SUMMARY

The scope of the work was to establish the correlation between the degree of hirsutism and serum levels of testosterone (T), free testosterone (fT), androstenedione (A), dehydroepiandrosterone sulphate (DHEAS), androstenediol glucuronide (ADION-G), sex hormone binding globulin (SHBG) and salivary testosterone (sT). The body mass index (BMI) was also taken into account. Serum SHBG and fT levels showed the highest correlation with the degree of hirsutism, while the correlation for sT, A and ADION-G was a little lower, but greater than for T and DHEAS. For hirsute women, a significant correlation between serum androgen levels and BMI was found, as opposed to normal group.

Key words: androgens, hirsutism

INTRODUCTION

Clinical manifestations of androgenization in women include hirsutism, acne and baldness of the masculine type. In severe cases, signs of virilization, like deepening of the voice, increased muscle mass and clitoromegaly are observed. The most common manifestation is hirsutism.

Hirsutism is more than a cosmetic problem that can attack a woman. It is the hormonal problem resulting from an excess of androgens and abnormal metabolism of androgens in hair follicle, caused by disorders in the ovaries or adrenal glands.

Androgens are C-19 steroids (containing 19 carbons) derived from cholesterol (Fig. 1) and secreted by the adrenal cortex and ovaries. Androgens may also be derived (not secreted) from the conversion of other steroids by the liver and some peripheral tissues (1). Principal androgens include testosterone (T) and its metabolite dihydrotestosterone (DHT), androstenedione (A), dehydroepiandrosterone (DHEA) and its metabolite dehydroepiandrosterone sulphate (DHEAS) (Fig. 2). An important metabolite of T and DHT is 3a,17β-androstenediol glucuronide.
Androgens in hirsutism

Figure 1. Synthesis of androgens from cholesterol

Slika 1. — Sinteza androgena iz kolesterola

70

BIOCHEMIA MEDICA god. 5, br. 2–3, 1995.
Figure 2. Metabolic pathways of testosterone degradation

Slika 2. Metabolički putovi razgradnje testosterona

BIOCHEMIA MEDICA god. 5, br. 2–3, 1995.
Androgens in hirsutism

Androgens in hirsutism (ADIOL-G). Although not androgenic itself, ADIOL-G serves as an effective marker of androgen action (2).

Several reports indicate that women with hirsutism have elevated levels of ADIOL-G in both serum and urine (3-5).

Since the plasma circulating androgens are the most readily demonstrable and the only obtainable biochemical parameters in routine evaluation of hirsute patients, we decided to study the correlation between the degree of hirsutism and serum levels of T, free testosterone (FT), A, DHEAS, ADIOL-G, sex hormone binding globulin (SHBG) and salivary testosterone (sAT).

The body mass index (BMI) was also considered, since androgen levels in obese women with mild hirsutism had been reported (6) to be higher than those in severely hirsute non-obese women.

PATIENTS AND METHODS

Our study included 46 women aged 17-39 years, mean age 25.2±3.2, referred to our outpatient clinic for hirsutism. The severity of hirsutism was assessed semiquantitatively as described by Ferryman and Gallwey (7). Blood samples for androgen determinations were drawn in the morning between second and sixth day of the menstrual cycle: three equal amounts of blood samples, drawn every 20 minutes, were pooled. The blood was centrifuged and the serum frozen until analysis at -20°C. Salivary samples were taken between the collection of blood samples without any additives for promotion of salivation.

\[\text{Figure 3.} \quad \text{Elution of different androgens from Celite column} \]

\[\text{Stiika 3.} \quad \text{Eluacija različnih androgena celitno kolone} \]

72

BIOCHEMIA MEDICA god. 5, br 2-3, 1995.
For all hormone measurements except ADIOL-G, conventional RIA methods using commercial kits were employed, as follows: T, A, DHEA-S, RIA by DPC (USA) for fT, RIA by Milab (Malmö, Sweden) for SHBG, and RIA by Sorin (Sallugia, Italy) for saT (8). Serum ADIOL-G was measured by the method of Samojlik (9) and is presented in short as follows: 1 ml of serum was extracted with ether to remove free steroids; the serum was then incubated at 45 °C for 48 h, β-glucuronidase (Helix pomatia). After incubation, approximately 1000 cpm Δ4-3 androstenediol were added to correct for procedural losses, and serum was extracted twice with water and evaporated to dryness. The resuspended extract was transferred to a 25 ml column impregnated with propylene glycol and eluted with isooctane progressively enriched with benzene. This system clearly separated A, T, and DHT from ADIOL (Fig. 3). The benzene-isooctane fraction (75:25) containing the ADIOL fraction was collected, and aliquots were taken to determine the procedural loss. The remainder was analyzed by RIA using a specific antibody raised against 3α-androstenediol conjugated to bovine serum albumin (BSA).

Normal hormone levels for women, established in our laboratory are: T 0.3 - 3.0 nmol/L, A 0.6 - 10.2 nmol/L, DHEA-S 3.6 - 13.4 μmol/L, fT 3.8 - 10.4 pmol/L, ADIOL-G 1.7 - 7.6 nmol/L, SHBG 27 - 58 nmol/L, and 58 - 71 pmol/L for saT. BMI was calculated by dividing body weight (in kg) by the square of body height (in m). For statistical evaluation, multiple regression analysis and correlation analysis were used.

RESULTS

Serum androgen levels in 46 hirsute women are shown in Table 1. Although the mean concentration of each androgen was elevated, only 17 (36.9%) had serum T elevated in excess of 3 nmol/L. Serum fT concentrations were elevated in 28 (60.9%) cases. Serum A concentrations in excess of 10.8 nmol/L were found in 33 (71.7%) hirsute women, and elevated serum DHEA-S levels in...
Androgens in hirsutism

Androgens in hirsutism J. Oroszlán, A. Kocian

only 2 (4.3%) hirsute women. By contrast, serum SHBG values were lower than the lower normal limit (27 nmoVL) in 27 out of 46 (58.7%) hirsute women. The mean serum ADIOL-G level in 46 hirsute women was 8.7 nmoVL, and serum ADIOL-G values were higher than the upper normal limit (7.6 nmoVL) in 22 out of 46 (47.8%) hirsute women. SaT values were elevated in 24 (52.2%) cases. Because the mean BMI in the women with hirsutism was greater than in normal women, we examined the relationship between serum androgen levels and BMI. No correlation was found for normal women, but for women with idiopathic hirsutism a weak but statistically significant correlation was observed.

If serum androgen levels do serve as markers of peripheral androgen metabolism, then correlations between serum levels and FG score, an index of the extent of hirsutism, might be expected.

DISCUSSION

As already mentioned, the concentrations of circulating androgens represent only one of the parameters determining the clinical picture of hirsutism. In our group, 6 patients (13%) had normal androgen levels, although all of them were hirsute. The determination of serum SHBG, and FT showed the highest correlation with the degree of hirsutism (r=0.51; r=-0.493) in our patients, in contrast to a previous study of ours(10). The correlation of serum T, saT and ADIOL-G was a little lower (r=0.284; r=0.298; r=0.207), but greater than the determinations of serum A and DHEA-S (r=0.12; r=0.127). On the other hand, we also showed a significant correlation between hirsutism and BMI. Our finding of a weak, but statistically significant, correlation between serum ADIOL-G levels and BMI suggested that body weight per se, rather than hirsutism, might be an important factor in determining serum ADIOL-G levels. The correlations of androgens determined and FG score showed a little different picture. The best correlations were found between saT (r=0.407) and FT (r=0.47) vs. FG score and the weakest between DHEA-S (r=-0.087) and ADIOL-G (r=0.248).

Hirsutism cannot be regulated only as a function of circulating androgens, but may result from the processes occurring in peripheral tissues. The hair follicle sensitivity has been shown to be higher in some women with hirsutism than in non-hirsute women (11). Much of the to date research supported the concept that serum ADIOL-G levels are related to 5a-reductase activity (2). In our group serum ADIOL-G levels were higher than those obtained by Horton (4) and Scanlon (12), and lower than those reported by Gompel (13). Determination of serum T, FT, A, DHEA-S, SHBG, ADIOL-G and saT represents the profile for clinical evaluation of hirsutism.

BIOCHEMIA MEDICA god. 5, br. 2–3, 1995.
KONCENTRACIJE ANDROGENIH HORMONA U ŽENA S HIRSUTIZMOM

SANETAK - Cilj rada bio je ustrezati korelaciji izmedu stupnja hirsutizma in serijskih koncentracijih ukupnog testosterona (T), slobodnog testosterona (fT), androstenediona (A), dehidroepiandrosterona sulfala (DHEAS), toksidol glucuronide (ADGOL-G), globalnih kajcev spolnih hormonov (SHBG) in testosterona v slizi (sT). Priseg je vselej sliz in serijskih izmedu mesce (BMI). Naljelj korelacijni upodoben v odnosu na stopnjo hirsutizma zanjo je v koncentraciji SHBG in sT, nevarje slabije korelacije nadana je z T, sT in ADIOL-G, in njenja za sA. Izmed razlik serijskih androgenov in BMI nadana je statistično značilna korelacija v grupi hirsutih žen.

Ključne riječi: androgensi hormoni, hirsutizam

REFERENCES


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