ORIGINAL ARTICLE
The Role of Alpha Diol G in ACNE Vulgaris in Females

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ABSTRACT

Background: Acne vulgaris in adult women is a chronic inflammatory disorder of pilosebaceous unit with many relapse cases. It commonly has psychological and social impact that interfere with the quality of life of many patients. Androgenic hormones have a very important role in the pathogenesis of acne. The aim of the study was to establish the relation between 3-alpha diol G levels and acne in female patients with normal androgenic status without menstrual dysfunctions in comparison with controls. **Methods:** This case control study was carried out at the outpatient clinics of Dermatology, Venereology and Andrology Department, Faculty of Medicine, Zagazig University. Levels of serum 3-alpha diol G were evaluated by ELISA. **Results:** There was statistical significance increase in the 3-alpha diol G level. **Conclusions:** The measurement of serum 3-alpha diol G in acne female patients as a diagnostic routine in cases of acne female patients without hyperandrogenism or menstrual dysfunctions is advisable.

Key words: Alpha DiolG ; Acne ; Females

INTRODUCTION

Acne vulgaris is a very common inflammatory disorder of pilosebaceous apparatus characterized by inflammatory (papules, pustules, nodules) and noninflammatory lesions (open and closed comedones) [1].

Acne vulgaris has a very complex physiological pathogenesis include: hormonally-stimulated sebum production, abnormal keratinization of the pilosebaceous duct and an inflammatory immune response to Propionibacterium acnes. In addition, diet, genetics and oxidative stress have an important role in the pathogenesis of acne[2]. In women, when ovulation is established, levels of estrogen affect acne improvement. After this period some patients still have acne lesions. Hyperandrogenism plays a very important role in the pathogenesis of acne. Androgens affect several functions and androgen receptors may have an important role in the development of the hyperandrogenism signs, which may be associated with the appearance of acne vulgaris[3].

The adrenal glands and the gonads produce many of the circulating androgens in females. Androgens also may be produced locally by the sebaceous gland from the hormones dehydroepiandrosterone (DHEA) , androstenedione. Testosterone (T) and dihydrotestosterone (DHT) are the main androgens which interact with the receptors that located in the basal layer of the sebaceous gland which called androgen receptors and in the keratinocytes which located in the outer root sheath of the hair follicle[4].

Testosterone and dihydrotestosterone mainly produced by the action of the enzymes 5 alpha-reductase 1 and 2 which are located in the peripheral tissues. Androgens, especially dihydrotestosterone, make a complexes with androgen nuclear receptors which interact with the DNA within the sebaceous cell nucleus for regulation the genes that involved in cell growth and regulation of lipid production[5].

The peripheral conversion of testosterone and androstenedione to DHT are mainly prevalent due to the action of 5 alpha-reductase enzyme or due to hypersensitivity of

the hormone receptors in the keratinocytes and sebocytes. The 5 alpha-reductase which act in the infrainfundibular region encourage the suspicion of androgens may influence the follicular keratinization[6].

3 alpha-androstanediol glucuronide (3-alpha diol G) is the main metabolite of 5 alpha-reductase which indirectly reflects the peripheral activity of the 5 alpha-reductase enzyme. It is considered a marker of the androgens in the pilosebaceous gland[7].

METHODS

This case control study was carried out at the outpatient clinics of Dermatology, Venereology and Andrology Department, Faculty of Medicine, Zagazig University Hospitals in the period from April till September 2017, after approval of The Institutional Review Board (IRB), an informed consent was taken from all the patients.

Apparently sixty healthy individuals, age and sex matched with the patients (sixty) were taken as control.

The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Acne vulgaris females, Age: ranging from (15 - 28 years).

Exclusion criteria: Females take contraceptive pills or any other hormonal treatment, those undergoing anti-androgen therapy, Females with menstrual dysfunctions, Females with polycystic ovary diagnosed by ultrasonography, Patients with increased serum levels of testestrone and dihydrotesterone hormones.

Methods:

All patients were subjected to full history, general examination and dermatological examination to assess acne grading by Adityan classification [8]. Each type of lesion is given a value depending on severity: no lesions =0, comedones = 1, papules = 2, pustules = 3 and nodules = 4. The score for each area (Local score) is calculated using the formula: Local score = Factor $\times$ Grade (0-4). The global score is the sum of local scores, and acne severity was graded using the global score. A score of 1-18 is considered mild; 19-30, moderate; 31-38, severe; and >39, very severe. Factor is calculated as shown in **Table (5).**

3 ml of venous blood were collected by vein puncture under complete aseptic precaution from both patients and control divided into two tubes. 1st tube: 1 ml of blood was added to anticoagulant tubes for measurement testestrone and dihydrotesterone. 2nd tube: 2 ml of blood were left to clot at 4°C in a sterile, clean, dry tube. After clotting, the samples were centrifuged for 10 minutes at 5000 rpm. Serum was separated and stored immediately at -20°C for measurement of 3-alpha diol G.

Levels of serum 3-alpha diol G were evaluated through an enzymatic immunoassay method (Androstanediol Glucuronide ELISA Kit) .

Statistical analysis:

The collected data were computerized and statistically analysed using SPSS program (Statistical Package for Social Science) version 18.0.

Qualitative data were represented as frequencies and relative percentages.

Chi square test was used to calculate difference between qualitative variables in different groups.

Mann Whitney test was used to calculate differences between quantitative variables in 2 groups.

Pearson correlation coefficient used to calculate correlation between quantitative variables.

We consider (+) sign as indication for direct correlation i.e. increase frequency of independent lead to increase frequency of dependent & (-) sign as indication for inverse correlation i.e. increase frequency of independent lead to decrease frequency of dependent, also we consider values near to 1 as strong correlation & values near 0 as weak correlation.

The significance Level for all above mentioned statistical tests done.

The threshold of significance is fixed at 5% level (P-value)

*P value of >0.05 indicates non-significant results.

*P value of <0.05 indicates significant results.

*P value of <0.01 indicates highly significant results.

RESULT

This study was conducted on sixty females patients with acne vulgaris, their age ranged from 15 to 28 years with mean 20.10 ± 3.17. Sixty healthy age matched females were taken as control their age range from 16 to 30 years **Table (1).** Using global acne grading system, 33patients (55%) the score was (19-30) grade II, while in 27 patients (45%) the score was (31-38) grade III **Table (2).** In present study 32 patients (53.3%) had elevated serum level of 3-alpha diol G (9.3-39) while in 28 pts (46.7%) the level was within normal range (0.5-4.2) ng/ml. All 60 control females (100%) had 3-alpha diol G level within normal range (0.22-4.64). There was statistically significance difference between patients and control groups (p<0.001) **Table (3).** There was statistical significance increase in the 3-alpha diol G level among cases with past history of acne (p=0.02) and those with diffuse hair loss (p=0.04) **Table (4).**

Table 1.Demographic data of patients and control:

Variable	Cases (n=60)	Control (n=60)	t	P
Age : (year) • Mean ± SD • Median • Range	20.10 ± 3.17 19.5 15 – 28	22.09 ± 3.23 20 16 – 30	0.43	0.67 NS

Table 2. Acne grading of patients:

Variable	No	%
Grade: • II • III	33 27	55 45

Table 3. Normal and elevated 3-alpha diol G levels in cases and control:

Variable	Cases (n=60)	Control (n=60)	MW	P
3α-diol G: (ng/ml)	32(53.3%) (9.3-39) 28(46.7%) (0.5-4.2)	60(100%) 0(0%) (0.22-4.64)	χ^2 **43.46**	**<0.001****

**Normal 0.22-4.64 ng/ml**
Elevated > 4.64 ng/ml

Table 4. Correlation between clinical data and 3-alpha diol G level:

Elevated 3α-diol G level (n=32)		Normal 3α-diol G level (n=28)		χ^2	P
No	%	No	%		
31 1	96.9 3.1	27 1	96.4 3.6	0.01	0.92 NS
26 6	81.2 18.8	28 0	100 0	5.83	0.02*
26 6	81.2 18.8	27 1	96.4 3.6	3.34	0.04*

Table 5. The global acne grading system regarding to the location of acne.

Location	Factor
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest and upper back	3
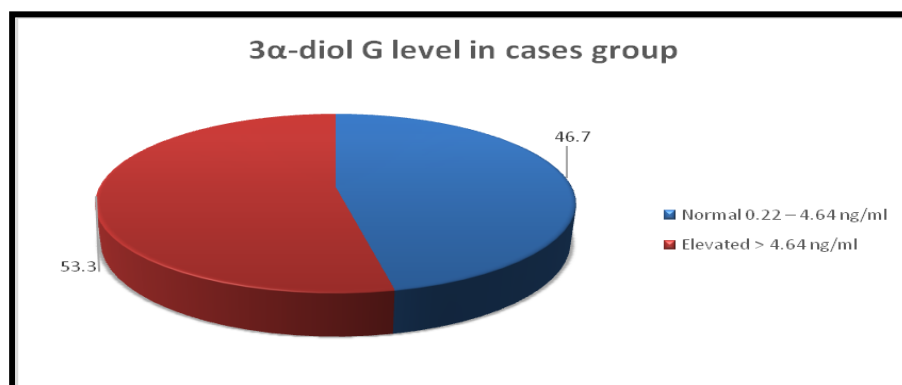
Figure (1): 3α-diol G level among cases

DISCUSSION

Acne vulgaris is a common chronic inflammatory disease of pilosebaceous apparatus. Acne can be a potential source of emotional stress and even psychiatric disorder because it is very common during adolescence [9]. The results showed a statistically significant increase of 3-alpha diol G level among patients of acne vulgaris compare to controls (p<0.001). Our result was in agreement with Cunha et al; [7]. study which investigated 26 patients 25 with grade II acne and one with grade III. The results showed a statistically significant increase of 3-alpha diol G between patients and control group which suggested that 3-alpha diol G has a role in acne.

Our findings support the results of Voegeli et al; [10] study which investigated 16 patients with acne and 16 healthy controls for serum 3-alpha diol G level, the results showed statistically significance increase of 3 alpha-diol G level in acne patients (p< 0.05).

On the opposite side in study carried by Toscano et al; [11] on 90 patients with mild to severe degree of acne, 52 patients with idiopathic hirsutism and 24 healthy control,

the serum level of 3-alpha diol G level was evaluated. The results revealed that all patients with hirsutism had increased level of 3 alpha-diol G whereas patients with acne had normal levels In the present study acne was classified to grade II and grade III. By comparing serum 3-alpha diol G level in the patients in relation to degree of acne, no statistically significant correlation was found between 3-alpha diol G level and degree of acne (p=0.47).

This result was in agreement with Cunha et al; [7] study which reported no significant difference correlation between 3-alpha diol G level and degree of acne (p=0.33).

In current study statistically significance was detected between serum level of 3-alpha diol G and diffuse hair loss (female pattern androgenic alopecia) which is androgen dependent. As all cases were normal androgen, so the peripheral response to testosterone is more important than its serum level.

Regarding to the age, the present study reveals that there was no significant correlation between the age and the mean 3-alpha diol G level among acne patients

(p=0.56). The same result was detected by Cunha et al [7] study (p=0.53).

It is considered as a preliminary study. It is an introduction for a future study, which will include a greater number of acne patients in an attempt to confirm the results here which obtained and for establish the measurement of the metabolite 3 alpha-diol G as a diagnostic routine in cases of acne in adult women without hyperandrogenism or menstrual dysfunctions.

CONCLUSION

The measurement of serum 3-alpha diol G in acne female patients as a diagnostic routine in cases of acne female patients without hyperandrogenism or menstrual dysfunctions is advisable.

Therefore, for most acne females with elevated serum level of 3-alpha diol G, the use of antiandrogenic drugs that block 5α-reductase action is recommended.

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