Clinical Study of Effect of High Fluoride on the Function of the Pancreatic Islet B Cells

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Objective: To study the effect of excessive fluoride intake on the function of pancreatic islet's B cells.

Methods: We performed x-rays, determined the [F] in the urine, conducted OGTT insulin and C-peptide releasing tests in the serum, and analyzed the drinking water quality of the exposed group and control group.

Results: (1) The [F] in drinking water and the geometrical mean of the [F] in the urine of the people of the exposed group were higher than those of the control group. (2) The fasting blood glucose concentration and the peak value after oral glucose in the exposed group were higher than those of the control group. The peak value was found later in the exposed group than in the control group. (3) The detectable rate of Diabetes and IGT in the exposed group was higher than that in the control group. (4) The blood-insulin and C-peptide in the exposed group were lower than in the control group, although the peak value after oral glucose was found later in the exposed group.

Conclusions: Excessive fluoride can do much harm to the function of the pancreas islet B cells and the effects change with the degree of fluorosis.

[**Key Words]** Fluoride poisoning; function of the pancreatic islet's B cells; Insulin; C-peptide

1. Materials and methods

1.1 Investigation subjects

1.1.1 The exposed group: Adults, 40 to 68 years of age, from a high fluoride village - a remote village of Gaomi without low-fluoride water or water improvement - were chosen as the exposed group. The [F] in the urine of 400 people (200 males and 200 females) were determined. According to the epidemiological survey, physical examination, and X-ray performed on the normotopia of their pelvic bone and right forearm, 31 patients with severe fluoride bone disease were detected.

Another 31 people without the disease but of the same gender, age and approximate BMI (21.3±2.2kg/m^2, 21.6±1.9kg/m^2, P>0.05) were randomly selected. These 62 subjects had the following in common: (1) They lived in the same village; (2) the [F] in their drinking water was stable; (3) the [F] in their urine was higher than that of the normal group; (4) they had no history of metabolic and endocrine disease, hypertension or liver and kidney disease; (5) they had no history of diabetes; (6) the patients with severe fluoride bone disease had typical X-ray changes [1].

1.1.2 The control group: 62 people from Gaomi were chosen as the control group whose incomes, life styles, and living conditions were basically the same as those of the exposed group. The fluoride concentration in their drinking water was lower than 1.0mg/L. They were of the same gender, age and approximate BMI (21.3±2.2kg/, 21.6±1.9kg/, P>0.05) as the exposed group and had no history of familial disease or other diseases.

1.2 Study Methods

1.2.1 Water quality analysis: K^+, Na^+, Ca^{2+}, and Mg^{2+} were determined through the atomic absorption method, F in the water, P^{3-}, and Cl^- were determined through fluoride selective electrode method, phosphorus ammonium molybdate colorimetric method, and silver nitrate titration method respectively.

1.2.2 Urine fluoride determination: The fluoride concentration in the urine of 400 people (200 males and 200 females) from each area was determined through fluoride selective electrode method to calculate the overall geometrical mean of urine fluoride.

1.2.3 Function check of pancreatic islet B cells: Oral glucose tolerance tests (OGTT), as well as insulin and C-peptide releasing tests, were conducted of the serum (the insulin and C-peptide levels were tested through Radio Immunity Analysis [2,3]). Ten days before the tests, the subjects stopped using any drug that could affect

glucose metabolism. 75g of glucose was put into 250ml of warm water and every subject was asked to drink it within 5 minutes. The blood glucose, insulin and C-peptide in the venous blood as well as glucose in the urine were determined in both the fasting state and 60, 120, and 180 minutes after the oral glucose was administered. The blood sampling was done within 3 minutes of time error.

1.3 Statistical Analysis

The data was presented with x ± s or percentage. The difference was assessed with *t* or chi-square.

2. Results

2.1 Water Quality Analysis

The [F] in the drinking water ranged from 7.39 to 8.68 mg/L and averaged 8.03mg/L in the exposed group, 13.4 times higher than that of the control group (0.5-0.7mg/L, average 0.6mg/L). Ca2+ content in the exposed group was lower than that of the control group and there was no obvious difference in terms of the two groups' K+, Na +, Cl-, Mg2+, and P3- content (P>0.05).

2.2 Urine Fluoride Determination

The overall geometrical mean of [F] in the urine of the exposed group was 6.32 mg/L, 5.64 times higher than the control group (1.12 mg/L). The difference was obvious (P<0.01). There was no remarkable difference regarding the geometrical mean of urine fluoride of males and females within the same group.

2.3 Function Check of the Pancreatic Islet's B Cells

Results of the OGTT insulin and C-peptide releasing tests in the serum are listed in Table 1. The results showed: (1) The fasting blood glucose concentration and the peak value after oral glucose in the exposed group were higher than that of the control group. The peak value was found 120min after the oral glucose was administered, 60 min later than the peak of the control group; (2) The detectable rates of diabetes and IGT[4] in the exposed group were 11.29% and 20.97% while the rates in the control group were both 0. The detectable rates among patients with severe fluoride bone disease were 22.58% and 35.48%, significantly higher than that of people without the disease (0, 6.5%). (3) The fasting blood glucose, insulin, and C-peptide in the exposed group were lower than in the control group. The peak value in the exposed group after administration of oral glucose was significantly higher than in the control group (P<0.05, P<0.01) and occurred later than in the control group (120min and 60min after the oral glucose, respectively). The above results indicate that the function of pancreatic islet B cells in the exposed group was worse than in the control group. As displayed in Table 2, it was also found that in the exposed group, there were great differences regarding the results of the OGTT, insulin, and C-peptide releasing tests in the serum of subjects with and without severe fluoride bone disease. Pancreatic islet B cell function among the patients

Table 1: Results of OGTT, Insulin, and C-peptide Releasing Test in the Serum of the Exposed Group and Control Group (x±s, n=62 **)**

Group	Fasting			60 min		
	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L
Exposed group	5.12±0.59	10.57±5.94	0.81±0.20	8.65±1.76	104.60±24.12	3.17±0.54
Control group	4.61±0.48	13.10±6.72	1.09±0.45	7.02±1.35	71.97±32.50	4.33±0.73
Group	**120min**			**180min**		
	Blood glucose mmol/L	**Insulin mU/L**	**C-peptide ug/L**	**Blood glucose mmol/L**	**Insulin mU/L**	**C-peptide ug/L**
Exposed group	8.92±1.58	110.64±28.40	3.96±1.96	4.69±0.87	37.43±18.40	1.78±0.86
Control group	4.97±1.14	47.27±26.56	3.21±1.71	4.28±0.59	13.68±7.82	1.45±0.69

Note: compared with that of the control group, P<0.05, P<0.01

Table 2: Results of OGTT, Insulin,and C-peptide Releasing Test in the Serum of Subjects with and without Fluoride Bone Disease (x±s, n=31)

Group	fasting			60min		
	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L
Skeletal Fluorosis	5.46±0.65	8.28±5.20	0.76±0.22	9.48±1.86	122.87±22.54	4.18±0.58
Without Skeletal Fluorosis	4.80±0.55	11.49±6.04	0.96±0.27	8.04±1.71	83.66±28.68	3.27±0.52
Group	**120min**			**180min**		
	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L	Blood glucose mmol/L	Insulin mU/L	C-peptide ug/L
Skeletal fluorosis	10.36±1.92	134.38±31.58	4.92±2.23	5.03±1.34	42.07±20.60	2.17±0.98
without skeletal fluorosis	7.63±0.84	76.39±27.01	3.71±1.82	4.42±0.71	28.92±16.64	1.62±0.76

Note: compared with that of subjects without fluorosis of bone, P<0.05, P<0.01

with severe fluoride bone diseases was worse than that of people without the disease, which indicates that excessive fluoride intake can do much harm to pancreatic islet B cells with this effect increasing with the degree of fluorosis. The OGTT insulin and C-peptide releasing tests showed no remarkable gender or age differences within the exposed group (P>0.05).

3. Discussion

Since Moller and Gudjonsson first identified fluorosis in 1932, foreign and domestic scientists have conducted a lot research on the link between fluoride and diseases. But studies on the effect of excessive fluoride intake on the pancreatic islet B cells have been lacking. This comparative study shows that excessive fluoride can do much harm to the function of pancreatic islet B cells and that the effects change with the degree of fluorosis. Due to the significant increase [5] in IGT, hypertension, hyperlipoproteinemia, and coronary disease prevalence among diabetics, more attention should be paid to fluoride's adverse impact on the function of pancreatic islet B-cells. Since fluorosis is highly prevalent in China, a great number of people affected still haven't been healed. Improving the drinking water quality and adopting protective measures in the fluorosis areas as soon as possible could thus have a far-reaching impact on decreasing the prevalence of fluorosis, IGT, and diabetes as well as the prevalence and death rate of hypertension and coronary disease in the affected areas and even across the globe.

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Submission date: April 5, 1999; **Revision date:** November 8, 1999

Financial assistance: Research fund of Gaomi

*Translated from Chinese into English by **FoxTranslate**, courtesy of the Fluoride Action Network (2012). For more translations of Chinese research on fluoride toxicity, see www.fluoridealert.org/researchers/translations/*