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Elevated serum levels of 8-hydroxy-2-deoxyguanosine in mild-moderate acne vulgaris

Selma Korkmaz[1], Eray Ozgun[2]

[1] *Suleyman Demirel University, Faculty of Medicine ,Department of Dermatology, Isparta, Turkey*
[2] *Trakya University, Faculty of Medicine ,Department of Biochemistry, Edirne, Turkey*

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Abstract

Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous unit. Although some mechanisms have been suggested in the etiopathogenesis of AV in several studies, they have not yet been clarified. This study aims to investigate the level of 8-hydroxy-2'-deoxyguanosine (8-OHdG) in acne vulgaris and its relationship with disease severity. Thirty-five patients with mild to moderate acne vulgaris and 30 healthy control participants were included in the study. The clinical severity of AV was determined by using the global acne score (GAS). The 8-OHdG level was measured by an enzyme-linked immunosorbent assay (ELISA). Total oxidant status (TOS), total antioxidant status (TAS), and oxidative stress index (OSI) scores were measured as oxidative stress markers. Levels of 8-OHdG were higher in AV compared to healthy controls ($P = 0.036$). A strong positive correlation between GAS and 8-OHdG was found in those with AV ($p = 0.007$, $r = 0.444$). And while TAS and TOS levels were significantly lower in AV patients, OSI levels were found to be significantly higher compared to healthy controls ($p < 0.001$, $p < 0.001$, and $p = 0.036$, respectively). The level of serum 8-OHdG is elevated in mild to moderate AV and this elevation become evident with the increase of disease activity.

Keywords: Acne vulgaris, oxidative stress, 8-Hydroxy-2'-Deoxyguanosine

Introduction

Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous unit. Ductal hyperkeratinization, increased secretion of sebum, and colonization of Propionibacterium Acnes (P. acnes) around the pilosebaceous gland are among the factors responsible for the etiopathogenesis of acne vulgaris [1-3]. Studies have also showed that oxidative stress contributes to the pathogenesis and progression of AV, and reactive oxygen species (ROS) and lipid peroxidation (LPO) contribute to the initiation and continuation of epithelial inflammation in the pilosebaceous unit. Additionally, it is believed that oxidants resulting from lipid peroxidation contribute to hyperkeratinization and thus increase comedogenity [4-9].

8-OHdG is an oxidative stress product that occurs after ROS lead to DNA damage [10]. Although it is widely used as an oxidative stress biomarker, until now 8-OHdG levels in AV patients had not been evaluated. In this study, we aimed to evaluate 8-OHdG levels in mild to moderate AV patients.

Material and Methods

The study was initiated upon obtaining approval from the Ethics Committee. Informed consent was obtained from all subjects prior to the study.

***Coresponding Author:** Selma Korkmaz, Suleyman Demirel University, Faculty of Medicine ,Department of Dermatology, 32260, Isparta, Turkey,
E-mail: selmakorkmaz35@gmail.com

Patient group and study protocol

The study included 35 patients (mean age 20.8±2.2 years; 27 females, 8 male) with mild and moderate severity acne vulgaris, aged from 18-30 years applying to the Skin and Venereal Diseases Clinic and 30 healthy volunteers (mean age 23.5±3.6 years; 17 female, 13 male). Apart from acne, patients with dermatological diseases, cigarette/alcohol use, systemic disease like cardiac, renal or hepatic disease, diabetes mellitus, diseases causing inflammation (acute infectious diseases, malignancy, inflammatory rheumatic diseases), pregnancy and any medication use within the previous month were not included in the assessment. Patient gender and ages were recorded. Dermatological examination was performed by a single dermatologist and the Global Acne Score (GAS) was used to calculate acne severity [11]. Those with GAS score above 30 were not included in the study. Those with GAS of 1-18 were accepted as mild severity, while those with GAS 19-30 were accepted as moderate severity.

Biochemical Analyses

Venous blood samples were taken in the morning and centrifuged 3000 g for 5 minutes and serum was separated. Sera were kept at -70 °C for subsequent biochemical analyses. All chemicals were purchased from Sigma-Aldrich Co. (St. Louis, MO, USA) or Merck (Darmstadt, Germany). All reagents were of analytical grade.

Measurements of 8-OHdG levels

Serum 8-OHdG levels were measured by using commercial

available ELISA kit (Elabscience, Wuhan, China) according to its original method.

Measurements of serum TAS levels

Serum TAS levels were measured spectrophotometrically according to Erel's method (TAS method) by using Trolox as standard. Results were expressed as mmol Trolox Eq/l [12].

Measurement of serum TOS levels

Serum TOS levels were measured spectrophotometrically according to Erel's method (TOS method) by using hydrogen peroxide as standard. Results were expressed as µmol H2O2 Eq/l [13].

OSI calculation

Oxidative stress index calculated by following formula: sOSI=[TOS (mmol H2O2 Equiv./l) / TAS (mmol Trolox Equiv./L)] X100 [14].

Statistical Analysis

Shapiro-Wilk test was used for checking the normal distribution of continuous variables. For comparison of 2 independent groups with normally distributed variables, the student t test was used (age, TAS, TOS); for those with non-normal distribution the Mann-Whitney U test was used. Comparison of categorical data used the chi-square test. The correlation between disease severity in AV patients with 8-OHdG and GAS was assessed with Spearman correlation analysis. Statistical analysis was done by the SPSS for Windows version 22.0 program and p<0.05 was accepted as statistically significant.

Results

The age and gender of the study groups were similar (p>0.05). The 8-OHdG levels in those with AV were found to be higher compared to the healthy control group (P=0.036). Of AV patients 12 had moderate acne while 23 had mild acne. In AV patients mean value of GAS was 16. In AV patients there was a strong positive correlation identified between GAS and 8-OHdG (p=0.007, r=0.444; Figure 1).

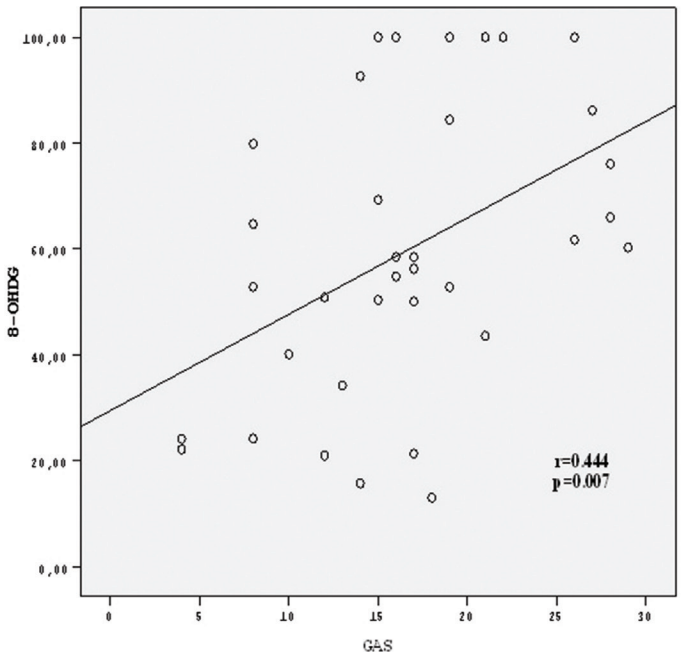

Figure 1. Correlation between GAS and 8-OHdG in acne vulgaris

TAS and TOS levels in AV cases were identified to be significantly lower compared to healthy volunteers (P<0.001, for each). However, OSI levels in AV cases were found to be significantly higher compared to healthy volunteers (p=0.036; Table 1). In AV cases there was no significant correlation between GAS and TAS, TOS and OSI (p>0.05). Additionally, there was no significant correlation between for 8-OHdG levels with TAS, TOS and OSI levels (p>0.05).

Table 1. Demographic and laboratory characteristics of groups

	Healthy Control	Acne Group	P
Age (year)	21.90±2.99	20.77±2.17	0.083
Gender (F/M)	17/13	27/8	0.111
8-OhDG (ng/ml)	41.75±22.60	58.46±44.29	0.036
TOS* (µmol H2O2 Equiv./L)	10.17±1.43	8.60±1.47	<0.001
TAS* (mmol Trolox Equiv./L)	0.71±0.11	0.53±0.09	<0.001
OSI	1.37±0.40	1.59±0.44	0.036

Data in which non-parametric tests were used and expressed as median±IQR and *mean±SS; 8-hydroxy-2'-Deoxyguanosine, 8-OHdG, Total Antioxidant Status, TAS; Total Oxidant Status, TOS; Oxidative Stress Index, OSI

Discussion

This study found that in cases with mild and moderate acne, the serum 8-OHdG levels increased and showed a positive correlation with GAS.

Many reactions trigger a physiological formation of ROS. In a healthy organism, the formation and removal of ROS is balanced. Some enzymes, known as antioxidants, suppress the formation of free radicals, thus reducing their activity and protecting the organism. However, when these free radicals are produced in an uncontrolled fashion, they damage basic cellular biomolecules like DNA, lipids, and proteins, disrupting the structure and functions of cells [15].

It is thought that oxidative stress plays a role in acne vulgaris [7,16]. because it contributes to the formation of free radicals, which in turn damage molecular structures. Al-Shobaili's study [17] found that, compared to healthy individuals, AV patients had higher serum malondialdehyde (MDA) levels with lower levels of antioxidant enzymes like superoxide dismutase (SOD), catalase, and total antioxidant capacity. Another study showed that AV patients had high levels of the oxidative stress markers, MDA and nitric oxide [16]. A study by Sarıcı et al. [6] found MDA and xanthine oxidase (XO) were significantly higher, and SOD and catalase levels were significantly low in the control group, which indicated that disruption of the antioxidant system, especially, may play a role in the pathogenesis of acne vulgaris. Arıcan et al. [2] found that the oxidative stress parameters of SOD and MDA levels were significantly higher in AV individuals. This study evaluated both the antioxidant levels of TAS, as well as the oxidant levels of TOS and OSI. In AV patients, a reduction was observed in both TAS and TOS scores, with an increased OSI score identified. This finding leads to the consideration that, in the early period of the disease, the reduction in antioxidants used to balance oxidants is not sufficient to prevent development of oxidative stress.

The most important oxidative stress marker showing ROS

damage to DNA is 8-OHdG. When DNA damage occurs due to oxidative stress, the DNA repair mechanisms come into play and antioxidant enzymes protect the cell from free oxygen radicals [18,19]. 8-OHdG levels were not assessed in AV. In this study the 8-OHdG levels were high in AV individuals and as disease severity increased, this rising became more defined. Considering these results, it is believed that DNA damage begins even in the early period of the disease. Preventing progression of the disease in the comedonal period may contribute to preventing DNA damage. A study by Georgala et al. [20] identified that isotretinoin used for acne vulgaris treatment increased 8-OHdG levels. In the future, development of reducing of 8-OHdG levels treatments may provide hope for new treatment alternatives.

In this study, there was no correlation identified between 8-OHdG and TAS, TOS and OSI levels. This situation may be related to the fact that oxidant radicals correlated with DNA damage were not studied. Additionally, other limiting factors were the cross-sectional nature of the study and the relatively low number of participants.

Conclusion

In conclusion, the level of the DNA damage marker of 8-OHdG was increased in mild and moderate AV. This increase became more pronounced as disease activity increased. We believe that future studies on this topic may contribute to understanding the etiopathogenesis of the disease and indicate new treatment targets.

Competing interests
The authors declare that they have no competing interest.

Financial Disclosure
The financial support for this study was provided by the investigators themselves.

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