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Detection of dihydrotestosterone (DHT) in female androgenic alopecia (FAGA)

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Abstract :

Female androgenetic alopecia (FAGA) is a kind of hair loss that does not result in permanent scarring. It is characterized by a widespread thinning of hair due to the gradual shrinking of hair follicles and a decrease in the quantity of hairs, particularly in the central , and parietal regions of the scalp. determine the concentration of DHT in women diagnosed with androgenic alopecia

The study included a sample of 60 women with androgenic alopecia and 30 healthy women, as a control group. Serum DHT levels were assessed using (ELISA)

The findings indicated that there were statistically significant disparities (p value < 0.05) in DHT concentration between the patients and the control group. Regarding age and weightThe results indicated statistically significant differences between the patients. (p value < 0.05) Namely, DHT increases with age and weight

Increased levels of dihydrotestosterone in women with female androgenic alopecia, as it is considered DHT is a contributing factor to the development of androgenic alopecia in women.

Keywords: Dihydrotestosterone (DHT). Female androgenetic alopecia(FAGA), Female pattern hair loss (FPHL),

الكشف عن هرمون ديهيدروتستوستيرون (DHT) في الثعلبة الأندروجينية عند الإناث (FAGA)

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مستخلص

الثعلبة الاندروجينية الانثوية (FAGA) هو نوع من تساقط الشعر لا يؤدي إلى حدوث ندبات دائمة. يتميز بتقليل كثافة الشعر على نطاق واسع نتيجة لتقلص تدريجي لبصيلات الشعر وانخفاض عدد الشعرات، خاصة في المناطق المركزية والجدارية من فروة الرأس. تهدف الدراسة إلى تحديد تركيز الديهيدروتستوستيرون (DHT) لدى النساء المصابات بالثعلبة الاندروجينية الانثوية .

شملت الدراسة عينة مكونة من 60 امرأة مصابة بالثعلبة الاندروجينية الانثوية و30 امرأة صحية كعينة تحكم. تم تقييم مستويات DHT في المصل باستخدام اختبار ELISA

أظهرت النتائج وجود فروق ذات دلالة إحصائية (p value < 0.05) في تركيز DHT بين المرضى ومجموعة التحكم. وبخصوص العمر والوزن، أشارت النتائج إلى وجود اختلافات ذات دلالة إحصائية بين المرضى p value (< 0.05))، حيث يتزايد مستوى DHT مع تقدم العمر وزيادة الوزن.

تشير زيادة مستويات الديهيدروتستوستيرون لدى النساء المصابات بالثعلبة الاندروجينية الانثوية إلى أن DHT يعتبر عاملاً مساهماً في تطور الثعلبة الاندروجينية الانثوية لدى النساء.

الكلمات المفتاحية: الديهيدروتستوستيرون (DHT)، الثعلبة الاندروجينية الانثوية (FAGA)، تساقط الشعر الانثوي(FPHL).

Introduction

Alopecia is a prevalent condition that affects more than half of the global population. Among the various types of alopecia, androgenetic alopecia (AGA) is the most prevalent[1].Female androgenetic alopecia (FAGA) is a pervasive condition characterized by non-scarring hair loss in women. [2]. The clinical presentation typically features diffuse hair thinning across the central scalp, while the frontal hairline remains relatively unaffected. Numerous studies have substantiated a diminished quality of life among women diagnosed with female androgenetic alopecia (FAGA). Undoubtedly, this condition exerts a significant psychological impact, often leading to increased levels of depression and anxiety [3] The involvement of androgens in the pathogenesis of hair loss in female patients remains uncertain. As a result, the term "female pattern hair loss (FPHL)" is favored over female androgenetic alopecia (AGA) [4]. The etiopathogenesis of female pattern hair loss (FPHL) is intricate, influenced significantly by genetic, environmental and hormonal-factors[5] .Three primary patterns have been identified in the presentation of female androgenetic alopecia (FAGA) [6]. In the first pattern, diffuse thinning occurs in the upper biparietal and vertex areas of the scalp, with preservation of the frontal hairline. This pattern is recognized in various hair loss scales, with Ludwig's scale being the most prevalent among them. The second pattern, as described by Olsen, involves thinning in the frontal, bitemporal, and vertex areas of the scalp, resembling a Christmas tree distribution. Lastly, the third pattern presents with thinning in the frontotemporal areas of the scalp, similar to what is observed in males, although this presentation is relatively rare[7]. Human hair undergoes a cyclic replacement process. The phases of hair growth include The anagen (growth phase), catagen (involution phase), telogen (resting phase), and exogen (shedding phase)[8-10]. The anagen phase of hair growth typically lasts for 3–5 years, while the catagen phase typically persists for a few weeks The resting period lasts known as telogen for approximately three months., Hair follicle regeneration typically occurs within the first week of the growth phase, and once rejuvenated, This phase persists until the hair reaches its ultimate length. The al-

terations in hair cycle dynamics, characterized by a shortened anagen phase and prolonged telogen phase, represent a critical component in the pathogenesis of androgenetic alopecia (AGA). In women with female pattern hair loss (FPHL) compared to controls, the decrease in total hair density primarily attributed to an increase in empty follicles is approximately five times greater than the increase in vellus hairs caused by hair follicle miniaturization. In androgenetic alopecia (AGA), the duration of the anagen phase progressively diminishes with each cycle, while the length of the telogen phase typically remains constant or may even be prolonged. This progression ultimately leads to a reduction in the ratio of anagen to telogen phases in androgenetic alopecia (AGA). Consequently, as each hair cycle shortens successively, the length of each hair shaft decreases. Eventually, the hair shaft becomes too short to reach the skin surface, leading to an empty follicular pore. In androgenetic alopecia (AGA), the substage of the telogen phase that is prolonged is known as kenogen. This phase follows exogen and results in the production of empty follicles. In the kenogen phase, the hair follicle undergoes a physiological resting period. In androgenetic alopecia (AGA), the kenogen phase lasts longer, resulting in a higher percentage of empty hair follicles, which contributes to the progression of balding[9]. The therapeutic options available for androgenetic alopecia (AGA) are constrained[11]. Topical minoxidil and Oral finasteride the primary treatments for androgenetic alopecia (AGA) [1]. Finasteride, a selective steroidal inhibitor of 5-α-reductase, inhibits the conversion of testosterone to DHT, leading to decreased levels of DHT in serum and the scalp. Minoxidil, on the other hand, induces vasodilation of peripheral vessels and enhances microcirculation, thereby promoting proliferation of dermal papilla cells (DPCs).[12]

Dihydrotestosterone (DHT) is widely recognized as the most potent hormone among androgens and is classified as a pure androgen due to its inability to convert into estrogen[13]. is the primary mediator of androgenetic alopecia (AGA). DHT is converted from testosterone by 5α-reductase type 2. Dihydrotestosterone binds to the androgen receptor (AR) of the dermal papillae, translocates into the nucleus, and induces processes such as apoptosis, which can affect hair formation.

Dihydrotestosterone suppresses proliferation and sustains the telogen phase. It disrupts the hair cycle by prematurely inducing the catagen phase and extending the telogen phase.[14]. The objective of the study is to ascertain the concentration of dihydrotestosterone (DHT) in women affected by androgenic alopecia.

Materials and methods

A total of 90 blood samples were collected from female participants aged 15 to 50,30 control blood samples from unaffected women And 90 blood samples from women diagnosed with androgenetic alopecia by expert dermatologists at the dermatology department of Tikrit Teaching Hospital. Sampling took place from August 2023 to February 2024. Confidential patient information was recorded using a dedicated questionnaire form. Weight and height were measured with participants wearing light clothing and barefoot. For calculating Body Mass Index (BMI), weight (in kilograms) is divided by the square of height (in meters squared) If the result is less than 18.5: the person is underweight. 18.5 to 24.9: the weight is normal. 25 to 29.9: the person is overweight. . A 3 ml blood sample was obtained and left to coagulate. Following coagulation, the samples underwent centrifugation to separate the serum, which was then stored at -20°C for subsequent analysis. The total concentration of dihydrotestosterone (DHT) was determined using ELISA kits sourced from Bioassay Korea.

statistical analysis

The statistical analysis of the results was performed using MINITAB version 17 statistical software. T-tests and ANOVA (F-test) were employed to assess significant differences between the study groups. Furthermore, Duncan's multiple range test was utilized to evaluate disparities in the means among the participating groups, with a significance level set at 0.05.

Results

The findings of the present study revealed a statistically significant increase ($p < 0.05$) in the average concentration of DHT among women experiencing hair loss compared to the control group.

Table 1: Comparison between affected and healthy women regarding mean DHT values		
Group	**Number**	**DHT ng/L mean ± SD**
C	30	1694 ± 79.9
P	60	2035 ± 100.9
p.value		0.048*
The test used t-test.C: control. P: patient DHT: Dihydrotestosterone, SD: Standard deviation		

The findings indicated significant age-related variations ($p < 0.05$), Both the middle and younger age groups exhibited lower hormone levels than the older age group, although all three groups demonstrated higher hormone levels than the control group.

Table 2 :Association between DHT level and the age			
Group	**Age**	**Number**	**DHT ng/L mean ± SD**
P	41-55	4	2300±148.6a
	26-40	24	2005±90.21b
	10-25	32	2024±105.5b
C		30	1694±79.9c
P-VALUE			0.044*
The test used F-test and Duncan's, DHT: Dihydrotestosterone, SD: Standard deviation The Duncan test yielded the highest value for the arithmetic mean (a), and if the subsequent value is statistically distinct from it, we assign it (b). The Duncan test indicates that when letters are similar, there is no statistically significant difference between them.			

Regarding weight, the current study recorded significant differences between the different weights (p value < 0.05). in the concentration of DHT, as the concentration of DHT in overweight women is higher than that of underweight and normal-weight women, and all of them have a higher DHT concentration than the control group.

Table3: Association between DHT level and the Weight			
Group	**WEIGHT**	**Number**	**DHT ng/L mean ± SD**
P	Underweight	22	1984±118b
	Normal	34	1937±75.8b
	Overweight	4	3152±147.8a
C		30	1694±79.9c
P-VALUE			0.034*

The test used F-test and Duncan's, Dihydrotestosterone, SD: Standard deviation
The Duncan test yielded the highest value for the arithmetic mean (a), and if the subsequent value is statistically distinct from it, we assign it (b). The Duncan test indicates that when letters are similar, there is no statistically significant difference between them.

Discussion

Results varied with[15] where an increase in the hormone concentration was found in patients and also in the control group. The results agreed with[16].Currently, the precise etiology and mechanism of androgenetic alopecia (AGA) remain incompletely understood. It is widely accepted that genetic factors, elevated androgen levels in localized tissues, and the overexpression of the androgen receptor (AR) are prominent contributors to the development of AGA. The Wnt/β-catenin signaling pathway is crucial in the cycling of hair growth, playing a critical role in the regeneration of hair follicles and the growth of the hair shaft. Recent research indicates that the inhibition of the Wnt/β-catenin pathway by dihydrotestosterone (DHT) represents a pivotal pathological mechanism in the development of androgenetic alopecia (AGA)[14]. The regulatory pathways influencing the development of the hair follicle cycle predominantly encompass the Wnt/β-catenin pathway, transforming growth factor-β (TGF-β) signaling, bone morphogenetic protein (BMP) signaling, and sonic hedgehog (SHH) signaling, among others. Of these pathways, the Wnt/β-catenin signaling pathway is crucial for hair follicle morphogenesis and the initial formation of primary hair follicles. Wnt signaling represents a highly conserved pathway critical for the development and maintenance of multicellular organisms' structure and function. Glycogen synthase kinase-3β (GSK-3β) plays a crucial role in regulating the self-renewal and functional

dynamics of cellular populations. Wnt signaling can negatively regulate Glycogen synthase kinase-3β (GSK-3β) by phosphorylating it at Ser9 residue, resulting in stabilization of β-catenin. In this signaling pathway, β-catenin, a key signal transducer, is stabilized and translocated to the nucleus, where it governs the expression of genes involved in renewal and proliferation.[1] Dickkopf 1 (DKK1)is one of the genes most upregulated by DHT in balding dermal papilla cells (DPCs). is secreted from dermal papilla cells in response to DHT stimulation, and it is recognized for its role in contributing to and exacerbating androgenetic alopecia (AGA). DKK-1 inhibited the growth of outer root sheath keratinocytes., a Wnt antagonist, inhibits Wnt action by binding to thelow-density lipoprotein-related protein (LRP)[17, 18]. DHT also upregulates interleukin-6 (IL-6) secretion in balding (DPCs). Moreover, IL-6 has been demonstrated to suppress the proliferation of outer root sheath keratinocytes and inhibit hair shaft elongation[19].

Regarding age, these results agreed with [20, 21]. The commencement of (FPHL) can occur at any point post-puberty, and its prevalence tends to rise with advancing age[6]. (FPHL) represents a prevalent hair disorder; however, studies assessing its prevalence frequently yield inconsistent findings, potentially stemming from the absence of universally accepted diagnostic criteria to precisely delineate the condition. While the incidence of (FPHL) varies among countries, it consistently escalates with age, notably affecting approximately 55% of women aged 70 and older. In a minority of cases, severe progression of the disease occurs during adolescence. Generally, (FPHL) exhibits an initial peak during the reproductive years and a subsequent peak following menopause[22]. This observation suggests a strong association between (FPHL) and hormonal fluctuations. Interestingly, the prevalence of (FPHL) also shows variation based on geographical location and ethnicity. For instance, an examination of prevalence among junior high school girls revealed an overall incidence of (FPHL) at 28.6%. This incidence was notably higher in rural settings compared to urban areas and showed a significant correlation with family history[23]. While (FPHL) can affect individuals of all racial backgrounds, studies have indicated a higher prevalence among Cau-

casian women compared to Chinese and Korean women[24]. In Caucasian women, the prevalence of female androgenetic alopecia (FAGA) rises with age, ranging from 3–12% during the third to fourth decade of life, increasing to 14–28% among postmenopausal women in their fifties, and reaching 29–56% in individuals aged over 70 years. The prevalence of female androgenetic alopecia (FAGA) in Asian women follows a similar age-related pattern, although it appears to be lower compared to Caucasian women[6]. Previous community-based or population-based research has identified variations in the prevalence of androgenetic alopecia (AGA), attributable to differences in ethnic and regional demographics, sample sizes, age distributions, and methodologies used for hormone measurement. Future studies should aim to evaluate the correlation between androgenetic alopecia (AGA) and factors such as lifestyle, environment, and related causes to enhance comprehension of these relationships.

Regarding weight, these results agreed with[5, 21]. These findings varied significantly when compared with[25]. Research indicates that androgen excess may exert an indirect influence on metabolic disorders in women through its impact on food intake[26, 27]. The hypothalamus, specifically the arcuate nucleus (ARC), serves as the primary regulator in maintaining homeostasis by energy expenditure balancing and food intake. The neuropeptide Y (NPY)/agouti-related peptide (AgRP) neurons located in (ARC) of the hypothalamus are responsible for synthesizing orexigenic peptides such as NPY and AgRP. Elevated levels of these peptides notably enhance food intake. Conversely, the proopiomelanocortin (POMC) neurons within the (ARC) of the hypothalamus produce the anorexigenic peptide α-MSH, which acts to reduce food intake. Insulin and leptin exert modulation on both NPY/AgRP and POMC neurons via their respective receptors, contributing significantly to feedback regulation that plays an important role in lipid and glucose metabolism. Dysregulation of these neurons can result in hypothalamic insulin and leptin resistance, leading to overexpression of POMC neurons and inhibition of NPY/AgRP neurons. Ultimately, these changes can guide to abnormal food intake and metabolic disturbances[28] . Some researchers employed a DHT-

induced PCOS rat model to investigate the impact of hyperandrogenism on hypothalamic neurons. findings revealed that prolonged exposure to elevated androgen levels resulted in increased food consumption, weight gain, and adiposity. Additionally, it impaired glucose tolerance and insulin sensitivity. Furthermore, DHT notably increased mRNA expression of Agrp and NPY in the hypothalamus. Specifically, DHT upregulated NPY expression and downregulated POMC expression in conjunction with leptin, while Agrp mRNA levels remained unaffected. Discrepancies observed between in vivo and in vitro experiments may stem from the varied complexities inherent in experimental conditions. In summary, excess androgens led to increased food intake and facilitated obesity through the downregulation of leptin and insulin signaling in the hypothalamus, consequently enhancing the expression of orexigenic genes[28].

CONCLUSIONS

Dihydrotestosterone exerts a substantial impact on women experiencing androgenetic alopecia, with the likelihood of developing this condition escalating with advancing age and increasing body weight.

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