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Full Length Research Paper

Fluoride and thyroid function in children in two villages in China

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Eighty two children, aged 8 - 13 years old, from Wamiao village (severe endemic fluorosis area), from Xinhuai village (nonendemic fluorosis area) were 88 (as a control group), were recruited in this study. The prevalence of dental fluorosis (DF) were 85.37% (Wamiao) and 6.82% (Xinhuai) in two village's children respectively; drinking water fluoride (F^-) in children's household shallow well from 0.62 - 4.00 mg/L in Wamiao and 0.23 - 0.76 mg/L in Xinhuai; serum total triiodothyronine (TT3), total thyronine (TT4), thyroid-stimulating hormone (TSH) were 1.47 ± 0.28 and 1.47 ± 0.33 ng/mL, 9.67 ± 1.76 and 9.22 ± 2.54 μg/dL, 3.88 ± 2.15 and 2.54 ± 2.07 μIU/mL in two villages children respectively. The prevalence of DF, drinking water F^-, serum TSH in Wamiao village was significantly higher than that in Xinhuai village. As the children in Wamiao village were divided into different subgroups according to their severity of DF, serum TT3 and TSH showed significant difference in different groups. The results in this study confirmed that the high F^- exposure can caused functional abnormalities of thyroid, and the different severity degree of DF may be relation to significant deviation in the serum levels of thyroid hormone.

Key words: Thyroid function, fluoride, dental fluorosis.

INTRODUCTION

Professor John Grevers had sent specimens of mottled teeth, found the identical condition in the teeth of people with goiter in Utrecht; Grevers also obtained laboratory evidence that there was a clear association of his clinical cases of goiter with mottled enamel; Goldemberg even became convinced that the goiters were, in fact, caused by excessive intake of fluoride (F^-) (Schuld, 2005).

Some animal studies indicated that the rats had thyromegaly, increasing or reducing of thyroid weight, reducing of follicle and atrophy of follicular epithelium of thyroid when the rats were exposed to F^- for 6 ~ 12 months (Editorial, 1976). The research results also indicated that F^- can affect the hormone secretion of the thyroid (Chuanhua et al., 1998; Desun et al., 1994; Fuzun et al., 2001; H Wang et al., 2009; Hu Aiwu et al., 2007; Juvenal et al., 1978; Liu Guoyan et al., 2008; Xiuan Z et al., 2006). Yaming et al. gave the results that excessive long-term intake of F^-, with or without adequate intake, are a significant risk factor for the development of thyroid dysfunction (Yaming et al., 2005). A few future studies on human showed different results. Xiaoli et al. (1999) reported that serum thyronine (T4) reduced significantly, but the triiodothyronine (T3); thyroid-stimulating hormone (TSH) increased significantly, in the 8 - 12 years old children in endemic fluorosis areas in China. T3 and T4 concentrations in the serum of the patients with endemic fluorosis were significantly below the Normal reference value (Guimin et al., 2001). Whereas the study by Mingyin F (Mingyin et al., 1994) and other researchers (Baum et al., 1981; Eichner et al., 1981) indicated that the high F^- intake does not have effects on thyroid-function. In order to get a better understanding between the F^- intake and the children's thyroid function, this study investigated the TT3 (total T3), TT4 (total T4), and TSH in the serum of the children in endemic fluorosis and

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Abbreviations: DF, Dental fluorosis; **F^-,** fluoride; **T3,** 3,5,3'-triiodothyronine; **TT3,** total 3,5,3'- triiodothyronine; **FT3,** free 3,5,3'- triiodothyronine; **T4,** thyronine; **TT4,** total thyronine; **FT4,** free thyronine; **TSH,** thyroid-stimulating hormone; **IDD,** iodine deficiency disorder.

Table 1. F^- in drinking water in children's household shallow well in two villages.

Village	No. of samples	F^- (mg/L) (M±S)	Range (mg/L)
Wamiao	82	2.36 ± 0.70	0.62 ~ 4.00
Xinhuai	88	0.36 ± 0.10	0.23 ~ 0.76

Note: t = -26.47, p = 0.000.

Table 2. Prevalence of DF in children in two villages.

Village	No. of samples	No. of DF	Prevalence of DF (%)
Wamiao	82	70	85.37
Xinhuai	88	6	6.82

Note: χ^2 = 105.94, p = 0.000.

Table 3. TT3 concentration in serum in the children in two villages (ng/mL).

Village	No. of samples	TT3 (M±S)	Range
Wamiao	62	1.47 ± 0.28	1.01 ~ 2.10
Xinhuai	68	1.47 ± 0.33	0.66 ~ 2.20

Note: t = 0.855, p = 0.394.

Table 4. TT4 concentration in serum in the children in two villages (µg/dL).

Village	No. of samples	TT4 (M ± S)	Range
Wamiao	58	9.67 ± 1.76	5.98 ~ 15.09
Xinhuai	61	9.22 ± 2.54	5.22 ~ 15.41

Note: t = 1.111, p = 0.269.

non-endemic fluorosis areas, the dental fluorosis (DF) and the drinking water F^- concentration in children's household shallow well were also analyzed.

MATERIALS AND METHODS

The investigation of age, gender, and DF was conducted from February, 2003 - June, 2003 in Wamiao village (a severe endemic fluorosis area) and Xinhuai village (a non-endemic fluorosis), and the samples of water and blood were also collected during this time. The basic information of these two villages was formerly reported (QY Xiang et al., 2004).

Fasting venous blood samples (2 - 2.5 mL) were collected and preserved in clean plastic centrifuge tubes, which were immediately centrifuged for 10 min at 3000 rpm. Serum was quickly removed to other clean plastic tubes and kept in a refrigerator at -40℃. The TT3, TT4 and TSH were measured at the time of September, 2006, with the Test Kit, which were bought from Hainan Huamei Medicine Co. LTD, manufactured by BioCheck, Inc. (Foster City, CA94404, USA).

The drinking water samples, which were collected from the household shallow wells in each child's family, were kept in clean plastic bottles and analyzed within two week. F^- in drinking water was measured with an F^- ion selective electrode according to the National Standard of China (National Standard of P.R. China, 1999). A dentist and a specialist in endemic fluorosis control and prevention examined the children for dental fluorosis with a mouth mirror, forceps, and a probe under natural light. Dean's classification was used for diagnosing dental fluorosis. The six grades of Dean's classification scale for dental fluorosis are: none (normal enamel) (the score marked for 0), suspected or questionable (0.5), very mild (1), mild (2), moderate (3), and severe (4) (Chinese Ministry of Health 1991). Statistical analysis of the prevalence of dental fluorosis was made according to the rates of DF%.

Data were analyzed using SPSS Software. Before the investigation, the informed consent must be signed by the children's parents. We have complied with all requirements of International Regulations for the human investigation.

RESULTS

There were 170 children in this study, 82 in Wamiao village (46 male and 36 female), 88 in Xinhuai village (52 male and 36 female). The average age was 11.00 ± 1.44 in Wamiao village and 10.84 ± 1.67 in Xinhuai village.

The F^- concentration in drinking water and the prevalence of DF in two villages were shown in Table 1 - 2. The results indicated that the drinking water F^- and the prevalence of DF in children in Wamiao village were significantly higher than that in Xinhuai village.

The TT3 and TT4 concentrations in children's serum in two villages were not have significant difference. But the TSH concentration in the children's serum in Wamiao village was higher than that in Xinhuai village, there was a significant difference between two villages. The details were shown in Table 3 - 5.

The means of TSH/TT3 and TSH/TT4 in Wamiao village were significant higher than that in Xinhuai village, but the means of TT3/TT4 in Wamiao village was

Table 5. TSH concentration in serum in the children in two villages (μIU/mL).

Village	No. of samples	TSH (M±S)	Range
Wamiao	62	3.88 ± 2.15	0.19 ~ 8.82
Xinhuai	67	2.54 ± 2.07	0.71 ~ 9.37

Note: t = 3.604, p = 0.000.

Table 6. Compared the difference in the values of TT3/TT4, TSH/TT3, TSH/TT4 between the two villages.

Village	TT3/TT4		TSH/TT3		TSH/TT4	
	No.*	Mean ± S	No.	Mean ± S	No.	Mean ± S
Wamiao	40	0.151± 0.037	55	2.735 ± 1.485	41	0.416 ± 0.218
Xinhuai	41	0.170 ± 0.044#	66	1.932 ± 1.813#	42	0.284 ± 0.191#

Note: * the number of subjects. # compared with Wamiao village.TT3/TT4: t = 2.028 p = 0.046; TSH/TT3: t = 2.628 p = 0.010 ; TSH/TT4: t = 2.925 p = 0.004.

Table 7. The correlation between the serum TT3, TT4, TSH in the children's serum and drinking water F^- in two villages.

Village	TT3 and F^-		TT4 and F^-		TSH and F^-	
	PC	p	PC	p	PC	p
Wamiao	0.087	0.502	0.057	0.672	0.023	0.858
Xinhuai	0.108	0.381	-0.167	0.198	-0.112	0.381

Note: F^- (drinking water fluoride). PC (Pearson correlation).

Table 8. The relationship between the DF score and the serum TT3, TT4, TSH in the children in Wamiao village.

DF (group)	TT3 (ng/mL)		TT4 (μg/dL)		TSH (μIU/mL)	
	No. of samples	TT3 (M ± S)	No. of samples	TT4 (M ± S)	No. of samples	TSH (M ± S)
1	11	1.19 ± 0.18	7	9.33 ± 1.92	8	3.31 ± 1.26
2	14	1.38 ± 0.28	15	9.20 ± 1.00	14	5.15 ± 2.68
3	22	1.54 ± 0.21	19	10.24 ± 2.18	25	3.50 ± 1.71
4	12	1.49 ± 0.34	12	9.46 ± 1.88	12	3.61 ± 2.50
5	3	1.40 ± 0.38	5	9.86 ± 1.04	3	3.74 ± 2.06

Note: TT3: 1 and 3, t = -4.680 p < 0.000; 1 and 4, t = -2.57 p = 0.018. TSH: 1 and 2, t = -2.183 p = 0.041.

significant lower than that in Xinhuai village. The details were shown in Table 6.

Each child's serum concentration of TT3, TT4, and TSH was compared with the drinking water F^- concentration in their household shallow well in two villages, there were not significant relationships between the TT3, TT4, TSH and the drinking water F^-. See Table 7.

As shown in Table 8, In Wamiao village, there were not significant trend between the dental fluorosis score (severity of DF) and the serum TT3, TT4, TSH concentration (the children with 0 and 0.5 DF score were divided into group 1, 1 score was group 2, 2 score was group 3, 3 score was group 4, 4 score was group 5). But the results of the comparison between each group indicated that the TT3 concentration has a significant difference between group 1 and group 3, group 1 and group 4; there were also significant differences between the group 1 and 2 in the TSH concentration. In Xinhuai

Table 9. The relationship between the DF score and the serum TT3, TT4, TSH in the children in Xinhuai village.

DF (score)	TT3 (ng/mL)		TT4 (μg/dL)		TSH (μIU/mL)	
	No. of samples	TT3 (M ± S)	No. of samples	TT4 (M ± S)	No. of samples	TSH (M ± S)
1	63	1.48 ± 0.33	56	9.34 ± 2.58	62	2.53 ± 2.09
2	5	1.30 ± 0.21	5	7.82 ± 1.55	5	2.72 ± 1.98

Table 10. The TT3, TT4, and TSH results by age and gender in Wamiao village.

	Age	TT3				TT4				TSH			
		No.	High	Normal	low	No.	High	Normal	Low	No.	High	Normal	Low
Male	8	2	0	2	0	1	0	1	0	2	1	1	0
	9	4	0	4	0	3	0	3	0	4	0	4	0
	10	5	0	5	0	4	1	3	0	5	0	5	0
	11	5	1	4	0	6	0	6	0	4	2	2	0
	12	10	0	10	0	11	1	10	0	9	2	7	0
	13	10	0	10	0	10	0	10	0	10	2	8	0
Total		36	1	35	0	35	2	33	0	34	7	27	0
Female	8	0	0	0	0	2	1	1	0	2	0	2	0
	9	2	0	2	0	2	0	2	0	2	1	1	0
	10	4	0	4	0	3	0	3	0	5	1	4	0
	11	8	0	8	0	8	1	7	0	10	2	8	0
	12	9	0	9	0	6	0	6	0	7	1	6	0
	13	3	0	3	0	2	0	2	0	2	0	2	0
Total		26	0	26	0	23	2	21	0	28	5	23	0

village there was not a significant difference between the two groups in TT3, TT4, and TSH (see Table 9).

In China as clinical diagnosis biomarkers, the reference normal values of TT3, TT4, TSH were 0.80 ~ 2.00 ng/mL, 5.00 ~ 13.00 μg/dL, 0.34 ~ 5.60 μIU/mL. As shown in Tables 10 - 11, there was 1 subject with high serum TT3 concentration in each village; and 4 in Wamiao, 5 in Xinhuai with high serum TT4; and 12 in Wamiao, 9 in Xinhuai with high serum TSH. There was not significant difference between the gender and total in the ratio of high TT3, TT4, and TSH in two villages indicated by the results of Chi-Square Tests.

DISCUSSION

In Wamiao and Xinhuai village primary school, the less economic development conditions are not allowed the school to provide food and drinking water for students and teachers; they must back to home to have meals for breakfast, lunch, and dinner; a few students may be bring boiling water in plastic or glass bottle from family to school. In our formerly investigation, the daily total intake of drinking water in two villages' children was: 156.0 ml crude water and 1085.1 ml boiled water included average 2 mL/child/day tea. The rate of crude water was only 14.38% for the total daily intake of drinking water. Each family has a household shallow well in the yard; the average use age of the shallow well was 5.16 ±3.12 years in Xinhuai village and 8.27 ±3.02 years in Wamiao village. Students in these two villages hardly ever move from one residential site to another, and hardly drink the market sell water. So the F^- exposure history of the subjects was relatively clear and the F^- in drinking water was the main source of the F^- intake (QY Xiang, et al 2004; QY Xiang et al. 2005). Therefore, it was relatively easy to explore the exact relationships between the drinking water F^- and the serum concentration of TT3, TT4, and TSH.

In 1990, the Government of China has an official commitment to the world that the hazard of IDD (iodine deficiency disorder) will be removed in China before 2000. So, in China, all the countrymen will eat the qualified iodize salt from 1994. In Wamiao and Xinhuai village the mean levels of iodine in children's urinary were over 280.70±87.16 μg/L and 300.96 ± 92.88 μg/L, and there was not significant difference in childrens' urinary iodine concentration in two villages (Q Xiang et al., 2003). Neither village was identified as being in an area of endemic iodine deficiency area according to The Manual of Prevention and Treatment of Endemic Iodine Deficiency published by Chinese Ministry of Health

Table 11. The TT3, TT4, and TSH results by age and gender in Xinhuai village.

		TT3				TT4				TSH			
	Age	No.	High	Normal	Low	No.	High	Normal	Low	No.	High	Normal	Low
Male	8	6	0	6	0	5	1	4	0	6	2	4	0
	9	3	0	3	0	3	1	2	0	3	0	3	0
	10	5	0	5	0	3	0	3	0	5	1	4	0
	11	9	0	9	0	10	1	9	0	8	0	8	0
	12	11	1	10	0	11	1	10	0	11	0	11	0
	13	4	0	4	0	5	1	4	0	5	0	5	0
Total		38	1	37	0	37	5	32	0	38	3	35	0
Female	8	4	0	4	0	0	0	0	0	4	2	1	1
	9	4	0	4	0	1	0	1	0	4	2	2	0
	10	5	0	5	0	3	0	3	0	4	0	4	0
	11	1	0	1	0	1	0	1	0	1	1	0	0
	12	9	0	9	0	10	0	10	0	9	1	8	0
	13	7	0	7	0	9	0	9	0	7	0	7	0
Total		30	0	30	0	24	0	24	0	29	6	22	1

(Chinese Ministry of Health, 1989). Thus urinary iodine levels do not appear to affect the differences in TT3, TT4, and TSH in children between the two villages.

In this study, there were not significant relationships between the drinking water F- and the serum concentration of TT3, TT4, and TSH. There was significant difference between the two villages in serum TSH, TT3/TT4, TSH/TT3, and TSH/TT4; the serum TSH, TSH/TT3, and TSH/TT4 were significantly higher in Wamiao village than that in Xinhuai village, but the values of TT3/TT4 was on the contrary which was founded in the study of H Wang in rats (H Wang et al., 2009). In the study of Susheela AK (Susheela et al., 2005) and his co-worker, the results indicated that in Two-thirds of the sample children have elevated TSH in the sample group with high drinking water fluoride, but none are below normal; in this study, as shown in Tables 10 - 11, there were 19.35% in Wamiao and 13.42% in Xinhuai with higher serum TSH than normal, and none are below normal. Serum TSH level in children in endemic fluorosis area was significant higher than that in non endemic fluorosis area in the study of (Xiaoli et al., 1999). With the increasing F^- in the diet, the serum TSH level was correspondingly increased in the young pigs and rats (Liu Guoyan et al. 2008; Xiuan et al. 2006). Those results were consistent with this study. But there were opposed results in the study of (Xiaowei et al., 1994). There were not significant differences between the residents of endemic fluorosis areas and non-endemic fluorosis areas in serum TSH in the study of Mingyin et al (Mingyin et al., 1994).

The results in this study indicated that there were not significant difference between two villages in serum TT3 and TT4 in the children. But in the study of Xiaowei (Xiaowei et al. 1994) indicated that serum TT3 and FT3 (free T3) were significant increased, serum FT4 (free T4) was significant reduced in adults in the higher F^- drinking water area compared with the control area. Serum T4 was significant lower, T3 was significant higher in the children in the endemic fluorosis area compared with the non endemic fluorosis area in the report of Xiaoli (Xiaoli et al., 1999).

It has long been suggested that DF is associated with IDD and thyroid dysfunction (Susheela et al. 2005). The results reported in Table 7 revealed significant deviations in the serum levels in TT3 and TSH in the children in Wamiao village between the different DF groups. The serum TT3 in Group 3 (with mild dental fluorosis) and 4 (with moderate dental fluorosis) were significant higher compared with group 1 (with normal and suspected dental fluorosis). The serum TSH in group 2 (with very mild dental fluorosis) was significant higher than that in group 1.

F^- and iodine are belong to chlorine group element, and F^- is more active than iodine. The mechanism of F^- causing the functional disorder of appendix cerebri - thyroid may be: 1. F^- can compete with iodine and influence the absorption and condensing of iodine in thyroid; 2. F^- can influence the biologic activity of functional enzyme system in thyroid; 3. F^- can influence the feedback mechanism of hypothalamus and adenohypophysis of appendix cerebri and control the secretion of thyroid directly (Xiaowei et al., 1994).

The statement in the guest editorial of Andreas Schuld said that: “In fact, DF is a developmental disorder-originating from aberrant thyroid hormone metabolism. It is well established that DF can only occur as a result of excessive fluoride exposure during crucial times of development Thyroid hormone (TH) deficiency leads to delayed tooth eruption. The more F^- ingested, the longer it takes for the tooth to erupt. The later in life maturation of enamel is completed, the greater is the severity of DF. At the same time, other risk factors known to influence DF are identical to those observed in thyroid dysfunction. Thus, while DF gets more severe at higher altitudes, the same is generally true for iodine deficiency" (Schuld, 2005).

The results in this study indicated or suggested that the high F^- exposure can caused the thyroid functional abnormalities, and the different severity degree of DF may be relation to deviation in the serum levels of thyroid hormone. There were different results in the past reports about these. So the exact relationship among fluoride, DF, and appendix cerebri-thyroid function need to further study.

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REFERENCES

Fuzun C, Xu C, Yonggui D, Yunxing C, Yawei H, Jing M, (2001). Effects of selenium at different concentrations on lipid peroxidation.the capacity of anti-oxidation and thyroid in rats with fluorosis. Chinese J. Control Endem. Dis. 16(4): 213-214.

Xiang QY, Liang LC, Wang CB, Chen XC (2003). Effect of fluoride in drinking water on children's intelligence. Fluoride 36(2): 84-94.

Xiang QY, Chen LS, Chen XD, Wang CS, Liang YX, Liao QL (2005). Serum fluoride and skeletal fluorosis in two villages in Jiangsu Province, China. Fluoride 38(3): 178-184.

Xiang QY, Liang YX, Chen BH, Wang CS, Zhen SQ, Chen XD (2004). Serum fluoride and dental fluorosis in two villages in China. Fluoride 37(1): 28-37.

Baum K, Borner W, Reiners C, Moll E (1981). Bone density and thyroid gland function in adolescents in relation to fluoride content of drinking water. Fortschr. Med. 99(36): 1470-1472.

Chinese Ministry of Health, Department of Endemic Diseases (1989). Manual of Prevention and Treatment of Endemic Iodine Deficiency.

Chinese Ministry of Health, Department of Endemic Diseases (1991). Manual of Prevention and Treatment of Endemic Fluorosis.

Chuanhua L, Xiaowei G, Jianchao B, Pin Y, Shumei Q, Yuan L (1998). An experimental study on effects of high fluoride and supplied selenium on thyroid in rats. Chinese J. Endemiol. 17(2): 105-107.

Desun X, Yanling W, Ye L (1994). Study the effect of fluoride on the 125I distribution in the thyroid in the rats. Chinese J. Control Endemic Dis. 9(4): 218-21.

Editorial (1976). Target organs in fluorosis. Fluoride 9(1): 1-4.

Eichner R, Borner W, Henschler D, Kohler W, Moll E (1981). Osteoporosis therapy and thyroid function. Influence of 6 months of sodium fluoride treatment on thyroid function and bone density. Fortschr. Med. 99(10): 342-348.

Guimin W, Zhiya M, Zhongjie L, Zhi C, Jiandong T, Ruilan Z (2001). Determination and analysis on multimark of test of th e patients with endemic fluorosis. Chinese J. Endemiol. [Chinese] 20(2): 137-139.

Wang H, Yang Z, Zhou B, Gao H, Yan1 X, Wang J (2009). Fluoride-induced thyroid dysfunction in rats: roles of dietary protein and calcium level. Toxicology and Industrial Health 25: 49-57.

Hu A, Liu Xiaoyang, Qin Yide (2007). Effect of fluorine on triiodothyronine and thyroxin in mice. J. Bengbu. Med. Coll. 32(4): 392-394.

Juvenal GJ, Kleiman de Pisarev DL, Crenovich L, Pisarev MA (1978). Role of neurotransmitters, prostaglandins and glucose on precursor incorporation into the RNA of thyroid slices." Eur. J. Endocrinol. 87(4): 776.

Liu G, Zhang W, Gu J, Chai C (2008). Effects of Fluoride on Morphological Structure and Function of Thyroids in Rats. J. Shanghai Jiaotong Univ. (Agric. Sci.) 26(6): 537-539.

Mingyin F, Enxiang G, Xioude Z, Yuting J (1994). The test and analysis of the thyroid function of the subjects in high fluoride areas. Shanghai J. Med. La. Sci. 9(3): 217.

National Standard of P. R. China (1999). Method for determination of fluoride in drinking water of endemic fluorosis areas (WS/T 106-1999).

Schuld A (2005). Is dental fluorosis caused by thyroid hormone disturbances?. Fluoride 38(2): 91-4.

Susheela AK, Bhatnagar M, Vig K, Mondal NK (2005). Excess fluoride ingestion and thyroid hormone derangements in children living in Delhi, India. Fluoride 38(2): 98-108.

Xiaoli L, Zhongxue F, Jili H, Qinlan W, Hongyin W (1999). The detection of children's T3, T4 and TSH contents in endemic fluorosis areas. Endemic disease bulletin 14(1): 16-17.

Xiaowei G, Xiaohong L (1994). The effects of high fluoride drinking water on the function of appendix cerebri–thyroid of the residents. Chinese J. Endemiol. 13(6): 378-9.

Xiuan Z, Jianxin L, Min W, Zirong X (2006). Effects of fluoride on growth and thyroid function in young pigs. Fluoride 39(2): 95-100.

Yaming G, Hongmei N, Shaolin W, Jundong W (2005). DNA damage in thyroid gland cells of rats exposed to long-term intake of high fluoride and low iodine. Fluoride 38(4): 318-23.