

The Survey of Serum Trace Element Profiles in Down's Syndrome

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Article information	Abstract
<p>Article history: Received: 19 June 2012 Accepted: 11 Nov 2012 Available online: 11 July 2012 ZJRMS 2014; 16(6): 77-79.</p> <p>Keywords: Down's syndrome Zinc Selenium Copper Manganese Atomic Absorption Spectroscopy</p>	<p>Background: Immunological, endocrinological, haematological and neurological abnormalities are relatively common in people with Down's syndrome (DS). Zinc (Zn), copper (Cu), selenium (Se) and manganese (Mn) are elements that act in the maintenance of normal function of these systems. The present study aimed to evaluate the concentration of these elements on DS symptoms.</p> <p>Materials and Methods: This case-control study was done from April to October 2011. Serum trace elements including Zn, Cu, Se and Mn were determined by using atomic absorption spectrometry (AAS) in 56 patients with DS and 60 healthy subjects.</p> <p>Results: There was no significant difference in the values of Cu and Se between two groups ($p > 0.05$). While, Zn and Mn levels were found to be significantly decreased in patients with DS compared to the control group ($p < 0.01$ and $p < 0.001$, respectively).</p> <p>Conclusion: Results of this study indicate zinc and manganese deficiency in more than 60% of DS patients. Some of the problems experienced by people with DS may be due to changed level of these trace elements.</p>

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Introduction

Down's syndrome (DS) is a genetic abnormality caused by a defect of chromosome 21. DS occurs in 1 every 700-800 live births and epidemiologic data give an estimated incidence of more than 200,000 cases per year worldwide [1]. People with DS have varying degrees of cognitive and developmental disabilities and suffer from a wide array of other symptoms, such as premature aging with development of Alzheimer's disease before the age of 40, frequent infections, autoimmune disease, hypothyroidism, and heart defects [2]. A number of studies have examined the nutritional status of people with DS. It is believed that the genetic defect that produces DS increases the need for antioxidants (nutrients that prevent free-radical damage) [2]. Antioxidants interact with free radicals and may prevent some of the damage free radicals might otherwise cause. Some of trace elements, such as Zn, Cu and Se are part of enzymes with antioxidant functions. It has been known for many years that chromosomes carry genes playing an important role in human development and disease. One of the genes over-expressed in DS is the one producing Cu/Zn superoxide dismutase 1 (SOD-1). The SOD-1 gene is located on human chromosome 21q22.1. Down's syndrome is caused by 3 copies of chromosome 21 being present in each (or most in the case of mosaic Trisomy-21) cell.

Measurements of SOD-1 activity in individuals with DS show that there is over-expression of this gene. SOD-1 converts oxygen radicals, which are normal by-products of cell metabolism, to hydrogen peroxide (H_2O_2) and water. Then, hydrogen peroxide can be converted by catalase (CAT) and (selenium-containing) glutathione peroxidase (GPX) to water. The triplication of

chromosome 21 leads to an imbalance in the ratio of SOD-1 to CAT and GPX, resulting in the accumulation of H_2O_2 and then more hydrogen peroxide will be available to cause peroxidative damage to the cell. The peroxide combines with iron, producing free radicals, while depleting antioxidants [3]. Fewer antioxidants and more free radicals lead to cell death in the brain. This theory claims that antioxidant supplements may prevent and even reverse damage by peroxidation. Zinc supplementation reduces SOD-1 levels in non-DS female subjects [4]. Zinc may be especially important in moderating the degree of metabolic disturbance from SOD-1 and hydrogen peroxide. Zinc is important in the homeostatic networks found to be altered in DS, namely nervous, neuroendocrine, immune and their interrelationship. This paper is being reported for the first time on determination of serum Zn, Se, Cu and Mn level in Tehranian DS patients. In the available studies reviewed here, no data on the serum status of trace elements in Iran has been obtained. Atomic absorption spectrometry (AAS) was used for the measurement of these elements. In this study, the measurements were done directly after dilution. This method is very simple and suitable for the routine measurements compared to previous studies.

Materials and Methods

This study involved two groups of subjects, living in Tehran. Group I (Down's syndrome) comprised 54 patients registered of State Welfare centers or schools for mentally retarded children. There were 25 males and 29 females, aged 6 to 38 years. Group II (controls) was

composed of 60 healthy subjects, 30 males and 30 females, aged from 6 to 40 years. Sample size determination for case-control studies are based on Cochran's formula ($z=1.96$, confidence level=95%). The exclusion criteria included diagnosis of chronic diseases such as diabetes mellitus, acute respiratory diseases, renal insufficiency or any serious heart defects, alcohol and drug addiction, smoking, consumption of any antioxidant supplements since 3 months ago. The donors belong to a middle socio-economic status with urban dietary habits. The purposes of the study had been previously explained to all the volunteers. Each participant or a legal guardian signed an informed consent form detailing the analyses and handling of the data. Zn, Cu, Se and Mn concentrations in serum were measured during the study and were compared to the control group. This evaluation was done from April to October 2011. The sampling of blood was performed in the Danesh laboratory (Tehran, Iran). 10 ml blood were taken at 8–9 a.m. after fasting and collected into polypropylene tubes containing lithium heparin (Vacuette, Geiner Labortechnik, Kremsmunter, Austria). Serum was separated within 2 h, and aliquots were kept frozen at -20°C until trace element analysis. All laboratory wares including pipette tips and autosampler cups were cleaned thoroughly with detergent and tap water, rinsed with distilled water, soaked in dilute nitric acid, and then rinsed thoroughly with deionized distilled water. For measurement of Zn and Cu, 1 ml of serum was mixed with 4 ml of 0.1 N hydro chloric acid [5]. Determination of these elements performed on a flame atomic absorption (FAAS) spectrometer equipped with deuterium background correction (SpectrAA 220, Varian, Australia). Se and Mn was determined by the graphite furnace atomic absorption spectrometry (GFAAS) equipped with pyrolytically coated graphite tubes and deuterium background correction (SpectrAA 220, GTA 110, Varian, Australia). The samples were diluted 1:5 and 1:2 with 0.1% v/v Triton X-100, respectively. The solution of Mg (NO₃)₂ was used as matrix modifier in GFAAS, addition an appropriate furnace program [5]. The accuracy of the measurement was evaluated based on analysis of quality control material (QCM) (SeronormTM Trace Elements Whole Blood, Level 1, Art. No. 201405, Norway). It was supplied freeze-dried and reconstituted by adding 3 mL of water [5]. Accuracy was 98.8 % for Zn, 99.4% for Cu, 97.5% for Se and 98.5% for Mn. The normality of the distributions was evaluated by the Chi square test. Statistical evaluation was carried out by using the SPSS

11.5 Version for Windows. Group means comparisons were tested for significance by student's *t*-test. All results were expressed as mean±SD, statistical significance was defined as $p<0.05$.

Results

Serum trace element concentrations for the total subjects are presented in table 1. On comparison between two groups, Zn and Mn levels were found to be significantly ($p<0.01$ and $p<0.001$, respectively) decreased in patients with DS (76.50 ± 12.84 µg/dL and 5.51 ± 2.38 µg/L, respectively) compared to the control group (92.25 ± 12.33 µg/dL and 9.19 ± 2.90 µg/L, respectively). While, Se and Cu levels were found to be 87.10 ± 14.31 µg/L and 85.17 ± 33.99 µg/dL in DS cases, and 94.10 ± 19.47 µg/L and 90.37 ± 13.33 µg/dL in the healthy subjects, respectively. No statistically significant differences were observed in serum Cu and Se concentrations. In addition, there were no significant differences between males and females in the DS group regarding levels of four elements.

Discussion

The means of these elements were normal in two groups, but Zn and Mn levels in patients (63 and 68%, respectively) were less than the normal range. Down syndrome is set of mental and physical symptoms that result from having an extra copy of chromosome 21. The triplication of chromosome 21 results in the accumulation of H₂O₂.

The hydrogen peroxide combines with iron, producing free radicals, while depleting antioxidants, especially Zn and Mn. Serum levels of Zn were normal in two studies of people with DS [6, 7], but others have found Zn levels to be low [8- 13]. The decreased levels of serum zinc in our studied cases compared to controls agreed with previous reported literature. Our findings has shown that Zn level is influenced by a number of external and internal factors. The correction of the Zn level is necessary for the control of biological processes in population with DS who are vulnerable to Zn deficiency. Therefore Zn level for an individual with DS may be judged to be deficient after comparing with the age-matched control group from the similar environment. The decreased levels of serum Mn in our work agreed with previous reported literature.

Table 1. Serum level of trace elements (mean±SD) in subjects with Down syndrome and control groups

		Zn	Cu	Se	Mn
		Serum (µg/dl)	Serum (µg/dl)	Serum (µg/l)	Serum (µg/l)
Total	Cases	76.50±12.84*	85.17±33.99	87.10±14.31	5.51±2.38**
	Controls	92.25±12.33*	90.37±13.33	94.10±19.47	9.19±2.90**
Male	Cases	78.11±13.47*	84.98±15.41	86.83±15.62	5.32±2.11**
	Controls	94.83±12.26*	87.06±12.89	88.28±18.33	8.82±2.97**
Female	Cases	75.12±12.57*	85.32±13.10	87.32±13.51	5.67±2.43**
	Controls	90.14±12.26*	93.08±13.36	98.86±19.48	9.57±2.88**

Values represent the mean±SD for patients (N=54) and controls (N=60). Asterisks denote the significance of differences between means of cases and controls (* $p<0.01$; ** $p<0.001$).

One study found that Mn levels in erythrocytes and thrombocytes were lower in children with DS [12]. The body needs Mn for normal growth and health. Because this element plays a role in a variety of enzyme systems, its deficiency can impact many physiological processes. This trace element is a component of some enzymes and stimulates the development and activity of other enzymes. Manganese helps to normal skeletal growth and development, glucose and lipid metabolism, pancreatic function and development, Prevention of sterility. It is important for protein and nucleic acid metabolism and thyroid hormone synthesis. Mn is also necessary for normal brain and nerve function. Manganese deficiency is associated with poor glucose tolerance (high blood sugar levels), excessive bone loss and compromised function of the reproductive system. DS patients have often been found to have elevated levels of Cu.

These elevations have been found in erythrocytes, neutrophils, platelets and serum [8, 11, 13]. One study has obtained normal copper levels in DS subjects [14]. Anneren et al. reported mean plasma Se concentration in patients with DS did not differ from that in healthy controls [15]. But other study found that Se levels in serum were lower in people with DS [8]. In the present

work, no significant difference was observed in serum Cu and Se level between two groups.

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Authors' Contributions

LF designed the study and analyzed data. The measurement of Zn and Cu in serum samples was done by FS and LK and the evaluation of Se and Mn in serum samples was done by LF. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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