Sex hormone–binding globulin and risk of hyperglycemia in patients with androgenetic alopecia

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Background: Low circulating levels of sex hormone–binding globulin (SHBG) are a strong predictor of the risk of type 2 diabetes. Androgenetic alopecia (AGA) has been related to an increase in cardiovascular risk, but the mechanism of this association has not been elucidated. AGA can be associated with low levels of SHBG and insulin resistance, which could be related to hyperglycemia and type 2 diabetes.

Objective: The objective of this study was to evaluate SHBG and blood glucose levels in men and women with early-onset AGA and control subjects to determine whether low levels of SHBG are associated with hyperglycemia.

Methods: This case-control study included 240 patients consecutively admitted to the outpatient clinic (Dermatology Department of San Cecilio University Hospital, Granada, Spain), 120 with early-onset AGA (60 men and 60 women) and 120 control subjects (60 men and 60 women) with skin diseases other than alopecia.

Results: Of patients with AGA, 39.1% presented with hyperglycemia (>110 mg/dL) versus 12.5% of controls ($P < 0.0001$). AGA patients with hyperglycemia or diabetes presented lower significant levels of SHBG than alopecic patients without hyperglycemia or type 2 diabetes, respectively. Patients with AGA and hyperglycemia presented significantly lower levels of SHBG than controls with hyperglycemia (22.3 vs 39.4 nmol/L for AGA patients and controls, respectively, $P = .004$). No significant differences in SHBG levels were noticed between patients and controls without hyperglycemia. Binary logistic regression showed a strong association between lower SHBG levels and glucose levels greater than 110 mg/dL in patients with AGA even after additional adjustment for sex, abdominal obesity, and free testosterone (odds ratio = 3.35; 95% confidence interval = 1.9-5.7; $P < .001$).

Limitations: The study of a wider sample of AGA patients would confirm these findings and would permit analysis of the pathogenic mechanisms underlying the increase in cardiovascular risk in patients with AGA.

Conclusion: An association between early-onset AGA, hyperglycemia/diabetes, and low levels of SHBG was observed in the current study. Low levels of SHBG could be a marker of insulin resistance and hyperglycemia/diabetes in patients with AGA. (J Am Acad Dermatol 2011;65:48-53.)

Key words: abdominal obesity; androgenetic alopecia; HOMA-IR index; hyperglycemia; insulin levels; SHBG; testosterone; type 2 diabetes.

INTRODUCTION

Sex hormone–binding globulin (SHBG) is a glycoprotein mainly produced by the liver cells that binds to sex and steroid hormones (estradiol, testosterone) to affect the bioavailable fraction and sequester circulating androgens and estrogens from biologic action. Low levels of SHBG are associated with polycystic ovary syndrome or hypothyroidism. Recently Ding et al[1] showed that low circulating levels of SHBG are a strong predictor of the risk of

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type 2 diabetes. Androgenetic alopecia (AGA) has been related to an increase in cardiovascular risk (eg, metabolic syndrome, diabetes, hyperlipidemia) by various authors,[2-8] but the mechanism of this association has not been elucidated. AGA can be associated with low levels of SHBG and insulin resistance. The objective of this study was to evaluate SHBG and blood glucose levels in men and women with early-onset AGA and control subjects to determine whether low levels of SHBG are associated with hyperglycemia.

CAPSULE SUMMARY

- Low circulating levels of SHBG are a strong predictor of the risk of type 2 diabetes. AGA has been related to an increase in cardiovascular risk, but the mechanism of this association has not been elucidated.
- An association between early-onset AGA in men and women, hyperglycemia/diabetes, and low levels of SHBG was observed in the current study.
- SHBG is an independent predictor of incident hyperglycemia (glucose levels >110 mg/dL) in patients with AGA even after adjusting for abdominal obesity, sex, and testosterone level (OR = 3.35; 95% CI = 1.9-5.7; $P < .001$).

MATERIAL AND METHODS

Study subjects and clinical parameters

This case-control study included 240 patients consecutively admitted to the outpatient clinic (Dermatology Department of San Cecilio University Hospital, Granada, Spain), 120 with early-onset AGA (60 women and 60 men) and 120 control subjects (60 men and 60 women) with skin diseases other than alopecia (mainly nevi, seborrheic keratosis, actinic keratosis, verruca, or basal cell carcinoma). Data were gathered on randomly selected days in randomly selected consulting rooms over a 10-month period by one examiner. Diagnosis of AGA was based on clinical findings: pattern of increased hair thinning on frontal/parietal scalp with greater hair density on occipital scalp for males; retention of frontal hairline (in females), the presence of miniaturized hairs and diversity of hair diameter by dermatoscopy. Family history of AGA was also asked. Inclusion criteria for patients with AGA were as follows: men and women 45-60 years of age, presence of early-onset AGA (age <35 years) with degree II on the Ludwig Scale or above for women and degree III or above on the Ebling scale for men and signing of informed consent statements to study participation. Patients with therapy with testosterone, contraceptives, corticoids, hormone replacement therapy, known cause of hyperandrogenism (eg, polycystic ovary syndrome, tumors), hypothyroidism, type 1 diabetes, treatment with insulin or oral antidiabetic medications, and psoriasis were excluded. Inclusion criteria for control subjects were as follows: age 45 to 60 years for men and women and signing of informed consent statements to study participation. Exclusion criteria for control subjects were the same as described above and the presence of AGA. The source population for cases and control subjects was the same.

Blood glucose, insulin, total testosterone, and SHBG levels were studied in samples drawn between 8 and 9 AM after a 12-hour fasting period; all blood analyses were carried out at one central hospital laboratory. Free testosterone was calculated by means of Vermeulen's formula.[9] The homeostasis model assessment of insulin resistance (HOMA-IR) index (given as microunits per milligram) was calculated (fasting insulin × fasting glucose/22.5). Data were also gathered on age, weight, height, body mass index (BMI; given as kilograms per square meter) and abdominal perimeter (midpoint between the anterior iliac crest and costal margin level, L4-L5), which was measured by one single examiner. The level of glucose greater than 110 mg/dL was chosen for numerical analysis, as this value is usually considered as a metabolic syndrome criterion.[10] New venous samples were taken in patients with glucose levels greater than 110 mg/dL. Patients with glucose levels greater than 126 mg/dL (twice) were diagnosed with type 2 diabetes mellitus.

Statistical analyses

The statistical analyses were performed with the SPSS/PC software (SPSS Inc, Chicago, IL; version 15.0 for Windows). The two-sample Student *t* test was used to compare mean values of quantitative variables as the two samples were obtained independently, the Shapiro-Wilk test to examine the normality of their distribution, and the Levene test to study the variance. Qualitative variables were analyzed with the chi-square test. Binary logistic regression models (Wald method), obtaining estimate-adjusted odds ratio (OR) and their 95% confidence interval (CI) were used to measure the association between SHBG and hyperglycemia/diabetes in a multivariate analysis. A *P* value less than or equal to .05 was considered significant in all analyses.