



Original Article

Total Testosterone Concentration and Severity of Hirsutism in a Group of Hirsute Women of Yaoundé

Dosage de la testostéronémie totale et sévérité de l'hirsutisme dans un groupe de femmes avec hirsutisme à Yaoundé

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ABSTRACT

Background. Hirsutism is the excessive terminal hair growth in androgen-dependent areas of the body in women, which grows in a typical male distribution pattern. This phenomenon results from simultaneous action of testosterone on the hair follicle and the sebaceous gland. The objective of this work was to establish a correlation between severity of hirsutism and testosterone levels in this group of women. **Material and Methods.** We conducted a prospective descriptive cross-sectional study, setting at Yaounde central hospital in the endocrinology unit. Participants were recruited by convenience sampling. The Ferriman and Gallway score was used for clinical classification of hirsutism. We measured total plasma testosterone using enzyme immunoassay ELISA. Spearman test was used to assess correlation between the study parameters. **Results.** Our study population consisted of 69 women aged 18 to 48 years. Hirsutism was mild in 63.7% (44/69) of women; moderate in 36.2% (25/69) of women. No women had severe hirsutism. Mean testosterone was 1.36 ± 1.00 ng / mL; 91.7% (66/69) of women with testosterone greater than 0.6 ng / mL. There was a weak but not significant negative correlation between degree of hirsutism and plasma total testosterone concentration ($r: -0.178, p: 0.138$). **Conclusion.** In women with mild or moderate hirsutism, the degree of hirsutism does not reflect total testosterone levels.

RÉSUMÉ

Introduction. L'hirsutisme est la croissance excessive des poils dans les zones du corps dépendant des androgènes chez les femmes, qui se développe dans un schéma de distribution masculine typique. Ce phénomène résulte de l'action simultanée de la testostérone sur le follicule pileux et la glande sébacée. L'objectif de ce travail était d'établir une corrélation entre la sévérité de l'hirsutisme et les niveaux de testostérone dans ce groupe de femmes. **Matériels et méthode.** Nous avons mené une étude prospective descriptive transversale dans l'unité d'endocrinologie de l'hôpital central de Yaoundé. Les participantes ont été recrutées par échantillonnage de convenance. Le score de Ferriman et Gallway a été utilisé pour la classification clinique de l'hirsutisme. Nous avons mesuré la testostérone plasmatique totale en utilisant un test immuno-enzymatique ELISA. Le test de Spearman a été utilisé pour évaluer la corrélation entre les paramètres de l'étude. **Résultats.** Notre population d'étude était composée de 69 femmes âgées de 18 à 48 ans. L'hirsutisme était léger chez 63,7% (44/69) des femmes ; modérée chez 36,2% (25/69) des femmes. Aucune femme ne souffrait d'hirsutisme grave. La testostérone moyenne était de $1,36 \pm 1,00$ ng / mL; 91,7% (66/69) des femmes ayant une testostérone supérieure à 0,6 ng / ml. Il y avait une corrélation négative faible mais non significative entre le degré d'hirsutisme et la concentration plasmatique totale de testostérone ($r : -0,178, p : 0,138$). **Conclusion.** En cas d'hirsutisme léger ou modéré, le degré d'hirsutisme ne reflète pas les niveaux totaux de testostérone.

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INTRODUCTION

Hirsutism is the development of excessive, hard and pigmented hair in areas where it is normally absent in women. In half of the cases it is suggestive of excess androgen which could either arise from the ovaries,

adrenal glands or peripheral potentiation of weak androgens [1]. Hirsutism affects about 5 to 10% of women of childbearing age in the world. The polycystic ovary syndrome (PCOS) is the main etiology and the idiopathic form is the most common [2]. In regard to reproduction,

hirsutism is often associated with disruption of the menstrual cycle, or infertility owing to hyperandrogenism. As a result, screening for hyperandrogenism must be systematic in a context of female infertility [3]. Testosterone is the main circulating androgen found in women. It is easily measured and does not undergo any significant variation during the menstrual cycle. Given that hirsutism reflects the action of androgens on pilosebaceous follicles, we therefore proposed to establish the correlation between testosterone concentrations and the degree of severity of hirsutism in a population of Cameroonian women in order to predict testosterone levels with regards to hirsutism.

MATERIALS AND METHODS

Study design

This was a descriptive cross-sectional study, carried out at the Department of Endocrinology and Metabolic Diseases of Yaounde Central Hospital over a period of 08 months.

Participants

Inclusion criteria

We included women aged 18 years to 50 years, who gave informed consent and had hirsutism with a Ferriman and Gallway (FG) score greater than or equal to 8.

Exclusion criteria

Women on corticosteroids or other medications (tamoxifene, antiepileptic drugs and thyroid hormones) that could modify the hormone cycle, or which could increase the Sex Hormone Binding Globulin and therefore the total testosterone level were excluded. Women on estrogen / progestin contraceptives; post-menopausal, pregnant or breastfeeding women were excluded. Sampling was consecutive and patients were recruited by advertisement.

Procedure

Step 1: Examination and physical examination

After explaining the purpose of the study and signing the informed consent, an appointment was made with each participant for the interview and the blood sample collection. Through a structured interview we obtained date of the last menstrual period, age at menarche, duration of the menstrual cycle and the date of onset of hirsutism. During physical examination, we looked for signs of virilization and hirsutism which was scored according to the Ferriman-Gallway score [4]. The FG score was assessed by three reviewers. The FG score assigned to each participant was the average of the scores obtained independently by each examiner. Every score with decimal was rounded up to the next upper whole number.

Step 2: Determination of total testosterone

Pre-analytical conditions: Samples were taken while fasting. All women with a regular menstrual cycle were sampled in the morning at 8am at the beginning of the follicular phase so that all were subjected to the same physiological conditions.

Analytical phase: total testosterone was assayed by competitive enzyme immunoassay ELISA. The intensity of staining was inversely proportional to the amount of antigen present in the sample. The results of the sample were obtained from the standard curve. Total testosterone was considered normal for a value between 0.1 and 0.6ng / ml.

Sensitivity: The lowest detectable concentration of testosterone that can be distinguished from the zero calibrator is 0.07ng/mL at the 95% confidence limit.

Specificity: The cross reaction of the antibody calculated at 50% according to the principles of biochemistry are 100% for testosterone, 16% for dihydrotestosterone and 0.8% for androstenedione.

Data analysis

Data was analyzed using SPSS software version 23.0. Qualitative and quantitative variables were presented as percentages and means, respectively. The association between variables was determined using Spearman's nonparametric correlation test. The threshold of significance was set for a value of $p < 0.05$.

Ethics approval and consent to participate

The study was approved by the Institutional Ethical Research Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I and Regional Ethical Research Committee N° 2016/04/752/CE/CNERSH/SP. In Cameroon and was conducted in accordance with the guidelines of the Helsinki Declaration. All participants provided written informed consent prior to enrolment.

RESULTS

General characteristics of the study population

We recruited 69 women with hirsutism whose mean age was 27.36 ± 6.69 years (range, 18 to 48 years).

The mean arterial pressure was $120/78 \pm 15/10$ mmHg. According to the grade of blood pressure, 6 (8.6%) patients had hypertension.

The average BMI was 27 ± 6 kg / m². BMI was normal in 42% (29/69) of participants; 33.3% (23/69) were overweight and 24.6% (17/69) were obese. The average waist circumference was 81.55 ± 11 cm; 76.8% (53/69) had a normal waist circumference; 23.1% (16/69) had central obesity. Table I summarizes all clinical characteristic of our participants.

Table I: Clinical characteristics of study population

Variables		Frequency (N=69)	%
BMI	Normal	29	42
	Overweight	23	33.3
	Obesity	17	24.6
Waist circumference	> 88cm	16	23.1
	< 88cm	53	76.8
SBP	> 140mmhg	6	8.6
	< 140mmhg	63	91.3
DBP	> 90mmhg	9	13
	< 90mmhg	60	86.9
Hirsutism	Mild	44	63.7
	Moderate	25	36.2
	Severe	0	0
Menstrual cycle	Regular	32	46.3
	Irregular	37	53.6
	Spaniomenorhea	08	11.5
Gestation	Yes	33	47.8
	No	36	52.1
Infertility		2	2.8

Evaluation of the severity of hirsutism and associated signs

Rating of hirsutism: Ferriman-Gallway Score

Rating of hirsutism according to Ferriman-Gallway is stated as follow: -Score <8: normal -Score between 8 and 14: light hirsutism -Score 15 and 17: moderate hirsutism -Score > 17: severe hirsutism. The average Ferriman score was 14.23 ± 4.40 with a minimum of 8 and a maximum of 25. Depending on the severity, 63.7% (44/69) of the participants had mild hirsutism (Ferriman and Gallway mean score 11.7 ± 2.2), 36.2% (25/69) showed moderate hirsutism (Ferriman-Gallway score 19.6 ± 2.7), and none of the participants had severe hirsutism.

Signs associated with hirsutism

Seborrhea was found in 79.7% (55/69) participants ; acne in 52.1% (36/69) and acanthosis nigricans in 17.4% (12/69). We found no signs of virilization.

Gyneco-obsterical profile of participants

The menstrual cycle

The mean age of first menses was 13 ± 1.7 years. 37 (53.6%) participants had an abnormal duration of the menstrual cycle with 8 presenting spaniomenorrhea. 32 (46.3%) had a regular menstrual cycle.

Gestation and parity

In this group of hirsute women, we found that 33 (47.8%) women had already been pregnant while 36 (52.1%) were nulligravid, including 2 (2.8%) who had confirmed primary infertility.

Assessment of total testosterone level and correlation between severity of hirsutism and testosterone

The average total testosterone was 1.35 ± 1.03 ng/ml. Testosterone was elevated in 66 (91.7%) patients with levels above 0.6ng/ml. The distribution of testosterone levels according to the severity of hirsutism is shown in Figure 1. There was a negative and statistically not

significant correlation between testosterone levels and the severity of hirsutism ($r: -0.178; 0.138$).

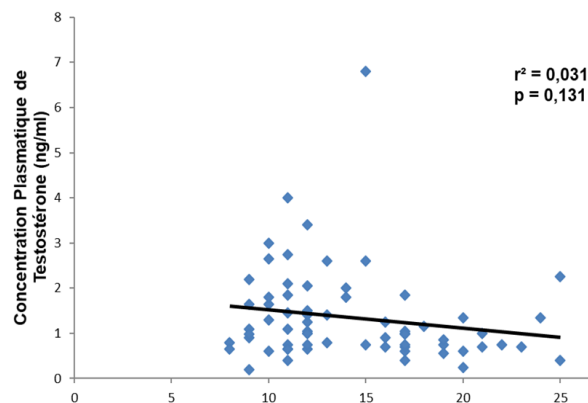


Figure 1: Correlation between severity of hirsutism and testosterone levels

DISCUSSION

According to the endocrine guidelines, total testosterone levels should be assessed as first-line in the presence of hyperandrogenism [3]. The assay technique is radioimmunoassay after pre-treatment of the sample. In our study, total testosterone was measured by the ELISA immunoassay technique [6]. Although it is the most used immunoassay technique, it has some flaws such as the hook effect that can be observed especially during competitive assays or interference especially with other physiological or synthetic steroids [7,8]. However, Radio immuno Assay by competition offers better sensitivity especially when working on low testosterone groups such as women. Mean testosterone was 1.35 ± 1.03 ng / ml and was high in 91.7% of participants, however, hirsutism was rather mild in this population and none of the participants had signs of virilization. With this mean testosterone levels, participants must be assessed for etiologies of hyperandrogenism. The most common cause in this case would be PCOS followed by congenital 21-hydroxylase deficiency in its non-classical form [2]. In addition, our patients were overweight or obese in 22% of cases, some presented with elements of the metabolic syndrome and others with ovulation disorders. Only 47.8% had experienced pregnancy. Two percent had already consulted a doctor and had primary infertility. These data strongly suggest PCOS as a cause of hyperandrogenism in this study population.

We found a negative and not statistically significant correlation between total testosterone levels and the severity of hirsutism. This negative correlation might suggest that the non-pathologic FG score in the studied population can be lower than the reference cut-off. Hair distribution having a variable expression according to ethnic group, the threshold for definition must be established according to the population to which it is applied. In the United States, a Ferriman score <8 is considered normal, while in some European regions the

authors define this <6 as normal. It should be noted that pubic hair overflowing on the white line and the inner thighs is not uncommon in women around the Mediterranean and can be considered normal [9]. Thus, it would be interesting to establish the FG threshold adapted to our population. Dinca Pavici in 2004 in his study also found a negative correlation between total testosterone and the degree of severity of hirsutism however this correlation was rather positive with free testosterone [10]. In another study, Sandra Karrer et al also found a strong correlation ($r: 0.309$) rather between the degree of severity of hirsutism and salivary testosterone concentrations [11]. Several mechanisms can explain this negative correlation: the increased sensitivity of peripheral tissues to dihydrotestosterone, which is the main androgen active at this level compared to total testosterone [11]. Also, the degree of hirsutism is a function of the sensitivity and polymorphism of tissue receptors to androgens [12]. The results obtained during our assays could have been overestimated, explaining on the other hand this level of total testosterone in discordance with hirsutism in the patients. The direct immunological assays as is the case in this study are certainly easy, fast and reproducible but also have some disadvantages such as interferences and matrix effect which result in quantitative errors (excess or deficiency) especially when the initial concentrations of steroids are low as observed in women [7]. Total testosterone concentrations were higher in patients with mild hirsutism and normal BMI. This result is in agreement with the literature. In fact, obesity is associated with a strong aromatization of androgens into estrogens. This relative excess of estrogen levels resulting from androgenic aromatization reduces GnRH pulsatility and as a result decrease testosterone levels in the obese subject [13].

CONCLUSION

The negative correlation between the severity of hirsutism and circulating total testosterone levels suggests that the degree of hirsutism does not reflect total testosterone levels. The cut-off for hirsutism might be lower to the reference Ferriman-Gallway score in our population.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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