

Evaluation of serum aldosterone level in patients with androgenetic alopecia

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a progressive patterned hair loss from the scalp occurring in both men and women. Polygenic heredity is assumed to be the primary cause, although testosterone hormone plays an important role in its pathogenesis. Androgenetic alopecia was found to be associated with coronary heart diseases and hypertension. Clinical studies have suggested the involvement of aldosterone in pathogenesis of AGA. The aim of this study was to evaluate serum level of aldosterone hormone in patients with AGA in order to elucidate its possible role in the pathogenesis of such disease and its relation to disease severity.

Patients and Methods: The study included 50 male patients with AGA and 40 healthy control subjects. Patients were classified clinically according to The Hamilton–Norwood scale for male pattern distribution into different grades of severity. For each patient and control, the serum level of free human aldosterone was measured using enzyme immunoassay (ELISA).

Results: Serum level of aldosterone hormone was statistically higher in patients than controls ($P < 0.001$). There was a significant positive correlation between serum levels of aldosterone hormone and the severity of disease ($P < 0.001$). There was also a significant positive correlation between serum aldosterone levels and Systolic, diastolic blood pressure and duration of the disease. However, there was no significant correlation between serum aldosterone levels and age of the patients.

Conclusions: Aldosterone might have a role in the pathogenesis of AGA and its serum level is related to disease severity. The use of the new antihypertensive selective aldosterone receptors antagonists might be a new therapeutic modality in treatment of AGA.

INTRODUCTION

Androgenetic alopecia (AGA) is considered the most prevalent type of hair loss in humans.¹ The etiology and pathogenesis of AGA are not fully understood yet. Hamilton² referred to mutual interplay of genetic factors, androgens, and age factors in the origin of AGA.^{3,4} Polygenic heredity is assumed to be the primary cause of AGA, although testosterone plays an important role, seemingly independent of genetic predisposition.¹ Androgenetic alopecia is considered to be associated with coronary heart disease but the explanation of this association remains unknown. Hypertension is highly prevalent in patients with

coronary heart disease. Essential hypertension is linked to hyperaldosteronism and spironolactone, an antihypertensive drug, which is a mineralocorticoid receptor antagonist, has been used for a long time in the treatment of androgenic alopecia.⁵ This study aimed at evaluation of serum level of aldosterone hormone in patients with AGA in order to elucidate its possible role in the pathogenesis of such disease and its relation to disease severity.

PATIENTS AND METHODS

The present study included 50 patients with androgenetic alopecia with different degrees of

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severity collected from the outpatients clinic of Dermatology and Venereology Department, Tanta University Hospital, Egypt. Forty, age and sex matched healthy persons, with no present or past history of AGA, were also included as controls. Patients who had a history of hyperaldosteronism or cardiovascular disease were not included in the study. Those who received hormone replacement therapy with testosterone or corticosteroid therapy for less than 1 month (chronic corticoid therapy) prior to commencement of the study were also excluded from the study.

All patients and controls were subjected to complete history taking, thorough general and full routine investigations. Careful dermatological examination involving scalp skin and hair, facial and body hair as well as the nails was done. The Hamilton–Norwood scale for male pattern distribution (AGA)⁶ was applied to classify the patients according to their stages. Five milliliters of venous blood were collected from each patient and control for quantitative determination of the levels of aldosterone in the serum using enzyme immunoassay (ELISA).

Enzyme immunoassay for aldosterone:

Aldosterone was measured using commercial kits (DRG® Aldosterone ELISA (EIA-4600)). Calibrator, control and patients serum samples were pipetted into correspondingly labelled wells in duplicate. The wells were incubated on a plate shaker for 1 hour at room temperature. TMB substrate was then pipetted into each well at timed intervals. The wells were incubated on a plate shaker for 10-15 minutes at room temperature (or until calibrator A attains dark blue colour for desired OD). Then, stopping solution added. The plate was read on a microwell plate reader at 450nm

within 20 minutes after addition of the stopping solution. A calibrator curve was drawn, and the optical densities of samples were read from these curves.

Statistical Analysis:

The data were collected, tabulated and statistically analyzed using SPSS software statistical computer package version 17. For quantitative data, the mean and standard deviation were calculated. The difference between two means was statistically analyzed by student t- test and Kruskal-Wallis Test. P-value ≤ 0.05 was considered statistically significant.

RESULTS

Clinical Results:

This study included 50 male patients of androgenetic alopecia. Their ages ranged from 22 to 75 years with a mean of 44.620 ± 12.467 years. The duration of their disease varied from 3 years to 35 years, with a mean of 14.64 ± 8.78 years. Forty healthy males were also included as controls. Their ages ranged from 20 to 63 years with a mean of 41.531 ± 11.242 years. There was no statistically significant difference between patients and control groups regarding age.

According to The Hamilton Norwood clinical grading scale of classification, the patients in this study was ranged from grade II to grade VII (Grade II: n=3, Grade III: n= 12, Grade IV: n=13, Grade V: n= 12, Grade VI: n=7, Grade VII: n=3) Out of the 50 patients, 42 patients had a positive family history of AGA. No correlation between family history of AGA among patients and their different grades could be detected (P= 0.77).

Regarding presence of hypertension, 20 patients (40%) and 6 (15%) controls were suffering from

hypertension. There was a statistically significant difference between patients and control ($P = 0.02$). Presence of hypertension was not correlated to the grades of AGA among patients Table 1. There was a statistically significant difference in values of systolic and diastolic blood pressure between patients and control groups ($P=0.012$ and $P<0.001$ respectively).

Table 1 Relation between number and percentage of patients in each grade of androgenetic alopecia and presence of hypertension

Grade	Hypertension					
	Negative		Positive		Total	
	N	%	N	%	N	%
II	3	6	0	0	3	6
III	9	18	3	6	12	24
IV	9	18	4	8	13	26
V	5	10	7	14	12	24
VI	4	8	3	6	7	14
VII	0	0	3	6	3	6
Total	30	60	20	40	50	100

Laboratory results:

Serum levels of aldosterone in patients group ranged from 50 to 440 pgm/ml with a mean of 87.50 ± 129.363 pgm/ml while that of controls ranged from 5 to 100 pgm/ml with a mean of 20.250 ± 29.326 pgm/ml. There was a statistically highly significant difference between both groups ($P < 0.001$). There was no significant correlation between serum aldosterone levels and age of the patients among the studied patients ($P = 0.919$). There was a positive significant correlation between serum aldosterone level and duration of the disease ($P < 0.001$). There was also a statistically highly significant positive correlation between serum aldosterone levels and grades of AGA among the studied patients ($P < 0.001$) as shown in Table 2. There were a positive significant correla-

tion between serum aldosterone levels and Systolic and diastolic blood pressure ($P < 0.001$ and $P=0.037$ respectively).

Table 2 Comparison between mean serum aldosterone levels in each grade of the studied patients

Grade	Aldosterone level		Kruskal-Wallis Test	
	Range	Mean \pm SD	χ^2	P-value
II	5- 5	5.00 \pm 0.00	45.37	<0.001*
III	5-10	7.082.57 \pm		
IV	10-40	20 \pm 8.90		
V	40-100	69.5822.61 \pm		
VI	100-380	278.57117.82 \pm		
VII	390-440	41026.46 \pm		

DISCUSSION

This study was an evaluation of serum levels of aldosterone among male patients of androgenetic alopecia in a trial to elucidate its role in such disease.

Regarding hypertension, in the present study there was a significant high BP values (systolic, diastolic or both) among patients (40%) than control (15%) and this finding was consistent with a study done by Hirsso *et al.* 2006⁷ who also found higher blood pressure values in patients with AGA than in a control group (65% vs 45%). Their study was carried out on 245 men aged 63 years, 58% of them reported extensive hair loss (grade III-VII). In another study done by Ahouansou, *et al.* 2007,⁸ they showed that hypertension was strongly associated to AGA (82% of hypertensive patients had alopecia versus 56% of non hypertensive patients). The study done on 250 Caucasian men aged 35-65 years to evaluate the prevalence of AGA between them. They found that 38% of them had hypertension and 65% had AGA (grade III-VII).

The result of the current study was also consistent with the study carried out by Mansouri *et al.* 2005⁹ who observed a positive correlation between AGA

and elevated BP values but in a female population. On the contrary, a study carried out on 727 young men aged 25-34 years with moderate to extensive AGA, failed to detect statistically significant differences for systolic or diastolic blood pressure levels in the studied patients.¹⁰ Moreover, in another study done¹¹ on female patients, they did not find any differences in BP in women with AGA and controls.

The association of hypertension and AGA could be explained by some authors by the binding of androgen to mineralocorticoid receptors (MR). This might be also responsible for the observed difference in the higher susceptibility to hypertension in men as compared to women.¹² Most studies detected no significant differences in testosterone values among AGA patients.^{5,13,14} Thus, other factors than androgen binding to MR were suggested to be responsible for the association between AGA and hypertension such as aldosterone level. Regarding aldosterone level, in the present study there were significantly higher levels in AGA patients than controls. These results were consistent with those of Arias-Santiago, et al. 2009.⁵ Their study included 40 male patients with AGA and 40 healthy male controls. Aldosterone levels were significantly higher in patients vs. controls. In addition, there were significantly higher systolic BP values but, no significant difference was found in mean diastolic BP values. They explained this result by the effect of antihypertensive drugs and the small sample size.⁵

In another study¹⁴ carried out on 40 female patients with AGA and 40 female controls. Patients with AGA showed significantly higher aldosterone levels vs. controls. There were also significantly higher systolic and diastolic BP values vs. controls. A positive correlation between aldoste-

rone levels and systolic and diastolic BP values was also detected.

The result of the present study was consistent with another comparative study done on female with AGA¹³ Aldosterone level was significantly higher in patients vs. controls. Also, mean systolic BP values were higher in patients than controls but they didn't find significant difference in the mean diastolic BP values between patients and controls. Several mechanisms have been proposed to account for aldosterone-related tissue damage, and AGA. Firstly, evidence from animal and human subjects suggests that aldosterone promotes vascular infiltration with monocytes, macrophages, and lymphocytes.^{15,16} Also, animal models treated with salt and aldosterone, resulted in the activation of NFκB, a key transcription factor of pro-inflammatory mediators such as tumor necrosis factor (TNFα), ICAM-1.¹⁶ Aldosterone has also been shown in vitro to directly regulate the expression of genes that encode inflammatory molecules such as IL-6. Increased expression of some IL-6 cytokine family members and other proinflammatory cytokines such as, transforming growth factor beta 1 (TGF β-1), interleukin-1alpha (IL-1α), and tumor necrosis factor alpha (TNF-α) might contribute to the promotion of apoptosis and hair loss.^{17,18,19} These deleterious inflammatory mediators are suspected to contribute to microinflammation and perifollicular fibrosis.

In addition, aldosterone excess is associated with functional changes in the cardiac and renal vasculature, probably due to increased production of nitric oxide and reactive oxygen species. Similar mechanisms have been reported to inhibit the growth of isolated hair follicles in culture.^{18,20,21}

In the present study, there was positive significant correlation between serum aldosterone level

and systolic and diastolic blood pressure. While the study done by Arias-Santiago, et al., 2009⁵ showed a relationship between systolic and diastolic hypertension and higher aldosterone values, but it was not significant.

In the current study there was positive significant correlation between the serum aldosterone level and the disease severity. To the best of our knowledge there are no previous reports supporting these observations.

Hyperaldosteronism is considered to be responsible for most of primary hypertension.^{5,8} This could be explained by the fact that aldosterone is a steroid hormone with mineralocorticoid activity, mainly recognized for its action on sodium reabsorption in the distal nephron of the kidney. Also aldosterone was associated with increased expression of cyclooxygenase 2 derived prostacyclin²² and thromboxane A2 in spontaneously hypertensive rats.²³

From the current study and the previously mentioned studies, the association of hypertension and AGA could be explained by the presence of hyperaldosteronism, that may also directly participate in the development of alopecia^{5,8,14} and AGA could be considered as a clinical marker of a risk to develop hypertension.

Aldosterone is classically known to bind the cytosolic MR.²⁴ Skin and hair follicles normally express MR and have all of the enzymes required for mineralocorticoid pathways.²⁵ This was confirmed by several experimental studies in which over expression of the mineralocorticoid receptor targeted to the skin lead to the development of Alopecia.^{8,26,27} This raising many exciting questions regarding the role of the MR in skin and hair biology. Moreover, clinical studies have illustrated the role of aldosterone in the inflammatory process

in humans.^{12,24,28} Chronic inflammation, which is more prevalent in patients with AGA, has served to explain the association with cardiovascular disease.²⁴

CONCLUSIONS

Aldosterone may have a potential role in the pathogenesis of androgenetic alopecia. Further studies should be done on a large scale of patients to clarify the role of aldosterone hormone and MR in the pathogenesis of AGA. Accordingly, the use of the newly selective aldosterone receptors antagonists in the treatment of hypertensive patients for controlling blood pressure can offer a new therapeutic modality in treatment of AGA. Hypertension and other cardiovascular diseases (CVD) screening tests should be considered in AGA patients for early detection of high risk individuals and for initiation of preventive therapy for CVD.

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