Free and Total Plasma Testosterone in Men and Women with Acne

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Androgens are important in the pathogenesis of acne, and free testosterone in the serum is regarded as the biologically active component. In this study, serum free and total testosterone levels were measured in men (34) and women (14), suffering from acne but otherwise healthy. The plasma values for both groups of patients did not differ significantly from those of the age matched control groups. *Key words: Serum free testosterone; Serum total testosterone; Percentage free testosterone.* (Received July 16, 1985.)

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Acne vulgaris is considered to be, at least in part, an androgen dependent condition (1, 2, 3, 4). Many investigations measuring protein-bound testosterone, sex-hormone binding protein and other androgen derivatives, have either confirmed or invalidated this assumption (3, 5, 6, 7, 8). Many of these studies were done measuring total testosterone and deriving indirectly the free testosterone. A few measured directly the free testosterone level, mostly in female acne patients (9, 10, 11, 12). Only one study was conducted in male acne patients (13). The aim of this study was to determine the serum level of free and total testosterone in men and women suffering from persistent acne vulgaris, in comparison with controls without acne.

MATERIALS AND METHODS

The patient population was mixed and consisted of 34 men and 14 women (age range 17–23 years), who were seen and followed at the Dermatology Clinic. These patients had moderate to severe acne. Otherwise they were in good health. The control population (medical students) consisted of 12 men and 10 women without acne, and within the same age range.

Total testosterone (TT) was measured by radioimmunoassay (14). The percentage of free testosterone (pFT) was evaluated by the method described by Granger-Watrin & DeMayer (15). In short, the free testosterone was determined by a simplified equilibrium-dialysis method. Equilibrium dialysis was performed using dialysing tubing (3.4 cm diameter, Union Carbide), and disposable 30 ml tubes. Plasma (0.5 ml) was diluted 1:2 in phosphate buffer (0.01 M, pH 7.4) containing 3-H-testosterone (10000 cpm) and dialysed against 5 ml of the same buffer for 18 hours at 37°C in a shaking water bath. The dialysable fraction was derived from the ration of radioactivity in free form, and the total radioactivity. The percentage of free testosterone was calculated with a diluting factor correction (1:22). The free (FT) testosterone was then computed from the pFT and the TT.

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The statistical analysis was done by the non-parametric bilateral U-test of Mann-Whitney.

RESULTS

In men the plasma total testosterone levels were quite similar in acneic patients (mean values 22.98±10.16 nmol/l) and control subjects (22.66±8.60 nmol/l)

The mean values of free testosterone were also within the same ranges for men with acne (0.36±0.12 nmol/l) and for control subjects (0.31±0.11 nmol/l). However, there was a significant ($p<0.005$) difference in the mean pFT between men with acne (1.58±0.22%) and control subjects (1.39±0.14%) (see Table I). In women the same picture emerged. Thus there was no significant difference between mean TT for women with acne (1.66±0.72 nmol/l) versus controls (2.14±0.49 nmol/l). The mean FT did not show any significant difference between affected patients 22.32±10.70 pmol/l) and controls (18.70±1.30 pmol/l). The only statistically significant difference ($p<0.005$) in females was found in the mean pFT between female patients with acne (1.59±0.53%) and control subjects (0.89±0.18%) (see Table II).

DISCUSSION

The role of androgens in the pathogenesis of acne is an important and pivotal one (2, 3, 4, 16). The origin of the excess precursor androgen, may be glandular (adrenal and ovary) or tissular (2). Most of the previous studies done on circulating androgens' influence in acne, involved measurement of total testosterone (TT) and sex hormone binding globulin (SHBG), deriving only indirectly the FT serum level. (6, 17, 18). Other studies suggest that the free androgen fraction in the serum is the biologically active component (16, 19). Therefore, measuring the free testosterone directly is more precise for detection of any abnormality or imbalance in acne patients.

Table I. *Total testosterone, percentage free testosterone, and free testosterone in 34 male acne patients and controls*

	Mean TT (nmol/l)	Mean pFT (%)	Mean FT (nmol/l)
Acne patients (34)	22.98±10.16	1.58±0.22	0.36±0.12
Range	7.24–46.14	1.03–2.02	0.12–0.74
Controls (12)	22.66±8.60	1.39±0.14	0.31±0.11
range	11.11–42.26	1.16–1.59	0.17–0.59
Significance	$p>0.05$	$p<0.005$	$p>0.05$

Table II. *Total testosterone, percentage free testosterone, and free testosterone in 14 female acne patients and controls*

	Mean TT (nmol/l)	Mean pFT (%)	Mean FT (pmol/l)
Acne patients (34)	1.66±0.72	1.59±0.53	22.32±10.70
range	0.62–2.97	0.98–2.87	6.07–48.95
Controls (10)	2.14±0.49	0.89±0.18	18.70±4.48
range	1.41–3.45	0.44–1.06	12.14–32.43
Significance	$p>0.1$	$p<0.005$	$p>0.1$

Is it still useful to measure the SHBG. Palatsi et al. have shown that there is no direct correlation between serum SHBG and free testosterone levels. Other factors, such as production and metabolic clearance of testosterone, may be of importance in the regulation of serum FT levels (20).

Even with the advent of these newer techniques, cheap and easy to perform for assaying FT directly, reports have shown a discrepancy between FT measurements in acne patients (9, 10, 12). The present study was carried out on male and female acne patients, measuring TT, and FT. Endrocrinological investigation is rarely called for in men with acne and to our knowledge only one study has been carried out where FT was measured directly in these patients (13). Our results in male acne patients, show that circulating TT are normal, and only one patient had a value above our normal upper limit for TT (normal range in our laboratory (12.1–34.5 nmol/l). The mean pFT showed a statistical difference which could not be explained. More significantly, normal mean values for FT were found, thus confirming the results of Van der Meeren & Thijssen (13). One can wonder why the FT values are not statistically different, when the pFT ones are highly significant. This can be explained by the fact that higher values of TT do no necessarily correspond to higher values of pFT. This is in concordance with most reports showing no correlation between plasma androgen and acne in men (1).

Our results in women with acne also show normal plasma TT values as compared to control subjects. The literature abounds with reports finding normal TT values (1, 3, 12) and others showing elevated plasma TT values (5, 6, 11, 21). Our results of FT plasma values were different but not statistically significant ($p>0.1$) between women controls and patients, confirming these reported by Lookingbill et al. (12) but contradicting those of Schiavone et al. (9), Lucy et al. (10) and Palatsi et al. (20).

Why the discrepancy in plasma FT value findings? It could not be due to the technique used, since Palatsi et al. and Lookingbill et al. used the same assay (the precipitation assay described by Tremblay & Dube (22) and yet obtained opposing results.

The mean pFTs in female acne patients and controls were significantly different, yet the mean FT was not. This can be explained when one looks at the mean TT values which are lower in acne vs. control subjects.

It seems that there might be many different types of androgen abnormalities in acne. Some patients have high plasma circulation androgens as mentioned earlier while others have a higher skin metabolism of androgens (12). Yet others could have a higher sensitivity to normal levels of circulating androgens, through possibly higher number of androgen receptors, at the cellular level.

Therefore it is more likely that more emphasis should be devoted to an abnormality of the pilo-sebaceous unit's sensitivity to normal serum androgens.

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