Original Investigation
Orijinal Araştırma

DOI: 10.4274/turkderm.89814
Turkderm-Turk Arch Dermatol Venereology 2017;51:115-8

Evaluation of ischemia-modified albumin level and parameters related with oxidative stress in early onset androgenetic alopecia

Erken başlangıçlı androgenetik alopeside iskemi modifiye albümin düzeyi ve oksidatif stres ile ilişkili parametrelerin değerlendirilmesi

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Abstract

Background and Design: Ischemia-modified albumin (IMA) is a biomarker, which is an indicator of ischemia and oxidative stress, and measured by the albumin cobalt binding test. Androgenetic alopecia (AGA) is the most important cause of hair loss in males. Hair loss that is affected by androgenic hormones, age, and ethnic, family and environmental factors, may lead to psychological, social and physical problems in some individuals. The aim of the present study was to investigate the factors affecting AGA, and the correlation between AGA and IMA.
Materials and Methods: Fifty male patients with AGA aged 18-35 years and 30 males of similar age without AGA were included in the study. Patients with AGA stage 3 or higher were included in the study group. Blood samples were collected after a 12-hour fasting period. Blood glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, insulin, testosterone, dehydroepiandrosterone-sulfate (DHEA-S), and albumin levels were analyzed using an autoanalyzer. IMA values were evaluated using a MINDRAY BS 2000 autoanalyzer.
Results: A total of 80 individuals were included in the study. There was no significant difference in mean age (p=0.179), body mass index (p=0.847), DHEA-S (p=0.247), testosterone (p=0.874), lipid profile [triglyceride (p=0.086), total cholesterol (p=0.492), HDL (p=0.993), LDL (p=0.544)], insulin resistance (p=0.399) and IMA (p=0.976) between study group and control group. Additionally, a family history of alopecia was found to be significantly higher in the study group (p=0.000). Moreover, there was a positive correlation between AGA grade and insulin resistance (r=0.296; p=0.037).
Conclusion: AGA, which leads to many cosmetic and psychosocial problems, was more frequent in individuals with a family history of alopecia; also, there was a positive correlation between AGA stage and insulin resistance. On the other hand, there was no significant correlation between AGA and IMA.
Keywords: Ischemia-modified albumin, androgenetic alopecia, insulin resistance

Öz

Amaç: İskemi modifiye albümin (İMA), albümin kobalt bağlama testi ile ölçülen, iskemi ve oksidatif stresin göstergesi olan bir biyomarkırdır. Androgenetik alopesi (AGA) erkeklerde görülen saç kaybının en önemli nedenidir. Androjenik hormonlar, yaş, etnik, ailesel ve çevresel faktörlerden etkilenen saç kaybı bireylerde ruhsal, sosyal ve fiziksel yetersizliklere yol açabilmektedir. Bu çalışmada AGA'yı etkileyen faktörler ve çeşitli alanlarda kullanılan önemli bir belirteç olan İMA ile AGA arasındaki ilişkinin ortaya konması amaçlanmıştır.
Gereç ve Yöntem: Çalışmaya AGA'sı olan 50 erkek olgu ile (18-35 yaş arasındaki) AGA'sı olmayan 30 erkek olgu (aynı yaş aralığında) alındı. Evre 3 ve üzerinde olanlar çalışma grubuna dahil edildi. Kan örnekleri 12 saat açlık sonrası alındı. Kan glukoz, total kolesterol, yüksek dansiteli

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lipoprotein (HDL), düşük dansiteli lipoprotein (LDL), trigliserid, insülin, testosteron ve dehidroepiandesteron-sülfat (DHEA-S) ve albümin değerleri otoanalizörde bakıldı. İMA örnekleri MINDRAY BS 2000 otoanalizörüne aplike edilerek çalışıldı.

Bulgular: Çalışmaya 50 AGA'lı 30 kontrol toplam 80 olgu alındı. Çalışma grubu ile kontrol grubu yaş ortalaması (p=0,179), vücut kitle indeksi (p=0,847), DHEA-S (p=0,247), testosteron (p=0,874), lipit profili [trigliserid (p=0,086), total kolesterol (p=0,492), HDL (p=0,993), LDL (p=0,544)], insülin direnci (p=0,399) ve İMA (p=0,976) açısından değerlendirildiğinde iki grup arasında istatistiksel olarak anlamlı fark yoktu. Buna karşın ailede kellik öyküsü çalışma grubunda istatistiksel olarak anlamlı derecede fazlaydı (p=0,000) ve AGA derecesi ile insülin direnci arasında pozitif yönde bir korelasyon vardı (r=0,296; p=0,037).

Sonuç: Kozmetik ve psikososyal birçok soruna neden olan AGA'nın ailesinde kellik öyküsü olanlarda daha sık gözlendiği ve AGA derecesi ile insülin direnci arasında pozitif yönde bir korelasyon olduğu saptandı. AGA ile İMA arasında ise anlamlı bir ilişki olmadığı belirlendi.

Anahtar Kelimeler: İskemi modifiye albümin, androgenetik alopesi, insülin direnci

Introduction

Ischemia modified albumin (IMA) is a biomarker the levels of which increase secondary to myocardial and skeletal muscle ischemia, and which is measured by the albumin cobalt binding test[1,2]. IMA levels can also increase in diseases in which oxidative stress is elevated, including obesity, type 2 diabetes mellitus (DM), hypercholesterolemia, preeclampsia and polycystic ovary syndrome[3-5]. Androgenetic alopecia (AGA) is the most important cause for hair loss in men. There is an important link between hair and identity as well as social life, mood and self-confidence of the individual. Hair loss makes individuals feel older and unconfident. The history of hair loss dates back 4.000 years. To date, various ethnic and familial factors, diseases and hormones have all been held responsible for the disease etiology[6-8].

Oxidative stress is known to cause cellular damage and aging[9]. In this context, it is thought that there may be a relationship between oxidative stress and follicle miniaturization, which is the primary cause of AGA.

The aim of the present study was to investigate the factors affecting AGA, and the correlation between AGA and IMA.

Material and Methods

Fifty male patients with AGA aged 18-35 years and 30 males of similar age without AGA were included in the study. The study were approved by the Fırat University of Local Ethics Committee (Date 11.08.15, number of meetings: 15, decision no: 11). The participants were informed about the study; all provided consent forms. The Norwood-Hamilton scale was used to stage the baldness level of the participants[10].

Patients with stage 3 or higher were included in the study group. Age, height, weight, and family history of baldness were recorded for all participants. Exclusion criteria were as follows: acute or chronic disease (hypertension, DM, thyroid diseases, etc.), regular medication use, and age <18 years or >35 years. Blood samples were collected after a 12-hour fasting period. Blood glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, insulin, testosterone, dehydroepiandrosterone-sulfate (DHEA-S), and albumin levels were analyzed using an autoanalyzer (MINDRAY BS 2000, Beckman Coulter DXI 800). Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) value, an indicator of insulin resistance, was calculated by using the following formula: HOMA-IR=Fasting glucose level (mg/dL) x fasting insulin (uIU/mL)/405. Patients with HOMA-IR <2.5 mg/dL were considered to be normal, whereas patients with HOMA-IR ≥2.5 mg/dL were considered to have insulin resistance. Body mass index (BMI) was calculated by using the following formula: weight/height^2 (kg/m^2). Patients with BMI <18 were considered underweight, patients with BMI between 18 and 24.99 were considered to have normal weight, patients with BMI between 25 and 29.99 were considered as overweight, and patients with BMI ≥30 were considered obese.

IMA test: IMA test was carried out according to the method by Bar-Or et al.[1] which is based on albumin-cobalt binding. Leftover serum samples were used for the test. Samples were analyzed using a MINDRAY BS 2000 autoanalyzer. In this modified method, 100 µL $CoCl_2$ reactive is added on 35 µL of serum, and this mixture is incubated for 5 minutes. During incubation, Co(II) binds to N-termini of unmodified albumins. When 50 microliters of dithiothreitol (DTT) reagent is added, DTT forms a colored complex with unbound Co(II). Color change is measured at 505 nm, and the results are recorded as absorbance unit.

Statistical Analysis

SPSS v.20.0 software (SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis. Data were expressed as mean±standard deviation for continuous variables. Categorical variables were represented by numbers and percentages. Student's t-test was used to compare continuous variables between independent groups. Chi-square tests were used to compare categorical variables between independent groups. Receiver operating characteristic curves were plotted to investigate the accuracy of how well age could indicate AGA stage in case of early-onset AGA. Correlation analysis was carried out to determine the potential correlation between the variables. Statistical significance was set at p<0.05.

Results

Fifty AGA patients and 30 control subjects were included in the study. The mean age in the AGA group was 25.88±4.79 years. The mean age in the control group was 24.63±3.40 years. There was no significant difference in age between the groups (p=0.179). In the presence of early-onset AGA, age had a high predictive power to indicate AGA stage (stage 3 AUC: 0.147; stage 4 AUC: 0.375; stages 5-6 AUC: 0.809). Forty patients (80%) in the study group and 10 control subjects (33.3%) had a family history of baldness. The difference was statistically significant (p=0.000).

The Norwood-Hamilton Scale was used to evaluate baldness level of the patients. According to the results, 8 patients (16%) had stage 3, 19 patients (38%) - stage 4, 19 patients (38%) - stage 5, and 4 patients (8%) had stage 6 baldness.

When we compared insulin resistance between the groups, the mean HOMA-IR value was 1.88±2.13 mg/dL in the study group, and 2.29±1.98 mg/dL in the control group. There was no significant difference in insulin resistance between the groups (p=0.399). On the

Table 1. Laboratory values for the study and control groups

	AGA + (n=50) Mean±SD (min-max)	Control subjects (n=30) Mean±SD (min-max)	p value
IMA (AbsU)	0.69±0.08 (0.44-0.84)	0.69±0.11 (0.37-0.84)	0.976
BMI (kg/m^2)	23.34±2.92 (16.33-29.86)	23.20±3.07 (15.76-29.67)	0.847
HOMA-IR score	1.88±2.13 (0.46-13.59)	2.29±1.98 (0.31-8.58)	0.399
Albumin (g/dL)	5.08±0.32 (4.1-5.7)	5.2±0.2 (4.7-5.5)	0.05
DHEA-S (µg/dL)	274.35±95.47 (100.5-487.2)	254.96±53.21 (95.5-324.8)	0.247
Testosterone (ng/mL)	3.78±0.92 (2.51-6.02)	3.74±1.04 (1.2-5.71)	0.874
Total cholesterol (mg/dL)	153.54±35.38 (79-245)	158.8±28.61 (103-229)	0.492
LDL (mg/dL)	92.6±32.59 (27-168)	96.8±24.59 (42-168)	0.544
HDL (mg/dL)	48.22±10.61 (25-92)	48.2±7.41 (31-65)	0.993
Triglyceride (mg/dL)	132.84±100.97 (28-459)	105.23±37.79 (40-180)	0.086

AGA: Androgenetic alopecia, IMA: Ischemia-modified albumin, BMI: Body mass index, HOMA-IR: Homeostatic Model Assessment - Insulin Resistance, DHEA-S: Dehydroepiandesterone-sulfate, HDL: High density lipoprotein, LDL: Low density lipoprotein, AbsU: Absorbance unit, min: Minimum, max: Maximum, SD: Standard deviation, p<0.05

other hand, there was a positive correlation between AGA grade and insulin resistance (r=0.296; p=0.037). The detailed information on laboratory parameters is shown in Table 1.

Discussion

AGA, also known as male-pattern baldness or male-pattern hair loss, is the most common cause of hair loss in males[6]. AGA is seen after puberty, but is most commonly seen in men between the ages of 20 and 40 years. In addition, the incidence of AGA increases with age. Thirty percent of 30-year-old patients and 50% of 50-year-old patients are affected from this condition. This rate increases to 70% with more advanced age[10]. In this study, we found that age had high power to indicate the AGA stage in case of early-onset AGA (stage 5-6 AUC: 0.809).

A family history of alopecia is another important factor in the etiology of AGA. It had been hypothesized that AGA is inherited via single dominant gene, whereas today it is known that the mode of inheritance is polygenic. For males, the risk of AGA increases with the number of family individuals with alopecia[11]. In the present study, history of familial baldness was significantly more common in AGA patients, compared to control subjects. (p=0.000).

Adrenal (androstenedione, DHEA-S) and testicular (testosterone, dihydrotestosterone) androgenic hormones have a key role in the regulation of hair growth. Long-term exposure to androgens leads to miniaturization in follicles[12]. Narad et al.[13] have investigated hormone profiles of 100 subjects (50 AGA patients and 50 control subjects). There were no significant differences in total testosterone and DHEA-S levels between the groups (p=0.885 and p=0.137, respectively). Two studies by Starka et al.[14] and Tsvetanova et al.[15] have yielded similar results between AGA and androgen levels (serum total testosterone and DHEA-S). Similar to the previous studies, we did not find a significant difference in androgen levels between the groups (p=0.874 and p=0.247, respectively).

Previous studies on the correlation between BMI and early-onset AGA have yielded contradictory findings. Sharma et al.[16] have investigated the correlation between coronary artery disease and AGA, and found that the mean BMI value did not differ significantly between the study group (23.11±1.59 kg/m^2) and the control group (22.60±1.60 kg/m^2) (p=0.89). Chakrabarty et al.[17] have investigated the correlation between AGA and metabolic syndrome in 85 AGA patients and 85 control subjects. The BMI in the study group was significantly higher compared to the control group (p=0.03). Obese participants were not included in the present study because they may affect the IMA levels. Therefore, we assume that there is no statistically significant difference between the groups in terms of BMI.

Sharma et al.[16] have evaluated lipid profiles of both groups, and found that AGA patients had significantly increased risk factors such as HD (p<0.002), LDL (p<0.0001) and triglyceride (p<0.0001). Arias-Santiago et al.[18] have found that triglyceride level is significantly higher in AGA patients. In another study that has investigated the correlation between insulin resistance and AGA, there was no significant difference in HDL (<35 mg/dL) and triglyceride (≥150 mg/dL) between AGA patients and control subjects (p=0.42 and p=1.00, respectively). On the other hand, total cholesterol (>200 mg/dL) was significantly higher in the control group, compared to AGA patients (p=0.003)[19]. In terms of dyslipidemia, there was no significant difference between the groups [triglyceride (p=0.086), total cholesterol (p=0.492), HDL (p=0.993), LDL (p=0.544)]. This is thought to be related to the fact that the study was done at a center in the eastern part of our country where the people consume natural foods instead of commercially manufactured and prepared foods such as fast-food.

Nabaie et al.[19] have investigated the correlation between insulin resistance and AGA in 97 AGA patients and 87 control subjects. The authors have not found a significant difference in insulin resistance between the groups (p=0.54). On the other hand, Matilainen et al.[20] have emphasized that early-onset AGA (<35 years) constitutes a risk for insulin resistance, and this can be used as an important marker. In the present study, there was no significant difference in insulin resistance between the groups (p=0.399). Similar to that in a study by Matilainen et al.[20], we found a positive correlation between AGA stage and insulin resistance (r=0.296; p=0.037).

IMA is a biomarker that is associated especially with acute coronary syndrome[1]. In addition, its importance in various diseases, including multiple myeloma, asthma, multiple sclerosis, psoriasis, acute appendicitis, gestational DM, and acute rheumatoid fever, has been

previously investigated[21-27]. To date, no study has investigated the correlation between male-pattern hair loss (AGA) and IMA. In the present study, there was no significant correlation between AGA and IMA (p=0.976).

Conclusion

In conclusion, we found that AGA was more common in patients with a family history of baldness. In addition, we found that AGA stage was positively correlated with insulin resistance. Furthermore, there was no correlation between AGA and IMA. In this context, new studies are needed to reveal the relationship between early-onset AGA, which is an important social problem in society, and oxidative stress.

Ethics

Ethics Committee Approval: The study were approved by the Fırat University of Local Ethics Committee (Date 11.08.15, number of meetings: 15, decision no: 11).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.N., F.Ç.G., Concept: H.N., S.N., Design: H.N., Z.K.K., Data Collection or Processing: H.N., F.Ç.G., B.D., Analysis or Interpretation: H.N., S.N., F.Ç.G., Literature Search: H.N., S.N., Writing: H.N., S.N.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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