Evaluation of serum vitamins A and E and zinc levels according to the severity of acne vulgaris

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Abstract
Background: Although hyperseborrhea, follicular hyperkeratinization, Propionibacterium acnes colonization and inflammation are found to be responsible in the pathogenesis of acne, the exact mechanisms are unknown. Vitamin A and E are basic antioxidants vital for health. Zinc is also an essential element for human. But these parameters of the effects on skin are not fully understood. We aimed to evaluate plasma levels of vitamin A, E and zinc in acne patients in relation to the severity of the disease.

Material and method: There were 94 acne patients who were referred to our clinic, all new diagnosed, and 56 age and sex matched healthy volunteers as control group. All patients are assessed according to Global Acne Grading System and grouped as mild, moderate, severe and very severe. Acne patients further grouped as group 1 consist of patients with mild to moderate disease; and group 2 consist of patients with severe to very severe acne. The patients with the controls and group 1 with group 2 was compared.

Results: The level of vitamin E, vitamin A and zinc were significantly lower than the control group (Table 1, p<0.001). When the patient group is compared among each other there was no statistically significant difference for plasma vitamin A levels between group 1 and 2 whereas vitamin E and zinc levels were significantly low in group 2 than group 1. Thus there was a negative correlation between acne severity and vitamin E and zinc levels.

Conclusion: Our study marks the importance of diet in patients with acne. We offer supportive dietary measures with foods rich in vitamin A and E and zinc in the acne prophylaxis and treatment. Supportive treatment with these vitamins and zinc in severe acne may lead to satisfactory results.

Introduction
Acne is a disease of pilosebaceous unit that affects adolescent and young adults. Although hyperseborrhea, follicular hyperkeratinization, Propionibacterium acnes colonization and inflammation are found to be responsible in the pathogenesis, the exact mechanisms are not known¹. The effect of diet on acne has been a debate in recent years. Thus, there are few studies that evaluate vitamin and mineral levels in acne patients to elucidate this relationship. Different results were achieved from these studies²³. For instance, vitamin A which is also used in treatment, measured by retinol binding protein levels, and low levels are reported⁴. On the other hand, in some studies, zinc levels are found to be low in proportion to acne severity, whereas no relation has been stated by some others⁵.

Vitamin A is an essential fat-soluble element in addition to its important role in vision, haematopoiesis, embryological development, function of immune system, gene transcription and many other physiological activities; it is also required for integrity and differentiation of skin and skin appendages. Deficiency of vitamins A and E can lead to some diseases. Vitamin A deficiency is observed in chronic illness, malabsorption, liver diseases as well as diet with low levels and may result with xerosis, follicular keratosis and metaplasia of mucous membranes. Toxicity is associated with high levels of vitamin A intake. Although synthetic derivatives of vitamin A have a wide range of side-effects, it may have excellent results when appropriate doses are used in dermatology⁶.

The role of vitamin E in skin biology has not yet been illuminated. It is known to protect biological membranes from free radicals by antioxidant activity. Free radicals are produced when body is exposed to environmental factors as foods, cigarette smoke and ionizing radiation. Vitamin E has a role in immune system and metabolic processes as well. Vegetable oils, nuts, seeds, grains and green leafy vegetables are sources known to be rich for vitamin E. Many people get enough levels of this vitamin. D-α-tocopherol is the
stabilizing unsaturated lipid form of vitamin E in plasma, known to protect against auto-oxidation. It accumulates lipoproteins and cellular membrane by rapidly reacting with free radicals and molecular oxygen, accentuates immune system, protects skin against UV radiation and preserves the membranes from peroxidation. For example, it is used in dermolytic epidermolysis bullosa although there are controversial results.

Among the essential elements, copper, zinc, iron and cobalt levels have been evaluated in acne patients. All these studies aimed at improved understanding of acne pathogenesis for better treatment results. Studies are particularly interested in zinc levels in acne patients. The vital role of this element was first published in 1963. The beneficial effects of zinc salts in mild and moderate acne lesions were also stated in studies. However, the mechanism of zinc salts is only partially understood yet. In fact, zinc inhibits leucocyte chemotaxis and proliferation of *P. acnes*, and increase phagocytic capacity of natural killer cells and granulocytes. The anti-inflammatory effect of zinc is by reduction of TNF-α and IL-6 production and modulation of expression of integrins, especially ICAM-1 and LFA-3. In vitro studies showed the specific effect of zinc on 5α-reductase.

We aimed to evaluate plasma levels of vitamins A and E and zinc in acne patients in relation to the severity of the disease.

Materials and methods

In total, 94 acne patients who were referred to our clinic between December 2010 and January 2011 and 56 age and sex matched healthy volunteers as control group were included in the study. The control group was not under any treatment and had no past or family history of acne. Both groups were not having any vitamin pills. Detailed procedure was discussed with all participants and they signed the informed consent. All patients were assessed according to Global Acne Grading System and grouped as mild, moderate, severe and very severe cases. Acne patients further grouped as group 1 consisted of patients with mild to moderate disease; and group 2 consisted of patients with severe to very severe acne.

Venous blood samples after 12–14 h fasting were collected in EDTA tubes. Tubes were centrifuged without delay, in slightly oblique position with low velocity cooling method (Hettich Zentrifugen D.78532; Tuttingen, Germany) and plasma was separated in 30 min. Plasma vitamins A and E concentrations were studied by high performance liquid chromatography method and serum zinc levels were measured spectrophotometrically. Vitamins A and E were dissolved by hexane and dried by nitrogen steam. The remnant was dissolved by diethyl ether and solvent is mixed before dilution with methanol. To avoid photodestruction of vitamins, light-protected, dark environment was supplied.

Data were recorded and analysed by using SPSS statistical analysis software version 18. A *p*-value of ≤0.05 was considered significant.

Results

Of the 94 patients included in the study, 61 were women and 33 were men. The mean age of patients was 28.54 ± 8.30. The level of vitamins E and A and zinc were significantly lower than the control group (Table 1, *p* < 0.001). When the patient group is compared among each other there was no statistically significant difference for plasma vitamin A levels between groups 1 and 2, whereas vitamin E and zinc levels were significantly low in group 2 than group 1. Thus, there was a negative correlation between acne severity and vitamin E and zinc levels.

Discussion

The pathogenesis of acne, a common disease in dermatology practice is not known exactly. There are some studies to understand relationship of diet and acne. Besides vitamin A, which is also used in the treatment, there are studies that evaluate vitamin E and minerals such as zinc and copper.

Vitamins A and E are a group of organic compounds, which are fat-soluble and naturally found in food. They are basic antioxidants vital for health. The deficiency of these vitamins can lead to many diseases. In addition to primary deficiency, secondary deficiency of vitamin A is observed when lipid and zinc absorption which are also necessary for vitamin A absorption, are impaired.

13-cis-Retinoic acid is a form of vitamin A that has inhibitory effects on sebaceous gland activity and on sebum secretion. Consequently, it leads to reduction in *P. acnes* population, which has an important role on inflammatory phase of acne. Retinoids suppress comedogenesis via effects on epidermal cell differentiation and keratin production. Thus, they are efficient at different stages ranging from comedones to more serious inflammatory lesions. The anti-inflammatory effects of vitamin A are also known. The low concentration of vitamin A leads to cell desquamation, increased adhesiveness of follicular cells and keratin production thus result in acne ranging in severity from mild comedonal to severe inflammatory lesions, also with prolonged duration of disease. These data are in parallel with

Table 1. The demographic data and laboratory measures of both acne and control groups.

<table>
<thead>
<tr>
<th>Patients (n: 94)</th>
<th>Controls (n: 46)</th>
<th><em>p</em> Value</th>
<th>Group 1 (n: 33)</th>
<th>Group 2 (n: 61)</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex female/male</td>
<td>61/33</td>
<td>44/12</td>
<td>0.02</td>
<td>26/7</td>
<td>35/26</td>
</tr>
<tr>
<td>Age</td>
<td>28.54 ± 8.30</td>
<td>30.45 ± 9.46</td>
<td>&gt;0.05</td>
<td>29.36 ± 10.32</td>
<td>28.04 ± 7.36</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>0.43 ± 0.26</td>
<td>0.60 ± 0.20</td>
<td>&lt;0.001</td>
<td>0.49 ± 0.24</td>
<td>0.40 ± 0.26</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>7.88 ± 3.00</td>
<td>11.06 ± 3.08</td>
<td>&lt;0.001</td>
<td>8.28 ± 3.12</td>
<td>5.66 ± 2.93</td>
</tr>
<tr>
<td>Zinc</td>
<td>62.15 ± 18.11</td>
<td>81.57 ± 20.43</td>
<td>&lt;0.001</td>
<td>68.14 ± 18.90</td>
<td>56.16 ± 16.74</td>
</tr>
</tbody>
</table>

*p* < 0.05 significant.
other studies. Acne severity is increased in patients with low levels of vitamin A. In addition, although the severe acne patients in our study had low levels of vitamin A, this was not statistically significant. These studies support the low levels of vitamin A as a risk factor for acne and improve acne lesions with oral vitamin A support this finding.

El Akawi et al. found low levels of both vitamins A and E in acne patients in comparison to control group and additionally, lower levels were obtained in severe acne patients when compared with mild patients. They suggest vitamin A level is low due to consumption in acne for its anti-inflammatory effects. Plasma lipoproteins or retinol binding proteins can affect transport, absorption and plasma concentration of vitamin A.

In our study, all three molecules, vitamins A and E and zinc levels, were found low and thus may reflect a relation between diet and acne. The low intake or secondary reasons for the low levels may be a risk factor for acne. The study by El Akawi et al. found that vitamin E levels were significantly lower than controls but they did not associate this finding with dietary factors. They thought that an indirect relation exists between low vitamin E level and acne. The low level was thought to be due to depletion as an antioxidant, produced against oxygen radicals during the inflammatory phase. Besides, the reactive oxygen radicals produced during inflammatory factors as smoking, were reported to deplete vitamins A and E levels. In the study, smokers were found to be high among those with low levels of vitamins A and E, but this was statistically not significant. The role of smoking should be investigated carefully in further studies.

Combined treatment of acne with oral vitamins A and E was reported to have a synergistic effect by regulating keratinization. Aktürk et al. showed that vitamin E levels decreased during isotretinoin treatment. We considered that some of the side-effects due to isotretinoin treatment might be related to this, and have suggested supplementation vitamin E during isotretinoin treatment. In our study, all the patients are evaluated, vitamin E levels are found significantly lower than the control group, even lower levels are yielded in severe acne patients. We had correlated acne severity and vitamin E levels. When the eating habits of our patients were asked, dominance of diet with high glycemic index, poor in fruits and vegetables were stated.

Zinc is an essential element for human, but the effects on skin are not fully understood. Zinc and vitamin A are essential for pubertal development and normal epithelial differentiation. About 6% of the zinc in human body is localized in the skin. In animal studies, zinc is shown to have an important role in retinol binding protein synthesis and/or increment in liver. The human retinol binding protein is a specific transporter protein with low molecular weight. Retinol binding protein reflects the vitamin A levels in target organs. Zinc is a co-factor for metalloenzymes in many cellular pathways. The basis of zinc utilization depends on anti-inflammatory activity. Cytokine production and antioxidant activity are not well known. It can be used in acne treatment based on its anti-inflammatory effects. Zinc levels are estimated to better understand acne pathogenesis and different results are yielded.

Weimar et al. reported that zinc appeared to have a somewhat beneficial effect on pustules but not on comedones, papules, infiltrates or cysts.

Nasiri et al. found low levels of vitamin A among Iranian acne patients but zinc levels were similar in both acne and control groups. In our study, zinc levels in all patients were decreased and this finding correlates with acne severity.

According to our results, the foods to offer in acne diet are yellow and green vegetables as spinach, squash, cabbage, carrots, bell peppers, lettuce, broccoli, cereals, olive oil, flax seed, fish oil, tuna fish, sardines, nuts, walnuts, egg yolks, tomatoes, potatoes, oatmeal, liver, cheese and meats.

Diet with high glycemic index may exacerbate acne as shown in studies. Saturated fatty acids, high glycemic index foods and abnormal carbohydrate metabolism are reported to aggravate acne. Milk is stated to exacerbate comedones via hormonal pathway.

Limitations in our study are: low number of study population, not having noted detailed dietary habits and smoking habits. On the other hand, these parameters should be given as treatment to note final effects in comparison to control group.

In conclusion, our study marks the importance of diet in patients with acne. In our patients group, depletion of foods with high glycemic index as fast foods are clearly important. We offer supportive dietary measures with foods rich in vitamins A and E and zinc in the acne prophylaxis and treatment. Supportive treatment with these vitamins and zinc in severe acne may lead to satisfactory results. Further studies with larger patient groups are required to understand the role of these vitamins and minerals in acne.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References