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SHORT COMMUNICATION

Effect of zinc supplementation on mood states in young women: a pilot study

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The relation of zinc (Zn) nutriture to brain development and function has been elucidated. The purpose of this study is to examine whether Zn supplementation improves mood states in young women. The study used a double-blind, randomized and placebo-controlled procedure. The major outcomes were psychological measures, somatic symptoms and serum Zn. Thirty women were placed randomly and in equal numbers into two groups, and they ingested one capsule containing multivitamins (MVs) or MV and 7 mg Zn daily for 10 weeks. Women who took MV and Zn showed a significant reduction in anger–hostility score ($P = 0.009$) and depression–dejection score ($P = 0.011$) in the Profile of Moods State (POMS) and a significant increase in serum Zn concentration ($P = 0.008$), whereas women who took only MV did not. Our results suggest that Zn supplementation may be effective in reducing anger and depression.
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Introduction

Zinc (Zn) is an essential mineral that has an important fundamental role in a wide range of biochemical processes relating to the growth and function of the brain (Sandstead *et al*., 2000). Poor Zn nutriture has been a prevailing worldwide public health problem (Yokoi *et al*., 2007) since the discovery of human Zn deficiency (Prasad *et al*., 1963). Relationships between Zn nutriture and brain function in humans have been reported (Sandstead *et al*., 1998).

Although we do not fully understand the relationship between Zn and behavioral activity, researchers have recognized that depression and impaired cognitive function are early clinical manifestations of human Zn deficiency (Sandstead *et al*., 2000; DiGirolamo and Ramirez-Zea, 2009). Halas *et al*. (1975) found aggression in intrauterine Zn-deficient rats and predicted a possible induction of anger and aggression by Zn deficiency in humans. The effects of Zn deficiency on behavior and development in humans are frequently assessed by the response to randomized trials of Zn supplementation conducted in populations thought to be marginal in Zn nutriture, based on the hypothesis that repletion of Zn might improve neuropsychological function.

With the hope of understanding the role of Zn on mood, a randomized controlled study with double-blind procedure was executed to investigate improvement of women's mood states by Zn supplementation.

Subjects and methods

This report describes a 10-week, randomized, double-blind, placebo-controlled trial of Zn supplementation in premenopausal women, executed from January 2006 to May 2007. This study was approved by the Bioethical Committee for Human Studies of the Seitoku University. Written informed consent was obtained from each subject.

Figure 1 shows the trial profile. Individuals living in the metropolitan area of Tokyo, Japan, who expressed potential interest to a posted notice, visited the Micronutrient Research Laboratory of the Seitoku University for informed consent, demographic and medical information interviews, and laboratory screening designed to examine any overt abnormality.

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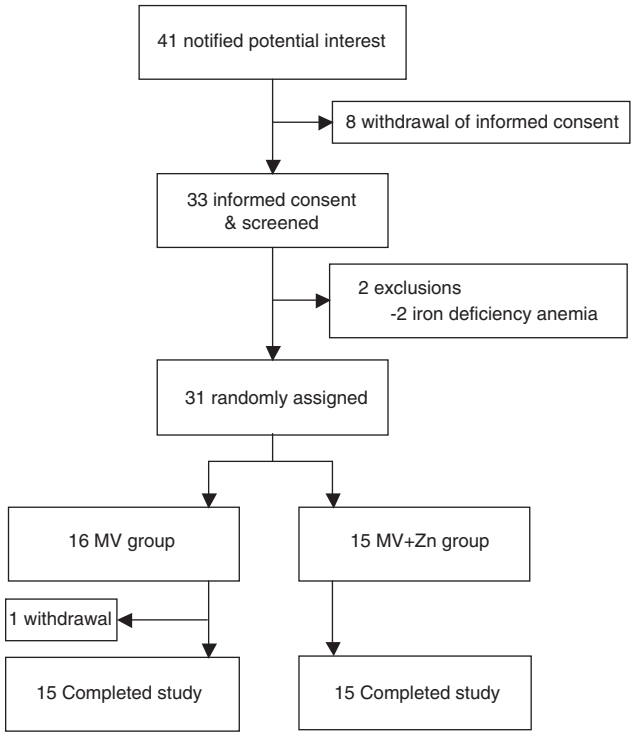

Figure 1 Trial profile. The inclusion criteria for subjects of this study were being aged between 18 and 21 years, being in good health, and having completed 12 grades of school. The exclusion criteria for subjects were iron deficiency anemia (hemoglobin <12 g/dl and serum ferritin <20 ng/ml), abnormal laboratory tests, chronic or recurrent illnesses, eating disorders, chronic medication and consumption of nutritional supplements that contained iron and/or Zn. MV = multivitamins.

Subjects were stratified according to the Fukamachi criteria (grades I, II, III and IV) for neurosis screening associated with the Japanese version of the Cornell Medical Index (CMI) (Kanehisa and Shinmachi, 1988). The subjects were randomly assigned by using a pseudo-random number generator to receive multivitamin (MV) capsules, or MV and Zn (MV–Zn) capsules, each to be taken once daily for 10 weeks. The MV capsule contained only MVs . The MV–Zn capsule contained MVs and 7 mg of Zn as an element (Zn gluconate; Tomita Pharmaceutical Co., Naruto, Japan). All capsules were identical in appearance, size and color. The MVs included vitamins A, D, B_1, B_2, B_6, B_{12}, niacin and folic acid, in amounts that were 50% of the Japanese Recommended Dietary Allowances (6th ed., 1999) for women of this age group. The MVs were given to all subjects to avoid possible vitamin deficiencies. Biochemical and psychological tests were conducted before and after supplementation.

Whole blood was collected in the morning after a 10–12 h fast, and the portion of serum was preserved for Zn analysis at $-80\,^{\circ}$C. Blood hematology and chemistry were performed by the Matsudo Medical Laboratory, Matsudo, Japan. Serum Zn content was determined by inductively coupled argon plasma-mass spectrometer ICPM-8500 (Shimadzu, Inc., Kyoto, Japan). Screening laboratory tests included hematology, serum ferritin and routine blood biochemistries.

Psychological tests were administered to each subject using a double-blind procedure. The A–L and M–R sections of the CMI were used to evaluate somatic symptoms, and mood and feelings, including anxiety, sensitivity, anger and tension. The Profile of Moods State (POMS) (Japanese version, Yokoyama and Araki, 1994) is a self-reporting questionnaire used to ascertain the mood state during the past week.

Data were analyzed with Wilcoxon's signed-rank test. Probabilities of less than 0.05 were considered significant.

Results

Both MV and MV–Zn groups were similar in terms of mean age (19.5 (s.d. 1.2) vs 19.3 (0.6) years); mean body height (1.58 (0.05) vs 1.59 (0.05) m); mean body weight (55.3 (9.0) vs 54.9 (7.9) kg) and mean body mass index (22.2 (3.2) vs 21.7 (2.2) kg/m^2). Both groups were similar in serum Zn concentration before intervention.

Neither intervention showed a significant change in serum ferritin and hemoglobin concentration. MV–Zn supplementation significantly increased serum Zn concentration, whereas only MV did not. Although the M–R sections of the CMI were not altered by either interventions, the A–L sections of the CMI were marginally decreased by MV–Zn supplementation ($P=0.069$). Women who took MV–Zn capsules showed a significant decrease in anger–hostility and depression–dejection scores on the POMS. However, there were no significant changes in other components, such as tension–anxiety, vigor, fatigue and confusion scores on the POMS (Table 1). Changes from baseline were not significantly different between MV vs MV–Zn groups by Mann–Whitney *U*-test (data not shown).

Discussion

In spite of a desirable body mass index for Asian origin (18.5–24.9 kg/m^2) and a normal hemoglobin level, symptom complaints were common in the subjects. Mood swings, one of the common symptoms of mild Zn deficiency, can be observed in industrialized countries (Levenson, 2006). The D score (depression–dejection) and A–H score (anger–hostility) on the POMS were significantly decreased by the intervention with Zn supplementation in the subjects (Table 1). Zn supplementation marginally decreased somatic symptoms (the A–L section of the CMI) in the present study. A negative relationship between serum Zn levels and severity of depression symptoms was reported in major depression (Nowak *et al*., 2003; DiGirolamo and Ramirez-Zea, 2009).

It is interesting that aggression secondary to intrauterine Zn deficiency was found only in female rats (Halas *et al*., 1975). Consistent with animal studies, we found an anger-reducing effect of Zn supplementation in female subjects.

Table 1 Biochemical parameters and scores of CMI and POMS before and after the 10-week intervention with and without Zn supplementation in women

	Multivitamin (n = *15*)			*Multivitamin + Zinc* (n = *15*)		
	Baseline	*Post-intervention*	P *value*	*Baseline*	*Post-intervention*	P *value*
Biochemical indices						
Hemoglobin (g/dl)	13.5 (0.8)	13.5 (1.0)	0.756	13.5 (0.9)	13.6 (0.9)	0.476
Serum ferritin (ng/ml)	27.6 (14.3)	38.8 (24.9)	0.059	38.8 (23.1)	34.5 (24.7)	0.239
Serum zinc (μg/ml)	0.87 (0.12)	0.89 (0.15)	0.776	0.84 (0.16)	0.92 (0.17)	0.011*
CMI						
Somatic symptoms, A–L	21.1 (16.6)[a]	19.6 (14.6)[a]	0.889	25.5 (13.1)	19.1 (10.7)	0.069
Mental symptoms, M–R	11.5 (10.0)[a]	12.5 (9.9)[a]	0.682	13.5 (9.8)	13.1 (9.8)	0.875
POMS						
Tension–anxiety, T–A	15.9 (7.1)	13.0 (7.6)	0.089	15.9 (6.2)	15.4 (6.8)	0.493
Depression–dejection, D	20.3 (11.0)	16.7 (13.7)	0.221	19.6 (10.4)	15.1 (10.6)	0.009**
Anger–hostility, A–H	14.3 (10.2)	12.5 (10.1)	0.393	11.7 (5.6)	8.4 (3.9)	0.012*
Vigor, V	9.3 (5.8)	10.2 (5.5)	0.972	9.5 (4.7)	9.1 (5.8)	0.309
Fatigue, F	12.7 (6.0)	12.9 (8.4)	0.864	12.3 (5.8)	11.5 (6.7)	0.151
Confusion, C	13.9 (4.8)	12.2 (3.7)	0.151	14.7 (5.1)	14.4 (5.5)	0.906

Abbreviations: CMI, Cornell Medical Index; POMS, Profile of Moods State.
Data are shown as mean (s.d.).
Significance level *$P<0.05$, **$P<0.01$.
[a]A number of subjects was 14 because of incomplete records in CMI.

Although our findings are preliminary and should be interpreted with caution, they may prompt further investigations to evaluate the relationship between Zn nutriture and mood states in women.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

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