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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Assessment of dehydroepiandrosterone sulphate and total serum testosterone in Iraqi women with post-adolescent acne

Iraklı adolesan sonrası akne'li kadınlarda dehidroepiandrosteron sulfat ve total serum testosteronun değerlendirilmesi

Samer A. Dhaher[1], Khalil I. Al-Hamdi[2], Jinan Q. Mohammed[3]

ABSTRACT

Objective: The aim of this study was to assess dehydroepiandrosterone sulphate (DHEA-S) and total serum testosterone (TST) in women with post-adolescent acne and their relationship to severity of acne and clinical markers of androgenicity.

Methods: Two hundred forty women with post-adolescent acne (PAA), 132 women with late- onset acne (LOA) and 108 women with persistent acne (PA) were recruited in this cross-sectional study. All patients were examined clinically and by ultrasound for evidence of polycystic ovaries (PCO), and serum DHEA-S and TST levels were measured.

Results: The results showed that there was an excess in androgens (DHEA-S) and TST levels. Serum androgens level were significantly correlated to the severity of PAA. In addition, clinical markers of androgenicity were frequently observed in women with PAA.

Conclusion: There is an increased level of circulating androgens in significant proportion of women with PAA and it seems that hyperandrogenism appears to play an important role in the etiopathogenesis of acne. In addition, there was a direct correlation between severity of acne and androgen levels suggesting that both ovarian and adrenal abnormalities are common at this patients group. *J Clin Exp Invest 2015; 6 (2): 121-125*

Key words: Dehydroepiandrosterone sulphate, total serum testosterone, post-adolescent acne

ÖZET

Amaç: Bu çalışmanın amacı adolesan sonrası akne'li kadınlarda dehidroepiandrosteron sulfat (DHEA-S) ve total serum testosteronun (TST) ve bunların akne şiddeti ve androjenikliğin klinik belirteçleri ile ilişkisini değerlendirmektir.

Yöntemler: Adolesan sonrası akne'li 240 kadın, 132 tanesi geç başlangıçlı akne ve 108 tanesi sürekli akneli kadın kesitsel çalışmaya alındı. Hastaların tümü klinik olarak ve polikistik over yönünden ultrasonografi ile değerlendirildi ve serum DHEA-S ve TST düzeyleri ölçüldü.

Bulgular: Veriler DHEA-S ve TST düzeylerinde fazlalık olduğunu gösterdi. Serum androjen düzeyi akne şiddeti ile anlamlı korelasyon gösterdi. Ayrıca adolesan sonrası akne'li kadınlarda androjenikliğin klinik belirtileri sıklıkla gözlendi.

Sonuç: Adolesan sonrası önemli sayıdaki akne'li kadında artmış dolaşan androjen düzeyleri ve öyle görünüyor ki bu akne etyopatogenezinde önemli bir rol oynuyor. Ayrıca akne şiddeti ile androjen düzeyleri arasında doğrudan bir ilişki olması, bu hasta grubunda hem over hem de adrenal anormalliklerin yaygın olduğunu telkin etmektedir.

Anahtar kelimeler: Dehidroepiandrosteron sülfat, total serum testosteron, adolesan sonrası akne

INTRODUCTION

Acne is a chronic inflammatory disease of the pilosebaceous units (PSU). It is a disease of adolescents that may persist for many years [1,2]. Post-adolescent acne (PAA) is defined as the presence of acne after the age of 20 years, it has been reported to be of mild to moderate severity, consisting predominantly of inflammatory lesions, more commonly found on the chin and with fewer comedones

[1] Assistant Prof. in Dermatology. Basra Medical College, Basra Iraq
[2] Prof. of Dermatology. Basra Medical College, Basra Iraq
[3] Consultant Dermatologist. Basra General Hospital. Basra Iraq

Correspondence: Samer A. Dhaher,
Assistant Prof. in Dermatology. Basra Medical College, Basra Iraq Email: sameralamir2@yahoo.com

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[3]. Observations of PAA confirm the presence of two clinical groups Persistent acne (PA), that persist from adolescence and they have strong family history of persistent acne, and Late-onset acne (LOA) which represents acne that occurs for the first time after puberty.

Persistant acne (PA) could be explained as a continuation of acne occurring during teenage years and could therefore share similar pathogenic features, namely: increased sebum production, ductal hypercornification, inflammation and increased bacterial activity [4].There is a significantly higher sebum excretion rate among adult women with PA, compared with non-acne female adults, suggesting that at least in PA there may be an underlying increase in sebogenesis [5]. It is more difficult to explain LOA which starts well after the hormonal changes accompanying puberty [6]. Patients with LOA, may represent a subgroup who have underlying abnormalities of ovarian, adrenal or local androgen metabolism, and require separate investigation [7].

METHODS

A cross-sectional study was conducted on a sample of patients who attended to the Dermatology and Venereology outpatient clinics in both Basra Teaching Hospital and Basra General Hospital in the south of Iraq during the period from January 2012 until October 2013.

Two hundred forty women with PAA (132 women with LOA and 108 women with PA after the age of 20 years were examined consecutively in outpatient units for acne vulgaris. Inclusion criteria were the absence of hormonal therapy during the past 6 months, and absence of therapy with systemic antibiotics or isotretinoin at the time of examination. Subjects who received oral contraceptives within the last 3 months of the study, or other drugs likely to interfere with androgen metabolism within 6 months of the study (e.g. cimetidine, spironolactone, or cyproterone acetate) were excluded from the study, as these agents may have had effects on clinical markers of androgenicity. Questionnaire including age of onset, age of menarche, family history of acne vulgaris, history of drug intake, history of premenstrual flare, menstrual irregularity in form of amenorrhea for at least 3 months or menstruation for more than 7 days,& marital status. Clinical and physical examination including; distribution and severity of acne vulgaris , distribution of both scalp and body hair, signs of hormonal irregularity such as hirsutism were carried out. Acne severity was generally assessed by counting the number, type, and distribution of lesions depending on Cunliffe et al classification (8). All patients were examined by ultrasound, and the morphology of the ovaries were assessed, the ultrasound findings of polycystic ovaries were12 or more follicles in each ovary, measuring 2-9 mm in diameter and/or increase ovarian volume.

Total serum testosterone (TST) and DHEA-S levels in serum samples obtained in the morning during the follicular phase (days 3-8 of the menstrual cycle) were measured by radioimmunoassay and ELISA respectively. The reference values for normal levels are TST levels 0.1-0.9ng/ml, DHEA-S values 0.4-2.17µg/ml (9).

RESULTS

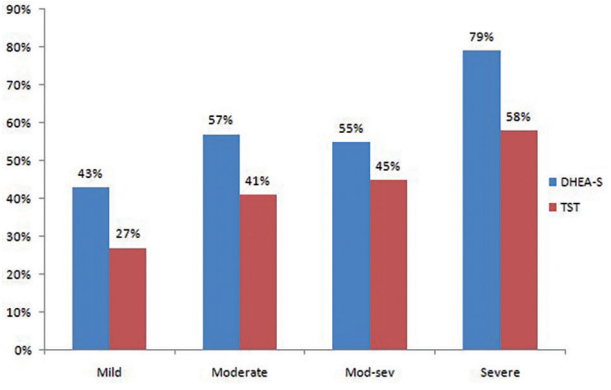
The results showed that there was an excess of androgen level in 176 (73.33%) patients; 81 patients (34%) in whom only DHEA-S was increased, 44 (18%) only TST was increased and 51 (22%) both DHED-S and TST were found to be increased. DHEA-S levels were elevated in 132(55%) of all patients, 66 women (50%) with LOA and 66 women (50%) with PA. Total serum testosterone (TST) level was increased in 95 (39.6%) of all patients, 50 women (52.6%) with LOA and 45 women (47.4%) with PA (Table 1). According to the severity of acne lesions, there were 76 (31.66%) patients with mild acne, 87 (36.25%) with moderate, 53 (22.08%) with moderately severe and 24 (10%) with severe acne. Serum androgens level were significantly correlated to the severity of PAA in which 33 (43.4%) women with mild acne showed raised DHEA-S compared to 21 (79.2%) women with severe acne, similarly TST levels were elevated in only 27.6% women with mild acne, while 58.3% women with severe cases had raised TST (Graphic 1). Results was statistically significant ($p<0.05$). In addition, clinical markers of androgenicity were frequently observed in women with PAA, where 210 patients (87.5%) had history of premenstrual flare, 144 (60%) had hirsutism , and 85 (35.4%) had ultrasonic confirmed polycystic ovary, furthermore, those patients with clinical evidence of androgenicity had statistically significant elevation of both serum DHEA-S and TST compared to those patients without clinical markers of androgenicity where 61.9% and 44.7% of patients with premenstrual flare had raised serum level of DHEA-S and TST respectively, while those patients with hirsutism 67.4% had raised DHEA-S and 48.6%

had elevated TST in their circulation and in patients with polycystic ovaries, 68.2% demonstrated raised DHEA-S and 78.8% had increased serum level of TST (Graphic 2).

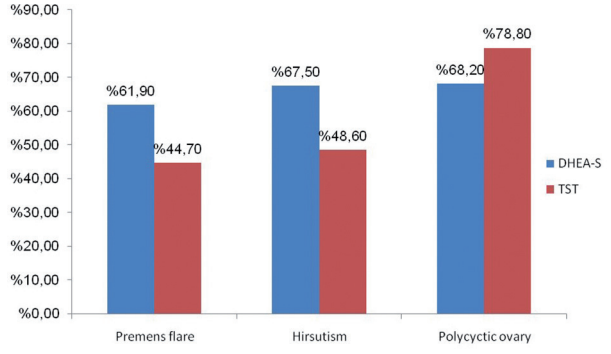
Table 1. Serum DHEA –S and TST levels in patients with PAA and its relation to the type of acne

Androgens level	Acne type		Total n (%)	p value
	Late onset acne n (%)	Persistent acne n (%)		
DHEA-S raised	66 (50.0)	66 (50.0)	132 (55.0)	0.112
TST raised	50 (52.6)	45 (47.4)	95 (39.6)	0.642

DHEA-S, dehydroepiandrosterone sulfate; TST, total serum testosterone



Graphic 1. Percentage of patients with elevated DHEA-S & TST in relation to the severity of acne



Graphic 2. Percentage of patients with raised levels of DHEA-S &TST in association with clinical androgen markers

DISCUSSION

The terms persistent and late onset acne are now generally accepted as describing the two types of post adolescent acne [7], and frequently causes discomfort and cosmetic disability. Although this problem was extensively investigated in the literature, no previous Iraqi study was carried out in this field, therefore this study was aimed to assess the serum levels of androgens including; DHEA-S and TST in Iraqi women with PAA, as well as to evaluate the relationship between the severity of acne and laboratory markers of androgenicity, and to determine the correlation between clinical parameters and the laboratory markers of Although the causes of PAA remained to be determined, it would appear that in some individuals there is an increased level of androgens in their circulation. The results of the study clearly demonstrated that there was a significant elevation of serum androgens levels in PAA women including both TST and DHEA-S. An abnormal androgenic parameters in adult women with acne was previously observed in many published studies [7,10,11], however the results were greatly variable. Mancschi et al. [12] reported mild and heterogeneous hyperandrogenism in 70% of women with adult acne. Vexiau et al. [13] reported hyperandrogenism in 86% of patients with persistent acne without signs of virilism. Darley et al [11] and Slayden et al. [14] reported abnormal levels of androgenic markers in 76% and 55% of patients with adult acne, respectively. Our results showed that at least 73% of our patients with PAA women had excess androgens levels in their circulation. This finding is consistent with some published studies [10,15].

The findings were also showed that the likelihood of having abnormal androgen hormones is more consistently documented in women with PAA. In addition, it has been suggested that these women may have an increased level of tissue-derived androgens which play a role in the pathogenesis of female acne [7,16].

Raised levels of DHEA-S in women with acne are well documented in literatures [10, 13]. We reported that DHEA-S level was significantly elevated in patients with PAA where 55% of all patients have raised value of DHEA-S and it is the only abnormal finding in about one third of patients. This observation suggesting that in these women, DHEA-S has

an important role in the pathogenesis of PAA and may represents remarkable clue for an underlying adult-onset congenital adrenal hyperplasia i.e. it is important to investigate for such problem in adult onset acne with raised level of DHEA-S.

In the present study, the TST level was raised in 40% of patients and it was the only abnormal androgen in about 18% of cases. These findings are consistent with other studies [15] which reported that the levels of total and free serum testosterone and sex hormone binding globulin are raised and within normal range. The role of normal and elevated circulating testosterone in the aetiopathogenesis of PAA is further supported by the findings of an increased local target tissue metabolism of testosterone and increased level of tissue derived androgens(3α-androstanediol glucuronide and androsterone glucuronide) in these women [16].

In our study, we demonstrated that there was positive correlation between acne severity and laboratory markers of androgenicity and we found that the levels of DHEA-S and TST were significantly elevated in severe form of acne compared with mild acne. It seems reasonable that raised androgen levels are considered as key factors in the etiology of acne, there should be an association between acne severity and the degree of androgen production, There are several previous studies discuss the relationship between acne severity and androgen levels but with inconsistent results. Walton et al. demonstrated a positive correlation between levels of androstenedione and DHEA-S and acne score, and a negative correlation between SHBG level and acne score [17]. Cibula et al.[18] didn't demonstrated any correlation between acne severity and clinical or laboratory markers of androgenicity, Hassan Seirafi et al. [10], found no overall correlation between hormonal level and acne severity ,these findings may suggest that end-organ hypersensitivity and not androgen level may be the central factor in severity of acne [7].

In our study we have separated PAA into two subgroups; persistent and late onset acne assuming that both may have different underlying ovarian or adrenal abnormalities, to clarify this we investigate both subgroups separately for evidence of circulating hyper androgenism. The result showed no statistically significant difference in hormonal levels between the two subgroups suggesting that both conditions have the same hormonal problem and both under the influence of ovarian and adrenal abnormalities.

Although anecdotal reports denoted that there were frequent occurrences of premenstrual flare-ups in late onset acne compared to persistent acne group [19]. It is now agreed that premenstrual flare-ups may occur in both groups of PAA. This was clearly demonstrated in our study. Interestingly, the majority (87.5%) of our patients reported premenstrual flare-ups of their acne lesions and in most of them there was significant elevation of androgens levels when compared with those patients without premenstrual flare-ups, suggesting that this symptom is influenced by hyperandrogenemia.

Our results confirmed the observation that hirsutism is frequently coexisting with acne and both are common manifestations of hyperandrogenism. An abnormally increased level of both DHEA-S and TST was found in 67.4% and 48.6% respectively, and this is in agreement with other studies [10,14,20,21]. In addition those patients with acne and hirsutism have significant overproduction of androgens than those with acne alone, and this is consistent with some reports [10,13].

The correlation between acne and polycystic ovary syndrome is well documented in the literatures. Persistent, severe or acne of late onset in women is suggestive of PCOS or another disorder of androgen excess [22]. In our study we reported that 35% of women with adult acne had polycystic ovary and this is in contrast to other study by Bunker et al. who reported that 83% of women with acne had PCOS [23], it seems that such high figure because that not all of these women met the diagnostic criteria for the diagnosis of PCOS [24]. The hormonal problem in PCOS is often variable; and in most women they had high normal or slightly elevated TST. We demonstrated that approximately 79% of women with PCOS had raised testosterone level, and about 68% of women had elevated DHEA-S level and was significantly greater than those without PCOS, this is similarly reported by others [25-27]. The mechanism for adrenal androgen excess in PCOS remain debatable, it has postulated that in PCOS the pituitary and ovarian responses to their respective trophic factors are exaggerated [28] ,while others demonstrated an alteration in the intrinsic behavior of the adrenal leading to hyper responsiveness of adrenal cortex to ACTH stimulation [29].

In conclusion, post-adolescent acne is a frequent manifestation in Iraqi women & there was an increased level of circulating androgens in significant proportion of them. As far as PAA was accepted as a feature of hyperandrogenism, there was a

direct correlation between the severity of acne and androgen level. Both DHEA-S and TST were significantly elevated in patients with PAA suggesting that both ovarian and adrenal abnormalities are common at this age group, and those patients may benefit from hormonal treatments, including inhibitors of ovarian or adrenal androgen production or androgen receptor blockers.

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