SERUM COPPER, ZINC, MANGANESE, AND MAGNESIUM STATUS OF SUBJECTS WITH CHRONIC FLUOROSIS

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SUMMARY: This study was designed to investigate the serum copper (Cu), zinc (Zn), manganese (Mn), and magnesium (Mg) status in a group of subjects with chronic fluorosis. Fifteen subjects diagnosed with fluorosis who live near Van, Turkey in the fluoride-polluted volcanic Tendurek Mountain region (altitude ca. 2000 m) were randomly selected to represent the fluorotic group. Fifteen healthy individuals living near this region matched for age, sex, body mass index, and smoking status were selected as controls. None of the participants had taken any vitamin or mineral supplements for at least 2 weeks before blood samples were drawn after overnight fasting. Subjects with chronic fluorosis had lower serum Cu, Zn, Mn, and Mg levels than did the controls, and it was therefore concluded that chronic fluorosis is associated with decreased serum levels of these minerals.

Keywords: Chronic Fluorosis; Serum copper; Serum magnesium; Serum manganese; Serum zinc.

INTRODUCTION

Chronic fluoride poisoning (fluorosis) is a condition in which characteristic toxic effects result from prolonged ingestion of elevated levels of fluoride in food and water.1 Prolonged exposure to excessive amounts of fluoride may cause adverse health effects in the musculoskeletal system in humans and animals.2,3 While a frequent cause of excessive fluoride in vegetation and water is industrial emissions, volcanoes can also produce high levels of fluoride in surrounding plants and water supplies.4,5 Consequently, a fluoride-rich volcanic mountain region in Eastern Anatolia, Turkey was chosen as the study area for the present research.

Minerals are required for both physiological and biochemical functions.6 Many disorders of the body are associated with the altered serum mineral levels. This study was conducted to investigate the serum copper (Cu), zinc (Zn), manganese (Mn), and magnesium (Mg) status of subjects with chronic fluorosis.

MATERIALS AND METHODS

Two groups of persons were included for study: adult subjects with chronic fluorosis and matched controls. Fifteen subjects living near Van, Turkey in the

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Tendurek Mountain region at an altitude of ca. 2000 m, who were diagnosed for chronic fluorosis through common clinical findings (skeletal abnormalities, painful gait, discoloration and softening of teeth, and difficulty in chewing), were selected randomly to represent the fluorotic group. Fifteen healthy individuals living close to this region were randomly selected as controls matched for age, sex, body mass index, and smoking status. None of the participants had taken any vitamin or mineral supplements for at least two weeks before blood samples were taken. The characteristics of the control and fluorotic subject groups are given in Table 1.

<table>
<thead>
<tr>
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<th>Controls</th>
<th>Fluorosis</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>55.7 ± 5.22</td>
<td>53.1 ± 6.67</td>
</tr>
<tr>
<td>Age range (yrs, youngest – oldest)</td>
<td>46 - 61</td>
<td>42 - 63</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.9 ± 3.88</td>
<td>24.1 ± 4.31</td>
</tr>
<tr>
<td>Sex (male : female)</td>
<td>13 : 2</td>
<td>12 : 3</td>
</tr>
<tr>
<td>Smoking (smokers : non-smokers)</td>
<td>11 : 4</td>
<td>12 : 3</td>
</tr>
</tbody>
</table>

Values are mean ± SD

The research was undertaken only after obtaining the voluntary consent of each participant. A full explanation of the study protocol was given to the subjects before consent was requested. The patients received care according to the criteria outlined in the Ethics of the World Medical Association. The research was undertaken only after obtaining the voluntary consent of each participant. A full explanation of the study protocol was given to the subjects before consent was requested. The patients received care according to the criteria outlined in the Ethics of the World Medical Association.7

Blood samples were drawn after overnight fasting in both groups. Determination of serum concentrations of Cu, Zn, Mn, and Mg was performed by atomic absorption measurements, which were made with a UNICAM-929 spectrophotometer (Unicam Ltd, York Street, Cambridge, UK). Data are expressed as mean with standard deviation (SD). Student’s t test was used to compare findings from fluorotic vs. control subjects.
RESULTS

Table 2 shows the serum concentrations of Cu, Zn, Mn, and Mg in the control and fluorotic subjects. Subjects with chronic fluorosis had significantly lower (P<0.05) levels of these minerals than the controls.

| Parameters | Controls | Fluorosis | Mean reference serum values
<table>
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<tbody>
<tr>
<td>Cu (µg/dL)</td>
<td>76.6 ±14.4</td>
<td>56.7 ± 13.3*</td>
<td>70 - 190</td>
</tr>
<tr>
<td>Zn (µg/dL)</td>
<td>75.0 ± 25.0</td>
<td>40.0 ± 20.0*</td>
<td>70 - 150</td>
</tr>
<tr>
<td>Mn (µg/dL)</td>
<td>5.6 ± 2.3</td>
<td>2.2 ± 0.7*</td>
<td>1.0 – 7.0</td>
</tr>
<tr>
<td>Mg (mg/dL)</td>
<td>2.7 ± 0.4</td>
<td>1.6 ± 0.3*</td>
<td>1.8 – 2.2</td>
</tr>
</tbody>
</table>

*P<0.05.

DISCUSSION

Chronic fluorosis is commonly seen in humans and animals living in volcanic regions of Turkey. Many studies have been conducted to evaluate the fluoride content of plants and waters in these regions, which often have extremely high levels of fluoride.8,9 The Tendurek Mountain area is one of these regions with high-fluoride drinking water.10 Prolonged ingestion of this fluoride-rich water produces debilitating chronic fluorosis in humans and animals living in the region.

Our study demonstrated that subjects with chronic fluorosis had lower serum micronutrient mineral levels than healthy subjects. These results are consistent with those of Chen et al,11 who studied the relationship between endemic fluorosis and serum concentrations of certain chemical elements in skeletal fluorosis patients and found a significant decrease in serum concentrations of Ca, Mg, and Cu, and an increase in serum Fe. The main clinical signs of chronic fluorosis are skeletal and dental. Premature crown wear and gingivitis occur in chronic fluorosis, hindering food intake and mastication.12 These restrictions limit the availability and utilization of food, thereby accounting for decreased mineral status in fluorotic subjects.

The present study showed a decreased level of serum Zn in chronic fluorotic subjects. Consistent with these results, significantly reduced liver and kidney levels of Zn, Cu, and Mn were found in fluoride-treated mice.13 Moreover, Bennis et al12 reported that plasma proteins decreased in chronic fluoride poisoning. Therefore, decreased Zn concentration in this study might be associ-
ated with a diminished plasma amino acid level, which is the circulatory factor to transfer Zn.\textsuperscript{14} However, decreased gastrointestinal absorption and tissue-specific absorption of Zn may also have contributory effects.

We also found that the level of serum Mg decreased in fluorotic subjects. Fluoride has been reported to be a potent nephrotoxic compound in both acute and chronic studies.\textsuperscript{15} Some degree of renal insufficiency could also account for the decreased serum level of Mg due to reduced tubular reabsorption and elevated urinary excretion of Mg in chronic fluorosis.

The present study also indicated that serum Cu level decreased in chronic fluorosis. Singh and Kanwar\textsuperscript{16} investigated changes in copper and iron in certain tissues resulting from experimental fluorosis. They found decreased concentrations of Cu in liver, kidney, and bone of fluoride-intoxicated mice along with increased iron in these organs. Cu has been known to be associated with lipid metabolism since 1973, and research in numerous animal models as well as in humans has shown that Cu deficiency can significantly increase plasma cholesterol concentration.\textsuperscript{17,18} Therefore, an inverse correlation between serum Cu and cholesterol levels could be expected, although we did not measure serum cholesterol in our fluorotic subjects. However, since it has been suggested that serum cholesterol levels are elevated in fluoride intoxication,\textsuperscript{19,20} the decreased Cu level in our fluorotic subjects might be due to (or the result of) an increased cholesterol level.

Finally, serum Mn levels of subjects with hepatoma and cirrhosis of the liver are known to be significantly lower than in healthy subjects.\textsuperscript{21} It has also been reported that chronic fluoride poisoning results in metabolic disturbances of energy metabolism and in liver disorders.\textsuperscript{11} Therefore, fluoride-induced liver disturbances might be responsible for the lower serum Mn levels in the subjects with chronic fluorosis.

In conclusion, our findings indicate that chronic fluorosis is associated with reduced levels of serum Cu, Zn, Mn, and Mg. However, more studies are needed to verify and clarify the relationship between serum mineral status and chronic fluorosis.

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