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Study on the correlation between daily total fluoride intake and children's intelligence quotient

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[**Abstract**] **Objective**: To explore the exact relationship between daily total intake of fluoride and children's intelligence quotient (IQ). **Methods**: Wamiao village (severely endemic fluorosis area, drinking water fluoride was 0.57-4.50 mg·L^{-1}) and Hinhuai village (non-endemic fluorosis area, drinking water fluoride was 0.18-0.76 mg·L^{-1}) in Shong County, Jiangsu Province, were selected for this study. All 8-13 years old students in two village's primary school were recruited as subjects in this study. Children's IQ, drinking water fluoride in children's household shallow well, daily total intake of diet and water, and fluoride level in indoor and outdoor air were investigated, and the daily total intake of fluoride was calculated. The children were divided into 5 subgroups according to the daily total intake of fluoride, which were: <1.00, 1.00-1.99, 2.00-2.99, 3.00-3.99, ≥4.00 mg·(per person·d)$^{-1}$. Children's IQ and the rate of IQ <80 in the subgroup were calculated. **Results**: Children's IQ in Xihuai village was significant higher than that in Wamiao village (100.41 ± 13.21 vs 92.02 ± 13.00). Children's IQ decreased and the rate of IQ < 80 increased according to the increasing of daily total intake of fluoride. There were significant dose-response relationship between the daily total intake of fluoride and the children's IQ ($y = -3.519x + 103.310$), and the rate of IQ <80 ($y = 5.779x - 1.347$). **Conclusions**: High level of fluoride intake may affect the development of cerebrum for infant and adolescent, and would resulte the lower IQ.

[**Key words**] daily total intake of fluoride; intelligence quotient; dose-response relationship

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In 1937, Roholm conducted a study and reported that among 68 cryolite industry workers with chronic exposure to fluoride, 84% suffered from skeletal fluorosis; among those with skeletal fluorosis, 22% had neurological systems such as fatigue, drowsiness, headaches, and dizziness.[1] Autopsies of persons afflicted with skeletal fluorosis have found nuclear vacuoles in nerve cells, cell reductions in the anterior horn, anterior funiculus, and lateral horns of the spinal cord, and reduction or partial clotting of Nissl bodies surrounding the cell membrane. These results suggested that fluoride may directly damage the nervous system.[2-3] The results of some studies[4-5] indicate that excessive quantities of fluoride in drinking water have a significant effect on children's intelligence quotient (IQ). No reports have been seen, however, on the correlation between total fluoride intake and child IQ. This study was intended to survey total fluoride intake and IQ among children in endemic fluorosis regions and non-endemic fluorosis regions in order to explore the correlation between total fluoride intake and child IQ, providing a reference for the prevention and treatment of endemic fluorosis and the protection of the health of children in endemic fluorosis regions.

1 Subjects and Methods

1.1 Survey Locations

Wamiao Village (a village in a region of severe endemic fluorosis, with concentrations of fluoride in drinking water of 0.57-4.50 mg/L) and Xinhuai Village (in a non-endemic fluorosis region, with concentrations of fluoride in drinking water of 0.18-0.76 mg/L) were chosen as the survey points for this study. The residents of both villages have hand-pumped well water for drinking water. The two villages are approximately 64 km apart, there is no significant difference in annual per capita income (t = 1.28, P>0.05), and transportation, education, medical conditions, the natural environment, and lifestyle are essentially consistent between the two. The two villages have no fuel coal or industrial fluoride pollution, and the residents do not drink Tibeti.

1.2 Survey Subjects

All primary students ages 8-13 currently in school in Wamiao Village and Xinhuai Village were surveyed. Children having suffered brain injury, with a history of brain disease, or having come from elsewhere or lived elsewhere for over two years were not taken as survey subjects. There were 236 children in Wamiao Village included in the survey (accounting for 97.12% of the total number of children, 236/243) and 290 in Xinhuai Village (accounting for 95.08% of the total number of children, 290/305).

1.3 Dietary Survey

Based on the survey method for total fluoride intake in Appendix A of the Health Industry Standard of the People's Republic of China *Health Standards for Population Total Fluoride Intake*, interview and weight measuring methods were combined to calculate the per-capita daily total fluoride intake for children; survey forms were designed according to the dietary survey requirements of the 2002 Chinese national nutrition and health survey. Residents of Wamiao Village were divided into five groups based on the fluoride content of the children's drinking water: a group with drinking water fluoride content of <1.0 mg/L (group A), a 1.0-1.99 mg/L group (group B), 2.0-2.99 mg/L group (group C), 3.00-3.99 mg/L group (group D), and ≥4.00 mg/L group (group E). Six families of residents were randomly selected from each group to be dietary survey households, with the intake of various foods by each person at each meal and intake of unboiled water, boiled water, and tea surveyed for four consecutive days.

1.4 Sample Collection and Measurement

Dietary surveyors collected food from dietary survey households (50 g or more of staples and vegetable samples of 100 g or more), sealed them in clean plastic bags, and promptly sent them for testing. Clean, dry polyethylene bottles were used to collect 50 mL of drinking water from each student's household to be used

to measure fluoride content. Five representative households were selected in each village based on geographic location, population distribution, housing structure, and other conditions, with indoor air samples collected once daily for five consecutive days to measure airborne fluoride content; outdoor air samples were collected once daily for five consecutive days at two points dividing each village into thirds on the East-West axis. Drinking water fluoride content was determined based on *Methods for the Determination of Waterborne Fluoride* in the National Standards of the People's Republic of China (GB5750-85). Airborne fluoride content was determined based on the People's Republic of China Industry Standards for Environmental Protection *Stationary source emissions- Determination of fluoride-Ion-selective electrode method* (HJ/T67-2001). The method for determination of foodborne fluoride content was based on the National Standard of the People's Republic of China *Methods for the Determination of Foodborne Fluoride* (GB/T 5009.18-1996).

1.5 Testing of Children

The Combined Raven's Test for Rural China (CRT-RC) was used to determine children's IQ. IQ testing was carried out in students' classrooms, with 20 students per group and one desk per student, with answer sheets completed independently under the guidance of 3 exam proctors. Testing methods, testing language, and testing conditions were all in strict accordance with the CRT-RC guidebook. Major testing personnel received necessary training by the Psychology Department of East China Normal University. The children undergoing IQ testing and the test scorers were kept double-blinded throughout the testing process. The CRT-RC standards for IQ classifications are: Very superior (IQ ≥130), superior (IQ 120-129) high average (intelligent) (IQ-110-119) intermediate (average) (IQ 90-109), low average (dull) (IQ 80-89), borderline (IQ 70-79) and mentally defective (IQ ≤60). The low IQ rate used in this study refers to the percentage of the surveyed children represented by children with IQs below 80.

1.6 Statistical Processing

Based on the method for calculation of total fluoride intake in Appendix A of the People's Republic of China Health Industry Standard *Health Standards for Population Total Fluoride Intake*, i.e. total fluoride intake (mg/person/day) = food borne fluoride intake + waterborne fluoride intake + airborne fluoride intake, total fluoride intake among children in the two villages of Wamiao and Xinhuai was calculated [as follows]: total fluoride intake (mg/person/day) = household drinking water fluoride content × daily unboiled water intake + household boiled water [level] × daily boiled water intake + foodborne fluoride intake + airborne fluoride intake. The SPSS software package was used to establish a database and perform statistical analysis of all data.

2 Results

2.1 Determination of drinking water fluoride content and airborne fluoride content in the two villages

See Table 1.

Table 1 Determination of household drinking water fluoride content for children in the two villages mg/L

Village	*n*	Drinking Water Fluoride Content	Fluoride Range
Wamiao	236	2.45 ± 0.80	0.57 – 4.50
Xinhuai	290	0.36 ± 0.11*	0.18 – 0.76

Compared with Wamiao Village, a $P<0.001$ ($t=45.13$)

Table 1 indicates that fluoride content in drinking water in Wamiao Village was significantly higher than in Xinhuai Village, and the range of fluoride content was relatively broad in Wamiao Village, providing a good survey site for investigating the dose-response relationship between fluoride and population health. Both villages were free of industrial fluoride emissions and coal burning fluoride emissions, and indoor and outdoor fluoride content were below the limit of detection in both villages.

2.2 Survey of total intake among children in the two villages

See Table 2.

Table 2 Results of the calculation of total fluoride intake among children in Wamiao and Xinhuai villages

Village	*n*	Total fluoride intake- mg/person/day	Range- mg/d
Wamiao	236	3.05 ± 0.99	0.73 – 5.57
Xinhuai	290	0.78 ± 0.13*	0.57 – 1.27

Compared with Wamiao Village, a $P<0.001$ ($t=38.72$)

Table 2 indicates that the mean daily average intake of fluoride among children in Wamiao Village was significantly higher than among those in Xinhuai Village, and exceeded the national health standard of 0.65 mg/person/day (the permissible limit of average daily fluoride intake for children ages 8-15 in endemic drinking water fluorosis regions is 2.4 mg/person/day WS/T87-1996).

2.3 Comparison of children's IQ between the two villages

See Table 3.

Table 3 Results of IQ survey of children ages 8-13 in the two villages ($\bar{x} \pm s$)

Village	Male children		Female children		Total	
	n	IQ	*n*	IQ	*n*	IQ
Wamiao	130	94.73 ± 13.09	106	88.72 ± 12.16[a]	236	92.02 ± 13.00(54 ~ 126)
Xinhuai	159	100.69 ± 13.52[b]	131	100.08 ± 12.87[b]	290	100.41 ± 13.21(60 ~ 128

Compared with male children in the same village, a $P<0.05$; compared with children in Wamiao Village, b $P<0.01$
Note: Figures in parentheses are the range of IQ

It may be observed from Table 3 that male, female, and overall IQ scores were all higher among children in Xinhuai Village that among those in Wamiao Village, and the differences were statistically significant ($P<0.01$). The IQs of male children were significantly higher than those of females in Wamiao Village, but there were no such findings in Xinhuai Village.

2.4 The dose-response relationship between total fluoride intake and children's IQ

See Table 4, and Figures 1 and 2.

It may be seen from Table 4 and Figures 1 and 2 that child IQ levels gradually decrease and the low IQ rate gradually increases as total fluoride intake increases, showing a marked dose-response relationship between total fluoride intake and children's IQ. The results of correlation analysis indicate that the correlation coefficient between total fluoride intake and children's IQ r= -0.332, $P<0.001$; the linear regression equation is y= -3.519x + 103.310 (F= 63.149, $P<0.000$), regression equation R^2= 0.1102. After fitting the model for the linear fit between total fluoride intake and the low IQ rate, the correlation coefficient r=0.966, with its linear regression equation being y= 5.779x – 1.347 (F= 41.322, P= 0.008), R^2= 0.966. If children of IQ ≥ 80 are given the value 0 and children of IQ < 80 are given a value 1, the results of logistic regression of low IQ and total fluoride intake, age and sex indicate that there was no correlation between age and sex and low IQ in children ($P>0.05$), but there was a significant correlation between total fluoride intake and low IQ in children ($P<0.01$); after eliminating the confounding effects of the factors of age and sex, the odds ratio OR of total fluoride intake was 1.106 (95% confidence interval of 1.052-1.163).

Table 4 Children's total fluoride intake and IQ in the villages of Wamiao and Xinhuai ($\bar{x} \pm s$)

Group	*n*	Total Fluoride Intake- mg/person/day	Children's IQ	Low IQ rate- %
A	268	0.75 ± 0.09	100.68 ± 13.07	6.02
B	60	1.34 ± 0.32	99.16 ± 13.32	3.51
C	77	2.61 ± 0.27	93.40 ± 13.19	13.33
D	84	3.52 ± 0.25	90.98 ± 13.40	17.50
E	37	4.51 ± 0.43	87.97 ± 11.99	26.47

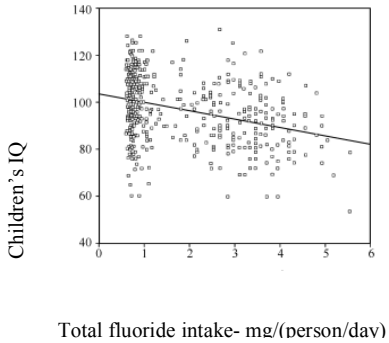

Figure 1 Fit curve of the dose-response relationship between children's total fluoride intake and IQ

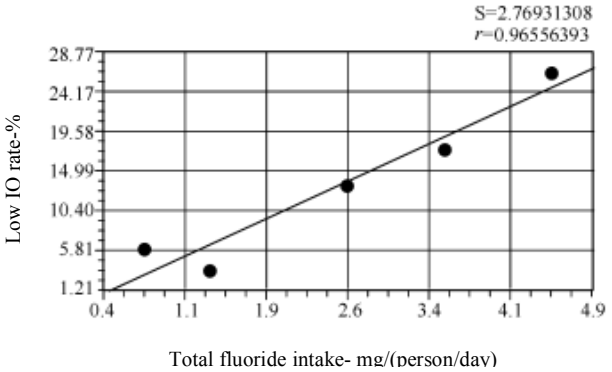

Figure 2 Fit curve of linear fit model of dose-response relationship between total fluoride intake and low IQ rate in children

3 Discussion

The effects of fluoride on the human body are bidirectional, being both beneficial and harmful. Insufficient intake is associated with increased incidence of tooth decay, while excessive intake can cause harm such as dental and skeletal fluorosis. The beneficial and harmful dose ranges of fluoride are relatively narrow. There is relatively little research data on the dose-response relationship between fluoride and its harmful and beneficial effects, with data on the dose-response relationship between total fluoride intake (including intake and absorption) and health effects being particularly scarce.[6-7]

There are relatively few research reports on the damage of fluoride to the nervous system, especially reports on populations.[4, 8] The development of the brain corresponds to a child's intellectual development; the brain develops most rapidly before three years of age, and

subsequently gradually slows. Eighty percent of the entire development of the human brain is complete before the age of five, and the structure and function of the brain are essentially similar to those in adults by the age of seven; the time before seven years of age is therefore the key period for intellectual development, with the time before three years of age most crucial. The school-age period refers to the period between entering primary school and the beginning of puberty (generally 6-12 years of age), during which time the form and structure of the brain is essentially complete, and intelligence develops relatively quickly. Exposure to high levels of fluoride during the period of time between birth and school age may therefore affect intellectual development in children. Research by Lu and Xiang *et al.*[4-5] found that high fluoride intake could lead to reduced IQ in children. Experimental studies in animals have found that fluoride can pass through the blood-brain barrier to enter the brain during the period of development in infancy and early childhood, thereby producing biochemical and functional effects on the nervous system.[9-10]

The results of this study indicate that children's IQ gradually decreases in the low IQ rate with increases in total fluoride intake, showing a marked dose-response relationship. These findings are consistent with the research results of Lu and Xiang *et al.*[4-5], further verifying that high fluoride intake can affect the intellectual development of children, leading to low IQ in children. Adopting a dietary survey method combining interview methods and weight measurement methods, this study surveyed children's intake of fluoride through different channels and calculated per capita daily total fluoride intake for children, and comprehensively analyzed the relationship between total fluoride intake and children's IQ, investigating the dose-response relationship between total fluoride intake and children's IQ, providing useful direction for on-site population studies of damage to the nervous system caused by fluoride. At the same time, the results of this study suggest that the issue of intake of fluoride through multiple channels should be given serious consideration in the work of preventing and treating endemic fluorosis, with multiple measures taken to reduce the hazards of fluoride to humans, particularly the effects of high fluoride intake on children's health.

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