

Serum lipoprotein (a) as an atherosclerosis risk factor in men with androgenic alopecia

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Conflict of interest : none to declare

*Received: December 30, 2010
Accepted: August 14, 2011*

Background: The association between coronary artery disease and androgenic alopecia has been demonstrated, but few studies have focused on the mechanism of this association. The aim of this study was to evaluate the lipid profile in male pattern alopecia.

Methods: In this case control study, 45 male patients with androgenic alopecia who were aged from 20 to 50 years and 45 men with a normal hair status aged from 20 to 50 years were enrolled as the case and control groups, respectively. Lipid parameters including cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, lipoprotein (a), apolipoprotein A1, apolipoprotein B were measured in cases and controls.

Results: A significant difference in serum lipoprotein (a) was observed between case and control groups ($p < 0.001$). We noted that 47.1 percent of the patients and 17.96% of the controls had a lipoprotein (a) level more than 30 mg/dl which is a critical level for coronary artery disease. There was no significant difference in other lipid parameters between two groups. The family history of androgenic alopecia and coronary heart disease was significantly higher in the cases than the controls.

Conclusion: Considering the results of the study and the important role of lipoprotein (a) as a risk factor for atherosclerotic heart disease, we suggest that all men with a male pattern hair loss should be investigated for lipid indices, especially lipoprotein (a).

Keywords: androgenic alopecia, lipid profile, lipoprotein (a), coronary artery disease, atherosclerosis risk factor

Iran J Dermatol 2011; 14: 81-85

INTRODUCTION

Androgenic Alopecia (AGA) has been always recognized as an androgen dependent hereditary disorder^{1,2}. A balding scalp is characterized by high levels of the potent androgen dihydrotestosterone and an increased expression of the androgen receptor gene¹. So, the association between AGA with coronary artery disease (CAD) has been investigated in many studies^{3,4}.

The gender difference in CAD cannot be explained on the basis of endogenous sex hormone exposure. None of the epidemiological studies in the literature have showed a positive

association between testosterone and CAD in men to suggest that high levels of this androgen may be a risk factor, with all the longitudinal studies consistently showing a lack of relationship. Data on women also do not suggest that endogenous testosterone plays a causal or protective role for CAD, but polycystic ovary syndrome (PCOS) patients undoubtedly have an adverse risk profile. Whether this leads to increased premature heart disease is currently unclear. Observational studies on dehydroepiandrosterone sulfate (DHEAS) do not support the hypothesis that DHEAS deficiency is a risk factor for CAD in men or women. Some researchers have revealed that low levels of free

testosterone may be related to the development of premature coronary artery disease⁵⁻⁷.

Several articles have indicated that AGA has a higher-than-normal risk for CAD⁸⁻¹⁵. Although an association between cardiovascular disease and AGA has been suggested in these studies, the explanation still remains unknown⁷. The effect of serum lipids, as a pathogenesis factors of male pattern alopecia, has been evaluated in a few studies^{4,16}. Lotufo et al, showed that AGA could serve as a clinical marker for an increased CAD risk, particularly in men with hypertension or high cholesterol¹¹. Sasmaz et al, showed that males with AGA had significantly higher levels of serum lipoprotein (a) compared to those with no AGA⁴ while Matilaiuen et al, failed to find higher levels of Lp (a) in AGA⁸. Farajzadeh et al, showed a remarkably higher level of lipoprotein (a) in women with female pattern alopecia¹⁵. In this study, we investigated the impact of serum lipid parameters on the relationship between AGA and CAD in males with AGA.

PATIENTS AND METHODS

In this case-control study which was conducted in Kerman, Iran, from July 2007 to April 2008, data were collected from men attending dermatology clinics affiliated to Kerman University of Medical Sciences and private dermatology clinics. Forty five male patients with AGA, aged between 20 and 50 years, were enrolled in the study. Forty five age-matched healthy men with a normal hair status were also recruited. An informed written consent was taken from each individual in the case and control groups. Men who were on any medication which could affect lipid metabolism, smokers, alcohol drinkers and those with Diabetes Mellitus (DM), CAD, hypertension (HT), familial hyperlipidemia, thyroid disease, chronic renal failure, liver disease, and cancer were excluded from both groups. The family history of DM, CAD, HTN, and androgenic alopecia was recorded. The baldness pattern was assessed by Hamilton

Baldness Scale, as modified by Norwood¹⁷. In this classification, hair loss was graded progressively from Type I (no loss) to Type VII (complete hair loss at the crown). The baldness groups were subcategorized into none (Type I), frontal-only (Types II and III) and vertex (Types III vertex, IV, V, VI and VII). For those whose pattern of hair loss was not compatible with Hamilton Baldness Scale, Ludwig classification was applied.

After 12 hours of fasting, a venous blood sample was taken for lipid profile including cholesterol, triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL), lipoprotein (a) (LP (a)), apolipoprotein A1 (Apo A1) and apolipoprotein B (Apo B). The immunoturbidimetric method was used to measure Apo A1, Apo B and LP (a) levels. Statistical analysis was carried out using SPSS 16. Data was analyzed using t- test and Chi square. A P-value less than 0.05 was accepted as evidence of statistical significance.

RESULTS

The mean age of the cases and the controls was 25.7 ± 6.26 and 27.16 ± 6.46 years, respectively with no significant difference between the two groups. The mean age of the patients with frontal and vertex baldness was 23.35 and 28.35 years, respectively ($p < 0.05$). Table 1 shows the family history of AGA, HTN, DM and CAD in the case and control groups. As this table shows, a positive family history of AGA and CAD was significantly more frequent in cases than the controls ($P < 0.05$). The pattern of hair loss was compatible with Hamilton pattern in 91.5% of all cases; 53.6% had frontal recession and 46.4% had vertex loss pattern; 2.1% of the patients had the Ludwig pattern hair loss and in 6.4%, the pattern was undetermined.

Table 2 shows the levels of total serum cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, LP (a), Apo A1 and Apo B. As it is shown in the table, the level of LP (a) was significantly higher in patients than controls ($P < 0.001$). 38.6% of the patients and only 4.4 % of the controls had an LP

Table 1. Family history of the study and control group

Group	AGA		HTN		DM		CAD	
	Number	Percent	N	P	N	P	N	P
case	47	100	12	25.5	11	23.4	12	25.5
control	20	44.4	8	17.8	5	11.1	3	6.7
P.value		0.000		0.36		0.12		0.014

Table 2. The mean values of the lipid parameters in study and control groups

Lipid profile	Group	Mean	SD	P. value
TG	Case	144.83	122.85	0.11
	Control	110.42	81.13	
Chol	Case	173.67	33.21	0.22
	Control	162.96	49.005	
LDL	Case	101.85	30.79	0.026
	Control	119.20	39.87	
HDL	Case	45	19.42	0.10
	Control	50.53	17.76	
APOA	Case	122.27	41.75	0.33
	Control	115.93	14.86	
APOB	Case	79.85	24.64	0.30
	Control	84.97	22.09	
LP(a)	Case	47.10	52.54	0.001
	Control	17.96	15.50	

APOA = Apolipoprotein A APOB= Apolipoprotein B Chol = Cholesterol LP (a) = Lipoprotein A HDL=High Density Lipoprotein
 LDL=Low Density Lipoprotein TG=Triglycerid

(a) level more than 30 mg/dl, which is the critical level for atherosclerosis ($P < 0.001$). The level of LP (a) was not significantly different in the alopecia subgroups; frontal only baldness vs. vertex baldness. There were no statistically significant differences in the mean levels of cholesterol, triglyceride, LDL, HDL-cholesterol, Apo A and Apo B between the patients and the controls.

DISCUSSION

There are inconsistent findings regarding the association of CAD and AGA in different studies. The basic question is whether MPA, regardless of its pattern, is statistically associated with CAD. The next questions are if the pattern (frontal baldness and vertex baldness) and the extent of baldness are important in this respect and finally what the mechanism of this association is.

The association between MPA and CAD was first suggested in 1972 by Cotton et al¹⁸. Several subsequent studies appeared to support the early findings^{3,12,14}. On the other hand, a few studies suggested that AGA was not a surrogate measure of an important risk factor for CAD¹⁹⁻²¹.

Few studies have investigated the mechanisms of association between AGA and CAD. Lotufo et al, and Trevisan et al, demonstrated a possible interaction between AGA and both blood pressure and cholesterol levels^{11,22}. Nassiri et al, showed a higher triglyceride and lower HDL cholesterol levels and total cholesterol/HDL cholesterol ratio in those with AGA than the controls²³. Although

Ellis et al, study was in contrast with the two previous studies⁷. The level of Lp (a) has not been assessed in these studies. A few studies investigated Lp (a) in male pattern alopecia. Sasmaz et al, showed that male patients with MPA had significantly higher levels of serum Lp (a) compared to male individuals with no MPA⁴. Lotufu et al, study revealed similar results⁶ while Matilaiuen et al, could not find higher levels of Lp (a) in MPA¹¹. Lp (a) is an important, independent and genetically determined risk factor for coronary heart disease²⁴. Measurement of Lp (a) levels has also been recommended for determination of the risk of myocardial infarction²⁵. In our investigation, the LP (a) level was remarkably higher in males with MPA as compared to counterpart males with a normal hair status.

Whether the pattern and severity of hair loss is an important factor in the association between MPA and CAD is still an issue of controversy. In their case-control study, Lesko et al, showed that vertex baldness, but not frontal pattern, was associated with CAD⁷. Using a retrospective cohort model, Lotufo et al, demonstrated that although the reported risk of CAD was increased in MPA, but the location and severity of baldness did not seem to be important¹⁵. Schnohr et al, conducted a prospective cohort study which reported an increased risk of myocardial infarction accompanied by vertex baldness and unexpectedly, a stronger association between frontal baldness and the incident of myocardial infarction¹². Herrera et al, showed strong associations between various

cardiovascular endpoints and the rate at which baldness progressed¹¹. Our study showed a lack of association between the pattern of baldness and CAD. In conclusion, the baldness pattern itself is not probably a risk factor for CAD.

There can be several rationalizations for disagreements reported in different studies regarding the aforementioned items including:

1. Investigation related factors including:
 - a. Study design: cross-sectional vs. case-control studies. The definition of groups also varied in some studies; some studies compared the frequency of alopecia between patients with CAD and healthy controls but others, such as our study, compared the CAD markers between alopecia and healthy subjects. These different kinds of study design can lead to variations in results.
 - b. Biased estimators resulting from confounding selection bias (Hospital based vs. population based study) or information bias.
 - c. Age: early onset vs. late onset baldness, some studies have showed that compared to late onset MPA, early onset baldness is associated with CAD.
 - d. Different definitions of CAD and baldness: in some studies, invasive methods such as coronary revascularization procedures have been regarded as the definition of having CAD but others, such as our study, measured some serum markers that would predict CAD.
 - e. different sample sizes
2. Existence of other protective factors for CAD in AGA which may balance the effect of risk Factors.
3. The possibility of a genetic trait that is a common cause of baldness and atherosclerosis may lead to a false correlation.

Considering the findings of our study and the important role of lipoprotein (a) as a risk factor for atherosclerotic heart disease, we suggest that all men with a male pattern hair loss should be investigated for lipid indices, especially lipoprotein (a), and they should be also referred to a cardiologist, if necessary.

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