*Clinical study*

# ANDROGEN HORMONE LEVELS IN WOMEN WITH MALE PATTERN BALDNESS

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## ABSTRACT

*Background* Adrogen hormones in women with androgenetic alopecia (AA) were studied.

*Materials and methods.* The prospective study included 50 women with androgenetic alopecia in fertile age. Blood and urine were taken on the 7th and 21st day of the same menstrual cycle. Free testosterone (T), androstanediole (A-DIOL) and dehydroepiandrosterone (DHA) were assayed in serum. In the 24-hour urine T, DHA, androsterone (A), etiocholanolone (E) and 17-ketosteroid (17-KS) levels were monitored. *Results.* Statistical deviation from physiological levels was observed for serum T.

*Conclusion.* It is suggested that A-DIOL was possibly the principal androgen in etiopathogenesis of AA in women. The hormonal disorder seems to be expressed in the estrogen phase of the menstrual cycle.

KEY WORDS

*alopecia, androgenetic, testosterone, androgen fractions, female sex*

## INTRODUCTION

The studies of metabolism and mechanisms of androgen action on the hair follicle as one of significant target units of androgenetic steroids have not significantly contributed to the solution of the basic dilemma: why and how do androgenetic hormones cause hair follicle involution constantly in the same regions of capillitium which are predisposed for androgenetic alopecia (AA), without disturbing the follicle function in the remaining regions? Neither do in vitro study methods (incubation of isolated hair roots with particular androgens and determination of metabolite concentration in incubates or fibroblast culture as a model of studying the androgen binding capacity by the skin) enable an exact insight into complex metabolic and biological processes induced by androgen steroids.

Special challenge in AA in women is due to the specificity of general hormonal milieu and to the fact that alopecia nevertheless represents stigmata of certain degree of androgenization[1]. This high incidence of AA in women is puzzling. Some authors

indicate the existence of metabolic disorders already on secretory level in women with AA[2-4], while others assume an androgen metabolic disorder on cellular effector level[5-13]. Although it has been proven that hair follicles posses enzymatic systems for metabolizing individual androgen steroids, metabolism is directed towards α-metabolic route.

## MATERIALS AND METHODS

The purpose of the investigation was to study the levels of relevant androgen hormones in women with AA. The prospective study included 50 women in fertile age (Figure 1.) in whom AA was diagnosed: Ludwig I type in 42% and Ludwig II type in 58% according to Ludwig's classification[18]. The study included female subjects without clinical signs of hirsutism in whom by gynecological examination an ovarian organic disease was excluded, and who did not receive oral hormonal contraceptives[19-24].

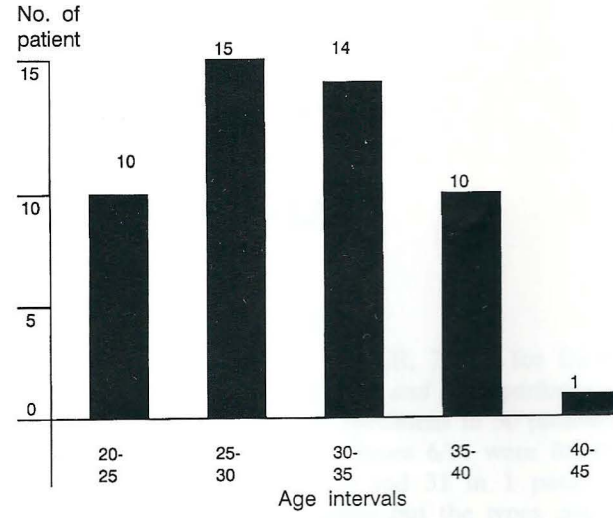


*Figure 1. Age distribution of 50 females with androgenetic alopecia*

The quantitative analysis of relevant hormones (free testosterone /T/, androstanediole /A-DIOL/, dehydroepiandrosterone /DHA/ in serum and DHA, androsterone /A/, etiocholanolone /E/, 17-ketosteroids /17-KS/ in 24-hour urine) were performed by adsorption thin layer chromatography[25]. The material (blood

*Table 1. Serum testosterone (T), dehydroepiandrosterone (DHA), androstanediole (A-DIOL) and urine dehydroepiandrosterone (DHA) levels in female patients with androgenetic alopecia type I and II (n = 50)*

| PARAMETERS | SERUM | | | | | | URINE | |
|---|---|---|---|---|---|---|---|---|
| hormone type (normal values) | [T] (ng%) (18 - 22) | | [DHA] µg% (40 - 60) | | [A-DIOL] µg% (20 - 40) | | [DHA] (mg/24h) (1,5-2) | |
| day of period | 7. | 21. | 7. | 21. | 7. | 21. | 7. | 21. |
| $x_{min}$ | 11 | 9,6 | 18 | 15 | 12 | 7 | 1,05 | 1,05 |
| $x_{max}$ | 60 | 37 | 105 | 100 | 72 | 90 | 5,52 | 3,62 |
| x | 26,1 | 23,4 | 48,6 | 52,6 | 31,8 | 33,4 | 2,01 | 1,98 |
| $SE_x$ | 11,0 | 7,9 | 18,5 | 20,6 | 15,2 | 16,2 | 0,84 | 0,58 |
| KV% | 41,6 | 33,5 | 37,6 | 39,3 | 47,2 | 48,3 | 41,1 | 29,1 |
| r | 0,12; NS | | 0,25; NS | | 0,60; p<0,01 | | 0,44 p<0,05 | |
| t | 1.396; NS | | 1.011; NS | | 0.502; NS | | 0.206 NS | |

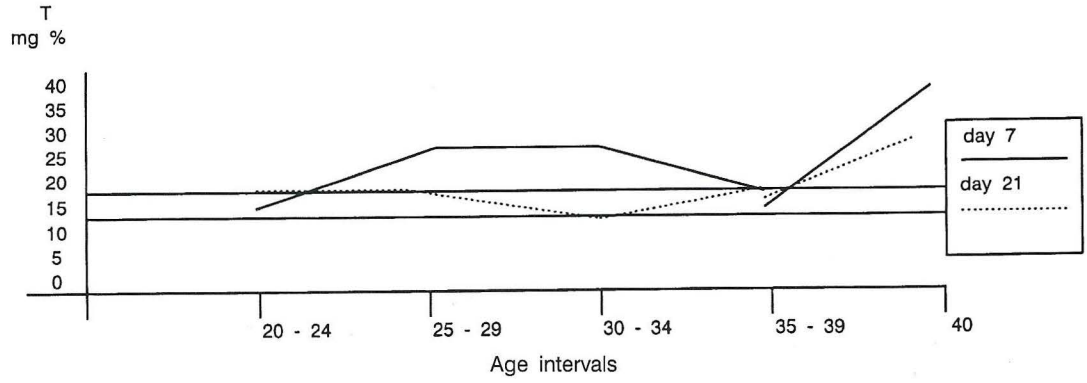


*Figure 2. Mean values of testosterone ( T ) in sera of 50 females with androgenetic alopecia. The samples were taken at day 7 and 21 of the same menstrual cycle*

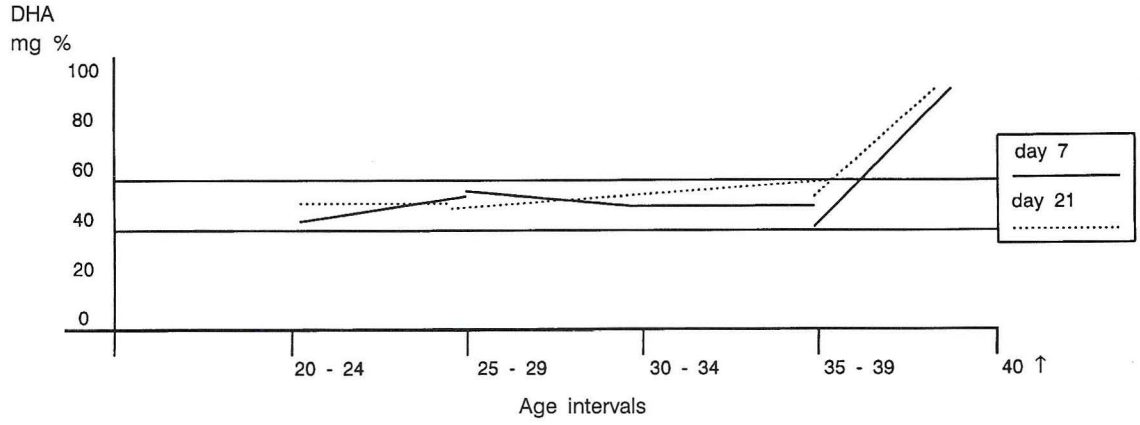


*Figure 3. Mean values of dehydroepiandrosterone (DHA) in sera of 50 females with androgenetic alopecia. Samples were taken at day 7 and 21 of the same menstrual cycle*

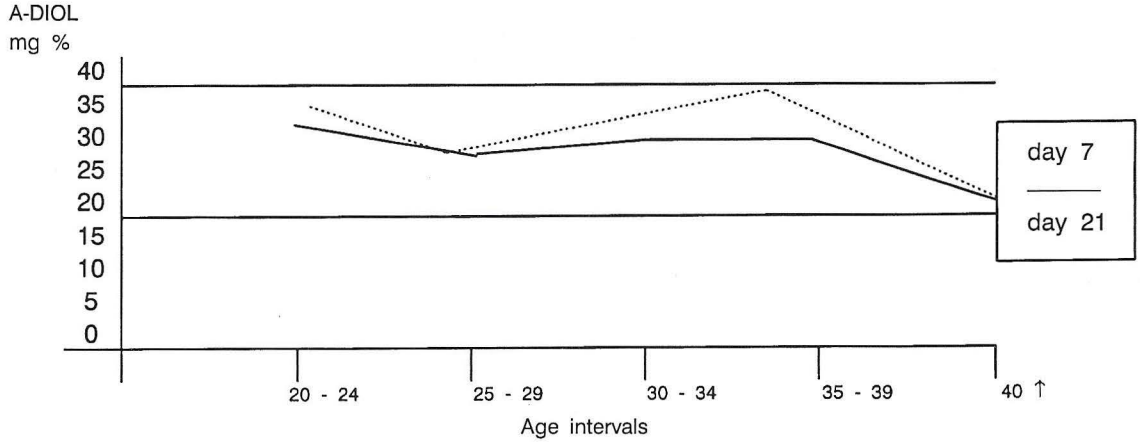


*Figure 4. Mean values of androstanediol (A-DIOL) in sera of 50 females with androgenetic alopecia. Samples were taken at day 7 and 21 of the same menstrual cycle*

samples in the morning biorhythm) and 24-hour urine were taken on the 7th and 21st day of the same menstrual cycle. The results of densitograms were compared with physiological level parameters for women in reproductive period:

T 18-22 ng/dl, A-DIOL 20-40 µg/dl, DHA 40-60

*Table 2. Dependence of dehydroepiandrosterone (DHA) and testosterone levels in the patients' sera*

| DHA (μg/dl) | | Testosterone (ng/dl) | | | | | | TOTAL | |
|---|---|---|---|---|---|---|---|---|---|
| | | decreased (≤ 17) | | physiologic (18 - 22) | | increased (≥ 23) | | | |
| day | | f | % | f | % | f | % | f | % |
| 7th | decreased (≤ 39) | 3 | 6 | - | - | 8 | 16 | 11 | 22 |
| 7th | physiologic (40 - 60) | 6 | 12 | 10 | 20 | 12 | 24 | 28 | 56 |
| 7th | increased (≥ 61) | 2 | 4 | 2 | 4 | 7 | 14 | 11 | 22 |
| | TOTAL | 11 | 22 | 12 | 24 | 27 | 54 | 50 | 100 |
| 21st | decreased (≤ 39) | 4 | 8 | 2 | 4 | 8 | 16 | 14 | 28 |
| 21st | physiologic (40 - 60) | 7 | 4 | 10 | 20 | 4 | 8 | 21 | 42 |
| 21st | increased (≥ 61) | 1 | 12 | 4 | 8 | 10 | 20 | 15 | 30 |
| | TOTAL | 12 | 24 | 16 | 32 | 22 | 44 | 50 | 100 |

*day 7 of the period: $X^2$ = 6.159; NS*
*day 21 of the period: $X^2$ = 11.142, $p<0,05$; c = 0,43; $p<0,05$*

μg/dl in serum and T 20-50 μg/dl, DHA 1.5 - 2 mg/24h, A 1-3 mg/24h, E 3-6 mg/24h and 17- KS 6 - 14 mg/24h in urine.

Since the literature data indicate the activities of α-series, directing T metabolism towards A-DIOL in hair follicles in general, and particularly in regions predisposed to AA, the statistical analysis of results was directed towards correlative relationships: serum T → A-DIOL, serum T → DHA, serum DHA → urine DHA. The outlined parameters were monitored particularly for the 7th and 21st days of the same menstrual cycle.

## STUDY RESULTS

The results of the statistical analysis of relevant steroids according to five-year age intervals showed that significant deviation from physiological levels was registered only for serum T (Figure 2). By F-test (variance analysis) it was evidenced that the female subjects' age did not influence either serum T levels or levels of other parameters. Thus, further analysis was performed for the female subject group as a whole. Since the study was directed towards the a-metabolic route of steroids and elevated serum T levels were registered, further statistical analysis of results was directed towards serum T, DHA and A-DIOL levels and DHA in urine (Table 1, Figures 3, 4). Statistical analysis (C- coefficient of association) showed that there was a proven association of serum T levels for the 7th and 21st day of the cycle ($C= 0.55$, $p<0.01$). For serum T, DHA (Table 2) and A levels there were no significant differences found in average values on the 7th and 21st day of the cycle. For serum A-DIOL levels ($p<0.01$) as well as urine DHA levels ($p<0.05$) there were found significant level dependencies between the 7th and 21st day of the cycle (Tables 3, 4). Further statistical analysis ($r_{xy}$ - coefficient of correlation) was directed towards correlative relationships: serum DHA → T, serum T → A-DIOL and serum DHA → urine DHA. Significant level dependency of serum DHA and T ($p<0.05$) was registered, as well as serum T and A-DIOL ($p<0.05$) on the 21st day of menstrual cycle, while for serum and urine DHA there was not significant level dependency either for the 7th or the 21st day (coefficient of correlation - $r_{xy}$).

*Table 3. Dependence of testosterone (T) and androstanediol (A-DIOL) levels in the patients' sera*

| | DHA (μg/dl) | Testosterone (ng/dl) | | | | TOTAL | |
|---|---|---|---|---|---|---|---|
| | | decreased (≤ 17) | | physiologic (18 - 22) | | increased (≥ 23) | | | |
| day | | f | % | f | % | f | % | f | % |
| 7th | decreased (≤ 19) | 1 | 2 | 1 | 2 | 8 | 16 | 10 | 20 |
| 7th | physiologic (20 - 40) | 6 | 12 | 7 | 14 | 13 | 26 | 26 | 52 |
| 7th | increased (≥ 41) | 4 | 8 | 4 | 8 | 6 | 12 | 14 | 28 |
| | TOTAL | 11 | 22 | 12 | 24 | 27 | 54 | 50 | 100 |
| 21st | decreased (≤19) | 2 | 4 | 1 | 2 | - | - | 3 | 6 |
| 21st | physiologic (20 - 40) | 7 | 4 | 6 | 12 | 18 | 36 | 31 | 62 |
| 21st | increased (≥ 41) | 3 | 6 | 9 | 18 | 4 | 8 | 16 | 32 |
| | TOTAL | 12 | 24 | 16 | 32 | 22 | 44 | 50 | 100 |

*day 7 of the period: $X^2$ = 3.625; NS*
*day 21 of the period: $X^2$ = 11.003, $p<0,05$*

## DISCUSSION

The sex hormone binding globulin (SHBG) levels were not determined due to technical reasons, which does not reduce the value of this study since the unbound T fraction is the only one which is biologically active[1, 26,27]. In healthy women 50-70% of T originates from peripheral androstenedione skin conversion. In 54 % of female subjects there were found elevated serum T levels on the 7th day of the cycle, and in 44% on the 21st day of the cycle. The association in T levels on the 7th day and 21st day correlated with the literature data[28,29]. In female subjects elevated T levels were not found in urine contrary to some other authors[2,3]. DHA is a precursor hormone for $C_{19}$ and $C_{18}$ steroids. The results did not suggest the presence of significant dependency between serum and urine DHA levels in women with AA. However, the significance of DHA for the studied pathology was confirmed by the analysis of the relationship of serum DHA → T, since DHA acted identically also on the level relation the 7th → 21st day of the menstrual cycle (according to well known α - metabolic pathway of androgen hormones).

Referring to the metabolism: DHA → androstenedione → T → A-DIOL, and having in mind high serum T levels in the majority of female subjects, it may be supposed that the metabolism is directed towards the level DHA → T in progesterone phase of the cycle. A significant dependency of DHA and T levels on the 21st day was registered. By statistical analysis T was shown as the targeted marker for AA in women, due to the proven level association for the 7th and 21st day of the cycle.

There was noticed a different behavior of individual steroids depending on the cycle phase, on the basis of which it may be concluded that the estrogen phase in female subjects was followed by hormonal dysbalance which in progesterone phase receives its targeted route (there was registered dependency at the level T → A-DIOL in the progesterone phase). This observation suggests the metabolic route of α-series of $C_{19}$ steroids in women with AA.

## CONCLUSION

The results indicate that in women with AA the estrogen phase is the one followed by hormonal dysbalance which in progesterone phase receives its targeted route and suggest the possible significant biological activity of A-DIOL as a peripheral steroid in etiopathogenesis of AA in women. A possible way to prove this hypothesis would be an in vitro study which is unfortunately at present technically not possible to apply as a standardized method.

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