Trace element concentration in various tissues following fluoride administration to female mice

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Brain, liver, kidney and muscles demonstrate significant changes in essential trace element (Cu, Zn, Mn and Fe) level in adult female mice given 30, 60 and 120 ppm sodium fluoride (NaF) in drinking water. These changes involve excess removal or accumulation of these trace elements in respective tissues. Changes observed were dose dependent and significant at 120ppm NaF concentration in drinking water.

Keywords: Fluoride in body tissues, Fluoride in drinking water, Trace elements

Interaction of fluoride with various trace elements and their metabolism is interesting as it has been shown that chronic ingestion of fluoridated water does influence systemic biochemical homeostasis in experimental animals as well as in humans. Significantly reduced Cu, Mn and Zn\(^{3+}\) in kidney and liver and also Zn\(^{2+}\) in hair have been reported. Boeckh et al.\(^3\) reported depletion of Zn ions in most tissues except kidney and submandibular gland in human. Chirayu\(^4\), observed that fluoride administration causes an increased urinary excretion of Ca, Mg, K and Na, though effects on trace elements have not been reported. Trace elements (Fe, Cu, Mn, I and F) though occur in low concentration in the body serve some useful functions and there imbalance may affect important biological functions in both animals as well as humans, including bone and teeth development, physical growth, psychomotor development, immunity, reproduction etc\(^5\). But whether excess fluoride intake results in removal or their accumulation in various body organs has not been observed so far. The purpose of the present communication is to report the effects of fluoride intake on some essential trace nutrients like Zn, Cu, Fe and Mn in various tissues (brain, kidney, liver and muscles) with an aim to provide evidence that higher intake of fluoride results in their excess removal or accumulation in an organ system.

Adult female, Swiss albino mice age 5 months were used for the study. Animals were procured from a supplier and acclimatized for two weeks to the laboratory conditions. They were kept in a well ventilated room and exposed to a 12 hr light and dark cycle at room temperature (27°±2°C). They were provided food and water ad-libitum. For experimental study, 20 animals each weighing 30±5 g were segregated into four groups- control (C) and three experimental groups-E1-E3; (N=5 for each group). Control animals were given deionized water, while E1 group animals were given 30 ppm, E2 group 60 ppm and E3 group 120 ppm sodium fluoride (NaF). At the end of the experiment, animals were sacrificed and their brain, liver, kidney and thigh muscles were quickly excised. Each tissue was washed thoroughly in physiological saline (prepared in deionized water), blotted dry and weighed. The tissues were then processed according to Kang et al.\(^6\) for preparation of samples. Acid washed glasswears were used during all steps of sample preparation for trace element studies. Metal concentrations in the tissue digest were determined by "Varian atomic absorption spectrophotometer Model No.AA-20BQ" at the following wave lengths Zn-213.8 nm; Cu-324.8 nm; Fe-248.3nm, Mn-279.5nm.

Statistical analysis of the means of treated and control groups was done with the Student's t-test. Data related to trace metal concentration in control and experimental tissues are summarized in Table 1. Changes observed in Cu, Fe, Mn and Zn level in brain, liver, kidney and muscles of the mice intoxicated by fluoride are consistent with earlier findings\(^1,6,7\). These changes are proportional to the intake of fluoride and specific for each tissue studied.
Deficiency or excess storage of these trace elements occur infrequently in animals and human beings, but evidences of close links between disturbances in trace element concentration and various biological activities and related disorders are available in literature.

Among the four essential elements studied, Cu is normally present in high concentrations in brain, liver and kidney therefore copper deficiency is a rare occurrence in these organs but in present study Cu level fell significantly in brain, liver and kidney while increased in muscles. Though loss of ability to utilize stored Fe for synthesis of hemoglobin in liver[12,13], hypomyelination, maldevelopment of central nervous system and lesions in liver and kidney[14], reduced noradrenaline synthesis[15], decreased capacity for oxidative phosphorylation in brain, liver and muscles are some of the reported consequences of Cu deficiency.

Fe level like Cu also fell significantly in brain and liver but increased in kidney and muscles. Fe is important in formation of hemoglobin molecule. It is an essential constituent of myoglobin and respiratory enzymes. Deficiency of Fe is related to restlessness, tiredness and imbalances in brain iron homeostasis during development which result into symptoms of neurodegenerative disorders[16,17]. Mn like Cu and Fe also catalyzes synthesis of haemoglobin. Mn also plays very important function in brain by stabilizing the membrane excitability, which otherwise result into epileptogenic lesions to increase the seizures activity[18,19]. High Mn is also associated with initial psychologic and neurologic effects but later a permanent crippling similar to Parkinson's disease occurs[17,19]. Deficiency of Mn is reported to disturb growth and skeletal abnormalities, glucose utilization etc. In present study Mn level fell significantly in liver and kidney but increased in brain and muscles.

Level of Zn fell significantly in brain, liver and muscles but increased in kidney. These observations are consistent with earlier reports. Zn is required for growth of every animal species[8,20]. Effects of low Zn includes skin lesions, poorly mineralized bone, impaired reproduction in both male and female, decreased learning ability and also reduced synthesis of protein and nucleic acids[13]. A close relationship between maternal Zn deficiency and congenital malformations of central nervous system have been also reported[20]. Acute toxicity of Zn is related to electrolyte imbalance, lethargy, muscular incoordination and renal failure. High Zn intake is also known to reduce Cu absorption[15]. Role of Zn and Cu in neuroprotection has been also reported[21].

These observations thus clearly demonstrate a close link between excess fluoride intake and possible consequences via imbalances in trace element levels of various tissues. Disturbance in trace elements observed in this study is very interesting as fluoride, a trace element is taken in excess causes both bone and dental fluorosis[21]. Role of fluoride in disturbing trace element concentration is due to its binding capabilities with tissue protein it is highly electronegative and thus forms complexes with proteins. Alternatively it...
binds with Cu, Fe, Mn or Zn to form complexes resulting in increased level of respective element.

In conclusion, study shows that excess fluoride intake disturbs essential trace element homeostasis in the body. These changes related with elimination or accumulation of specific element in a tissue may be implicated with various disorders not only of the nervous system but also involving other systems as well.

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References