

A Comparative Study on Systolic Time Interval of Populations in Mild and Severe Endemic Fluorosis Regions

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Abstract: Comparative study on STI of populations in regions mildly and severely affected by endemic fluorosis demonstrated significant differences between these two affected regions in the detection rate of abnormal STI as well as QS_2 and PEP/LVET, indicating that endemic fluorosis may injure the heart.

Keywords: Endemic fluorosis, systolic time interval

Endemic fluorosis (hereinafter referred to as "EF") is a kind of chronic systemic disease; aside from dental fluorosis and skeletal fluorosis which are widely recognized, there is an increasing amount of research into EF's non-skeletal effects^[1]. This paper aims to clarify the effects of fluorine on the cardiac functions of populations in the affected regions via the changes of cardiac systolic time interval (STI) on ECG.

Subjects and Methods

All subjects came from Lianhe Village of Gaoping Township and Zhongxin Village of Xinshui Township of Jinsha County, Guizhou Province. For the subjects from Lianhe Village, the incidence of dental fluorosis in the 8-15-year-old populations born locally was 100%, and that of grade-III dental fluorosis was 83.6%; the incidence of skeletal fluorosis in the over-16-year-old populations was 94.0%, and that of grade-III skeletal fluorosis was 21.0%. The population's urine fluoride concentration $G = 14.8$ ppm, with a range of 1.9-46.6 ppm. For the subjects from Zhongxin Village, the incidences of corresponding populations were 91.9%, 29.2% and 13.3%, respectively; there were no patients with grade-II or grade-III skeletal fluorosis; the population's urine fluoride concentration $G = 3.1$ ppm, with a range of 0.5-19 ppm.

Based on the provisions in the "Working Standards for Prevention and Control of Endemic Fluorosis (Tentative)" formulated by the "Chinese Association for Endemic Disease Prevention and Control" in 1981, Lianhe Village was deemed as a severely affected region and Zhongxin Village as a mildly

affected region.

In both villages, all males 27-39 years old and females 27-44 years old were listed as the subjects and underwent medical history inquiry, physical examination, routine ECG tracing and STI determination. For those requiring differential diagnosis, corresponding special examinations were performed additionally.

The STI recording instrument was a model-5153 three-stylus ECG machine made in Japan, which could simultaneously record the electrocardiogram, phonocardiogram and carotid arteriogram. The subject rested for 15 minutes before the examination, and lay on his/her back with the head slightly shifted leftwards for recording; the rheomicrophone (model TK-2118 made in Japan) and the pulse transducer (model TF-111S made in Japan) were placed at the routine positions. The limb leads with significant Q waves were chosen for conducting ECG [monitoring], with the machine turned on when holding the breath at the end of expiration. The paper speed was 50 mm/S.

Various STI time courses were measured by the blinded method; that is, the measurement was completed by a person who did not participate in the field investigation and knew nothing about subject grouping. The total electromechanical duration (QS_2) and the left ventricular ejection time (LVET) were measured by the conventional method and the pre-ejection period (PEP) was calculated by QS_2 minus LVET and substituted into Weissler's HR-STI regression equation to obtain the corresponding index values of the

above time courses, in order to eliminate the effects of heart rate.

Results

For Lianhe Village, 119 people were planned to be examined; 111 people were actually examined, with an actual examination rate of 93.3%; five people with factors affecting the observation (2 people with borderline hypertension and 3 people with hypertension) were removed, thus only 106 people were included in the data analysis (45 males and 61 females, with a sex ratio of 0.74); for Zhongxin Village, 125 people were planned to be examined; 112 people were actually examined, with an actual examination rate of 89.6%; eight people with factors affecting the observation (3 people with borderline hypertension, 1 person with hypertension, 1 person with congenital heart disease, 1 person with rheumatic heart disease, 1 person with pulmonary heart disease and 1

person with cirrhosis complicated by severe ascites) were removed, thus only 104 people were included in the data analysis (43 males and 61 females, with a sex ratio of 0.71).

See Tables 1 and 2 for various STI index values and the abnormal STI detection rate of the populations from both villages. It could be seen from Tables 1 and 2 that, compared with the mildly affected region, the PEP/LVET ratio of the severely affected region was significantly greater and the QS₂ was significantly prolonged, and the abnormal STI detection rate was also significantly increased, suggesting that the cardiac systolic functions of the populations with severe endemic fluorosis were significantly lower than those of the populations with mild endemic fluorosis.

See Table 3 for the abnormal STI constitution of the populations from both villages.

Table 1 Comparison of STI Values between the Two Villages

		QS (ms)		LVET (ms)		PEP (ms)		PEP/LVET	
		\bar{x}	SD	\bar{x}	SD	\bar{x}	SD	\bar{x}	SD
Lianhe (n = 106)	Actual value	302.17	27.63	290.99	23.13	101.27	16.35	0.35	0.06
	Index value	533.47	16.80	408.74	14.17	129.93	16.14		
Zhongxin (n = 104)	Actual value	397.19	25.52	299.01	20.97	99.03	15.29	0.33	0.06
	Index value	534.01	16.18	408.00	15.73	125.71	14.58		
U	Value		1.96		0.36		1.95		2.41
P	Value		=0.05		>0.05		>0.05		<0.05

QS: Total electromechanical duration LVET: Left ventricular ejection time

PEP: Pre-ejection period n: Number of cases

Except for the PEP/LVET ratio, all the statistical tests adopted the index values for testing.

Table 2 Comparison of Abnormal STI Detection Rate between the Two Villages

	Number of Subjects	Normal (PEP/LVET ≤ 0.39)	Abnormal (PEP/LVET ≥ 0.40)	Abnormal Detection Rate %
Lianhe	106	82	24	22.64
Zhongxin	104	92	12	11.54
Total	210	174	36	17.14

$X^2 = 4.56 P < 0.025$

Table 3 Comparison of Abnormal STI (PEP/LVET) Constituent Ratio between the Two Villages (%)

	0.40-0.43		0.44-0.52		0.53-0.60		Total	
	Number	Constituent Ratio	Number	Constituent Ratio	Number	Constituent Ratio	Number	Constituent Ratio
Lianhe	17	70.8	6	25.0	1	4.2	24	100.0
Zhongxin	8	66.7	4	33.3	--	--	12	100.0
Total	25	69.4	10	27.8	1	2.8	36	100.0

For the subjects with different degrees of dental fluorosis, none of the various STI index values

For the subjects with different degrees of dental fluorosis, none of the various STI index values and the normal and abnormal constituent ratios of cardiac function between the two villages showed significant differences (the former adopted variance analysis, and the latter used chi-square test).

Discussion

Fluorine is an essential element for the human body; however, long-term excessive fluorine intake could cause fluorosis^[1]. It has been reported in the literature^[2, 3, 4] that fluorine at certain concentrations in the body could inhibit the activities of acid phosphatase, alanine aminotransferase, aspartate aminotransferase, cytochrome oxidase, succinate dehydrogenase (SDH) and isocitrate dehydrogenase (ICDH) as well as biologically oxidative phosphorylation of cells, consequently leading to blocked tricarboxylic acid cycle and reduced energy production.

The above biochemical changes could also be reflected by the material metabolism and energy metabolism of the myocardium. Scholars including Bogin *et al*^[2] had already discovered in 1978 that myocardial ICDH activity of white rats was reduced after they were given 100 ppm water containing fluorine. Therefore, if the fluorine content in the body is too high, the myocardial citric acid cycle may be blocked, and subsequently the hydrogen supply from Nicotinamide Adenine Dinucleotide (NAD) I and SDH would be disturbed, leading to inhibited biological oxidation process of the myocardium and reduced ATP levels, which is extremely detrimental to the myocardium, which has significant energy consumption and very little ATP stored^[5]. In addition, Susheela^[6] found that collagen is the main target on which fluorides exert effects, and there are already abundant collagenous fibers in the myocardial interstitium^[7]. As a result, the reduction of myocardial systolic function is absolutely possible in the case of chronic fluorosis, which is supported by the investigational results of this paper. Although the PEP index values and LVET index values between the two affected

regions showed no significant difference, the PEP/LVET ratios were significantly different, which may be caused by the fact that the ability of the PEP/LVET ratio to identify left ventricular dysfunction is better than that of PEP and LVET^[8].

The quantitative criteria proposed by Weissler for determining left ventricular function with the PEP/LVET ratio are as follows: (1) Normal range: 0.35 ± 0.04 ; (2) Mildly impaired left ventricular function: 0.44-0.52; (3) Moderately impaired: 0.53-0.60; (4) Severely impaired: > 0.60 ^[9]. As shown in Table 3, most abnormal STIs of both affected regions were within the range of above normal to mildly impaired left ventricular dysfunction that should belong to subclinical cardiac insufficiency, which is consistent with the general clinical findings of EF.

Moreover, the STI changes of patients with different degrees of dental fluorosis showed no significant differences, the causes of which remain to be further investigated.

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