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ORIGINAL ARTICLE

Study of obesity associated proopiomelanocortin gene polymorphism: Relation to metabolic profile and eating habits in a sample of obese Egyptian children and adolescents

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KEYWORDS

Childhood obesity;
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Abstract *Background:* Melanocortinergic system represents a known system involved in the central regulation of body weight with the central proopiomelanocortin (POMC) neurons forming a potent anorexigenic network. Polymorphisms in the POMC gene locus are associated with obesity phenotypes.

Aim: To assess the contribution of the POMC gene 9-bp insertional polymorphism in the susceptibility to obesity and its relation to body mass index (BMI) and adiposity-related co-morbidities in obese children and adolescents; as well as binge eating behavior.

Patients and methods: Fifty obese children and adolescents with simple obesity were screened for Binge Eating Disorder (BED) by The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), they were compared to 50 age, sex and pubertal stage-matched non obese controls. Anthropometric measurements, blood pressure, abdominal ultrasound for fatty liver, measurement of fasting lipid profile, fasting insulin, fasting blood glucose and assessment of POMC gene 9-bp insertional polymorphism were done.

Results: Obese patients had significantly higher anthropometric measurements, blood pressure percentiles, fasting glucose, fasting insulin, homeostasis model assessment for insulin resistance (HOMA-IR) and fasting lipid profiles, and higher frequency of occurrence of non alcoholic fatty liver disease and BED. Allelic frequencies of POMC gene 9 bp insertional polymorphism were comparable in patients and controls ($p = 0.956$). Fasting insulin levels were significantly higher in the heterozygous cases having the polymorphism than in wild homozygous cases; whereas no difference was observed among the controls.

Conclusion: This polymorphism was associated with higher fasting insulin levels in the obese patients only. These findings support the hypothesis that the melanocortin pathway may modulate

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glucose metabolism in obese subjects indicating a possible gene-environment interaction. POMC variant may be involved in the natural history of polygenic obesity, contributing to the link between type 2 diabetes and obesity.

1. Introduction

Childhood obesity is a worldwide health concern with a multifaceted etiology [1]; which includes modifiable and non-modifiable risk factors [2]. Genetic factors estimated to account for >40% of the population variation in BMI, where clear differences exist in obesity susceptibility among individuals exposed to the same obesogenic environment, implicating genetic risk factors [3].

The genetic influences are likely to be particularly powerful in people with severe and early-onset obesity [4]. In the past few years, scientists have been trying to localize the genes responsible for obesity which code for hormones and neurotransmitters regulating satiety; where the alteration in these genes or their pathways are implicated in the pathology of obesity [5].

Monogenic obesity caused by single gene polymorphism accounts for about 5% of the cases of obesity, of which 11 genes are identified including leptin (LEP), LEP receptor, preproopiomelanocortin, and melanocortin-4 receptor (MCR4) [6].

The central proopiomelanocortin (POMC) neurons form a potent anorexigenic network [7] where it regulates feeding and energy homeostasis by integrating long-term adiposity signals from the hypothalamus and short-term satiety signals from the brainstem [8]. Polymorphisms in the POMC gene locus are associated with obesity phenotypes [9] which is a risk factor of several short term and long term complications including type 2 diabetes, hypertension, cardiovascular disease, orthopedic and psychological problems [10].

All this genetic evidence for POMC pathogenesis in obesity made us choose the POMC gene as a candidate to search for 9 bp insertional polymorphism that might correlate with childhood obesity [11].

2. Subjects and methods

This case-control study included fifty children and adolescents with simple obesity recruited from the Pediatric Obesity Clinic, Children's hospital, Ain Shams University during the period from January 2014 till the end of August 2014. Obesity was defined as body mass index (BMI) > 95th percentile [12]. Cases were compared to fifty age-, sex- and pubertal stage-matched healthy non obese children and adolescents as a control group. The work was carried out in accordance with "The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments in Human". A written informed consent was taken from the legal guardians of cases and controls.

2.1. Methods

(A) Full medical history: age, sex, complications of obesity (diabetes mellitus, hypertension, heart disease, breathing problems, sleep disorders) and family history of obesity, hypertension, diabetes mellitus, liver disease or cardiac disease were recorded.

(B) Thorough physical examination laying stress on:

(1) Blood pressure: measured by sphygmomanometer in the right arm of a relaxed, seated child with comparison of values to normal reference percentiles for age/height according to National High Blood Pressure Education Program [13].

(2) Auxological measurements:

- Weight: was measured on a digital scale in kilograms and to the nearest 0.1 kg with the subjects standing motionless without shoes and with minimal clothing. Weight for height SDS (standard deviation score) was calculated according to the norms of— [14].
- Height: was measured to the nearest 0.1 cm on a wall mounted stadiometer without shoes. The participants were asked to stand with their back against the wall-mounted stadiometer with their back (scapulae), buttocks and both heels touching the wall-plate. The shoulders are relaxed and arms are relaxed and hanging loosely at the sides. The head should be in the "Frankfort Horizontal Plane" in which the lowest point on the inferior orbital margin and the upper margin of the external auditory meatus form a horizontal line and the participant was asked to look straight ahead. Height SDS was calculated according to the norms of Tanner et al. [14].
- Body mass index (BMI): was calculated as follows: weight (kg)/height $(m)^2$ according to Cole [12]. BMI SDS was calculated from the age- and sex-specific reference values [12].
- Waist circumference: was measured midway between the lowest rib and the top of the iliac crest. Waist circumference SDS was calculated and compared to normal references for age and sex according to Schwandt et al. [15].
- Hip circumference: was measured in a horizontal plane at the extension of the buttocks. Hip circumference SDS was calculated and compared to normal references for age and sex according to Schwandt et al. [15] till the age of 11 years and according to Moreno et al. [17] above 11 years.
- Waist/hip ratio: was calculated and compared to normal age and sex reference range together with calculation of waist/hip ratio SDS according to Schwandt et al. [15] till age of 11 years and according to Mederico et al. [16] above 11 years.