
Wang SS, et al. [19]	27	189	32	128	6.80%	0.50 [0.28, 0.89]	2004	
Huang YK, et al [22]	166	1263	315	1263	8.60%	0.46 [0.37, 0.56]	2006	
Qi FS et al. [34]	72	828	159	856	8.20%	0.42 [0.31, 0.56]	2011	
Subtotal (95% CI)		2464		2394	31.10%	0.45 [0.39, 0.53]		
Total events	323		575					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.77$, df = 3 (P = 0.86); $I^2 = 0\%$								
Test for overall effect: Z = 10.08 (P < 0.00001)								
2.1.5 duration of observation: 7-12 Months								
Wang SS, et al. [19]	133	879	274	827	8.50%	0.36 [0.28, 0.45]	2004	
Wang Ml et al. [24]	2	48	10	44	2.60%	0.15 [0.03, 0.72]	2006	



Li ZJ et al. [23]	6	125	33	138	5.00%	0.16 [0.06, 0.40]	2006	
Li ZJ et al. [27]	19	317	33	300	6.70%	0.52 [0.29, 0.93]	2008	
Xu QH et al. [33]	5	193	74	440	4.90%	0.13 [0.05, 0.33]	2010	
Subtotal (95% CI)		1562		1749	27.80%	0.27 [0.17, 0.45]		
Total events	165		424					
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 10.11$, df = 4 (P = 0.04); $I^2 = 60\%$								
Test for overall effect: Z = 5.17 (P < 0.00001)								
2.1.6 Duration of Observation: 18 Months								
Zhao XF et al. [20]	43	184	62	118	7.20%	0.28 [0.17, 0.45]	2004	
Chen JS et al. [21]	171	993	321	943	8.50%	0.40 [0.33, 0.50]	2005	
Subtotal (95% CI)		1177		1061	15.80%	0.36 [0.25, 0.51]		
Total events	214		383					
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 1.90$, df = 1 (P = 0.17); $I^2 = 48\%$								
Test for overall effect: Z = 5.80 (P < 0.00001)								
Total (95% CI)		8406		8408	100.00%	0.27 [0.20, 0.36]		
Total events	1000		2575					
Heterogeneity: $Tau^2 = 0.27$; $Chi^2 = 139.52$, df = 15 (P < 0.00001); $I^2 = 89\%$								
Test for overall effect: Z = 8.47 (P < 0.00001)								
Test for subgroup differences: $Chi^2 = 79.04$, df = 5 (P < 0.00001), $I^2 = 93.7\%$								

Table 3: Effect of IFSS on anemia prevalence in age groups of intervened subjects.

Study Group or Subgroup	Favours IFSS Events	Total	Favours Non-IFSS Events	Total	Weight	Odds Ratio MH, Random,95%CI	
2.1.1 Age, >=3 Years							
Chen JS et al. [14]	171	993	321	943	0.085	0.40 [0.33, 0.50]	
Subtotal (95% CI)		993		943	0.085	0.40 [0.33, 0.50]	
Total events	171		321				
Heterogeneity: Not applicable							
Test for overall effect: Z = 8.37 (P < 0.00001)							
2.1.2 Age, 3-6 years							
Wang SS et al. [19]	27	189	32	128	0.068	0.50 [0.28, 0.89]	
Zhao XF et al. [20]	43	184	62	118	0.072	0.28 [0.17, 0.45]	
Subtotal (95% CI)		373		246	0.14	0.36 [0.20, 0.65]	
Total events	70		94				
Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 2.38$, df = 1 (P = 0.12); $I^2 = 58\%$							
Test for overall effect: Z = 3.39 (P = 0.0007)							
2.1.3 Age, 3-18 Years							
Huang YK et al. [22]	166	1263	315	1263	0.086	0.46 [0.37, 0.56]	
Subtotal (95% CI		1263		1263	0.086	0.46 [0.37, 0.56]	
Total events	166		315				
Heterogeneity: Not applicable							
Test for overall effect: Z = 7.44 (P < 0.00001)							
2.1.4 Age, 6-19 Years							
Fang ZF et al. [25]	22	376	48	299	0.07	0.32 [0.19, 0.55]	
He SL et al. [26]	8	68	73	95	0.052	0.34 [0.14, 0.80]	
Huo JS et al. [12]	1	77	972	81	0.017	0.00 [0.00, 0.01]	
Li LJ et al. [28]	265	2600	159	2648	0.087	0.20 [0.17, 0.23]	
Qi FS et al. [34]	72	828	73	856	0.082	0.42 [0.31, 0.56]	
Sun J et al. [17]	2	82	274	81	0.026	0.00 [0.00, 0.01]	
Wang SS et al. [19]	133	879	74	827	0.085	0.36 [0.28, 0.45]	



Xu QH et al. [33]	5	193		440	0.049	0.13 [0.05, 0.33]
Subtotal (95% CI		5103		5327	0.47	0.16 [0.09, 0.27]
Total events	508		1700			
Heterogeneity: Tau^2 = 0.43; Chi^2 = 90.44, df = 7 (P < 0.00001); I^2 = 92%						
Test for overall effect: Z = 6.72 (P < 0.00001)						
2.1.5 Age, 21-38 Years						
Li ZJ et al. [23]	6	125	33	138	0.05	0.16 [0.06, 0.40]
Li ZJ et al. [27]	19	317	33	300	0.067	0.52 [0.29, 0.93]
Wang MI et al. [24]	2	48	10	44	0.026	0.15 [0.03, 0.72]
Subtotal (95% CI)		490		482	0.144	0.26 [0.10, 0.67]
Total events	27		76			
Heterogeneity: Tau^2 = 0.42; Chi^2 = 5.69, df = 2 (P = 0.06); I^2 = 65%						
Test for overall effect: Z = 2.82 (P = 0.005)						
2.1.6 Age,s >55 Years						
Wang SS et al. [16]	58	184	69	147	0.075	0.52 [0.33, 0.82]
Subtotal (95% CI)		184		147	0.075	0.52 [0.33, 0.82]
Total events	58		69			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.85 (P = 0.004)						
Total (95% CI)		8406		8408	1	0.27 [0.20, 0.36]
Total events	1000		2575			
Heterogeneity: Tau^2 = 0.27; Chi^2 = 139.52, df = 15 (P < 0.00001); I^2 = 89%						
Test for overall effect: Z = 8.47 (P < 0.00001						
Test for subgroup differences: Chi^2 = 15.03, df = 5 (P = 0.01), I^2 = 66.7%						

IFSS Production and Consumption

The IFSS production data was collected from manufacturers by Food Fortification Office. Social marketing has been conducted national wide and IFSS sells mainly in supermarkets and grocery stores. The average annual IFSS production was 67,500 MT ranged from 2.6 to 10.0 MT in different years. The accumulated IFSS production from 2004 to 2013 is 675,000 MT (Figure 1). It was theoretically estimated that 207.78 million populations have consumed IFSS in the period and that the consumption of 8.9 g soy sauce per person per day is assumed. Among those IFSS consumption population, the IFSS effective population is 83.11 million adjusted by 40.0%, the ratio of regular and constant IFSS consumers. Further calculation according to the equation described in the methods part, using 0.27 odd ratio between IFSS effective population to none IFSS population, the IFSS reduced anemia population was estimated as 23.8% of the total reduced anemia population.

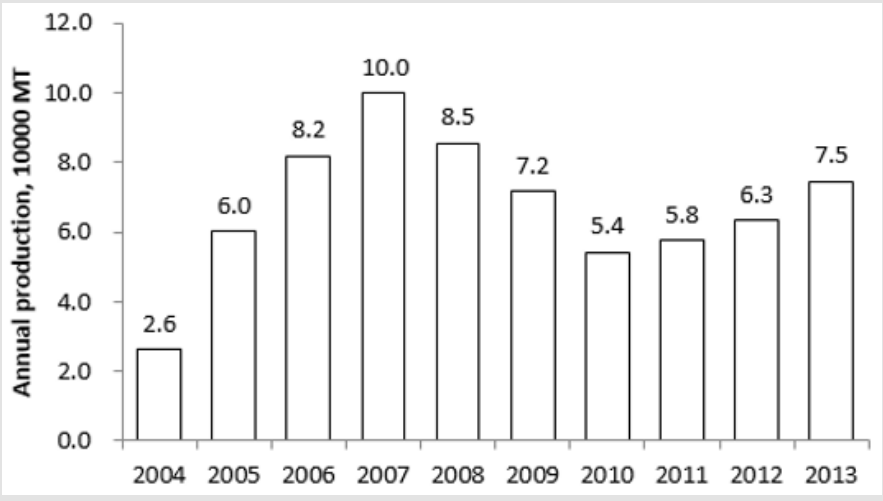


Figure 1: IFSS production from 2004 to 2013.

Discussion

IFSS project is a voluntarily food fortification project implemented from 2004 to 2013 in Mainland China. The project tried to use a new working mechanism to scale up the use of IFSS in consumers which is named the government leading partnership model. Data from national nutrition surveys showed that the anemia prevalence has decreased significantly in the past decade. Economic development, more adequate of food supply, awareness on anemia and IFSS project should be the main causes for this nutrition improvement [30]. But there seems lack of suitable method to estimate the contribution of IFSS among the various casual factors. We defined in this study the contribution of IFSS on anemia reduction as percentage of anemia reduction in terms of population by IFSS to the total anemia reduction population. The calculation was conducted through several assumptions and available national survey data. Results showed that the estimated contribution by IFSS was 23.8% to the total reduction of anemia population during past decade, which suggests a remarkable impact of the IFSS project. Accuracy of original data including anemia population reduced, production and consumption of IFSS, and effectiveness of IFSS on anemia, etc. are crucial to the validity of the estimation. The net increase of population from 2003 to 2014 in China is 62 million which is included in the calculation as their anemia status could be impacted by IFSS.

Data of anemia prevalence used in this study represents the population, since the surveyed population covered major high-risk age groups for anemia. There are 16 high quality RCT studies with a total sample size of 8406 subjects covered different age groups and intervention duration. Results of systematic analysis showed the effectiveness of IFSS intervention, but there were no significant differences among groups in different ages and intervention duration. It could be explained by homeostasis of iron and Hb in human body. Iron depletion or inadequacy could be recovered by increase of iron intake, but when body iron store reaches the normal range, its absorption or bioavailability would be decreased that could stop the further increase of body iron level. Hemoglobin level would be lifted to the normal range as a result of iron getting enough but remain stable if iron intakes satisfying the physiological requirement. IDA population accounted for about 50% of the total anemia in Chinese population [31]. Other types of anemia would not be affected by IFSS. Therefore, anemia prevalence would not be reduced to zero by increase dietary iron intake and the effects of IFSS could not continuously increase with prolonged intervention time.

IFSS production data was collected each year from soy sauce manufactures which are partners to IFSS project organized by Food Fortification Office, China CDC. There are some uncertainties and imprecision in the IFSS production data as well as soy sauce consumption data. For example, the production data should not accurately represent consumption data at the same time point. However, since production of each batch of IFSS is rather small and in most cases, manufactures would produce IFSS according to orders from traders or distributors. Therefore, the production data are reasonably reliable to be used in this study as a represent data of consumption. The daily soy sauce consumption data was obtained from the national survey in 2002. A wide range of consumption was observed, and we used the average daily consumption for the calculation of IFSS effective population. Bias would be introduced by the estimation. It would be preferred for this study with detailed survey data of IFSS consumption such as data from every year, data in various regions and different social-economic classes etc. The consumption pattern of IFSS should be another uncertainty for the analysis. IFSS consumers could be roughly divided into several groups, such as occasional, intermittent, constant and regular. Each of the consumption patterns would be related with the effectiveness on anemia reduction. In this study, we included regular and constant IFSS consumers as the effective IFSS population which would underestimate the contribution of IFSS as there would be benefit from other patterns of IFSS consumption. The underestimation of IFSS contribution would also come from the lack of nutrition knowledge.

IDA, as a widespread malnutrition issue, could results in heavy losses at both personal and social context. Elimination of IDA as one of the public health goals has been continuously worked on by many countries and organizations. Wheat flour fortification with iron and other micronutrients has played key roles in IDA control and accumulated enough international experiences [32]. In China, wheat flour fortification was promoted in poor regions and showed positive effects in IDA prevention, but the product of fortified wheat flour is not widely available in the market. Comparatively, iron fortified soy sauce as a food fortification project had no international experience to borrow, but it applauded by soy sauce producers as predominant part of condiment industry because of needing of new technology in this traditional industry. IFSS project being an action on combating IDA launched by Chinese government used a new working mechanism in the scaling-up promotion, which is neither mandatory nor voluntary, but a government leading partnership model. IFSS is promoted and encouraged to use by consumers by the government and partners such as government officials and public health professionals calling on the consumers to consume IFSS in television, broadcast and newspapers, but purchased by consumers. Communication and public education were focused on at-risk population groups, including the rural and the vulnerable groups in urban, as well as women, elderly and children in both rural and urban areas. Consumers even in the poorest regions could purchase IFSS in the market with the same price or a little higher price within the market tolerance. Most of those who are anemic or whose family members are anemic would prefer to buy and consume IFSS [33,34]. Although the total production of IFSS is still very low compared with the total soy sauce production but has been considered as sustainable with slow but continuous increase in the market.

This study showed that 23.8 % reduction of anemia population is owning to IFSS consumption. It evidenced that the IFSS project contribute significantly to anemia control as a low cost and sustainable approach. It should be emphasized this study needs further work with more detailed survey data. And, sophiscated cost-benefit analysis of IFSS application in the control of anemia should be carried out, in order to further promote the use of IFSS in China.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest to this study.

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