A CLINICAL AND BIOCHEMICAL STUDY OF CHRONIC FLUORIDE TOXICITY IN CHILDREN OF KHERU THANDA OF GULBARGA DISTRICT, KARNATAKA, INDIA

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SUMMARY: The prevalence of dental and skeletal fluorosis was determined among children of Kheru Nayak Thanda of Gulbarga district, where the fluoride concentration in drinking water ranges from 0.6 to 13.4 ppm and the water has low levels of copper and zinc. These children were investigated clinically, radiologically and biochemically. The study revealed that 89% of the children had dental fluorosis and 39% exhibited skeletal fluorosis. Serum samples of these children showed elevated levels of alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), and decreased levels of total protein, albumin, and potassium. Radiographic changes suggestive of osteoporosis, osteosclerosis, and genu valgum were observed.

Keywords: Fluorosis, Genu valgum, Genu varum, Osteoporosis, Osteosclerosis.

INTRODUCTION

Fluorine is the most electronegative element, distributed ubiquitously as fluorides in nature. Water is the major medium of fluoride intake by humans.[1] Fluoride can rapidly cross the cell membrane and is distributed in skeletal and cardiac muscle, liver, skin,[2] and erythrocytes.[3] Fluorosis is a major public health problem resulting from long-term consumption of water with high fluoride levels. It is characterized by dental mottling and skeletal manifestations such as crippling deformities, osteoporosis, and osteosclerosis.

In India, as many as 15 states are affected by endemic fluorosis, and an extensive belt of high fluoride in water and soil is reported in South India.[4-7] Gulbarga District of Karnataka was found to be a fluorosis endemic area by Nawlakhe *et al*,[8] and AK Susheela.[9] However, a detailed survey for clinical manifestations attributable to fluoride toxicity has not been recorded. Children residing in Kheru Nayak Thanda, a village 35 km north of Gulbarga city, exhibited skeletal deformities from the waist downwards. In November 1998, the parents of these children brought them to the District General Hospital, Gulbarga, to be certified as physically handicapped. A survey was therefore carried out in the village. Drinking water samples were collected and analyzed for fluoride, copper, and zinc. The affected children were investigated clinically, radiologically and biochemically. Our findings are presented in this report.

MATERIALS AND METHODS

Kheru Nayak Thanda was created by the Karnataka State Government 8 years ago to provide shelter for the migrating, low socio-economic class of people. The area is a dry land with the temperature reaching 46ºC in summer.

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Fourteen families have resided in this thanda for the last 8 years and make their living by working in agricultural fields and building construction. Most of them are illiterate. Jowar and maize form the staple diet, and three bore wells are the only sources of water for drinking and cooking. Ten boys and 8 girls out of 46 children in the thanda were affected with skeletal deformities.

The fluoride content of the water samples of the three bore wells was estimated by the zirconium – SPADNS spectrophotometric method[10] in our laboratory and cross-checked by analysis with a fluoride ion selective electrode (ORION 710-A). Copper and zinc levels of water samples were analyzed by atomic absorption spectrophotometry (Thermo Jorrell Ash, Smith-Hieftje 1000). All the 46 children of the age group 3-10 years were examined clinically, and those exhibiting skeletal manifestations were examined radiologically. X-rays were taken of the skull, pelvis, forearm, vertebral column, and legs. Blood samples of the children with skeletal manifestations were collected, and the serum was separated and used for biochemical investigations. Alkaline phosphatase (ALP), transaminases (ALT, AST), total protein, albumin, sodium, potassium, calcium, phosphorus, urea, and creatinine were estimated by standard methods with a Technicon RA-XT auto-analyzer. Statistical significance of the results was analyzed by Student's t-test.

Age- and sex-matched children of Gulbarga city consuming water having fluoride levels within the 1.0 ppm permissible limits, according to WHO,[1] were used as controls.

RESULTS

Analysis of Water Samples: Water samples from the three bore wells showed fluoride levels of 3.96 ppm, 13.4 ppm, and 0.6 ppm, respectively (mean: 5.98 ppm) by the zirconium – SPADNS method, and 3.5 ppm, 12.6 ppm and 0.5 ppm, respectively (mean: 5.53 ppm) by the fluoride ion-selective electrode suggesting comparable sensitivities and accuracy of these methods. Copper levels were below 0.001 ppm. The zinc content of one of the samples was 0.055 ppm and in two others below 0.001 ppm (Table 1).

Clinical Features: Typical clinical findings are shown in Figure 1. Out of 46 children, 41 (89%) have dental fluorosis. An overall skeletal fluorosis preva-

Table 1. Water Analysis

Bore well sources	Levels of Trace Elements (ppm)		
	Fluoride	Copper‡	Zinc‡
1	3.96* 3.5†	<0.001	0.055
2	13.4* 12.6†	<0.001	<0.001
3	0.6* 0.5†	<0.001	< 0.001

*Estimated by Zr-SPADNS method. †By using fluoride-selective electrode.
‡By atomic absorption spectrophotometry.

lence of 39% (18 out of 46) was observed; these children had joint and back pain, back stiffness and restriction of movement. Three children were crippled with severe leg deformities; two had bow legs and one had knock-knee.

Figure 1. Children with skeletal manifestations of fluorosis

Radiological Features: Radiographs of the skull (Figure 2) had a ground-glass appearance, lacked diploid spaces and showed increased bone density and osteosclerosis. The vertebral bodies showed middle osteoporotic portions with upper and lower osteosclerotic portions (Rugger-Jersey Vertebrae). Vertebral heights were smaller and widths were above normal (Figure 3). The pelvis and leg bones showed varying combinations of osteoporosis and osteosclerosis with increased bone density. Medial bowing of femurs with medial/lateral bowing of leg bones was also seen as well as evidence of genu valgum and varum (Figure 4).

Figure 2. X-Ray of the skull of a child with skeletal fluorosis

Biochemical Findings: There was a significant increase in serum levels of ALP, ALT and AST, and significant reduction of total protein and albumin levels of fluorotic children (Table 2). Serum potassium and urea levels were markedly reduced, whereas creatinine and calcium were significantly increased. No significant difference in serum levels of phosphorus and sodium was found (Table 3).

Figure 3.
X-Ray of osteosclerotic spine

Table 2. Serum parameters (Values: mean ± S.D.)

	Alkaline phosphatase (IU/L)	ALT (IU/L)	AST (IU/L)	Total protein (grams/dL)	Albumin (grams/dL)
Control (n=15)	250.27 ± 6.98	15.03 ± 2.36	25.47 ± 4.39	7.12 ± 0.26	4.9 ± 0.16
Fluorotic (n=18)	447.67 ± 111.5	26.83 ± 4.91	47.11 ± 6.47	6.45 ± 0.39	4.57 ± 0.41
Statistical significance	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.005$

Table 3. Serum parameters (Values: mean ± S. D.)

	Calcium (mg/dL)	Inorganic phosphorus (mg/dL)	Sodium (mEq/L)	Potassium (mEq/L)	Urea (mg/dL)	Creatinine (mg/dL)
Control (n=15)	8.49 ± 0.36	4.74 ± 0.54	135.6 ± 1.84	3.93 ± 0.2	25 ± 4.36	0.63 ± 0.07
Fluorotic (n=18)	9.4 ± 1.29	4.95 ± 0.55	134.67 ± 1.61	3.47 ± 0.38	19.7 ± 4.79	0.84 ± 0.23
Statistical significance	$p<0.01$	--	--	$p<0.001$	$p<0.005$	$p<0.001$

Figure 4. X-Ray of deformed femurs and leg bones with genu valgum and genu varum

DISCUSSION

The mean fluoride content of the drinking water sources of Kheru Thanda was higher than the permissible level of 1 ppm according to WHO.[1] Although fluoride levels in the water from the three bore wells ranged from 0.60 to 13.4 ppm, we do not have information regarding the relative use of the three wells.

Earlier studies have indicated that the incidence and severity of chronic fluoride intoxication are greatly influenced by socio-economic, climatic, and nutritional status.[11-13] The relationship between the levels of fluoride in drinking water and the incidence of dental fluorosis vary from place to place. Enamel mottling at 0.5 ppm and 0.9-1.0 ppm fluoride levels has been reported.[14,15] At 6.0 ppm, 100% prevalence of dental fluorosis has been reported.[16] Choubisa *et al* have observed a prevalence of 25.6% and 84.4% of grade II dental fluorosis in children at fluoride levels of 1.4 ppm and 6.04 ppm, respectively.[17] Among the children of Kheru Thanda, 89% (41 out of 46) have dental fluorosis.

Several workers have reported skeletal and crippling fluorosis at fluoride levels above 1.4 ppm and 3.0 ppm respectively.[11,16,17] Here an overall prevalence of skeletal fluorosis with severe symptoms among 18 (39%) of the children at a mean fluoride level of 5.98 ppm was observed. The prevalence of skeletal fluorosis was marginally higher in males.

Fluoride toxicity affects children more severely and after shorter exposure to fluoride than adults, owing to the greater and faster accumulation of fluoride in the metabolically more active growing bones of children.[18] In the present study, we found the prevalence of fluoride toxicity and associated deformities were restricted to the children. None of the adults have visible symptoms of skeletal toxic effects. However, a few of them complained of vague back pain and stiffness. Steyn and Jackson found that 2.6 ppm fluoride in water caused deformities in children and referred to it as Kenhardt bone disease.[19,20,21] Major skeletal manifestations observed in various studies of fluorosis are bowed legs (genu varum) or knock-knee (genu valgum), and stiffness of the cervical and lumbar spine.[4,12,13,22-24] Our study also revealed skeletal fluorosis with crippling bone deformities.

Low levels of copper and zinc, and high levels of molybdenum in water and food contribute to the development of the genu valgum syndrome in fluorotic patients in South India with no symptoms of genu valgum in endemic fluorosis areas containing more than 0.1 ppm copper in water.[4,12] However, genu valgum has not been observed in areas of endemic fluorosis in other parts of India.[25]

Although the molybdenum level could not be estimated in the present study, copper and zinc levels were lower than the average. However, the mean high fluoride level of 5.98 ppm could by itself be responsible for the skeletal deformities and radiological features which resemble the symptoms of genu valgum described by earlier investigators.[12,23,24]

The alterations in bone metabolism in fluorosis seem to be multifactorial. Deposition and resorption of bone increase, presumably because of overproduction of parathyroid hormone.[26] Elevated plasma alkaline phosphatase and parathyroid hormone levels support the diagnosis of associated metabolic bone disease and secondary hyperparathyroidism in fluorosis.[13] A marked increase in serum ALP levels was also observed in our study, which is consistent with the observations of Teotia *et al* in juvenile fluorosis (696 IU/L).[27]

Serum ALT and AST, well-known markers of liver function were significantly elevated in the fluorotic children, indicating liver cell damage and disturbed liver function. Similar results have been reported in earlier studies on fluorotic individuals[28,29] and experimental animals.[30,31] Fluoride is known to inhibit protein synthesis mainly due to impairment of peptide chain initiation and by interfering with peptide chains on ribosomes.[28,29] In the present study, a slight but significant decrease in serum total protein and albumin levels has been observed.

CONCLUSIONS

In addition to typical manifestations of dental and skeletal fluorosis, the clinical and radiological picture of the children in Kheru Thanda resembles genu valgum as an expression of environmental fluoride toxicity. This finding is also associated with impaired liver function as assessed by biochemical parameters. In view of high fluoride content of the bore well water and associated fluoride toxicity among the children, our team has advised the local administration to provide an alternative drinking water supply.

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