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EFFECT OF FLUORIDE IN DRINKING WATER ON CHILDREN'S INTELLIGENCE

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SUMMARY: The Intelligence Quotient (IQ) was measured in 512 children, aged 8–13 years, living in two villages in Sihong County, Jiangsu Province, China, differing in the level of fluoride in their drinking water. In the high-fluoride village of Wamiao (water fluoride: 2.47±0.79 mg/L; range: 0.57–4.50 mg/L), the mean IQ of 222 children was significantly lower (92.02±13.00; range: 54–126) than in the low-fluoride village of Xinhuai (water fluoride: 0.36±0.15 mg/L; range: 0.18–0.76 mg/L), where the mean IQ of 290 children was higher (100.41±13.21; range: 60–128). The children's IQs were not related to urinary iodine, family income, or parent's education level. Higher drinking water fluoride levels were significantly associated with higher rates of mental retardation (IQ <70) and borderline intelligence (IQ 70–79). The Benchmark Concentration (BMC) for the concentration-response relationship between IQ <80 and the drinking water fluoride level was 2.32 mg/L, and the lower-bound confidence limit (BMCL) of the BMC was 1.85 mg/L. Taking dental fluorosis and other sources of dietary fluoride into account, the reference value concentration (RfC) for fluoride was calculated to be 0.925 mg/L, which is very close to the current national Chinese standard of <1.0 mg/L. In endemic fluorosis areas, drinking water fluoride levels greater than 1.0 mg/L may adversely affect the development of children's intelligence.

Keywords: Children's intelligence; China; Fluoride in village water; Intelligence Quotient.

INTRODUCTION

In 1937, Kaj Roholm published his classic study on 68 cryolite workers chronically exposed to fluoride, 84% of whom had skeletal fluorosis with 22% of them having neurological symptoms involving excessive tiredness, sleepiness, indisposition, headache, and giddiness.[1] In that same year, Shortt *et al* reported 10 cases of fluorosis complicated by central nervous system damage with symptoms of pressure on the spinal cord including tingling sensations, loss of pain, temperature, touch, vibration sensation in the lower limbs, altered reflexes, impotence, and loss of sphincter control but with unimpaired mental powers.[2] In 1961, Singh and Jolly reported that 10% of patients with skeletal fluorosis had nervous system damage.[3] Animal studies show that brain fluoride levels increase with increasing exposure to fluoride,[4-5] and further studies on humans, particularly in China, have been published.[6-14] Investigations by Zhao *et al*[13] and by Lu *et al*,[14] conducted in different regions of China, indicated an association between higher levels of drinking water fluoride and a lower IQ in children, whereas a study by Hu *et*

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al, did not.[15,16] The relationships between drinking water fluoride, urinary fluoride, and IQ are examined further in the present study.

MATERIALS AND METHODS

Two villages, Wamiao and Xinhuai, located 64 km apart in Sihong County, Jiangsu Province, that are near Lake Hongze, which is about 215 km inland from the east coast of the People's Republic of China and about 730 km southeast of Beijing, were selected for study. Wamiao in northeast Sihong County, about 32 km northeast of Sihong (*ca.* 33° 28' N and 118° 12' E), lies in a severe endemic fluorosis area. Xinhuai in the southwest part of Sihong County, about 32 km southwest of Sihong, is in a nonendemic fluorosis area. Neither village has fluoride pollution from burning coal or other industrial sources. None of the residents reported drinking brick tea.

The study was conducted between September and December 2002 and included all eligible children in each village. A questionnaire, completed with the assistance of parents, was used to collect information on personal characteristics, medical history including illnesses affecting the nervous system and head trauma, educational level of the children and parents, family socioeconomic status, and lifestyle. Children who had been absent from either village for two years or longer, or who had a history of brain disease or head injury, were excluded. In Wamiao, 93% of the children (222 out of 238) were included for the study, while in Xinhuai, 95% were included (290 out of 305). The children in Wamiao were divided into five subgroups according to the level of fluoride in their drinking water: <1.0 mg/L (group A), 1.0–1.9 mg/L (group B), 2.0–2.9 mg/L (group C), 3.0–3.9 mg/L (group D), >3.9 mg/L (group E), while those in Xinhuai (0.18–0.76 mg F/L in the drinking water) were considered as a single group (group F).

The Intelligence Quotient (IQ) of each child was measured with the Combined Raven's Test for Rural China (CRT-RC), published by Huadong Normal University in 1989.[17] The test was administered to the children in a school class, working independently, in a double-blind manner, under the supervision of an examiner and two assistants, according to the directions of the CRT-RC manual for the test administration conditions, instructions to be given, and the test environment.[17] The scores for IQ in the CRT-RC were ranked as: mental retardation (IQ <70), borderline (IQ 70–79), dull normal (IQ 80–89), normal (IQ 90–109), bright normal (IQ 110–119), superior (IQ120–129), and very superior (IQ >129).

Fluoride in the drinking water and urine was measured with a fluoride ion selective electrode.[18-19] Iodine in urine was measured with the Test Kit manufactured by the Center for Disease Control and Prevention, Hubei Province.[20] Urine samples were collected in the early morning, and the drinking water was collected from the wells in clean plastic bottles. Children

for urine testing were chosen by random sampling: in Wamiao, 155 for fluoride and 46 for iodine; in Xinhuai, 135 for fluoride and 40 for iodine.

Data were analyzed using SAS and Benchmark Concentration software (BMCS).

RESULTS

Fluoride levels in the drinking water and urine, and iodine levels in the urine are shown in Tables 1–5. The results indicate that significant differences were present between the villages in the levels of fluoride in the drinking water and urine, but not in the urinary iodine levels.

Table 1. Fluoride drinking water levels in Wamiao and Xinhuai

Village	No. samples	Fluoride in drinking water (mg/L)		t	*p*
		Mean±SD	Range		
Wamiao	222	2.47±0.79	0.57–4.50	44.97	<0.001
Xinhuai	290	0.36±0.15	0.18–0.76		

Table 2. Urinary fluoride in children in Wamiao and Xinhuai

Village	No. samples	Urinary fluoride (mg/L)		t	*p*
		Mean ±SD	Range		
Wamiao	155	3.47±1.95	0.90–12.50	13.82	<0.001
Xinhuai	135	1.11±0.39	0.37–2.50		

Table 3. Ratio of urinary fluoride to creatinine in children in Wamiao and Xinhuai

Village	No. samples	Urinary fluoride/Cre (mg F/mmol Cre)		t	*p*
		Mean ±SD	Range		
Wamiao	155	0.82±0.75	0.13–4.69	8.96	<0.001
Xinhuai	135	0.24±0.10	0.09–0.71		

Table 4. Urinary iodine in children in Wamiao and Xinhuai

Village	No. samples	Urinary iodine (μg/L)		t	*p*
		Mean ±SD	Range		
Wamiao	46	280.70±87.16	131.31–497.05	1.04	>0.3
Xinhuai	40	300.96±92.88	148.46–460.89		

Table 5. Ratio of urinary iodine to creatinine in children in Wamiao and Xinhuai

Village	No. samples	Urinary iodine/creatinine (μg I/mmol Cre)		t	*p*
		Mean ±SD	Range		
Wamiao	46	93.24±46.86	36.86–251.03	1.07	>0.28
Xinhuai	40	81.27±55.91	22.76–298.74		

In the two villages there were significant differences between male, female, and total children's IQ. A significant difference was present between male and female children's IQ in Wamiao but not in Xinhuai. Details are shown in Tables 6 and 7.

As seen in Table 7, most of the children's IQs were distributed in the normal range of 90–109. In Xinhuai, 27.59% of the children tested in the range of bright normal (110–119) or higher, whereas only 8.11% did so in Wamiao. Moreover, 15.31% of the children in Wamiao were borderline intelligence IQ (70–79) or lower, but only 6.20% were in these classifications in Xinhuai.

Table 6. Children's IQ in Wamiao and Xinhuai

Village	Male		Female		Total		
	N	Mean ±SD	N	Mean ±SD	N	Mean ± SD	Range
Wamiao	122	94.73±13.09	100	88.72±12.16[*]	222	92.02±13.00	54-126
Xinhuai	159	100.69±13.52[#]	131	100.08±12.87[†]	290	100.41±13.21[†]	60-128

[*] p <0.01 compared with male data. [†] p<0.01 compared with Wamiao.

Table 7. IQ distribution of children in Wamiao and Xinhuai

IQ	Wamiao				Xinhuai			
	Male	Female	Total	(%)	Male	Female	Total	(%)
≥130	0	0	0	(0)	0	0	0	(0)
120-129	5	0	5	(2.25)	11	3	14	(4.83)
110-119	9	4	13	(5.86)	38	28	66	(22.76)
90-109	62	43	105	(47.30)	75	75	150	(51.72)
80-89	31	34	65	(29.28)	25	17	42	(14.48)
70-79	12	14	26	(11.71)	9	4	13	(4.48)
≤69	3	5	8	(3.60)	1	4	5	(1.72)
Total	122	100	222	(100)	159	131	290	(100)

When compared with the children in Xinhuai (Group F), the children in Wamiao exhibited, as the level of fluoride in the drinking water increased, a decrease in IQ and an increase in the rates of mental retardation (IQ <70) and borderline intelligence (IQ 70–79) (Table 8).

Table 8. Level of fluoride in drinking water and children's IQs

Village	Group	F in drinking water (mg/L) No. samples	Water F level (Mean±SD)	No. children	IQ and rate of retardation IQ (Mean±SD)	Rate of IQ<80 (%)
Xinhuai	F	290	0.36±0.15	290	100.41±13.21	6.55
Wamiao	A	9	0.75±0.14	9	99.56±14.13	0.00
	B	42	1.53±0.27	42	95.21±12.22*	9.52
	C	111	2.46±0.30	111	92.19±12.98†	14.41*
	D	52	3.28±0.25	52	89.88±11.98†	21.15†
	E	8	4.16±0.22	8	78.38±12.68†	37.50†

*p<0.05. †p <0.01 compared with group F.

The concentration-response relationship between the level of fluoride in the drinking water and an IQ score <80 (borderline intelligence and mental retardation) in the children is shown in Figure 1. The BMC and BMCL were 2.32 mg F/L and 1.85 mg F/L, respectively.

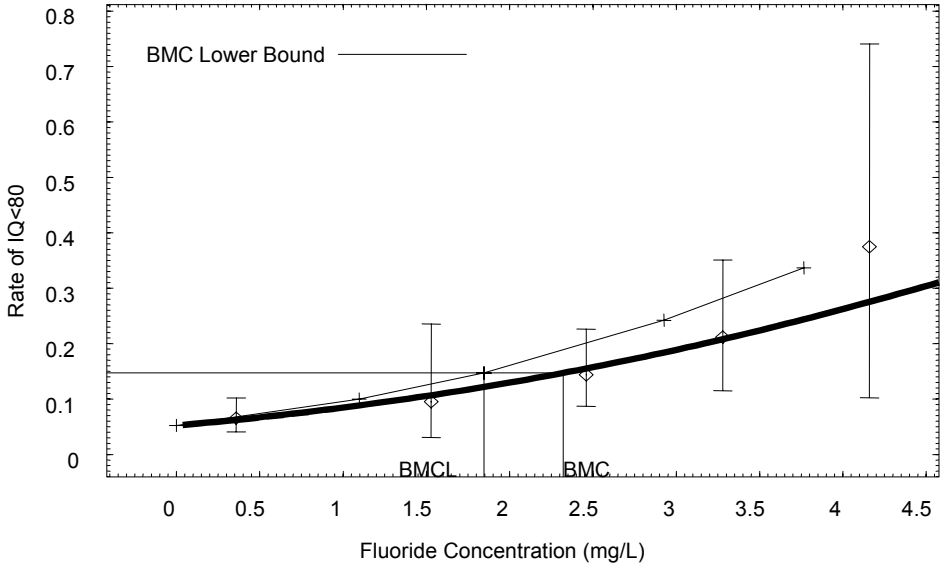

Figure 1. Concentration-response relationship between an IQ<80 score and the level of fluoride in drinking water

As shown in Figures 2 and 3, when the data from the 512 children in the two villages were considered as a whole, a significant inverse correlation

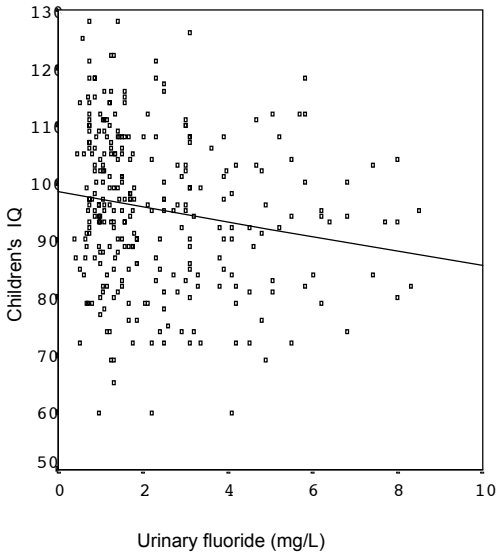

Figure 2. Correlation between urinary fluoride (directly measured) and IQ

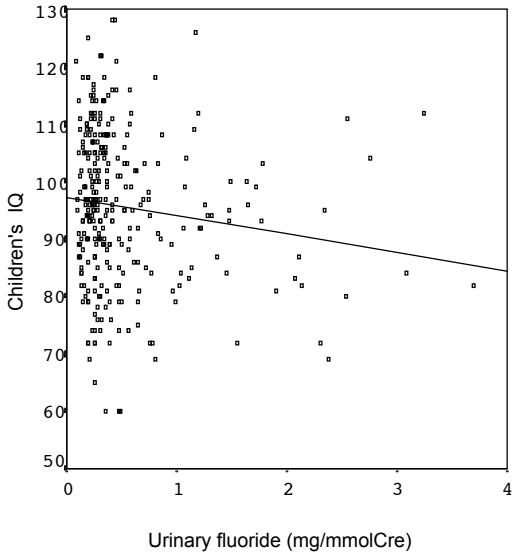

Figure 3. Correlation between urinary fluoride (creatinine-adjusted) and IQ

was found between IQ and the level of fluoride in urine, both when measured directly, as mg F/L, (Pearson correlation coefficient –0.174 , $p = 0.003$) and when adjusted for creatinine, as mg F/mmol Cre, (Pearson correlation coefficient –0.164, $p = 0.005$).

A further significant relationship was evident between the levels of fluoride in drinking water and in urine, both when the latter was measured directly, as mg F/L (Pearson correlation coefficient: 0.653, $p < 0.001$) and when adjusted for creatinine, as mg F/mmol Cre (Pearson correlation coefficient: 0.503, $p < 0.001$) (Table 9).

Table 9. Fluoride in drinking water and in urine (Mean±SD)

No. samples	Drinking water F (mg/L)	Urinary fluoride (mg/L)	Urinary fluoride mg/mmol Cre
142	0.39±0.15	1.14±0.49	0.25±0.22
32	1.15±0.29	2.59±1.70	0.61±0.47
80	2.44±0.30	3.67±1.97	0.85±0.67
32	3.22±0.18	3.77±1.86	0.86±0.81
4	4.05±0.01	4.65±2.39	2.17±1.73

As seen in Table 10, the average IQ of the children in each age group in Xinhuai was higher than in Wamiao. Above age 10, the IQ had a tendency to decrease, but it did not do so significantly in either village. Correlation analysis showed that there was a significant relationship between IQ and age in Xinhuai (Pearson correlation coefficient: –0.216, $p < 0.01$) but not in Wamiao (Pearson correlation coefficient: –0.083, $p = 0.218$). When combined, the data of the two villages indicated the existence of a significant relationship between age and IQ (Pearson correlation coefficient: –0.207, $p < 0.01$).

In regard to family income and children's IQ, there were no significant relationships in both Wamiao and Xinhuai (Pearson correlation coefficients: –0.096 and 0.027, respectively, $p > 0.05$). Children's IQ in each group by family income in Xinhuai was higher than that in Wamiao (Table 11).

Table 10. Mean IQ by age in Wamiao and Xinhuai

Age (yrs)	Wamiao No. children	Wamiao IQ(Mean±SD)	Xinhuai No. children	Xinhuai IQ (Mean±SD)
8	11	94.09±16.50	39	103.39±11.58
9	20	91.25±14.81	46	104.04±13.80
10	20	96.35±14.04	31	105.45±10.57
11	43	92.77±12.43	60	97.45±14.60
12	60	91.15±12.74	61	99.41±14.20
13	68	90.94±12.27	53	96.64±10.47
Total	222	92.02±13.00	290	100.41±13.21

Table 11. Mean IQ of children and family income in Wamiao and Xinhuai

Family income (yuan/yr)	Wamiao		Xinhuai	
	No. children	IQ (Mean±SD)	No. children	IQ (Mean±SD)
≤1000	42	93.88±12.04	40	99.45±11.82
1001-2000	128	91.73±12.41	173	100.54±13.23
2001-3000	39	93.36±15.24	59	100.34±14.39
>3000	13	84.85±13.37	18	101.61±12.88
Total	222	92.02±13.00	290	100.41±13.21

As shown in Table 12, no significant relationships were present between the children's IQ and education level of parents, in both Wamiao and Xinhuai (Pearson correlation coefficient: –0.119 and 0.113, respectively, $p > 0.05$). At each parent's education level, the children's IQ in Xinhuai was higher than in Wamiao.

Table 12. Mean IQ and education level of parents in Wamiao and Xinhuai

Parent's education level	Wamiao		Xinhuai	
	No. children	IQ (Mean±SD)	No. children	IQ (Mean±SD)
Primary school and below	74	93.26±12.69	38	103.50±11.72
Junior high school	118	92.16±12.59	131	100.09±13.19
Senior high school and above	30	88.43±15.05	121	99.79±13.64

DISCUSSION

The villages of Wamiao and Xinhuai in Sihong County, Jiangsu Province, People's Republic of China, are situated in isolated low-income areas with less economic development and a relative lack of communication with the outside world, resulting in poor living conditions for the majority of the residents, especially the elderly and children. This study found a significant inverse concentration-response relationship between the fluoride level in drinking water and the IQ of children. As the fluoride level in drinking water increased the IQ fell and the rates of mental retardation and borderline intelligence increased.

No significant difference was found between the two villages of this study in the levels of iodine in the urine of the children. Neither village was identi-

fied 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.[20] Thus urinary iodine levels do not appear to affect the differences in IQ in children between the two villages.

These results are consistent with the findings recorded by Li *et al*, Zhao *et al*, and Lu *et al* of an inverse correlation between intelligence and dietary fluoride from either contaminated food or drinking water.[12-14] However, the significant relationship reported by Zhao *et al*[13] between IQ and age and between IQ and the parent's educational level was not found in the present study. Similarly, no relationship was found between IQ and family income. There was, however, a significant difference between the male and female children's IQ in Wamiao, but not in Xinhuai. The reason why there was the tendency for IQ to decrease with increasing age is not clear. Possibly, the total intake of fluoride/kg body weight per day or lifetime was the main cause, or there is a sensitive period for the effect of fluoride on children's intelligence development. Xu *et al* [21] and Li *et al*[22] found that adolescence is a period significantly affected by fluoride. The exact relationship between age and IQ, especially in endemic fluorosis, needs further study. It is known, however, that fluoride is able to cross the blood-brain barrier producing biochemical and functional impairment of the nervous system during the developmental periods of infancy and childhood.[4,5,23]

The Benchmark Concentration (BMC) of 2.32 mg F/L and the lower-bound confidence limit of the BMC (BMCL) of 1.85 mg F/L were calculated from the concentration-response relationship between the rates of mental retardation (IQ <70) and borderline intelligence (IQ 70–79) and the level of fluoride in the drinking water. The reference value concentration (RfC) is modeled after the equation RfC = BMCL/(UF×MF) (where UF is an uncertainty factor and MF a modifying factor).[24] After considering the result obtained from a human epidemiological study, particularly with 8–13 year-old children, the UF and MF were both set at 1. This gave the result of RfC = 1.85 mg F/L, meaning that more than 95% of children will have an IQ >80 when the fluoride in drinking water is below 1.85 mg/L (the theoretical distribution of IQ below 80 is 8.9%.).[18] However, by considering dental fluorosis and other adverse effects of fluoride, plus additional sources of fluoride intake, the UF could be set at 2, giving an RfC = 1.85/(2×1) = 0.925 mg F/L. This result is very close to the current national fluoride standard for China of <1.0 mg F/L and suggests that the current national standard is safe enough to protect 90% of children, aged 8–13 years, from adverse effects on their intelligence development. In endemic fluorosis areas, drinking water fluoride levels greater than 1.0 mg/L may therefore adversely affect the development of children's intelligence.

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