Effects of zinc supplementation on serum zinc concentration and ratio of apo/holo-activities of angiotensin converting enzyme in patients with taste impairment

Tsukasa Takaoka a, Nobuko Sarukura b, Chizuru Ueda b, Yoshiaki Kitamura a, Bukasa Kalubi a, Naoki Toda a, Koji Abe a, Shigeru Yamamoto b, Noriaki Takeda a, *

a Department of Otolaryngology and Communicative Neuroscience, Institute of Health Bioscience University of Tokushima Graduate School, 3-18-15 Kuramoto, Tokushima 770-8503, Japan
b Department of International Public Health Nutrition, Institute of Health Bioscience University of Tokushima Graduate School, 3-18-15 Kuramoto, Tokushima 770-8503, Japan

Received 16 April 2009; accepted 5 July 2009
Available online 28 August 2009

Abstract

Objective: The aim of the present study was to evaluate the effects of zinc supplementation on hypogeusia, serum zinc concentration and the ratio of apo/holo-activities of angiotensin converting enzyme (ACE ratio) in patients with taste impairment. ACE ratio was used as an index of zinc nutritional status.

Methods: Forty patients complaining of taste impairment were divided into two groups: zinc deficiency taste impairment (n = 12) and idiopathic taste impairment (n = 28). Patients with zincemia values of less than 63 μg/dl with no history of other disorder or medication known to cause dysgeusia were diagnosed as zinc deficiency group, while those with the same condition and values more than 64 μg/dl were considered to belong to the idiopathic group. Patients orally received 150 mg of polaprezinc containing 33 mg of zinc every day. Subjective symptom was scored according to visual analogue scale (VAS).

Results: Zinc supplementation improved hypogeusia in both idiopathic and zinc deficiency groups. The mean improvements of VAS were 3.02 ± 3.03 in the idiopathic group and 3.13 ± 2.53 in the zinc deficiency group. Thus, there were no significant differences in idiopathic and zinc deficiency groups. Significant correlations were found between the improvement of VAS score and the ACE ratio after zinc supplementation in both idiopathic and zinc deficiency groups. On the contrary, significant correlations were not found between the improvement of VAS score and the zinc concentration in the serum after zinc supplementation in both groups.

Conclusion: The results of the present study indicated that zinc deficiency is a predominant factor underlying taste impairment and ACE ratio may be a predictor of the prognosis for taste impairment after zinc supplementation, in addition to a more sensitive indicator of zinc nutrition than zinc concentration in the serum.

© 2009 Published by Elsevier Ireland Ltd.

Keywords: Taste impairment; Zinc supplementation; Angiotensin converting enzyme; Visual analogue scale

1. Introduction

Zinc is an essential trace element playing a role in several functions in both humans and animals. In fact, zinc deficiency has been associated with growth disturbance, special senses including vision, taste and smell [1,2]. Especially, several lines of clinical evidence suggested that taste impairment is one of the symptoms of zinc deficiency [3–8], as corroborated by double-blind, placebo-controlled studies that have shown the efficacy of zinc supplementation in the taste recovery in several zinc deficient patients [9–11].

However, zinc concentration in the serum which has been widely used to assess zinc deficiency is known to be
modified by several factors, including acute stress and inflammation [12]. In addition, zinc is a trace element, rapidly transferred into the cells and of particular significance, especially in cells with a high-rate turnover, such as cells of the taste buds [13,14]. In fact, it was reported the therapeutic effect of zinc supplementation in patients with idiopathic taste disorder with normal zinc levels in the serum [15,16].

Inquiry into more reliable tests has lead to the observation that the activity of zinc-metallo enzyme, such as angiotensin converting enzyme (ACE) is a more reliable test for the assessment of zinc deficiency. In the previous study, we showed that the ratio of apo/holo-ACE activities (ACE ratio) in the serum was a more sensitive indicator of zinc nutrition than zinc concentration in the serum [17,18]. In the present study, we used ACE ratio to evaluate the zinc nutrition and the effects of zinc supplementation in patients with taste impairment.

2. Materials and methods

The present study includes patients who visited the Department of Otolaryngology, Tokushima University Hospital complaining of taste impairment and were diagnosed as zinc deficiency taste impairment (n = 12) and idiopathic taste impairment (n = 28). Informed consent regarding the purpose of this study and measurements of zinc concentration and ACE activity in the blood was obtained from each patient. This study was approved by the Ethical Committee of Tokushima University Hospital and performed in accordance with the Declaration of Helsinki.

Zinc concentration in the serum was measured by means of atomic absorption spectrometry [19] by Mitsubishi Kagaku Bio-Chemical Laboratories Inc. (Tokyo, Japan). Normal ranges of zinc concentrations in the serum are from 64 to 111 μg/dl. On the one hand, zinc deficiency taste impairment was diagnosed in patients with no history of therapy or any other underlying disorders susceptible to cause taste disturbance including smell disturbance with zinc concentration of less than 63 μg/dl in the serum. On the other hand, idiopathic taste impairment was considered in patients with the same condition, but with zinc levels of more than 64 μg/dl in the serum.

ACE activity in the serum was measured spectrophotometrically as that of holo-ACE. ACE color Kit (Fujirebio Inc., Tokyo Japan) was used, which is based on colorimetry of the quinoneimine dye product from pHydroxyhippuril-L-histidyl-L-leucine as the substrate of ACE with hippuricase and peroxydase [20]. Since ACE is a zinc-metallo enzyme, holo-ACE with zinc shows full ACE activity. After measuring ACE activity in the serum, it was further measured after addition of zinc (80 μM in phosphate buffer at pH 8.3) to the serum in vitro. The increase of activity over the initial holo-ACE activity was determined as that of apo-ACE in the serum. The ratio of apo/holo-ACE activities is calculated as follows: ACE ratio (%) = (apo-ACE activity/hoio-ACE activity) \times 100 [17,18].

Subjective symptom was measured by visual analogue scale (VAS) on a scale ranging from 0 to 10 [21]. Patients with both zinc deficiency taste impairment and idiopathic taste impairment orally received 150 mg of polaprezinc containing 33 mg of zinc every day. The mean period for zinc supplementation was 17.7 weeks (4–97 weeks). Zinc concentration and ACE ratio in the serum and VAS score were measured every two weeks after zinc supplementation. The improvement of VSA score was calculated as the initial VAS score minus the final one.

Unpaired Student’s t-test and Pearson correlation analysis were used for statistical analysis. P < 0.05 was considered significant.

3. Results

The mean concentration of zinc in serum was 76.8 ± 8.6 μg/dl (mean ± S.D.) in the idiopathic group and significantly decreased at 57.2 ± 5.6 μg/dl in the zinc deficiency group. The mean ACE ratios were 13.1 ± 8.0% in the idiopathic group and 13.1 ± 6.9% in the zinc deficiency group (Fig. 1). The mean ACE ratio in both groups was much higher than that in healthy subjects (1.10 ± 0.6%, n = 30) [17].

Zinc supplementation improved subjective symptom in both idiopathic and zinc deficiency patients. The mean improvement of VAS score was 3.02 ± 3.03 in the idiopathic group and 3.13 ± 2.53 in the zinc deficiency group (Fig. 2). Thus, there were no significant differences in idiopathic and zinc deficiency groups.

Significant correlations were not found between the improvement of VAS score and the zinc concentration in the serum at the final VAS score after zinc supplementation in both idiopathic and zinc deficiency groups (Fig. 3). On the contrary, significant correlations were found between the improvement of VAS score and ACE ratio at the final VAS score after zinc supplementation in both idiopathic and zinc deficiency groups (Fig. 4).

4. Discussion

In the present study, the concentration of zinc in the serum of idiopathic group of patients with taste impairment was significantly lower than that in idiopathic group of patients with taste impairment. On the contrary, ACE ratio in idiopathic group was not different from that in zinc deficiency group (Fig. 1). ACE ratio in both groups was much higher than that in healthy subjects [17]. Since our previous study showed that the ACE ratio is a sensitive indicator of zinc nutrition [17,18], it is suggested that zinc deficiency is predominant factor underlying taste impairment even when zinc concentration is within...
normal ranges in the serum. This assumption was proved by the finding that zinc supplementation improved taste impairment evaluated by VAS score in both idiopathic and zinc deficiency groups (Fig. 2).

Although there were no correlations between the improvement of VAS score and the zinc concentration in the serum after zinc supplementation (Fig. 3), significant correlations were found between the improvement of VAS score and ACE ratio after zinc supplementation in both idiopathic and zinc deficiency groups (Fig. 4). However, we could not find the correlations between the improvement of VAS score and the improvement of ACE ratio calculated as the initial ACE ratio minus the final one (data not shown). The reason is probably that ACE ratio after zinc supplementation, but not the improvement of ACE ratio, indicates the improvement of zinc nutrition. ACE ratio is the ratio of apo/holo-activities of ACE and apo-ACE molecules lacking zinc is inactive [22]. Therefore, it is suggested that the better zinc nutrition means the less apo-ACE, resulting in the less ACE ratio. These findings demonstrated that ACE ratio is a more sensitive indicator of zinc nutrition than zinc concentration in the serum, suggesting that it is a predictor of the prognosis for taste impairment after zinc supplementation.

In the previous study, we showed that the dietary intake of zinc was not different between patients with taste impairment and age-adjusted healthy subjects [18]. Therefore, it was suggested that patients with taste impairment have malabsorption of dietary zinc. Zinc is mainly absorbed in the small intestine [23,24]. Intestinal lesions can explain malabsorption of dietary zinc in patients with Cronkhite-Canada syndrome with many hyperplastic polyps in the intestine [25], but not in patients with no apparent disorders except taste impairment. Mineral absorption in the small intestine proceeds by two mechanisms: an active transcellular process that takes place in the duodenum and a passive paracellular process throughout the small intestine [24]. It was reported that several zinc transporters such as ZIP and CDF play an important role in the active absorption process of zinc [26] and that tight-junction permeability regulates the passive absorption of various nutrients including zinc [27]. Dysfunction of zinc transporters or tight-junctions may disturb the absorption of dietary zinc from the small intestine in patients with taste impairment.
5. Conclusion

In the present study, we used ACE ratio to evaluate the nutrition of zinc and examined the effect of zinc supplementation in patients with taste impairment. Zinc supplementation improved taste impairment evaluated by VAS score in both idiopathic and zinc deficient patients. The improvement of taste impairment by zinc supplementation in both idiopathic and zinc deficiency groups significantly correlated with ACE ratios after zinc supplementation. These findings indicated that the ACE ratio is a sensitive indicator of zinc nutrition and may be a predictor of the prognosis for taste impairment after zinc supplementation.

Acknowledgements

We are grateful to Dr. H. Kobayashi for his technical supports. This study was partly supported by a Grant-in-Aid for Scientific Research from Japan Society for the Promotion of Science.

References