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MEASURES DESIGNED TO PREVENT ENDEMIC FLUOROSIS CAUSED BY BURNING COAL IMPROVE THE HEALTH OF MOST RESIDENTS IN THE AREA OF GUIZHOU, CHINA, BUT NOT OF THE ELDERLY

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ABSTRACT: Our aim was to evaluate the health of the residents living in an area of the coal-burning type of endemic fluorosis, particularly the elderly, after five years of integrated attempts to control this disease (e.g., by the adaptation of stoves and improved health education). A total 153 individuals living in this area and 167 residents of an area unaffected by fluorosis were compared with respect to the numbers of red blood cells (RBC), white blood cells (WBC), and platelets (PLT), the level of hemoglobin (HGB) in the blood, and the serum levels, measured with biochemical procedures, of alanine aminotransferase (ALT), aspartate transaminase (AST), uric acid (UA), blood urea nitrogen (BUN), and creatinine (CREA). The level of education and the family economic status were also surveyed. The results showed that for the individuals below 60 years of age living in the area of endemic fluorosis, these biological parameters were similar to those of the controls. However, for the residents aged 60 years or older in the fluorosis area, the values for RBCs, HGB, PLTs, and BUN were all decreased, and levels of ALT, AST, and CREA were elevated. No differences in the level of education or family economic status were present in the residents aged 60 or more years living in the fluorosis and non-fluorosis areas. These findings indicate that even though integrated control results in an obvious improvement of the health of the individuals below 60 years of age in the area of the coal-burning type of endemic fluorosis, the health of elderly residents, aged ≥60 years, in the fluorosis area was not significantly improved, possibly because their fluorosis was more severe as a result of having been present for a longer duration.

Key words: Biological parameters; Coal-burning type of endemic fluorosis; Economic status; Education; Residents with different ages;

INTRODUCTION

In addition to the typical dental and skeletal changes, endemic fluorosis, resulting from an excessive intake of environmental fluoride, damages the human body in many other ways.[1-2] Since Dr. Lyth first reported in 1946 in the *Lancet*[3] the presence of endemic fluorosis in the Guizhou (Kweichow) province of China, many studies have concluded that this type of fluorosis was due to the consumption of food contaminated by smoke from the indoor burning of coal containing a high level of fluoride.[4-6]

This type of endemic fluorosis occurs in the major coalfield districts in the southwest of China, where the humidity is usually high and the residents burn coal to both dry harvested grain for long-term storage and to provide warmth in the wintertime.[7,8] The stoves involved have no chimney and the soot is emitted directly into the indoor space, contaminating with fluoride not only the air but also grain, chili, and vegetables. Eating the fluoride-contaminated food and breathing the polluted air for long periods results in excessive fluoride deposition in the body and the development of chronic fluorosis.

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In China, endemic fluorosis due to burning coal occurs in 13 provinces with more than 34 million people living in affected areas, of whom 18 million exhibit dental fluorosis and 1.5 million have skeletal fluorosis. In Guizhou province, where this type of endemic fluorosis was first recognized and is most severe,[4] the total population is 37 million, more than 15 million live in affected areas, 10 million have dental fluorosis, and 0.8 million have skeletal fluorosis.[9]

Since the 1980's, much effort has been put into eliminating the coal-burning type of endemic fluorosis in China,[9] including campaigns to adapt local family stoves to eliminate fluoride pollution and to educate the residents in the areas concerned about the hygiene required. As a result, the fluoride contamination of food and indoor air and the incidence of dental and skeletal fluorosis have all declined. Indeed, endemic fluorosis might even be eliminated totally in the near future.

Populations around the world are ageing rapidly, primarily due to better living standards and progress in medical technology, which lengthen life expectancy and reduce mortality from disease, and to a declining birth rate. Between 2000 and 2050, the proportion of the world's population older than 60 years of age will double, from approximately 11% to 22%, which corresponds to an increase from 605 million to approximately 2 billion people. The ageing of populations is poised to become the next global public health challenge,[10] with an increasing proportion of elderly individuals subject to dementia, tumor, cardiovascular and cerebrovascular diseases, chronic inflammation, diabetes, and osteoarthritis.[11] Although, in general, the health level in the areas where fluorosis due to coal burning is endemic has improved significantly, it is unclear whether the health of the elderly population in these areas has been improved and which factors influence their health.

Accordingly, in the current investigation, the health of the residents living in these areas was compared to that of age-matched controls from areas unaffected by endemic fluorosis.

MATERIALS AND METHODS

Materials: The reagents for the fully automatic blood cell analysis were obtained from the Sysmex Corporation, Japan. All other chemicals were purchased from Sigma Aldrich, USA.

Subjects: One hundred and fifty-three residents of the area affected by endemic fluorosis in the Shuicheng and Qixingguan counties in the Guizhou province of China and 167 from unaffected areas, all 18–83 years old, were selected and divided into three groups, with ages of 39 years old or younger, 40–59 years, and 60 years or older. For more than 5 years, the areas with endemic fluorosis had been subjected to extensive attempts to eliminate this condition, including designing stoves scientifically with an exhaust leading outdoors and education about hygiene. The blood samples were collected after obtaining informed consent.

Blood parameters: The numbers of red blood cells (RBC), white blood cells (WBC) and platelets (PLT), the level of hemoglobin (HGB), the serum activities of alanine aminotransferase (ALT) and aspartate transaminase (AST), and the serum levels of uric acid (UA), blood urea nitrogen (BUN) and creatinine (CREA) were all determined with a fully automatic blood cell analyzer (Sysmex XT 1800i, Japan) or biochemical procedures.

Survey concerning education and family economy: The education of the residents was divided into three levels, i.e., primary school or below, junior high school, and high school. The family economy was designated as lower (living in relative poverty), middle (an average standard of living), or good (a more comfortable life). These levels were based on a questionnaire survey.

Fluoride content in the urine and the occurrence of dental or skeletal fluorosis: The fluoride content of the urine was quantified with a fluoride ion specific electrode. Dental fluorosis was determined by observation and skeletal fluorosis by the examination of X-rays.

Statistical analysis: All values are presented as means±SD, and the analyses were performed with the GraphPad Prism 5.0 and SPSS 22.0 software (SPSS Inc., USA). Data were analyzed by one-way analysis of variance (ANOVA) followed by the Bonnferoni or the two-paired Student's *t* test. Differences present of at least $p<0.05$ were considered to be statistically significant.

RESULTS

General examination: In all three age groups in the area with endemic fluorosis, the fluoride content in the urine (1.37–2.15 ppm) was obviously higher than that in controls (0.59–0.67 ppm) (Table 1).

Table 1. Urinary fluoride content and the prevalence of dental and skeletal fluorosis in the different age groups from the areas affected and unaffected (control) by the coal-burning type of endemic fluorosis

Age (years)	Group	n	Fluoride (ppm)	Dental fluorosis (%)	Skeletal fluorosis (%)
≤39	Control	58	0.59±0.23	0 (0/58)	0 (0/58)
	Fluorosis	53	1.37±0.58*	52.8 (28/53)	28.3 (15/53)
40–59	Control	57	0.67±0.37	0 (0/57)	0 (0/57)
	Fluorosis	54	1.89±0.95*	66.7 (36/54)	37.0 (16/54)
≥60	Control	52	0.63±0.73	0 (0/52)	0 (0/52)
	Fluorosis	46	2.15±0.82*†	87.0 (40/46)	63.0 (29/46)

Compared to the control group: *$p<0.01$;
compared to the other groups in the area with fluorosis: †$p<0.05$.

The incidence of dental and skeletal fluorosis was 52.8% and 28.3%, respectively, in those aged 39 years or younger, 66.7% and 37.0%, respectively, in the group aged

40–59 years, and 87.0% and 63.0%, respectively, in individuals aged 60 years or older (Table 1). In contrast, the residents in the area without fluorosis exhibited no increased level of fluoride in their urine and no dental or skeletal fluorosis (Table 1).

Blood parameters: Among the residents of the area of endemic fluorosis, the blood parameters for those aged 39 years or younger were the same as for the control individuals. Those aged 60 years of age or older had reduced numbers of RBCs and PLTs, and a reduced level of HGB. In addition, the number of RBC and the level of HGB in this oldest group were lower than normal (4.3–5.8×10^{12}/L and 130–175g/L, respectively (Table 2).

Table 2. The numbers of circulating red blood cells (RBC), white blood cells (WBC), and platelets (PLT) and the level of hemoglobin (HGB) in the groups from the areas affected and unaffected (control) by coal-burning type of endemic fluorosis

Age (years)	Group	n	RBC[a] (×10^{12}/L)	WBC (×10^{9}/L)	PLT (×10^{9}/L)	HGB[b] (g/L)
≤39	Control	58	5.49±0.27	6.88±0.98	293.5±67.8	139.8±6.3
	Fluorosis	53	5.22±0.34	6.12±1.06	241.9±33.1	133.2±6.6
40–59	Control	57	5.21±0.44	6.38±1.24	287.5±28.6	142.3±8.5
	Fluorosis	54	4.62±0.23*	6.19±1.38	253.2±64.6	132.7±10.4
≥60	Control	52	4.87±0.19	6.33±1.85	272.3±49.4	138.2±3.7
	Fluorosis	46	4.10±0.15†	5.97±1.77	194.1±30.4*	122.5±3.7*†

[a]The normal range for the RBC, as measured by the hospital, is 4.3–5.8×10^{12}/L, [b]the normal range, as measured by the hospital, for the level of hemoglobin is 130–175 g/L. Compared to the control group: *$p<0.05$; compared to the normal value measured by the hospital: †$p<0.01$.

Compared to controls, the group aged 60 years or older from the area of endemic fluorosis had elevated activities of ALT and AST (Table 3), and an increased level of CREA and a decreased content of BUN (Table 4). Moreover, the AST activity in this group was higher than normal (15–40 U/l) (Table 3). On the other hand, no significant changes in these blood parameters were found for those aged 39 or younger and only an increased activity of AST was determined in the 40–59-years-old group from the areas of fluorosis compared to controls (Tables 3–4).

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Table 3. Serum activity of alanine aminotransferase (ALT) and aspartate transferase (AST) in the different age groups from the areas affected and unaffected (control) by the coal-burning type of endemic fluorosis

Age (years)	Group	n	ALT (U/L)	AST[a] (U/L)
≤39	Control	58	28.4±11.3	32.9±6.6
	Fluorosis	53	28.9±11.6	35.4±14.3
40-59	Control	57	28.1±7.6	30.3±2.8
	Fluorosis	54	32.5±10.7	39.5±5.6*
≥60	Control	52	26.7±3.2	34.8±9.4
	Fluorosis	46	42.7±7.8*	52.9±4.5*†

[a]The normal level of AST, as measured by the hospital, is 15–40 U/L.
Compared to the control group: *p<0.05; compared to the normal value measured by the hospital: †p<0.01.

Table 4. Serum levels of uric acid (UA), blood urea nitrogen (BUN), and creatinine (CREA) in the different groups from the areas affected and unaffected (control) by coal-burning fluorosis

Age (years)	Group	n	Fluoride (ppm)	Dental fluorosis (%)	Skeletal fluorosis (%)
≤39	Control	58	281.1±39.7	6.40±1.47	66.5±9.8
	Fluorosis	53	251.6±36.4	6.59±2.17	60.3±7.3
40–59	Control	57	271.8±43.8	6.41±0.40	67.9±43.8
	Fluorosis	54	269.9±41.2	5.07±0.98	269.9±9.5
≥60	Control	52	296.0±97.8	4.65±0.89	75.9±4.6
	Fluorosis	46	288.0±64.6	3.60±0.70*	98.9±2.2†

Compared to the control groups: *p<0.01, †p<0.05.

Level of education and family economic status: The level of education and family economic status for the different age groups in the areas affected and unaffected by fluorosis were similar (Table 5).

Table 5. Level of education and family economic status in the different age groups from the areas affected and unaffected (control) by coal-burning fluorosis (PSB = primary school or below; JHS = junior high school; HS = high school; LI = lower income; MI= middle income; GI = good income)

Age (years)	Group	n	Level of education			Family economic status		
			PSB (%)	JHS (%)	HS (%)	LI (%)	MI (%)	HI (%)
≤39	Control	58	62 (36/58)	33 (19/58)	5 (3/58)	33 (19/58)	54 (31/58)	13 (6/58)
	Fluorosis	53	57 (30/53)	36 (19/53)	7 (4/58)	30 (16/53)	58 (31/53)	12 (6/53)
40-59	Control	57	71 (41/57)	25 (14/57)	4 (2/57)	38 (22/57)	53 (30/57)	9 (5/57)
	Fluorosis	54	75 (40/54)	22 (12/54)	3 (2/54)	32 (17/54)	60 (32/54)	8 (4/54)
≥60	Control	52	79 (41/52)	19 (10/52)	2 (1/52)	47 (24/52)	51 (27/52)	2 (1/52)
	Fluorosis	46	82 (38/46)	17 (8/46)	2 (1/46)	49 (23/46)	50 (23/46)	2 (1/46)

DISCUSSION

In the current investigation, the urinary fluoride content of residents from the areas affected by the coal-burning type of endemic fluorosis was significantly higher than those living in unaffected areas. Following the accumulation of large amounts of fluoride in the body, fluoride excretion via the urine is a long-term process. The prevalence of dental fluorosis and skeletal fluorosis found in the residents was 68.8% and 42.8%, respectively, which was significantly lower than the values found in the same area in 2003, over 95% and 57.5%, respectively.[12] Thus, stove adaptation and preventive education appear to have gradually reduced the prevalence of both dental and skeletal fluorosis.[13] However, the high rate of skeletal fluorosis still present in those aged 60 years or older living in the area of endemic fluorosis, 63.0%, indicates that the long-term deposition of fluoride in the bones is difficult to attenuate. The high prevalence of dental fluorosis in those aged 60 years or older living in the area of endemic fluorosis, 93.5%, was not unexpected as dental fluorosis in teeth cannot be reversed to normal once the teeth are affected by dental fluorosis.[16] However, discoloured teeth can be masked by bleaching, microabrasion, removal of the maturation enamel with fine polishing burs, alone or in combination with a strong acid, composite resins, porcelain veneers, and sometimes full coverage restorations.[16,17]

Fluoride released from tissues into the blood can reduce the numbers of circulating RBCs,[14] influencing the activity of APP on the surface of these cells and the transport of sodium and calcium, thereby changing their shape. Excessive fluoride also interferes directly with oxygen metabolism and promotes the formation of free radicals,[15] which may damage RBCs and cause anemia. Therefore, the numbers of RBC and PLT and the serum level of HGB are highly important indicators of the health of residents in the area of endemic fluorosis. In a previous study performed in 2009, the numbers of RBC and the levels of HGB in these residents[18] were significantly lower than those in the present investigation, indicating the improvement resulting from five years of integrated control in the area of endemic fluorosis. For the participants from the affected area younger than 60 years of age, only a small decrease in the numbers of RBC in comparison to the controls was detected. However, for those aged 60 years of age or older, the levels of RBC, PLT, and HGB, but not WBC, were lower than those of the control individuals with the RBC and HGB values being significantly lower than normal.

The serum activities of ALT and AST are valuable indicators of damage to the liver and mice or rats exposed to high levels of fluoride exhibit increases in the activities of these enzymes,[19,20] indicating hepatotoxicity. In addition, an excessive intake of fluoride can induce renal lesions and dysfunction.[21,22] In the current study, we found elevated activities of ALT and AST, an increased level of CREA, and a decreased BUN in those 60 years of age or older living in the area of endemic fluorosis compared to the controls, with their AST activity being higher than normal. In the case of the other two age groups, only the AST activity was increased in the 40–59 years old living in the area of endemic fluorosis. These findings indicate that even after several years of comprehensive control, the health of the elderly residents of the area of coal-burning fluorosis had not recovered to an optimal level.

The level of education and family economic status of the different age groups from the areas affected and unaffected by endemic fluorosis were similar and could thus not explain the differences in the blood parameters.

CONCLUSION

Even though, in general, the health of the residents living in the area of coal-burning type of endemic fluorosis was greatly improved after five years of integrated control, the health of the elderly residents in this area was not. This difference could not be explained on the basis of the level of education or the family economic status, but might be due to the fluorosis being more severe as a result of having been present for a longer duration. Accordingly, special attention, including drug treatment and medical care, should be paid to the health of the elderly population in areas of the coal-burning type of endemic fluorosis.

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