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Original Article

Association of zinc intake & serum zinc levels with acne severity

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Abstract

Background: Recent studies have suggested the relationship between diet and acne, and zinc plays a role through its anti-inflammatory mechanism. This study aimed to determine the association between zinc intake and serum zinc levels with acne severity.
Methods: A comparative cross-sectional study was conducted to assess the difference in zinc intake and serum zinc levels with acne severity based on Indonesian Acne Expert Meeting (IAEM) criteria. Sixty patients with acne in Dr. Cipto Mangunkusumo General Hospital were selected. The effect of zinc intake on acne severity was analyzed via unpaired T test, whereas the effect of serum zinc levels on acne severity was examined with Mann–Whitney test. Data were further evaluated using SPSS 20.0.
Results: Zinc intake in all the subjects was below the Indonesian recommended daily allowance, and the mean of zinc intake and serum zinc levels in the mild acne group was higher than that of the moderate–severe acne group. The zinc intake significantly differed between the mild and moderate–severe acne groups ($p < 0.01$). Likewise, serum zinc levels significantly varied between mild and moderate–severe acne group ($p = 0.048$).
Conclusion: Although this study showed a significant difference between zinc intake and serum zinc levels with the severity of acne vulgaris, further follow-up studies should be performed to assess zinc for acne vulgaris therapy.

Keywords: *zinc intake, serum zinc level, acne severity*

Background

Acne vulgaris is a chronic inflammatory disease of pilosebaceous glands, commonly afflicted by adolescents and adults worldwide.[1] Acne cases continue to increase yearly, according to the Indonesian Cosmetics Dermatology Study Group, acne cases increased from 60% in 2006 to 90% in 2009.[2] Acne vulgaris becomes a problem because of common sequelae of erythematous macule, hyperpigmentation, or scarring.[1] Acne may also cause psychiatric problems or social, physiological, and emotional disorders.[1] In another study, the more severe degree of acne, the greater the impairment of a patient's quality of life.[3] In Indonesia, the degree of acne severity is assessed in accordance with the 2015 Indonesian Acne Expert Meeting (IAEM) criteria that classify the severity of acne into mild, moderate, and severe based on the number of lesions of comedones, pustules, or nodules.[4]

The association of various nutrients with the incidence of acne has been widely explored. For example, the association of acne with zinc has been investigated. Zinc is an essential micronutrient present in the skin, especially the epidermis, and needed for cell differentiation.[5] Zinc likely plays a role in reducing acne severity through its activity as an anti-androgen by modulating 5α-reductase, the anti-inflammatory effect on immunity by inhibiting toll-like receptor-2 (TLR-2), activates natural killer (NK) cells and phagocytes, and the antibacterial effect by reducing the number of *Cutibacterium acnes*.[6] However, studies examining the association between zinc and acne severity are limited, and

inconsistent results have been obtained among studies.[6,7,8]

Zinc in the body comes from food and endogenous zinc originating from the pancreas and intestinal mucosal cells. Food sources high in zinc derived from animal proteins, such as seafood, red meat, and dairy products. Limited studies have explored the status of zinc in the body because of the lack of specificity and sensitivity. Serum zinc level is considered to reflect the zinc status of a population. The combination of intake, biochemical, and physiological functional examinations is the most ideal for evaluating the status of zinc in the body.[9]

This research aimed to determine the association between zinc intake and serum zinc levels with acne severity in accordance with the IAEM criteria.

Methods

This cross-sectional study was conducted in Cipto Mangunkusumo General Hospital, Jakarta. The sample size was determined in accordance with Browne[10] recommendation for a pilot study; a minimum of 30 subjects were included per group, and approximately 10% of the subjects dropped out, so the total number of the samples was 33 subjects per group. However, the sum of the subjects who completed the study was 60 subjects.[10] Inclusion criteria were as follows: male or female patients who attended the Dermatology–Venerology Polyclinic in Cipto Mangunkusumo General Hospital, were diagnosed with acne by a dermatovenereologist, aged between 19 and 49 years old, and were willing to participate by signing the informed consent. Exclusion criteria were as follows: pregnant and lactating mothers, patients who consumed hormonal drugs, patients who were taking antibiotics or corticosteroids in the last 28 days before sample collection, patients who were receiving oral isotretinoin or topical retinoid within the last 3 months, and patients who had liver disorders.

The data of 60 consecutive patients who fulfilled the inclusion/exclusion criteria were collected in October until November 2017. Blood samples were obtained once at first visit, and basic data were collected. The subjects' characteristics, including age, gender, education, and income, were obtained through one-on-one interview. Zinc intake was assessed using a semiquantitative food frequency questionnaire (Appendix 1, page 6), and the collected data were processed via a nutrisurvey 2007 application. Anthropometric measurement covered body height, body weight, and body mass index in accordance with a standard procedure. Body weight was measured with calibrated weight scale (seca®, German) and body height was measured using a microtoize stature. Serum zinc levels were examined by collecting 3 ml of blood from the cubiti vein. The collected blood was then centrifuged at a speed of 3000 rpm to separate the serum, which was later stored at −80 °C. The serum was analyzed through atomic absorption spectrophotometry (GBC Scientific Model GBC933AA, Australia) to measure the serum zinc level after all the subjects were completed.

Data were analyzed using Statistical Package for Social Sciences version 20.0. A Shapiro–Wilk test was conducted to assess the normality of numerical data. Normally distributed data were presented as mean and standard deviation, whereas data that were not normally distributed were presented as median and minimum–maximum range. An unpaired T test was conducted to compare the different zinc intake values on the mild acne subject group and the moderate–severe acne subject group. A Mann–Whitney test was carried out to assess the difference in serum zinc levels between the mild acne subject group and the moderate–severe acne subject group.

Results

A total of 60 subjects with acne vulgaris participated in this study. Of these subjects, 30 had mild acne and 30 had moderate–severe acne. Most subjects were males (80%). The median age of the mild group was 22 (19–41) years, and the median age of the moderate–severe group was 22 (19–30) years. The subjects' characteristics based on age, gender, education, income, and body mass index are shown in Table 1.

Serum zinc levels were examined in SEAMEO RECFON Laboratory. The median serum zinc levels in the mild acne group and the moderate–severe group were 12.5 (9.2–17.6) and 12.0 (7.6–14.4) µmol/L, respectively. Statistical analysis with Mann–Whitney test showed a significant difference in serum zinc levels between the two groups (p = 0.048; Table 2).

All the subjects (100%) had a zinc intake below the recommendation dietary allowance in Indonesia with means of 8.51 ± 1.02 mg/day for the mild acne vulgaris group and 5.24 ± 0.84

mg/day for the moderate–severe acne vulgaris group. The mean zinc intake level derived from vegetables in both groups was larger than that derived from animals. Statistical analysis through unpaired T test revealed that the zinc intake between the two groups significantly differed (p < 0.001; Table 3).

Discussion

In this study, the median serum zinc levels in the mild acne group were higher than those in the moderate–severe acne group. Previous study done in 2015 obtained similar results, which showed that the

Table 1. Distribution of subjects based on sociodemographic characteristic and body mass index

Variable	Acne Severity		Total	*p*-value
	Mild (n=30)	Moderate–Severe (n=30)	n (%)	
Age (year)	22 (19–41) *	22 (19–30) *		0.254 ‡
19–29 (%)	26 (86.6)	29 (96.6)	55 (91.6)	
30–49 (%)	4 (13.4)	1 (0.4)	5 (8.4)	
Gender				
Male (%)	6 (20)	6 (20)	12 (20)	1.000 §
Female (%)	24 (80)	24 (80)	48 (80)	
Education				
Very low-moderate (%)	14 (46.7)	20 (66.36)	34 (56.7)	0.193 §
High (%)	16 (53.3)	10 (33.3)	26 (43.3)	
Income				
Adequate (%)	22 (73.3)	17 (56.7)	39 (65)	
Inadequate (%)	8 (26.7)	13 (43.3)	21 (35)	
BMI	23.99 ± 0.99†	22.43 ± 0.81†		
Underweight (%)	3 (10)	6 (20)	9 (15)	0.176 *c*
Normoweight (%)	9 (30)	12 (40)	21 (35)	0.204 *c*
Overweight (%)	8 (26.7)	5 (16.7)	13 (21.7)	
Obese (%)	10 (33.3)	7 (23.3)	17 (28.3)	

*Mean, †median, ‡*Mann–Whitney,* §*Chi-square, and* *c* unpaired T test, BMI = body mass index, n = number of patient

Table 2 Difference between serum zinc levels and acne vulgaris severity

Variable	Acne Severity		*p*-value
	Mild (n=30)	Moderate–Severe (n=30)	
Serum zinc levels (µmol/L)	12.5 (9.2–17.6)*	12.0 (7.6–14.4)*	0.048
Adequate, n (%)	2 (6.7)	5 (16.7)	
Deficiency, n (%)	28 (93.3)	25 (83.3)	

* Median (minimum–maximum), n = number of patient

Table 3. Difference between zinc intake and acne vulgaris severity

Variable	Acne Severity		*p*-value
	Mild (n=30)	Moderate–Severe (n=30)	
Zinc intake (mg/day)	8.5 ±1.02*	5.24 ± 0,84*	≤0.001
Animal derived zinc (mg/day)	3.12 ± 0.19*	1.71 ± 0.14*	
Plant derived zinc (mg/day)	5.46 ± 0.25*	3.57 ± 0.15*	

*Mean ± standard deviation, n = number of patient

median serum zinc levels are 11.15 (10.23–14.21) and 9.93 (6.72–10.69) μmol/L in the mild and severe acne groups, respectively.[11] The percentage of the subjects who had low serum zinc levels was higher in the moderate–severe acne group (16.7%) than in the mild acne group (6.7%).

Mann–Whitney analysis test was carried out to assess the difference between serum zinc levels with the degree of acne severity, and the results were significant (p = 0.048). Previous studies taken in different country show same results as ours but there also a study showing different result .[9,11,12,] These different results were probably due to the usage of the International Consensus Conference on Acne Classification System criteria in determining the severity of acne in Kaymak's study. According to these criteria, acne is classified into three degrees of severity, but qualitative aspects do not have clear limits on the number of lesions (few, many, and some).[13] This classification was more subjective than the IAEM 2015 classification because different results might have been examined by different reviewers.

Unpaired T test was conducted to assess the difference between zinc intake with acne vulgaris severity, and reveal significant results (p < 0.001). The zinc dietary intake of all the subjects in this study did not reach the RDA in Indonesia, that is, 10 mg/day for females and 13 mg/day for males. The source of zinc intake in this study was largely derived from a plant protein. In the mild acne vulgaris group, the mean zinc intake derived from a plant protein was 5.46 ± 0.25 mg/day, and the mean zinc intake derived from an animal protein was 3.12 ± 0.19 mg/day. In the moderate–severe acne vulgaris group, the mean of zinc intake derived from the plant protein was 3.57 ± 0.15 mg/day, and the mean of zinc intake from the animal protein was 1.71 ± 0.14 mg/day. According to interviews, most subjects rarely consume high-zinc-containing foods, such as beef, poultry, and seafood, including shellfish, fish, and shrimp. Most subjects also consume food derived from plant sources. Meat, which is a protein source that can increase zinc absorption; conversely, phytate, which is widely found in plants, can act as a zinc inhibitor.[14]

This result was consistent with the theory that zinc is associated with acne vulgaris. Zinc functions as an anti-androgen. Zinc deficiency can cause an increase in DHT hormone that induces changes in keratinocytes, resulting in hyperkeratinization and increasing inflammatory cells. Zinc deficiency can also cause an increase in TLR-2, which stimulates cytokine expression. The release of proinflammatory cytokines, such as IL-1, IL-8, IL-12, and TNF-α, leads to inflammatory acne.[8] Zinc is also known to inhibit polymorphonuclear cell chemotaxis, inhibit *C. acnes* growth, modulate integrins, especially ICAM-1 and LFA 3, activates the phagocyte capacity of granulocytes, and activates NK cells.[9] In another mechanism, zinc plays a role in retinol binding protein synthesis and secretion in the liver, which may describe the amount of vitamin A available in the tissues. Vitamin A and zinc are essential for normal epithelial development.

In this study, all the subjects showed low zinc intake; however, only a small percentage was found to have low serum zinc levels. This observation was probably due to a highly efficient zinc homeostatic regulation in human body. Zinc homeostasis in the body is influenced by variations in zinc absorption and endogenous zinc excretion in the intestine. In low zinc intake, zinc absorption is more effective through active transport.[15] Zinc absorption under fasting conditions increased to 60%–70%, whereas the average absorption of zinc under nonfasting conditions was 33%. If zinc intake is low for long periods or under extreme zinc deficiency conditions, homeostasis response results in changes in urinary excretion of zinc, turnover rate of zinc, and release of zinc from various tissues, such as bones.[16]

Conclusion

The result of our study shows an association between zinc intake and serum zinc levels with severity of acne. A lower serum zinc level in moderate-severe acne group compared to mild acne group suggest that zinc might have play a role in acne pathogenesis thus further study is needed

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Appendix 1. Semi quantitative food frequency questionnaire

Name: **Age:** **Date:** **Subject's Code:**

Food list	Never/ <1x/ month	Frequency								Serving	Gram
		1x /day	2–3 x /day	4–5x /day	≥6x /day	1x /week	2–4 x/ week	5–6x /week	1–3x /month		
Fruits											
Ambon's banana											
Gold banana											
King banana											
Others….											
Cerealia											
Rice											
Pasta											
White bread											
Wheat bread											
Peas											
Cashew nut											
Others											
Vegetables											
Jelly fungus											
White mushroom											
Red spinach											
Green spinach											
Broccoli											
Green beans											
Carrot											
Papaya leaf											
Chayote											
Others											

Daily zinc intake from animal source : mg/day (%)
Daily zinc intake from plant source : mg/day (%)
Daily zinc intake : mg/day