

Study on the Cardiovascular System Damage in Skeletal Fluorosis Patients

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[Abstract] Objective To understand the damage to the cardiovascular systems of patients with different degrees of skeletal fluorosis after stopping fluorine exposure. **Methods** 65 patients with mild, moderate and severe skeletal fluorosis and 23 subjects without skeletal fluorosis as the control group were selected for detailed inquiry of cardiovascular disease history, blood pressure measurement and ECG examination. **Results** The rate of skeletal fluorosis patients with cardiovascular system symptoms accounted for 70.77%, and the difference was statistically significant as compared with that of the control group ($P < 0.05$); the pairwise comparisons of various parameters indicated that the rate of patients with symptoms showed an upward trend along with the exacerbation of the patients' condition, and the differences between the control group and the severe skeletal fluorosis group were all statistically significant ($P < 0.05$). There were 42 cases of skeletal fluorosis patients with ECG abnormality, with a detection rate of 35.38%; and 17 cases of ECG abnormality in the control group, with a detection rate of 26.09%; all intergroup comparisons showed no statistically significant differences ($P > 0.05$). [As seen from] the comparison of ECG parameters, the P-R intervals of the severe skeletal fluorosis group were significantly prolonged and statistically different as compared with those of the control group ($P < 0.05$). There was no significant difference in the blood pressures of the investigated groups ($P > 0.05$). **Conclusion** The normal physiological functions of cardiovascular systems of skeletal fluorosis patients are still subject to a certain level of interference after 18 years of water quality improvement and fluoride reduction. The abnormal ECG changes can be significantly recovered in mild and moderate skeletal fluorosis patients, but in severe skeletal fluorosis patients, the recovery speed may be very slow. The long-term effects of severe skeletal fluorosis on the changes in patients' ECGs remain to be further investigated.

[Keywords] Skeletal fluorosis; cardiovascular damage; drinking water-type fluorosis

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Drinking water-type fluorosis, especially at the stage of skeletal fluorosis, can have impacts on the functions of multiple organs and significantly damage the cardiovascular system. It is reported that skeletal fluorosis patients' abnormal ECG rate could reach 43.52%^[1], and it is also reported that fluorine could cause changes of blood pressure and lead to vascular lesions. In order to understand the impacts of fluorine on the cardiovascular system of patients with skeletal fluorosis, in 2003, an investigational study was conducted on the skeletal fluorosis patients in the former high-fluoride area of Kuitun, Xinjiang, which had implemented a water quality improvement program for 18 years, and where the current characteristics and degrees of cardiovascular system damage in skeletal fluorosis patients are reported as follows.

1 Subjects and Methods

1.1 Subjects under Investigation

Residents that had been living in formerly high-fluoride areas (water fluoride content being 8.2-17

mg/L before water quality improvement in 1985 and 0.7 mg/L after water quality improvement) for more than 20 years and definitely diagnosed with skeletal fluorosis (by combining field data of epidemiologic investigation with the results of X-ray signs analysis) were chosen as the case group and divided into the mild, moderate and severe skeletal fluorosis patient groups based on the skeletal fluorosis conditions determined by X-ray signs^[2]. There were 23 cases in the mild skeletal fluorosis group, with 10 males and 13 females, aged 31 to 71 years, with an average age of 51.13; 23 cases in the moderate skeletal fluorosis group, 13 males and 10 females, aged 31 to 76 years old, with an average age of 53.74; and 19 cases in the severe skeletal fluorosis group, 10 males and 9 females, aged 35 to 74 years old, with an average age of 55.95. Permanent residents in neighboring non-high-fluoride areas (drinking water fluoride content 0.6 mg/L) that had no abnormal skeletal changes as confirmed by X-ray diagnosis were chosen as the blank control group (23 cases), of which there were 9 males and 14 females, aged 45 to 58 years old, with an average age of 49.13.

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1.2 Methods and Measurement Indexes

The measurements were conducted after all instruments used were respectively calibrated. (1) A uniform health physical examination form with items including the occupational history, subjective symptoms, personal and family histories, smoking history, etc. was used, and a trained person in charge was designated for inquiring, examining and completing the physical examination form; (2) A domestically-produced model ECG-6511 ECG machine was used and operated routinely, and any measurements beyond the normal ECG ranges would be determined as abnormal ECG changes; (3) Blood pressure was measured by a desk-model sphygmomanometer, and the median value was taken after two routine measurements.

1.3 Statistical Analysis

The SPSS11.5 statistical software was used for statistical treatment, and single-factor variance analysis was adopted if the variances were equal; if not, a rank-sum test was used instead. The chi-square test was adopted for the enumeration data.

2 Results

2.1 Main Cardiovascular System Symptoms

The rate of skeletal fluorosis patients with cardiovascular system symptoms reached up to 70.77%, among which patients with two or more symptoms accounted for 56.92%, significantly different from that of the control group ($P < 0.05$). All observed items showed significant differences between various skeletal fluorosis patient groups and the control group ($P < 0.05$). It was found by the pairwise comparisons of each item that the rate of patients with symptoms showed an upward trend along with the exacerbation of the patients' condition, and the differences between the control group and the severe skeletal fluorosis group were all statistically significant ($P < 0.05$); see Table 1.

2.2 Comparison of Blood Pressure

The blood pressure differences between various skeletal fluorosis groups and the control group were not statistically significant ($P > 0.05$); see Table 2.

Table 1 Comparison of main symptoms of cardiovascular system between various skeletal fluorosis groups and the control group (%)

	Control group (n = 23)	Mild group (n = 23)	Moderate group (n = 23)	Severe group (n = 19)
Without symptoms	16 (69.57)	12 (52.17)	4 (17.39) ^Δ	3 (15.79) ^Δ
With symptom(s)	7 (30.43)	11 (47.83)	19 (82.61) ^Δ	16 (84.21) ^Δ
Dizziness	6 (26.09)	8 (34.78)	13 (56.52)	13 (68.42) ^Δ
Palpitation	6 (26.09)	9 (39.13)	12 (52.17)	14 (73.68) ^Δ
Shortness of breath	6 (26.09)	10 (43.48)	13 (56.52)	13 (68.42) ^Δ
Chest pain	1 (4.35)	5 (21.74)	5 (21.74)	9 (47.37) ^Δ

Note: As compared with the control group $^{\Delta}P < 0.05$, some patients had two or more symptoms at the same time.

Table 2 Comparison of blood pressures between various skeletal fluorosis groups and the control group (mmHg)

Group	N	Diastolic Pressure	Systolic Pressure
Control group	23	78.83 ± 12.32	116.65 ± 20.04
Mild group	23	80.83 ± 12.21	124.96 ± 21.81
Moderate group	23	77.61 ± 16.07	118.35 ± 22.72
Severe group	19	85.74 ± 14.94	133.00 ± 17.78

2.3 Comparison of ECG Changes

The investigation results showed that there were 42 cases of skeletal fluorosis patients with ECG abnormality, with a detection rate of 35.38%; there were 17 cases of ECG abnormality in the control group, with a detection rate of 26.09%. Both the overall and pairwise comparisons of each abnormal ECG change between various skeletal fluorosis groups and the control group showed no statistically significant differences ($P > 0.05$); see Table 3.

Table 3 Comparisons of each abnormal ECG change (%)

ECG Change	Control group (n = 23)	Mild group (n = 23)	Moderate group (n=23)	Severe group (n=19)	P Value
ECG abnormality					
Various kinds of arrhythmia	6 (26.09)	7 (30.43)	11 (47.83)	5 (26.32)	> 0.05
Sinus arrhythmia	4 (17.39)	2 (8.70)	5 (21.74)	2 (10.53)	> 0.05
Occasional atrial premature beats	3 (13.04)	1 (4.35)	1 (4.35)	0 (0)	
Frequent atrial premature beats	0 (0)	0 (0)	0 (0)	1 (5.26)	
Sinus tachycardia	0 (0)	0 (0)	1 (4.35)	0 (0)	
Sinus bradycardia	1 (4.35)	1 (4.35)	2 (8.70)	1 (5.26)	
Various kinds of conduction block	0 (0)	0 (0)	1 (4.35)	0 (0)	> 0.05
Complete right bundle branch block	1 (4.35)	0 (0)	2 (8.70)	0 (0)	
Left anterior fascicular block	1 (4.35)	0 (0)	1 (4.35)	0 (0)	
T wave abnormality	0 (0)	1 (4.35)	1 (4.35)	0 (0)	> 0.05
T wave abnormality of limb leads	0 (0)	1 (4.35)	1 (4.35)	0 (0)	
T wave abnormality of precordial leads	0 (0)	0 (0)	0 (0)	0 (0)	
Atrioventricular hypertrophy	0 (0)	1 (4.35)	1 (4.35)	2 (10.53)	> 0.05
Left atrial and ventricular hypertrophy	0 (0)	0 (0)	0 (0)	1 (5.26)	
Bilateral ventricular hypertrophy	0 (0)	0 (0)	0 (0)	1 (5.26)	
Left ventricular hypertrophy	0 (0)	1 (4.35)	0 (0)	0 (0)	
Others	1 (4.35)	3 (13.04)	0 (0)	1 (5.26)	> 0.05
Myocardial damage	1 (4.35)	3 (13.04)	3 (13.04)	0 (0)	
Left axis deviation	0 (0)	0 (0)	2 (8.70)	1 (5.26)	
u wave inversion	0 (0)	0 (0)	1 (4.35)	0 (0)	

It was found during the statistical analysis of ECG parameters of various skeletal fluorosis groups and the control group that the difference of P-R intervals between the control

group and the severe skeletal fluorosis group was statistically significant ($P < 0.05$), but other parameters were not different; see Table 4.

Table 4 Comparisons of ECG parameters between various skeletal fluorosis groups and the control group ($\bar{x} \pm s$)

Parameter	Control group ($n = 23$)	Mild group ($n = 23$)	Moderate group ($n = 23$)	Severe group ($n = 19$)
Heart rate (beats)	80 ± 13.80	78.96 ± 11.23	81.57 ± 15.16	77.95 ± 14.62
P-R interval (s)	0.1404 ± 0.0152	0.1461 ± 0.0192	0.1478 ± 0.0213	0.1532 ± 0.0197^A
QRS interval (s)	0.0852 ± 0.0156	0.0930 ± 0.0499	0.0848 ± 0.0095	0.0842 ± 0.0084
Q-Tc interval (s)	0.3962 ± 0.0153	0.3987 ± 0.0236	0.3979 ± 0.0208	0.3927 ± 0.0262

Note: As compared with the control group $^A P < 0.05$.

3 Discussion

Fluorine is an active non-metallic element that is susceptible to binding with blood calcium and blood magnesium which can lead to disturbance of calcium metabolism, and, as a consequence, functional and organic damage to systems such as the cardiovascular system [3]. WANG Jing-li [4] believed that the ECG changes of fluorosis patients were mainly manifested as arrhythmia, especially sinus arrhythmia and sinus bradycardia, followed by lowered or biphasic T waves, but the changes of P-R interval and Q-T interval were not significant. However, some literatures also demonstrated that the heart rhythm disorders of fluorosis patients were mainly sinus tachycardia, and the S-T segment intervals of the skeletal fluorosis groups were shorter than those of the control group, while the P-R intervals varied by gender. JI Xin *et al* [5] discovered in a preliminary observation on the cardiovascular systems of 40 fluorosis patients that the clinical manifestations of their cardiovascular systems were a group of syndromes, namely dizziness, palpitation, arrhythmia, reduced cardiac output and aortic abnormality, etc., but with no characteristic lesion. Fluorosis patients with cardiovascular system symptoms reached up to 77.50%, among which patients with two or more symptoms accounted for 50.0%; the differences were significant compared with the control group, but symptoms were non-specific. SU Li *et al* [6] investigated the ECGs of residents in high-fluoride areas and found that the incidence of abnormal ECG changes of such residents were significantly higher than that of the control population, and their myocardial damages were diffuse. It was also found by animal experiments that rats drinking high-fluoride water (1.58 and 2.63 mmol/L, respectively) for 8 months showed reduced T wave amplitude and shortened Q-T interval in their ECGs [7]. Other investigations also showed that, as compared with the control group, the P-Q intervals shown by ECGs of sheep with skeletal fluorosis were significantly prolonged; the diseased group had sinus bradycardia that caused decreased heart rhythm, where the heart rates of the control group were (110 ± 15) beats/min, and those of the diseased group were (75 ± 10) beats/min, and the intergroup comparison showed a statistically significant difference [8]. All of the above data show that high fluorine levels can induce changes of the cardiovascular system.

This paper conducted an investigation on 65 cases of non-cured skeletal fluorosis patients in former areas of endemic fluorosis, of which the results showed that the rate of skeletal fluorosis patients with cardiovascular system symptoms reached up to 70.77%, among which patients with two or more symptoms accounted for 56.92%, significantly different from that of the control group. The pairwise comparisons of each item indicated that the rate of patients with symptoms showed an upward trend along with the exacerbation of the patients' condition, and the differences between the control group and the severe skeletal fluorosis group were all statistically significant. The results of blood pressure changes demonstrated that the comparison of blood pressure among each investigational group had no statistical difference. There were 42 cases of skeletal fluorosis patients with ECG abnormality, with a detection rate of 35.38%; there were 17 cases of ECG abnormality in the control group, with a detection rate of 26.09%; all intergroup comparisons showed no statistically

significant differences. It was found through the comparisons of ECG parameters of all groups that the P-R interval difference between the control group and the severe skeletal fluorosis group was statistically significant. As compared with the results of literature reports, the normal physiological functions of the cardiovascular systems of skeletal fluorosis patients are still subject to a certain level of interference after 18 years of water quality improvement and fluoride reduction; the markedly increased rate of skeletal fluorosis patients with cardiovascular system symptoms is associated with the severity of disease, and considered to be related to the long-term effects of fluorine on the body or the symptoms' lack of specificity. In addition, the P-R intervals of the severe skeletal fluorosis group were significantly prolonged as compared with those of the control group, and other ECG changes had no difference, indicating that the ECG parameters and abnormal changes of mild and moderate skeletal fluorosis patients could be recovered after stopping drinking high-fluoride water for 18 years, but the ECG changes of severe skeletal fluorosis patients may be irreversible or recover at a relatively slower speed. The long-term effects of severe skeletal fluorosis on the changes in patients' ECGs remain to be further investigated and explored.

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