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Oxidant: Antioxidant Status In Obese Adolescent Females with Acne Vulgaris

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Running title: Oxidative stress in Obese female with acne.

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Abstract: background & objectives :Acne vulgaris is a distressing skin condition

which can carry with it significant psychological disability. Oxidant/antioxidant imbalance leads to increased free radicals production that causes many diseases. Some nutrients, along with systemic oxidative stress have been implicated in acne vulgaris. The goal of the present study is to assess oxidant and antioxidant status in correlation with the incidence of acne vulgaris in adolescent obese females. Methods: A total of 60 adolescent females age (16-22 years) divided into four groups (15 each) as following: The first including obese females with acne; the second including obese without acne ; the third including nonobese with acne and the fourth including nonobese without acne. Fasting serum Malondialdehyde (MDA), β -carotene, vitamins A, E ,C were measured, in addition platelet monoamineoxidase (MAO), and erythrocyte catechol-o-methyltransferase (COMT) activities were determined . Results :It was found that, serum MDA was statistically significant decreased in obese and nonobese with acne as compared with without acne ($p < 0.05, < 0.001$) respectively. In contrast the levels of β -carotene, vitamins A,E and C and the activity of MAO were significantly decreased in obese and non obese with acne versus obese and nonobese without acne. Interpretation: in obese subjects increased fat content facialte free radical production and lipid peroxidation as indicated by increased MDA level which scavenged by antioxidant vitamins . The decreased activity of MAO may be inhibited by free radicals that causes psychological depression in adolescent . While there was non significant changes in the activity of COMT among the studied groups. Conclusion . The nutritional factors, a weakened antioxidant defense system may interplay to increase the risk of psychological sequelae in acne vulgaris.

Keywords: Oxidative stress, Acne vulgaris , Obese female, adolesecent.

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Abstract

background & objectives :Acne vulgaris is a distressing skin condition which can carry with it significant psychological disability. Oxidant/antioxidant imbalance leads to increased free radicals production that causes many diseases. .Some nutrients, along with systemic oxidative stress have been implicated in acne vulgaris. The goal of the present study is to assess oxidant and antioxidant status in correlation with the incidence of acne vulgaris in adolescent obese females.

Methods: A total of 60 adolescent females age (16-22 years) divided into four groups (15 each) as following: The first including obese females with acne; the second including obese without acne ; the third including nonobese with acne and the fourth including nonobese without acne. Fasting serum Malondialdehyde (MDA), β -carotene, vitamins A, E ,C were measured, in addition platelet monoamineoxidase (MAO), and erythrocyte catechol-o-methyltransferase (COMT) activities were determined .

Results :It was found that, serum MDA was statistically significant decreased in obese and nonobese with acne as compared with without acne ($p < 0.05, < 0.001$) respectively. In contrast the levels of β -carotene, vitamins A,E and C and the activity of MAO were significantly decreased in obese and non obese with acne versus obese and nonobese without acne.

Interpretation: in obese subjects increased fat content facialte free radical production and lipid peroxidation as indicated by increased MDA level which scavenged by antioxidant vitamins . The decreased activity of MAO may be inhibited by free radicals that causes psychological depression in adolescent . While there was non significant changes in the activity of COMT among the studied groups.

Conclusion . The nutritional factors, a weakened antioxidant defense system may interplay to increase the risk of psychological sequelae in acne vulgaris.

Key words: Oxidative stress, Acne vulgaris , Obese female, adolesecent.

Introduction

Acne vulgaris is a distressing skin condition which can carry with it significant psychological disability. Patients with acne are more likely to experience anger and are at increased risk of depression, anxiety, suicidal ideation. Certain nutrients which have been implicated as influencing the pathophysiology of acne have also been identified as important mediators of human cognition, behavior and emotions (1). Zinc, folic acid, selenium, chromium and ω -3 fatty acids are all examples of nutrients which have been shown to influence depression, anger and/or anxiety. These same nutrients, along with systemic oxidative stress have been implicated in acne vulgaris. may interplay to increase the risk of psychological sequelae in acne vulgaris (2).

Lipid peroxidation and the value of systemic antioxidants have been reported to be of value in acne (3). Important antioxidant enzymes, including glutathione peroxidase and super oxide dismutase have been reported to be significantly lower in the blood of acne patients (4). Higher levels of oxidative stress have been documented in social anxiety a condition more common in those with acne. While depression and anxiety can certainly influence oxidative stress, the oxidative stress theory of depression/anxiety also dictates that some of the symptoms may be directly mediated by free radical damage to lipid components of the central nervous system (5). In keeping with this theory, experimental data shows anxiolytic and antidepressant effects of antioxidant rich polyphenols green tea, turmeric and berries (6).

Ascorbate has a great reducing potential and reacts with many reactive oxygen and nitrogen species in vitro. Ascorbate effectively quenches singlet oxygen, superoxide, hydroxyl and water soluble peroxy radicals, and hypochlorous acid (7). The reaction between ascorbate and those reactive species generates a one electron oxidation product (ascorbyl radical) that can be oxidized further to result in dehydroascorbate. Cellular reducing molecules (e.g., nicotinamide adenine dinucleotide reduced form [NADH], nicotinamide adenine dinucleotide phosphate reduced form [NADPH], and glutathione) can reversibly reduce one- and two electron oxidation products to ultimately regenerate

ascorbate (8). In addition, ascorbate can recycle the vitamin E radical (tocopheroxyl), thereby forming the ascorbyl radical, which can be regenerated (9).

Monoamines (MAOs) are integral proteins of outer mitochondrial membranes in various cells (both neuronal and non-neuronal in the CNS and peripheral organs) where they oxidatively deaminate biogenic and xenobiotic amines (10). In the CNS they play a pathophysiological role by indirectly generating cytotoxic free radicals during aging and in neurodegenerative diseases.

The therapeutic potential of selective reversible MAO inhibitors lies in their ability not only to increase the biological half-life of monoamine transmitters (symptomatic effects) but also to slow down the process of neurodegeneration (neuroprotective effects) (12). Monoamine oxidase B (MAO) and catechol-0-methyltransferase (COMT) are pivotal enzymes in the catabolism of several neurotransmitters. MAO-B and COMT activity can be reliably measured in human platelets and erythrocytes, respectively (13).

This study aimed to assess the oxidative stress status in obese adolescent females with acne and its correlation with psychological depression during this period

SUBJECTS AND METHODS

This study was conducted on a total 60 adolescent females their age between 16-22 years (mean, 18.5 years) divided into 4 groups (each 15) as following. The first including obese with severe acne. The second including obese without acne, the third including non obese with acne and the fourth including non obese without acne.

Mild acne was defined as up to 10 lesions, moderate acne between 11 to 25 lesions, and severe acne more than 25 lesions, this is according to International Consensus conference on acne classification system. Obesity involving body mass index (BMI) > 27 kg/m², waist to hip ratio (WHR) > 0.8 according to Garrow and Webster (15).

All cases were selected from outpatient of Dermatology unit of the University Hospital King Abdulaziz University (Jeddah, SA). They were submitted to clinical examination (non-diabetic, free from any neuroendocrine disorders, no history of hypertension, liver, kidney or heart disease) and not under any treatment.

10 ml of fasting blood samples were withdrawn from all cases divided into three portions, the first for serum separation, the second for platelets separation and the third for erythrocyte separation. Serum Malondialdehyde was determined according to Satoh, (16). Serum vitamin A, E and β -carotene levels were determined by HPLC according to Lee (17) and vitamin C according to MC Cormick and wright (18). Platelet collection and determination of MAO activity were carried out by fluorimetric method of Mc Entire (19). Platelet MAO activity was calculated in terms of nmol/h/mg protein. COMT activity in erythrocytes was determined fluorimetric according to described method of Axerod and Tomchicr (20). COMT activity in erythrocytes was calculated in terms of pmol/h/mg hemoglobin.

Statistical analysis

The results were expressed as mean \pm SD. Statistical comparisons were made using the student *t* test, nonparametric chi square, and kruskal-wallis tests. *P* less than 0.05 was accepted as the significance level.

Results

The Sociodemographic data in table (1) revealed that , the age of the adolescent females selected in this study between 16 to 22 years. There was a significant elevation in body mass index (BMI) in obese female with or without acne as compared with non obese with or without acne ($p<0.05$).

Serum malondialdehyde (MDA) and antioxidant vitamins levels were presented in table (2). It was found that , Serum MDA level was highly significant elevated in obese female with acne versus obese without acne ($p<0.001$) , in nonobese with acne versus nonobese without acne ($p<0.05$) and in obese with acne versus nonobese with acne ($p<0.001$).

In contrast , the levels of serum b-carotene, vitamins A, E and C were statistically significant decreased in obese with acne versus obese without acne ($p<0.05, <0.01, <0.01$ and <0.001) respectively. and decreased in nonobese with acne versus nonobese without acne ($p<0.001, <0.01, <0.01$ and 0.01) respectively. Comparing obese with acne versus nonobese with acne, it was revealed that, there was a significant decrease in vitamin c level in obese female ($p<0.05$) and no changes in the levels of other vitamins.

Table (3) reveled that the activity of platelet MAO was statistically significant decreased in obese with acne versus obese without acne ($p<0.001$) and in nonobese with acne versus nonobese without acne ($p<0.05$).however the decrease in obese is more than nonobese .The activity of erythrocyte COMT showed nonsignificant changes among obese with or without acne versus nonobese with or without acne.

A positive correlation between the elevation in MDA level and the decreased the activity of MAO ($r = 0.61$).

Discussion

Lipid peroxidation and the value of systemic antioxidants have been reported to be of value in acne for decades . Only recently have investigators used sophisticated techniques to establish that not only is oxidative stress and lipid per oxidation a local issue these patients are under systemic oxidative stress . Antioxidant enzymes, including glutathione peroxidase and super oxide dismutase have been reported to be significantly lower in the blood of acne patients . Higher levels of oxidative stress have been documented in social anxiety (21) a condition more common in those with acne. While depression and anxiety can certainly influence oxidative stress, the oxidative stress theory of depression/anxiety also dictates that some of the symptoms may be directly mediated by free radical damage to lipid components of the central nervous system (22).

The goal of this study is to interpreted the causes of depression in adolescent females in correlation to the acne vulgaris.

It was found that, Serum MDA level was significantly elevated while the levels of β -carotene, vitamins A,E and C were significantly decreased in obese with acne versus obese without acne and in nonobese with acne versus nonobese without acne.

Recently it was reported that in 100 patients with acne (vs. matched controls) the systemic levels of vitamins A and E were much lower overall, and the lower the levels of vitamins A and E, the more severe the acne (23). As with most chronic medical conditions characterized by both oxidative stress and inflammation, it is likely that the blood levels of antioxidants are used up more readily in those with acne because there is a greater demand to deal with free radicals. In the context of the psychological sequelae in acne, we make reference to the oxidative stressacne connection because it has been shown that depressive symptoms are independently correlated with oxidative stress (24).

We suspect that in acne increased risk of psychological sequelae would be low levels of certain nutrients which can further increase that risk. Prospective trials which evaluate mood, emotions and yet are also inclusive of nutritional assessments and related blood

markers would help to shed light on the complex relationships between diet, the risk of acne and its individual mental health consequences.

Ascorbate, not tocopherol, normalizes epidermal lipid profiles (in particular glucosphingolipids and ceramides) in reconstructed epidermis. Until recently, its instability in cosmetic forms has limited its use. Ascorbic acid is commonly used in a number of cosmetic products claiming to protect the skin from environmental insults and photo aging. However, in many, but not all cases, ascorbic acid is present at a low concentration, is not stable, or is not delivered efficiently to the skin. In addition, vitamin E exhibits scavenging activities against a wide spectrum of free radicals including singlet oxygen, superoxide, and hydroxyl radicals. In vitro, tocotrienol scavenges peroxy radicals and is recycled more efficiently than tocopherol (25)

It is our contention that nutritional factors may be setting the stage for a higher risk of depression, anxiety and other emotional symptoms related to acne. It is likely that a significant group of teenagers and young adults are already on the pathway to an increased risk of psychological impairment before the acne even becomes evident. Emerging studies with matched controls shows that acne patients are more likely to consume carbohydrates, fast foods, soft drinks and sweets (26) .

Regardless of the controversial impact such dietary choices may have on clinical acne, it is possible that nutritional voids in subgroups of acne may influence the emotional realm. Research also shows that the psychological sequelae in acne can be long term, and in some cases, resistant even after clinical improvement in acne . To test this hypothesis it would be interesting to evaluate young children for the signs of depression and anxiety and later determine who might go on to experience acne. Investigations of this nature have already determined that depressive and anxious symptoms in early school years can predict later overweight and obesity when followed up (27).

The monoamine oxidases are flavoenzymes play an important role in the catabolism of biogenic and xenobiotic by oxidative deamination both In the human brain, MAO-A preferentially deaminates adrenaline, MAO-B and COMT activity in humans can be reliably measured in peripheral tissues easily accessible for sampling. MAO activity in platelets has been shown to be an accurate model of neuronal MAO activity (28).

The activity of MAO was significantly decreased in obese females with acne versus without acne , this inhibition increased monoamines levels in those subjects that causes psychological depression. However non significant changes was observed the activity of COMT among the studied groups. COMT in human erythrocytes reflects activity in the liver, kidney and lung. The autoxidation and monoamine oxidase (MAO)-mediated causes a continuous production of hydroxyl radical ($\bullet\text{OH}$), which is further enhanced by the presence of iron. It has been found Consequently monoamines has been shown to be a double-edged sword, because it displays antioxidant properties in relation lipid peroxidation and exhibits pro-oxidant properties by causing both generation $\bullet\text{OH}$ and oxidation of mitochondrial proteins (29).

It is recommended that body weight must be reduced and increase intake of nutrients rich in its antioxidant activity and vitamins to overcome this psychological depression period.

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Table (1): Sociodemographic characteristic of obese and nonobese females with or without acne (mean \pm SD)

| Groups Parameters | Obese | | Non obese | |
|----------------------|--------------|----------------|--------------|-----------------|
| | (with Acne) | (without Acne) | (with Acne) | (without Acne) |
| Age | | | | |
| Mean \pm SD | 18 \pm 1.3 | 20 \pm 1.9 | 17 \pm 1.4 | 18 \pm 1.62 |
| t ₁ (p) | N.S | _____ | N.S | _____ |
| t ₂ (p) | N.S | N.S | _____ | _____ |
| BMI | | | | |
| Mean \pm SD | 30 \pm 2.1 | 29 \pm 1.7 | 26 \pm 2.1 | 25 \pm 1.9 |
| t ₁ (p) | N.S | _____ | N.S | _____ |
| t ₂ (p) | 1.3 (p<0.05) | p<0.05 | _____ | _____ |

t₁ (p): t test and significance between obese female with acne Vs without acne & nonobese with acne Vs without acne

t₂ (p): t test and significance between obese female with acne or without acne Vs non obese with or without acne.

N.s: non significant