An Assessment of the Selenium Status of Iodine-Deficient and Non-Iodine-Deficient Filipino Children

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ABSTRACT

The aim of this study is to examine and compare blood selenium levels in iodine-deficient and non-iodine deficient children. Two groups of children were examined: one group with iodine deficiency (n = 31) and the other group with normal iodine status (n = 32). Blood was extracted by venipuncture from children aged 6-10 years attending first grade in Commonwealth Elementary School in Quezon City. Whole blood selenium was examined by electrothermal atomic absorption spectrophotometry (AAS). Iodine status was determined by goiter palpation and urinary iodine excretion. Mean selenium levels of deficient and non-deficient children were compared using T-test. Using a cut-off value of 60 µg Se/L whole blood, the proportion of children with normal and deficient iodine status who fell below this cut-off was compared using chi-square test. Whole blood selenium values ranged from 17.6 to 133.6 µg/L. There were no significant differences in mean selenium levels between children with normal and deficient iodine status. Children with normal iodine status had a mean blood selenium level of 55.87 ± 26.3 µg/L while children with deficient iodine status had a mean level of 58.76 ± 26.4 µg/L. Sixty percent of children had blood selenium levels below the arbitrary cut-off of 60 µg/L with no significant difference between groups (p = 0.165), indicating that selenium deficiency is prevalent in this group of children regardless of iodine status. Since selenium deficiency limits the response to iodine supplementation, further investigation is needed to determine whether the same situation exists in children from other areas.

Key words: selenium status, iodine deficiency, schoolchildren, nutritional status

INTRODUCTION

Iodine deficiency is presently a public health problem in the Philippines. Results of the Fifth National Nutrition Survey (FNRI, 1998) showed that the country has a mild iodine deficiency problem. Iodine is an essential trace element required for the synthesis of thyroid hormones, which are involved in normal growth and development. One consequence of iodine deficiency is the development of goiter or enlargement of the thyroid gland. During pregnancy, iodine deficiency has deleterious effects on the fetus, the most severe of

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which is endemic cretinism. Cretinism is characterized by mental retardation, squinting, deafness, primitive brain reflexes, severe growth stunting, and sexual immaturity (Maberly, 1994; Hetzel, 1986). At lower levels of deficiency, modest but detectable neurological changes occur, such as impaired learning capacity and performance in school or reduced capacity to handle formal tests of psychomotor function (Stanbury, 1998).

Children and adults with endemic iodine-deficient goiter have been shown to have impaired mental function associated with reduced levels of circulating thyroid hormones. Because of its impact on the nation's intellectual productivity, the government has launched a nationwide salt iodization program in order to correct and prevent iodine deficiency.

Aside from iodine, other essential trace elements are also needed to improve iodine status. Selenium is one trace element that is closely involved in iodine metabolism and thyroid function. There are two known roles of selenium. One is its role as a component of the enzyme glutathione peroxidase, which acts as the cell antioxidant system to protect cells from injury by free radicals. The other role of selenium is as component of iodothyronine deiodinases, enzymes which convert the thyroid hormone thyroxine (T_4) to its biologically active form triiodothyronine or T_3 (Arthur et al., 1993). Studies have shown that selenium deficiency affects thyroid hormone metabolism and the activity of thyroid hormone deiodinases. Under normal circumstances, increased plasma T_4 results in a reduction in plasma thyroid stimulating hormone (TSH) produced by the pituitary. During selenium deficiency, the pituitary is unable to recognize increased plasma TSH concentrations. Rats given a selenium-deficient diet exhibited hyperthyroxinemia (increased levels of plasma T_4) accompanied by increased plasma TSH. Selenium deficiency in rats also resulted in lower plasma T_3 concentrations due to the inhibition of deiodinase enzyme activity. An increase in thyroidal T_4 and T_3 synthesis at the expense of a decrease in total thyroidal iodine has been observed during selenium deficiency even when there is an adequate supply of iodine in the diet. The result is a 15 to 20 percent decrease in the total concentration of thyroidal iodine, T_4 and T_3. Since iodine deficiency also decreases thyroidal iodine, T_4 and T_3 concentrations, it is therefore aggravated by selenium deficiency (Arthur et al., 1993).

The response to iodine intervention is influenced by pre-existing selenium status. It has been shown that goitrous children aged 6 to 12 years who were selenium-deficient had a less vigorous response to oral supplementation with iodized oil (Zimmermann et al., 2000). Percentage decrease in thyroid volume was lower among the more severely selenium deficient children than in those whose deficiency was less severe. Aside from its role in thyroid activity, other functions of selenium are currently being studied. These include its role in the prevention of cancer and cardiovascular disease (Shortt et al., 1997; Ip, 1998).

Unlike iron and vitamin A, there are no current standard cut-off levels to define selenium deficiency or adequacy (Gibson, 1990; WHO, 1996). Studies use arbitrary cut-off points to define selenium deficiency on the basis of results obtained from enzyme function tests. No local study has so far examined the selenium status of any population group in this country. This study aims to determine blood selenium levels in iodine-deficient and non-iodine deficient schoolchildren and compare these values with those obtained in studies from other countries.

MATERIALS AND METHODS

This study is part of a larger study that examined several factors (i.e., dietary, biochemical, health, and environmental factors) affecting iodine status in schoolchildren, and compared the psychomotor and cognitive functions of iodine-deficient and non-iodine deficient children. Only the results for selenium analysis are reported here.

Subjects

This portion of the study included 63 children aged 6 to 10 years (30 males and 33 females) from Commonwealth Elementary School in Quezon City. All the children were in first grade. The children were distributed in three classroom shifts: 6:00-10:00 a.m.; 10:00 a.m.-2:00 p.m.; and 2:00-6:00 p.m. Two classes from each time shift were randomly selected for inclusion in the study. The consent of the parents of the children participating in the study was obtained.

A two-stage sampling procedure was used to select the study sample. The first stage was the initial screening of 290 children from the three classroom shifts for

urinary iodine excretion and goiter palpation. The second stage was the selection of a purposive sample of 40 children classified as having adequate iodine status and 40 children with deficient iodine status. Due to attrition during the study period, only a total of 77 children participated in the entire study.

Children with normal iodine status did not have goiter and had urinary iodine excretion of >100 µg/L. Children with iodine deficiency had urinary iodine excretion below 90 µg/L and had either grade 1 or grade 0 goiter. Parents of 63 children agreed to have their children's blood samples taken. These samples were included in this study. Thirty-two children with normal iodine status and 31 children with iodine deficiency were examined for blood selenium levels.

Determination of urinary iodine and enlargement of the thyroid gland

Spot casual urine samples were collected from the children during class hours. Samples were labeled, stored in ice, and immediately brought to the Biological Research Laboratory of the Department of Health for determination of urinary iodine. The method prescribed by WHO/ UNICEF/ ICCIDD (1994) was used in the analysis. Urine was digested with chloric acid under mild conditions and iodine was determined by its catalytic role in the reduction of ceric ammonium sulfate in the presence of arsenious acid. Duplicate tests were done on each sample.

Palpation of the thyroid gland was done by visually inspecting the size of the thyroid gland when the subject swallowed. Goiter was classified as grade 0 (no visible goiter), grade 1 (palpable but not visible when the neck is in the normal position), and grade 2 (swelling in the neck is visible when neck is in the normal position) following the criteria set by WHO (1994). In order to avoid inter-observer variability, a single trained researcher conducted the examinations.

Analysis of whole blood selenium

Blood samples were collected from the children by venipuncture. Approximately 2.5 ml blood was extracted and placed in heparin-lined test tubes. Samples were diluted by adding 2.5 ml distilled water and 17.5 ml Triton X-100 (0.1%). Diluted samples were mixed with 22.5 ml palladium-Triton X matrix modifier solution (Sigma cat. No.P-4400) and analyzed by electrothermal atomic absorption spectrophotometry (Shimadzu model 6501-S atomic absorption spectrometer with HGA-600 graphite furnace). Values were calculated using a standard curve following the standard addition method described by Fidanza (1991). The coefficient of variation (CV) for every addition of the standard was ± 5.0%. Analyses were done by the Analytical Services Laboratory, Institute of Chemistry in U.P. Diliman.

Data analysis

Data were analyzed for normality using Kolmogorov-Smirnov test. Whole blood selenium values were normally distributed. Mean selenium values for iodine-deficient and non-iodine deficient children were compared using Student's t-test. An arbitrary cut-off value of 60 µg Se/L whole blood was used to define normal and low blood selenium levels (Neve, 2000). Using this cut-off, the proportion of iodine-deficient and non-iodine deficient children whose selenium levels fell within each category were analyzed using chi-square test.

RESULTS

Whole blood selenium values ranged from 17.6 to 133.6 µg/L. The mean selenium level in the entire study sample was 57.3 ± 26.2 µg Se/L whole blood. Ashour et al. (1999) showed that mean plasma selenium level in children with kwashiorkor was 47 ± 10.4 µg/L, while in children with marasmus had a mean level of 56 ± 10.4 µg/L. A control group of healthy children had a mean plasma selenium level of 64 ± 1.8 µg/L. The results of the present study showed that the children from Commonwealth Elementary School have low selenium levels, similar to the values obtained for children with protein-energy malnutrition.

A comparison of the mean values of selenium in iodine-deficient and non-iodine deficient children showed that there is no significant difference between the two groups (Table 1).

In selenium deficiency, there is a strict hierarchy of supply to specific tissues and also to different selenoenzymes within a tissue (Arthur & Beckett, 1999). Studies in rats showed that with insufficient selenium intake, the deiodinase is preferentially supplied

with the element. This suggests that selenium requirement for the activity of deiodinase is lower than that for optimum glutathione peroxidase (GSHPx) activity, and that GSHPx activity is therefore a good indicator of selenium requirement (Behne et al., 1992; Levander & Burk, 1996). Normal values that are adequate for the expression of red blood cell glutathione peroxidase activity were shown to fall within the range of 60 to 220 µg Se/L whole blood (Neve, 2000). The present study examined the number of children who would fall below 60 µg Se/L whole blood. Table 2 shows that if this arbitrary cut-off level is used, majority of the children (60%) would be considered selenium-deficient with no significant difference between groups.

Aside from selenium deficiency, the condition of selenium toxicity has been reported in some population groups. Since there are as yet no sensitive and specific indicators of dietary selenium overexposure, toxicological standards for selenium have been proposed on the basis of clinical signs of selenosis. These include loss of hair and nails, skin lesions, tooth decay, and abnormalities of the nervous system (Levander & Burk, 1996).

The common clinical sign of selenosis, i.e., loss of hair and nails, was not observed in the present study sample.

DISCUSSION

The present study showed that whole blood selenium values in this group of schoolchildren ranged from 17.6 to 133.6 µg/L. The mean selenium level was 57.3 ± 26.2 µg Se/L whole blood. Children with normal iodine status had 55.87 ± 26.3 µg Se/L while children with iodine deficiency had 58.76 ± 26.4 µg Se/L whole blood, with no significant difference between groups.

The study of van Bakel et al. (2000) on children aged 9 to 13 years with phenylketonuria (PKU) and hyperphenylalaninemia (HPA) who are fed selenium-free diets during therapy showed plasma selenium levels of 41.08 ± 15.8 µg/L and 72.68 ± 16.59 µg/L for PKU and HPA patients, respectively. A comparison group of healthy children had a mean plasma selenium level of 97 ± 11.05 µg/L. Malnourished children examined by Ashour et al. (1999) had mean plasma selenium levels ranging from 47 to 56 µg/L while a comparison group of healthy children had a mean plasma selenium level of 64 µg/L. Zimmerman et al. (2000) used a cut-off value of 67 µg/L serum selenium to define selenium deficiency in schoolchildren. The values for selenium that were obtained in the present study (55.87 ± 26.3 µg/L and 58.76 ± 26.4 µg/L for children with normal and deficient iodine status, respectively) fall within the range of values obtained in studies done on children

Table 1. Mean levels of whole blood selenium by children's iodine status

	Children with normal iodine status (n=32)		Children with iodine deficiency (n=31)			
	Mean	± S.D.	Mean	± S.D.	t-value	Sig.
Whole blood selenium (µg/L)	55.87	26.3	58.76	26.4	-0.435	0.665

Table 2. Selenium deficiency by iodine status using an arbitrary cut-off level of 60 µg Se/L whole blood.*

Whole blood selenium (µg/L)	Children with normal iodine status (n=32)		Children with iodine deficiency (n=31)		Total	
	No.	%	No.	%	No.	%
≥ 60 µg Se/L	10	31.3	15	48.4	25	39.7
< 60 µg Se/L	22	68.7	16	51.6	38	60.3
Total	32	100.0	31	100.0	63	100.0

*Chi-square value = 1.932; df = 1; Significance = 0.165

with protein-energy malnutrition and those fed selenium-free diets.

Neve (2000) reported published experimental values for whole blood selenium, ranging from 60 to 220 µg/L, that were found adequate for the expression of red blood cell glutathione peroxidase activity. Using the lower level of 60 µg Se/L whole blood as arbitrary cut-off point to define adequacy, a majority of the children in the present study (i.e., 60.3%) were classified as selenium-deficient.

The effects of selenium deficiency have been demonstrated in certain areas in China that were once afflicted with Keshan disease. Keshan disease is a selenium-responsive endemic cardiomyopathy that mainly affects children and women of child-bearing age (WHO, 1996). Its main clinical features are acute or chronic episodes of heart disorder characterized by cardiogenic shock and/or congestive heart failure. Very low selenium concentrations were pointed out as the fundamental cause of Keshan disease (Ge & Young, 1993), although it is now known that Keshan disease is due to a virus that causes heart damage – the coxsackie virus. Once the disease is established, selenium is of little or no therapeutic value (WHO, 1996). Levander & Beck (1999) found that selenium-deficient mice suffered more extensive heart damage when infected with a coxsackie B_4 virus than mice supplemented with selenium. Selenium deficiency also increased the virulence of an already virulent strain of coxsackie B_3 virus and allowed the conversion of a non-virulent strain to virulence. When the non-virulent strain was inoculated into mice deficient in selenium or vitamin E, the strain caused a moderate amount of heart damage, whereas the same strain given to mice fed nutritionally adequate diets caused no apparent damage. The benign virus that replicated in selenium-deficient mice was then inoculated into normal mice. A moderate amount of cardiac damage was observed in these mice, indicating that selenium-deficient mice had somehow altered the benign strain of the virus such that it was now able to cause heart damage even in a selenium-supplemented mouse. When the benign virus from the selenium-deficient mice was sequenced, six nucleotide changes were found. These nucleotides correspond with those found in the genome of a virulent strain. Further studies showed that selenium deficiency leads to mutations in the viral genome via reduced glutathione peroxidase activity (Beck, 2000). The increased oxidative stress causes nucleotide changes that result in a normally avirulent virus changing into a virulent one. RNA viruses, such as those responsible for influenza, hepatitis, polio, or AIDS have high mutation rates and lack proofreading capability. Outbreaks of these diseases may actually be the result of infection by a virus whose pathogenicity has changed as a result of replicating in a nutritionally deficient host. Beck (2000) proposed that the current paradigm of nutritional deficiency affecting the host immune system, which leads to increased susceptibility to infection, be changed to one in which nutritional deficiency affects both the host and the pathogen.

Aside from selenium deficiency, selenium toxicity has also been reported based on the clinical signs of excess selenium. In China, high-selenium areas with toxicity have reported whole blood selenium levels of 3200 µg/L, while high selenium areas without toxicity have levels of 440 µg Se/L whole blood (Diplock, 1993). In Venezuela, high selenium areas have whole blood levels of 813 µg/L while a moderate selenium area has 355 µg/L. The range of whole blood selenium values obtained in the present study (i.e., 17.6 to 133.6 µg/L) indicates that the local situation is more inclined towards selenium deficiency rather than toxicity.

The study of Ashour et al. (1999) on children with protein-energy malnutrition showed that plasma levels of selenium and other antioxidants decreased in parallel with glutathione peroxidase activity in the presence of malnutrition (i.e., marasmus and kwashiorkor). They concluded that malnourished children were susceptible to high oxidative stress.

The two groups of iodine-deficient and non-iodine deficient children in the present study may not have differed in their selenium status since both groups were generally malnourished. The findings of Ashour et al. (1999), indicating high oxidative stress in malnourished children, might be applicable to the present study since 70.6% of the children in the present sample were stunted (results not included in this report) which is a sign of chronic undernutrition (Amarra, 2001). Aside from having low calorie and nutrient intakes (results also not presented here), the low selenium levels in these children

increase the potential for viral mutation in the event of an infection (Amarra, 2001). Further investigations among children in other areas are needed to determine whether the same situation of low selenium levels also exists.

SUMMARY

The study has shown that Filipino schoolchildren living in an urban poor area tend to have low blood selenium levels, concurrent with iodine deficiency. Aside from inhibiting the response to iodine supplementation, recent studies have shown that selenium deficiency in the host may induce the mutation of viruses, causing non-virulent strains to become virulent. Given the recent outbreaks of infectious diseases such as influenza among schoolchildren, there may be a need to further examine the selenium status of children in urban poor areas and determine whether selenium supplementation in addition to iodine is called for.

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