Biochemical Evaluation of Testosterone Levels Pre- and Post-Treatment in Individuals with Acne Vulgaris: An Analysis using A Case-Control Study Design

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ABSTRACT

Objective: The objective of this study was the biochemical assessment of the levels of free testosterones in women presenting with acne vulgaris.

Methods: This study was carried out at a tertiary care hospital in Peshawar-KP, Pakistan, from January to December 2022. The ethical approval was obtained from the institutional review board. Of 120 enrolled patients with acne vulgaris within a year, they were classified I-IV according to Pillsbury's scale. 100 participants attended a follow-up, while the rest were lost to follow-up. Data from 90 patients was entered into SPSS version 22 and analyzed. 0.05 value was considered significant statistically.

Results: The study found mean free testosterone levels of 1.80 ± 1.00 pg/mL before and 1.50 ± 0.84 pg/mL after treatment, showing statistical significance (p = 0.006). For grade III patients, pre-treatment levels were 1.40 ± 1.22 pg/mL, post-treatment were 1.0 ± 0.66 pg/mL, with no statistical significance. In grade IV patients, pre-treatment levels were 1.62 ± 1.11 pg/mL, post-treatment were 1.34 ± 0.80 pg/mL, showing statistical significance (p = 0.007).

Conclusion: As Acne vulgaris and free testosterone are mutually associated, it should be needed to measure free testosterone levels in subjects reporting with acne vulgaris, particularly in cluster of 16–35 years of age. The anti-androgen treated and treatment-resistant cases might be designated in cases with raised free testosterone levels.

Keywords: Acne vulgaris, inflammatory disease, Testosterones, Androgens.

Introduction

Acne vulgaris is a most common skin disease affecting human and which is treated most commonly by the physicians.[1] Its incidence is more common in female gender than in male. The prevalence is around 15% in all age groups.[2,3] This chronic, inflammatory disease of the pilo-sebaceous unit results from numerous reasons including inflammation, upsurge production of the sebum, induced levels of androgen, transformed keratinization and bacterial annexation of hair follicle on facial area, neck, back and chest.[4]

Of all the hormones, androgens are supposed to be the powerful hormone causing acne-genesis. The major androgen hormone that intermingle with androgenic receptors are testosterone and dihydrocortisone.[5] The human skin is a most favorable target for testosterone which causes major metabolic processes in the endothelium of sebaceous gland. Amplification and overstimulation of this gland causes overproduction of sebum in addition with slothful exfoliation process which causes blockage of pores and onset of acne.[4] Other reasons that contribute towards the onset of acne may include like poor hygiene, dietary habits, exposure to sun light, stress and most probably genetic reasons. Papules, seborrhea, pustules, comedones are the clinically characteristics of acne vulgaris, nodules and scars.[6] Inflammatory acne can results when the contents of comedones are ruptured into the dermis.[7] This disease can afflicts the majority of the adolescents and a large number of adult community. The adult population can be grouped as "persistent" which occurs particularly in women whereas in boys, acne fades after puberty period. Some cases of delayed commencement of acne (>25 years) are also reported.[5] As no local data was available regarding the level of free testosterone in acne patients in Peshawar, the rational of this study was the biochemical assessment of the level of free testosterones before and after treatment in patients with Acne vulgaris in Peshawar, KP.

Methodology

This case control trial was conceded from January 2022 to December 2022 at a tertiary care private hospital of Peshawar. Institutional review board of the hospital approved the study. 120 patients were enrolled in the study who were reported with Acne vulgaris during the period of one year.

Female patients in an age group 16-45 with grade III and IV acne were included in the study whereas patients with confirmed cases of pituitary or thyroid, having BMI >30kg/m^2, CAD (coronary disease), DM (diabetes mellitus), CRF (chronic renal failure), pregnancy/lactation, patients on vitamin therapy were excluded from the study.

Detailed history of the study participants was taken at their first visit to OPD. During this visit, clinical examination was also done. Free testosterone levels were also recorded during their visit. Treatment was prescribed and patients were asked to come for second visit after 3 months period. All their demographics were recorded in an excel file. At follow up visit of the patients, their examination was done and testosterone levels were measured again in order to compare the levels with the one at their first visit. We used a manual kit (Biomereux, France) for the estimation of serum testosterone levels, which works on competitive ELISA principle. All the collected data was subjected to SPSS version 21 for statistical analysis. A P value of ≤0.05 was considered statistically significant.

Results

According to the results of our study, 34% (n=34) patients reported with an age 16-22, 49% (n=49) with an age 23-35 and rest of the 17% with an age 36 to 41 years. A large number of patients were presented in an age group of 23-35. The mean age of the study group was 27 years ± 5.20. The results are mentioned in table I.

In our study, we observed the mean free testosterone levels as 1.80 ± 1.00 pg/mL before treatment and 1.50 ± 0.84 pg/mL after treatment. A statistical significance was observed in these values (p = 0.006). In patients with grade III, the mean levels before starting the treatment were 1.40 ± 1.22 pg/mL and after taking the treatment were observed as 1.0 ± 0.66 pg/mL. A statistical insignificance was observed in these values. Similarly, in patients with grade IV acne, the mean levels before the onset of treatment were calculated 1.62 ± 1.11 pg/mL and

after taking the treatment were recorded as 1.34 ± 0.80 pg/mL. A statistical significance was observed in these values (p = 0.007). These results are mentioned in figure 1 and table II.

Table I: Age wise distribution of the patients.

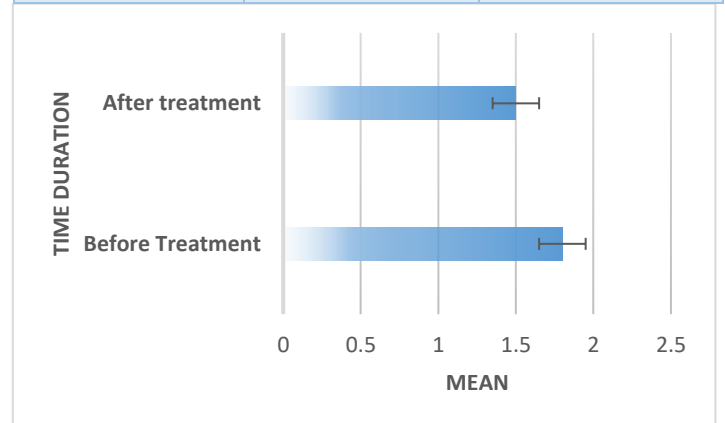| Age Group	No of Patients	Percentage
16-22	34	34
23-35	49	49
36-41	17	17
Total	100	100

Figure 1. Mean free Testosterone levels in the study group.

Table II: Mean levels of free Testosterone in grade III & grade IV patients

Patients with Grade III acne	Testosterone Levels before Treatment (pg/mL)	Testosterone Levels after Treatment (pg/mL)	P value
	1.40 ± 1.22	1.0 ± 0.66	0.08
Patients with Grade IV acne	1.62 ± 1.11	1.34 ± 0.80	0.007

According to our findings, the free testosterone levels in patients having age less than 23 years before treatment were recorded as 1.88 ± 1.00 pg/mL and 1.58 ± 1.22 pg/mL after treatment. A statistical significance was observed in the values (p=0.008). Furthermore, the levels in the patients having an age group 23-35 years were recorded before treatment as 1.38 ± 1.10 pg/mL and after treatment as 1.18 ± 0.80 pg/mL. A statistical insignificance was observed in the values (p=0.10). Our results further reported the free testosterone levels in an age group 36-41 years before and after treatment as 1.30 ± 1.00 pg/mL and 1.19 ± 0.78 pg/mL respectively. The values were insignificant statistically (p=0.11). These results are mentioned in table III.

Based on the treatment received, we designated the study participants into three groups.

One group received doxycycline and benzoyl peroxide treatment, the second group received azithromycin

and isotretinoin and the third group received doxycycline and salicylic acid. The mean free testosterone levels in various treatment duration in all these groups are mentioned in table IV.

Table III: Comparative analysis of Testosterone levels in various age groups.			
Age Groups	T levelsbefore treatment (pg/mL)	T levelsafter treatment (pg/mL)	P value
age<23 years			
Free T levels	1.88 ± 1.00	1.58 ± 1.22	0.008
Range	0.10-8.0	0.20-5.0	
Age 23-35			
Free T levels	1.38 ± 1.10	1.18 ± 0.80	0.10
Range	0.08-9.0	0.20-3.20	
Age 36-41			
Free T levels	1.30 ± 1.00	1.19 ± 0.78	0.11
Range	0.25-5.0	0.20-4.0	

Table IV: Comparative analysis of acne in various treatment stages			
Groups	T levels before treatment (pg/mL)	T levels after treatment (pg/mL)	P value
Group1 (Doxycycline/benzoyl peroxide)	1.37 ± 1.47	1.12 ± 0.7	0.04
Group 2 (Azithromycin/isotretinoin)	1.28 ± 0.95	1.33 ± 1.19	0.004
Group 3 (doxycycline/salicylic acid)	2.35 ± 1.77	1.89 ± 0.98	0.006

Discussion

Acne vulgaris is considered to be the most common cosmetic disorder presenting a sign of an underlying disease. This disease commonly occurs in young adults or teen agers. In the present clinical study, 34% patients fall within the age group of 16-22, 49% in 23-35 years, and 17 patients in an age group of 36-41 years. We documented and reported a highest number of patients in 23-35 years group. The mean age in this group was calculated as 27 years ± 5.20. These results are consistent with the statement of Rocha & Bagatin.[8]

Similarly, Rehman et al.,[9] reported a mean age of 22.43 ± 5.2 years in their findings. Number of studies suggest that women are more commonly affected by acne vulgaris than male population. The exact reason for this argument is controversial among the researchers. In a study conducted by Skroza et al[10], a peak incidence was reported in adults of age 14-19 years.

The incidence of acne is usually seen before the start of puberty, when maximum androgen is produced by the adrenal gland and when the sebaceous action is ordinarily and majorly dependent on androgenic sex hormones. Therefore, the occurrence of acne vulgaris in our study in the age group of 23-35 is steady with the idea of incidence of teenage acne.

Many studies are evident of the presence of free testosterones in patients suffering from grade III and IV acne gets declined. The findings of our study are consistent with the results of another researchers.[11-12] Free testosterones are a more steadfast reflection of its' biologic activity because of difference in the binding capability and percentage of total testosterone which are bound to serum proteins.[13, 14] It has been reported by researchers that females having acne vulgaris had possessed a relatively higher levels of testosterones in comparison with the control. Some researchers reported the levels within the normal range in patients suffering from acne vulgaris.[15, 16] According to an assumption, diffusion is the process through which, free testosterone goes inside the cellular structure of the targeted tissue. But, due to the ability of the skin to metabolize testosterone to its bioactive strong form, it is not the only androgenic stimuli receptor. It might be better to involve bigger number of patients and while in this study only 100 individuals included and this is one of the limitations of the study.

A study has shown augmented echelons of free dihydrotestosterone and free testosterone in patients reported with moderate and severe acne. In these patients, androsterone, total testosterone, dihydrotestosterone and SHBG values were insignificantly varied from those in the control

group.[17] Many studies have shown the role of androgens in the pathogenesis of acne vulgaris but the circulating levels of these hormones were found in a normal range. Perhaps, hypertestosteronemia occurs due to imperfection in the affinity for receptors, metabolism at the receptors site, number of receptors and voracity with which they are bound.

As Acne vulgaris and free testosterone are mutually associated, it should be needed to measure free testosterone levels in subjects reporting with acne vulgaris, particularly in cluster of 16–35 years of age. The anti-androgen treated and treatment-resistant cases might be designated in cases with raised free testosterone levels.

Conclusion

LIMITATIONS It needs to be acknowledged that our study was a single center study with less study participants. More multicenter studies with a larger no of patients are needed to make generalization.

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