Iodine deficiency disorders after a decade of universal salt iodization in a severe iodine deficiency region in China

Yanling Wang^{*,**}, Zhongliang Zhang[†], Pengfei Ge^{**}, Yibo Wang^{*} & Shigong Wang[‡]

*The Gansu Key Laboratory of Arid Climate Change & Reducing Disaster, College of Earth & Environment Sciences, Lanzhou University, **Gansu Center for Diseases Control & Prevention, †The First People Hospital of Lanzhou City & ‡College of Atmospheric Sciences, Lanzhou University, Lanzhou Gansu, PR China

Received January 28, 2008

Background & objectives: Universal salt iodization (USI) was implemented in all counties of China in 1995. This study was undertaken to assess the status of iodine deficiency disorders control and prevention after 10 years of implementation of USI in a severe iodine deficiency region in China.

Methods: Thirty primary school were selected in Gansu province utilizing cluster sampling methodology for the years 1995 and 2005. In each selected school, 40 children aged 8-10 yr were randomly selected for thyroid and IQ examination, and urinary samples were collected from 12. On the spot casual urine samples and salt samples were collected from a subset of children included in the study. In 2005, casual urine samples were also collected from 50 pregnant and lactating women in each cluster. Effect of health education was studied by a combination method of giving questionnaires to and observing students and families.

Results: The total goiter rates (TGR) were found to be 13.5 and 38.7 per cent in 2005 and 1995 respectively. The medians urinary iodine excretion levels of children were 191.8 and 119.9 μ g/l in 2005 and 1995. The median urinary iodine excretion level of women was 161.9 μ g/l. The mean intelligence quotient (IQ) was 96.9 in 2005 significantly more than that in 1997 (*P*<0.05). The health education pass rate of children and women were 21.1 and 51.1 per cent respectively.

Interpretation & conclusion: After ten years of universal salt iodization (USI), iodine nutrition of people improved and the current iodine nutrition status of population was adequate. Decrease in TGR and increase in IQ showed that IDD control and prevention had made great progress through ten years USI, salt iodization played the key role in IDD control and prevention for sustained elimination of IDD, the programme of USI and other measures like health education should be persisted and enforced.

Key words Goiter - health education - intelligence quotient (IQ) - iodine deficiency disorders (IDD) - salt iodization - urinary iodine excretion (UIE)

Iodine is an essential ingredient for the synthesis of thyroid hormones. Iodine deficiency (ID) causes goiter and different forms of physical and mental retardation. Iodine deficiency disorders (IDD) affect the poor, pregnant woman and preschool children^{1,2}. Normal levels of thyroid hormones are required for neuronal migration and myelination of the foetal brain, and lack of iodine irreversibly impairs brain development³.

Severe ID during pregnancy increases risk for stillbirths, abortions, and congenital abnormalities^{4,6}. Cross-sectional studies of moderate to severely iodinedeficient children have generally reported impaired intellectual function and fine motor skills. Two metaanalyses estimated that populations with chronic ID experience a reduction in intelligence quotient (IQ) of 12.5-13.5 points^{7,8}. Iodized salt has been recognized as the most effective way to control and prevent IDD. Universal salt iodization (USI) has been remarkably successful in many countries. Over 30 countries have achieved the goal of USI (>90% of households using iodized salt), and many others are on track¹. USI was implemented in China in all counties in 1995. The initial iodization level was set at 50 mg/kg (50 ppm), later reduced in 2000 to 35 (± 15) ppm after national monitoring of urinary iodine concentration showed this intake to be excessive; the medians of urinary iodine of school children, at provincial level, were over 300 µg/lin 18 and 14 provinces in 1997 and 1999, respectively ^{9,10}. IDD is a significant public health problem in China11. Monitoring of iodized salt was carried out at county level one time per year in higher iodized salt coverage counties and two time per year in lower iodized salt coverage counties. A national survey in 1995 found the prevalence of goiter among school children to be ≥ 10 per cent in 27 of 30 provinces¹². This study was in conducted 1995 when USI was implemented and a decade later in 2005 with the objectives to assess the effects of USI on the status of IDD in a severe iodine deficiency region in China.

Material & Methods

Study area: Gansu province in China was classified in 1995 as having a severe level of IDD according to WHO/UNICEF/ICCIDD criteria¹² with a total goiter rate in school children of 38.7 per cent and median urinary iodine level of 119.9 µg/l. It is located in the west part of China. Gansu has twelve cities and two autonomous prefectures and 87 counties (cities and districts) directly under its jurisdiction. The province total area is 454,400 square kilometers and its population is 26.0625 million at the end of 2006¹³. Gansu is a landlocked, mountainous area with little rain that is far from sea. In more than 90 per cent samples of drinking water the iodine contents was less than 10 µg/l¹⁴ in surveillance in 1999. 850,000 patients had visible goiter, cretins were 20000 according to investigation in Gansu province.

The school enrollment rate of children in the age group of 8-10 yr was more than 90 per cent in Gansu

province and hence, a school based study was conducted in 1995 and then in 2005 using the same methods. The 30 clusters sampling methodology recommended by WHO/UNICEF/ICCIDD¹ was utilized for selecting the clusters. Thirty schools were selected and in each school, 40 children aged 8-10 yr were selected randomly for thyroid examination and IQ test; urinary samples were collected from 12 of these 40 children randomly^{9,10} as the number of urinary samples can represent the urinary iodine level of the people¹⁵. The goiter was graded according to the criteria recommended by the joint WHO/UNICEF/ICCIDD in 1994¹⁶ (grade 0, no goiter; grade 1, thyroid palpable but not visible; and grade 2, thyroid visible with neck in normal position). When in doubt, the immediate lower grade was recorded. The intra- and inter- observer variation was controlled by repeated training and random exam inations of goiter grades by another author. The results were recorded in a pre-designed questionnaire. The sum of grades 1 and grades 2 provided the total goiter rate (TGR) of the study population¹⁶. If the requisite number of children could not be completed from the selected cluster/school, then the nearest adjointing school was included to complete the total number of subjects to be covered in the cluster.

Intelligence quotient (IQ) of children included in the study was tested with Combined Raven's Test Rural and City in China^{17,18}. The Ravens was designed to reduce the biases that language differences can have on measuring IOs. It allows children to show patternrecognition, attention to details, memory, and spatial reasoning. This test is suitable for group measurement and is less likely to be affected by environment, culture, and acquired knowledge¹⁹. The Chinese norm was applied to calculate the age-adjusted IQ value for each child¹⁷. The IQ value of superexcellence was >130, excellence 120-129, upper middling 110-119, middling 90-110, below middling 80-89, verge mental retardation 70-79, mental retardation ≤ 69 , and a prevalence of mentally retarded children in normal group was 2.2 per cent according to Chinese norm¹⁷.

On the spot casual urine sample were collected from 12 of 40 children selected in each school. Because pregnant and lactating women, and infants are most susceptible to iodine deficiency disorders²⁰, we added pregnant and lactating women as study subjects in 2005. Fifty pregnant and lactating women were selected in the same administrative village (or community) with the chosen school in 2005. A total of 1751 pregnant and lactating women were included in the study. Plastic

bottles with screw caps were provided to children and women for the urine samples. The samples were stored in the refrigerator until analysis. The urinary iodine excretion (UIE) levels were analyzed using the acid-digestion method²¹. All iodine analyses were conducted in the provincial iodine laboratory, which is accredited by National IDD Reference Laboratory. Urinary iodine analysis of 18 blind control samples at three concentration levels conducted by the provincial laboratory did not demonstrate any bias compared to the results from National IDD Reference Laboratory. The children were provided with auto seal polythene pouches with an identification slip and to bring two tea spoons of salt (about 10 g) from their family kitchen and the iodine content of salt samples was analyzed by the National standard method of titration²². Health education plays an important role in IDD control and prevention, so health education was surveyed by a combination method of giving questionnaires to students and women and at the same time observing behaviour of women in 2005. Twenty children were selected randomly in one class of the 5th grade in

Table I. R	esults of thyro	oid examin	ation of child	dren (8-10	yr) in 2005			
Age	Number	Go	Goiter grade (%)					
group		0	Ι	II	goiter			
(yr)					rate (%)			
8	375	89.3	10.4	0.3	10.7			
9	439	87.9	11.6	0.5	12.1			
10	427	82.7	16.4	0.9	17.3			
Total	1241	86.5	12.9	0.5	13.5			

the chosen school, and questionnaire survey was conducted. Also five pregnant or lactating women from the same administrative village (or community) with the chosen school, were selected randomly and given the questionnaires.

Before the study, women groups and parents of children were explained about the study and consents were obtained. The study protocol was approved by ethical committee of Gansu Center for Diseases Control and Prevention.

Statistical analysis: Results were analyzed by SPSS (version 10.0). Medians were used to describe the iodine concentration in urine and salt. Chi square test was used to compare prevalence of goiter.

Results

Goitre: A total of 1241 children in the age group of 8-10 yr were included in 2005 & (49.8 % boys 50.2% girls). The total goiter prevalence was found to be 13.4 per cent in boys and 13.5 per cent in girls. The TGR was found to be 13.5 per cent in 2005. It was observed that the total goiter rate increased with the increase in age (Table I). Compared with the study of 1995, the TGR decreased from 38.7 to 13.5 per cent (P < 0.05).

Urinary iodine concentration: The proportion of children with urinary iodine excretion (UIE) levels 0-19.9, 20.0-49.9, 50.0-99.9 and \geq 100 µg/l was 2.0, 8.4, 14.0 and 75.6 per cent in 2005. The median UIE of the study children was found to be 191.8 µg/l in 2005 and 119.9 µg/l in 1995 (Table II). The median UIE of pregnant and lactating women was 172.2 and 159.2

Table II. Urinary iodine excretion levels of children (8-10 yr old)

Year n	n	Median urinary iodine concen-	Frequenc	n level (%)		
		tration (µg/l)	0-19.9	20-49.9	50-99.9	$\geq \! 100 \ \mu\text{g/l}$
1995	362	119.9	0.6	5.2	11.1	83.1
2005	356	191.8	2.0	8.4	14.0	75.6

Table III.	Urinary iodine	excretion lev	vels of women	in 2005
------------	----------------	---------------	---------------	---------

Population group	Number	Median urinary iodine concentra-	Frequency distribution of urinary iodine excretion level (%)				
		tion (µg/l)	0-19.9	20-49.9	50-99.9	$\geq 100 \ \mu g/l$	
Pregnant women	487	172.2	2.5	7.6	15.4	74.5	
Lactating women	1264	159.2	3.4	10.1	16.5	70.0	
Total	1751	161.9	3.1	9.4	16.2	71.3	

	Table IV. Results of iodized salt estimation at household level in 1995 and 2005								
Year	N	Iodine median of iodized salt (ppm)	Non-iodized salt rate (<5p pm) (%)	5-20 ppm (%)	Consumption rate of qulified iodized salt (%)	Qualified iodized salt (%)			
1995	1200	23.5	7.1	32.5	55.5	59.9			
2005	1147	30.0	7.7	2.8	88.9	96.6			

Table V. Intelligence quotient (IQ) level and its distribution of school-age children in 2005

Year	n	IQ		Frequency distribution (%)					
		(mean±SD)	<69	70-79.9	80-89.9	90-99.9	110-119.9	120-129.9	<u>≥</u> 130
2005	1102	96.9±15.6	4.6	8.8	17.9	48.0	13.5	6.8	0.4
Theory distribution ¹⁹	—	100±15	2.2	6.7	16.1	50.0	16.1	6.7	2.2

Table VI. The outcome of health education of children and women in 2005

Population group Number		Knowing IDD harm (%)	Knowing iodized salt can Mean score prevent IDD (%)		Pass rate (%)
Children	555	24.3	48.5	34.6	21.1
Women	133	15.8	45.9	56.3	51.1

 μ g/l respectively. The total median UIE of women was 161.9 μ g/l (Table III).

Salt iodine level: Median level of iodine in salt was 23.5 ppm in 1995 and 30.0 ppm in 2005. A total of 32.5 and 2.8 per cent salts had iodine content 5-20 ppm and the consumption rates of qualified iodized salt (20-50 ppm) were 59.9 and 96.6 per cent respectively in 1995 and 2005, reflecting the quality of iodized salt has been improved greatly (Table IV). The consumption rate of qualified iodized salt was 55.5 per cent in 1995 and 88.9 per cent in 2005.

Intelligence quotient: IQ of 1102 children included in the study was tested in 2005. The mean IQ was 96.9 (Table V). The mean IQ of children has been improved compared with that of 91.0 in 1997²³ (P<0.05). But IQ values still showed a positive skewed distribution.

Health education: The health education pass rate of children and women was 21.1 and 51.1 per cent respectively (Table VI) indicating health education measures were very week.

Discussion

Salt iodization has been an effective, safe and convenient measure to control and prevent IDD. After ten years of USI, the consumption rate of qualified iodized salt increased in Gansu province, but did not reach the standard of National IDD elimination (>90%). The total goiter rate increased with the increase in age. May be at the beginning of USI, the consumption rate of qualified iodized salt was very low, the older children (born in 1995) have higher risk of exposure to iodine deficiency than younger children (born in 1996 and 1997). The iodine nutrition of people has improved. The median urinary iodine excretion levels of children and women has reached the criterion recommended by the WHO¹ and the current iodine nutrition status of population was adequate. Though the TGR decreased greatly from the year 1995, the TGR of children was still 13.5 per cent. One reason is that the TGR represent the chronic iodine deficiency while the urinary iodine excretion (UIE) levels indicate the current iodine nutrition. The size of the thyriod gland changes inversely in response to alterations in iodine intake, with a lag interval that varies from a few months to several years, depending on many factors. These include the severity and duration of iodine deficiency, the type and effectiveness of iodine supplementation, age, sex, and possible additional goitrogentic factors¹. Another reason was the consumption rate of disqualified iodized salt was still high. The IQ values had improved from 91.0 in 1997 to 96.9 in 2005, but the brain development of children was still damaged³.

After ten years of USI, IDD control and prevention had made great progress in Gansu province. Iodine nutrition of people had reached to an appropriate level. Salt iodization played key role in IDD control and prevention. In order to achieve the goal of IDD sustained elimination, the Universal Salt Iodization Programme should be persisted and the quality of iodized salt provided to the beneficiaries should be monitored continuously. In addition, emphasis need to be given on health education.

Acknowledgment

This work was supported by National Support Project for Science and Technology in China (2007BAC29B03) and the Project of National Natural Science Foundation of China (40675077).

References

- WHO/UNICEF/ICCIDD. Assessment of iodine deficiency disorders and monitoring elimination. 3rd ed. Geneva: WHO; 2007.
- Delange F, Hetzel B. The iodine deficiency disorders. In: DeGroot LE, Hannemann G, editors. *The thyroid and its diseases*. Available from: *http://www.thyroidmanager.org/S*, accessed on January 18, 2008.
- Morreale de Escobar G, Obregon MJ, Escobar del Rey F. Role of thyroid hormone during early brain development. *Eur J Endocrinol* 2004; *151*(Suppl. 3): U25-37.
- 4. Pharoah POD, Buttfield IH, Hetzel BS. Neurological damage to the fetus with severe iodine deficiency during pregnancy. *Lancet* 1971; *i* : 308-10.
- Dillon JC, Milliez J. Reproductive failure in women living in iodine deficient areas of West Africa. *Br J Obstet Gynaecol* 2000; 107: 631-6.
- Cobra C, Muhilal, Rusmil K, Rustama D, Djatnika, Suwardi SS, *et al.* Infant survival is improved by oral iodine supplementation. *J Nutr* 1997; *127*: 574-8.
- Bleichrodt N, Garcia I, Rubio C, Morreale de Escobar G, Escobar del Rey F. Developmental disorders associated with severe iodine deficiency. In: Hetzel B, Dunn J, Stanbury J, editors. *The prevention and control of iodine deficiency disorders*. Amsterdam: Elsevier; 1987. p. 65-84.
- Qian M, Wang D, Watkins WE. The effects of iodine on intelligence in children: a meta-analysis of studies conducted in China. *Asia Pac J Clin Nutr* 2005; 14: 32-42.
- Chen JX, Li ZZ, Xu HK, Hao Y. *China national IDD surveillance in 1997*. Beijing: People's Health Publishing House; 2000. p. 3-21 (in Chinese).

- Chen JX, Li ZZ, Hao Y, Xu HK. *China national IDD surveillance in 1999*. Beijing: People's Health Publishing House; 2002. p. 3-34 (in Chinese).
- WHO/UNICEF/ICCIDD. Global prevalence of iodine deficiency disorders, Micronutrient Deficiency Information System Working Paper No.1. Geneva: WHO; 1991.
- 12. Comprehensive evaluation and planning mission. Report of the Mission's Observations and Recommendations, Program of International Cooperation for the Elimination of IDD in China by the year 2000. Program against micronutrinent malnutrition, Atlanta, USA; July 1-15, 1996.
- Population and Family Planning Comission of Gansu. The population data of every city and country in 2006 in Gansu province. Available from: http:// www. gsjsw. gov.cn /html / gsrksj /17_19_20_183.html.
- Zhang YX, Zhu XN, Li L, Yang HX, Yang CH, Tian DL. The investigation about relationship betweent iodine deficiency and intelligence of children in Gansu province, China. *Chin J Endemiol* 2000; *3-1* : 145-7.
- Yan Y, Chen Z. Correct or standardized application of the biological indicator-Urinary Iodine. *Chin J Endemiol* 2002; 6: 512-4.
- WHO/UNICEF/ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodization. Geneva: World Health Organization; 1994.
- Wang D, Qian M, Gao Y. Re-standardization of Combined Raven Test Norm (CRT-C2) for Chinese children. In: *Scientific development of intellectual test for new century*. Taipei: Taiwan Psychological Publishers;1999. p. 387-401.
- Wang D, Qian M. A report on the revision of combined Raven Test for rural China. *Xin Li Tong Xun* 1989; 5: 23-7.
- GaoY, Qian M, Wang D. The ten year comparision study on intelligence development of children in China – The analysis of new established Combined Raven Test Norm. *Chin J Clin Psychol* 1998; 3: 185-6.
- Francois Delange. Iodine deficiency in Europe and its consequences: an update. *Eur J Nuclear Med Mol Imaging* 2002; 9:404-16.
- Dunn JT, Crutchfield HE, Gutekunst R, Dunn D. Two simple methods for measuring iodine in urine. *Thyroid* 1993; 3:119-23.
- State Bureau of Quality Technical Supervision. *General test method for measuring iodine in salt.* (Chinese criteria). Beijing: Publishing House; 1999, GB/T 13025.7-1999.
- Zhang YX, Yang HX, Zhu XN, Li L, Yang CH, Cao YQ, et al. The study on iodine deficiency caused intelligence damage in Gansu province, China. Chin J Epidemiol 2003; 1: 76-7.

Reprint requests: Dr Yibo Wang, College of Earth & Environment Sciences, Lanzhou University, Lanzhou Gansu 73000, P.R. China e-mail: wylxiao@126.com