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Analysis on Serum Lipids in Patients with Fluorine-Associated Aortic Sclerosis

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Abstract *In this paper, we analyzed the quantification of serum lipoprotein performed on 30 cases (the mean age being 41 years old) with fluorine-associated aortic sclerosis, and 31 healthy adults (the mean age being 40.5 years old) were included in the control group. The determination of T-ch, HDL, LDL, VLDL and HDL/T-ch was performed on [all cases] in these two groups; the significance of differences was verified with the t test, and correlation analysis was made. Results demonstrated that HDL and HDL/T-ch for the fluorosis group were significantly lower than those for the control group, and VLDL for the fluorosis group was higher than that for the control group, but all those values did not exceed the normal ranges. VLDL, LDL and T-ch were positively correlated to the thickness of aortic wall measured by two-dimensional echocardiography, r being 0.45, 0.54 and 0.55 respectively. The relation between the pathogenesis of fluorine-associated aortic sclerosis and serum lipids was discussed, and the conclusion was as follows: The increased incoming Ca++ may cause the functional failure of muscle cells and their subsequent necrosis, resulting in local calcification and ulceration; in addition, the pathogenesis of fluorine-associated aortic sclerosis may be related to the important synergic action of fluorine ions with the enzyme system in the human body; the excessive uptake of fluorine may cause dysfunction of the enzyme system in the human body, leading to the elevation of VLDL and the reduction of HDL in the blood, and subsequent pathological changes of vascular walls.*

Key words *Fluorine-associated aortic sclerosis; serum lipoprotein; human being*

We carried out a study on the changes in echocardiography in a group of patients with endemic fluorosis in 1986 [1], and we discovered sclerotic changes such as remarkable thickening of aortic walls in those patients; therefore we proposed [the concept of] fluorine-associated aortic sclerosis and made a preliminary inference on its pathogenesis. In this paper, we analyzed the quantification of serum lipoprotein performed in 30 cases with fluorine-associated aortic sclerosis, in order to further probe into the pathogenesis of fluorine-associated aortic sclerosis and the relation between fluorides and lipid metabolism.

I. Information and methods

Thirty cases with fluorine-associated aortic sclerosis were chosen from the affected region of endemic fluorosis in Hongshawo, Zhangye City, Gansu Province. In this affected region, the content of fluorine in drinking water reached 3.0–10.0 mg/L; the incidence of dental fluorosis reached up to 85.4% and the incidence of skeletal fluorosis reached up to 31.9%; patients at grade-III clinical stage accounted for 8.9%. All 30 cases in this group were diagnosed with fluorine-associated aortic sclerosis by two-dimensional and M-mode echocardiography and X-ray, including 12 male cases and 18 female cases, at the ages of 31–61 years old, the mean age being 41 years old. The content of fluorine in the drinking water was 3.0 ml/L for 2 cases, 3.5 ml/L for 6 cases, and 10.0 ml/L for 22 cases. Two-dimensional echocardiography showed that the mean thickness of aortic wall was 8.2 ± 0.5 mm, and chest X-ray revealed 27 cases with thoracic aortic sclerosis. Another 31 healthy adults free of cardiovascular diseases were chosen additionally as controls, including 11 male cases and 20 female cases, the mean age being 40.5 years old.

The dextran sulfate-Mg++ precipitation method was adopted, and the reagents were prepared at the Shanghai Second Medical College. The determination of T-ch, HDL, LDL, VLDL and HDL/T-ch was performed on [all cases] in these two groups, the significance of differences was verified with the *t* test, and correlation analysis was made.

II. Results

The comparison of serum lipoprotein between the 30 cases with fluorine-associated aortic sclerosis and the control group is as shown in Table 1.

As shown in Table 1, HDL and HDL/T-ch for the fluorosis group were significantly lower than those for the control group, and VLDL for the fluorosis group was higher than that for the control group, but all those values did not exceed the normal ranges. VLDL, LDL and T-ch were positively correlated to the thickness of aortic wall measured by two-dimensional echocardiography, r being 0.45, 0.54 and 0.55 respectively.

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Table 1 Comparison of serum lipoprotein between the fluorosis group and the control group ($\bar{x} \pm SD$, unit: mmol/L)

Items	Fluorosis group n = 30	Control group n = 31	*t*	P
T-ch	4.43 ± 0.55	4.26 ± 0.78	1.02	>0.5
HDL	1.17 ± 0.12	1.43 ± 0.37	3.92	<0.01
HDL/T-ch	0.27 ± 0.04	0.34 ± 0.09	4.13	<0.01
LDL	2.41 ± 0.49	2.29 ± 0.75	0.77	>0.5
VLDL	0.85 ± 0.42	0.53 ± 0.41	3.07	<0.01

III. Discussion

All cases with fluorine-associated aortic sclerosis in this study were patients with skeletal fluorosis who drank water with high levels of fluorine exceeding the physiological index (fluorine content in drinking water within 3.0–10.0mg/L) for more than 30 years consecutively, and all of them manifested symptoms of endemic fluorosis, such as: increased content of fluorine in blood and urine, skeletal fluorosis, dental fluorosis, and clinical palpitation and polypnea manifestations of different degrees; their X-ray chest films revealed changes associated with aortic sclerosis and calcification; their ultrasound examinations revealed manifestations of reduced aortic diameters, thickened vascular walls, intensified echoes, reduced mobility and ageing-related aortic sclerosis of different degrees.

The biochemical mechanism of atherosclerosis includes two parallel and correlated processes: first, platelet-endothelial interaction causing the proliferation of connective tissue components in the aortic wall; second, lipids infiltrating blood vessels and settling within [2]. Aortic smooth muscle cells (SMC) swallow a lot of lipids to form foam cells, and this process is inhibited by the self-regulation of LDL receptors of the cells. However, serum LDL may promote the proliferation of SMC, and is therefore related directly to the genesis of atherosclerosis, while the elevation of HDL concentration may prevent atherosclerotic injury [3]. Furthermore, the precipitating factor of atherosclerosis is generally considered to be the endothelial injury caused by the interaction of mechanical or hemodynamic stress with antigen-antibody complexes or chemical substances. Multiple [study] results have demonstrated that the sclerosis is negatively correlated to the levels of HDL and HDL/T-ch, and positively correlated to the levels of VLDL and triglycerides. The data obtained from the current study also demonstrated the aforesaid result.

Certain prospective studies show that a definite relationship exists between certain environmental, biochemical, physical, genetic and pathological conditions and atherosclerosis. For patients in the current study, their fluorine-associated aortic atherosclerosis is due to the lipid metabolism disorder caused by long-term accumulation of fluorides exceeding the physiological index in the human body and the precipitation of fluorapatite formed through the binding of fluorides with calcium ions and other cations on the aortic wall. In the current study, the fluorosis group's serum Ca++ level (2.56 ± 0.21 mmol/L) was significantly higher than that for the control group (2.25 ± 0.19 mmol/L), $P < 0.01$. The elevation of serum Ca++ and the precipitation of fluorapatite exacerbated calcification of the aortic wall; furthermore, the elevation of the Ca++ concentration outside myocardial cells would cause more Ca++ to enter the myocardium and muscle cells in the aortic wall under certain conditions, which may lead to functional failure of muscle cells and their subsequent necrosis, resulting in local calcification and ulceration. Fluorine is an essential microelement for the human body, and a proper amount of F^- may protect the myocardium, yet the effect of fluorine on the great vessels and the related mechanism remain to be made clear. Microelements have key biological actions, and they have important synergic actions with the enzyme system in the human body; as both exhilarants of enzyme activity and enzyme inhibitors, microelements may penetrate the center of enzyme activity and control multiple enzymes to affect the secretion of hormones, thus playing important roles in the regulation of metabolism. Consequently, the amount of their uptake, differences of their content in different regions, and the disorder of their regulating function may cause pathological and physiological changes in the heart and blood vessels. Multiple materials have reported that high levels of fluorine may inhibit the activity of multiple enzymes, such as lipase, osseous phosphatase, urease, various saponification enzymes and glycogen lytic enzymes, causing disordered substance metabolism, which may be related to changes of serum lipoprotein seen in patients with fluorine-associated aortic sclerosis.

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