The LEP G-2548A Polymorphism is not Associated with Breast Cancer Susceptibility in Obese Western Mexican Women

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Abstract

Breast cancer incidence and the prevalence of obesity have considerably increased in Mexican women. The LEP G-2548A polymorphism has been associated with obesity and breast cancer risk in several ethnic populations. We hypothesize that G-2548A LEP polymorphism could be associated with breast cancer risk in women Mexican population. A total of 319 women were included in this study, 130 breast cancer patients and 189 control women. The data collected included anthropometric measurements and menopausal status, and a blood sample was obtained to evaluate SNPs using a PCR-RFLP analysis. No statistically significant associations were identified between breast cancer risk and the LEP G-2548A polymorphism in obese or normal-weight subgroups regardless of menopausal status. Our findings suggest that the LEP G-2548A polymorphism is not associated with breast cancer risk in obese western Mexican women. Our results indicate that, for western Mexican women, the LEP G-2548A polymorphism does not affect breast cancer susceptibility in obese or normal-weight subgroups regardless of menopausal status.

Keywords: Leptin; Polymorphism; Obesity; Breast cancer

Introduction

Leptin is a multifunctional adipokine produced primarily by white adipose tissue. The main role of leptin is the regulation of food intake and energy balance at the hypothalamic level [1], and plasma leptin is highly correlated with body mass index in rodents and obese humans [2]. Additionally, recent in vitro studies have shown that leptin stimulates breast cancer growth [3] and that leptin and the leptin receptor are overexpressed in breast cancer tissue and lymph node metastases [4,5].

Mammes et al. were the first to report an association between the LEP G-2548A polymorphism and overweight and variations in leptin levels [6]. Obesity is a well-established risk factor for postmenopausal breast cancer [7], and the prevalence of obesity in Mexican adults has increased markedly [8]. We hypothesised that the LEP G-2548A polymorphism is associated with breast cancer risk in Mexican women. In the present study, we evaluated obese and normal-weight breast cancer patients for the LEP G-2548A polymorphism.

Materials and Methods

Study Population

This study included 319 unrelated female residents from western Mexico (130 breast cancer patients and 189 controls). All participants provided written informed consent, and the study was performed in accordance with the Helsinki Declaration.

Data and sample collection

Data were collected on anthropometric measurements and menopausal status, and a blood sample was taken. The patients and controls were categorised as obese (BMI >30 kg/m²) or normal weight (BMI <24.9 kg/m²).

Genomic DNA extraction and genotyping

Genomic DNA was extracted from peripheral blood leukocytes using a standard protocol [9]. The LEP G-2548A polymorphism was identified using polymerase chain reaction (PCR). The PCR products were digested with 3 U of the restriction enzyme CfoI (Promega®).

Homzygous and heterozygous (LEP-2548AA and GA, respectively) genotype samples were included in each run.

Statistical analysis

The allele and genotype frequencies are presented as percentages. The χ² test was used to evaluate Hardy-Weinberg equilibrium and genotype samples were included in each run.

Table 1: Genotype distribution and allele frequencies of the LEP G-2548A polymorphism in control subjects and patients with breast cancer.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients (n=130)</th>
<th>Controls (n=189)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-dominant model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG</td>
<td>37 (28.5)</td>
<td>48 (25.4)</td>
<td>0.66 (0.35-1.11)</td>
</tr>
<tr>
<td>AA</td>
<td>22 (16.9)</td>
<td>46 (24.3)</td>
<td>0.62 (0.31-0.12)</td>
</tr>
<tr>
<td>Dominant model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG*</td>
<td>71 (54.6)</td>
<td>95 (57.2)</td>
<td>0.96 (0.57-1.64)</td>
</tr>
<tr>
<td>AA</td>
<td>22 (16.9)</td>
<td>46 (24.3)</td>
<td>0.62 (0.31-0.12)</td>
</tr>
<tr>
<td>Recessive model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GG* + GA</td>
<td>108 (83.1)</td>
<td>143 (75.7)</td>
<td>0.66 (0.35-1.11)</td>
</tr>
<tr>
<td>AA</td>
<td>22 (16.9)</td>
<td>46 (24.3)</td>
<td>0.62 (0.31-0.12)</td>
</tr>
<tr>
<td>Allele</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>145 (55.8)</td>
<td>195 (51.0)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>115 (44.2)</td>
<td>187 (49.0)</td>
<td></td>
</tr>
</tbody>
</table>

OR: Odds Ratio; CI: Confidence Interval.

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Results

Genotype and allele frequencies of the LEP G-2548A polymorphism

The observed genotype frequencies were in Hardy-Weinberg equilibrium in both the patient and control groups (p=0.22 and p=0.94, respectively). The genotype and allele frequencies did not differ between breast cancer patients and controls (Table 1). An association test showed no statistically significant correlation between the LEP G-2548A polymorphism and breast cancer risk. To determine the influence of obesity on the relationship between the LEP polymorphism and breast cancer risk, the patient and control groups were further stratified into obese and normal-weight subgroups. A lower frequency of the homozygous genotype AA was observed in normal-weight breast cancer patients (14%). However, there were no differences in polymorphism frequency between obese and normal-weight patients and controls (Table 2). There was no significant relationship between the LEP G-2548A polymorphism and breast cancer risk regardless of menopausal status (Table 3).

Discussion

In this study, we found no association between the LEP G-2548A polymorphism and breast cancer risk (Tables 1 and 2). By contrast, studies conducted in other countries have associated the LEP polymorphism and breast cancer risk, although some have shown inconsistent results [10,13-16].

An association between the LEP G-2548A polymorphism and breast cancer risk has been shown in previous studies. For example, Tunisian women carrying the -2548AA genotype (OR=1.30; 95% CI=1.01–1.66) in European-American women [18].

Obesity is a risk factor for postmenopausal breast cancer [7]. We classified breast cancer patients and controls according to menopause status and observed no significant changes in LEP G-2548A genotype frequencies (Table 3), which is in agreement with other studies [15,17]. The discrepancies observed between this and other studies may be attributable to several potential effect modifiers, such as differences in ethnicity, sample size, BMI, age and sex.

A few reports have described the functional effect of the G-2548A LEP polymorphism. Hoffstedt et al. reported that this polymorphism...
influences leptin expression, possibly at the transcriptional level, and therefore also leptin secretion by adipocytes [19]. More recently, Terrasi et al. conducted a functional analysis of the LEP G-2548A polymorphism in breast cancer cell lines and demonstrated differences in leptin mRNA expression [20]. We were unable to evaluate the leptin levels in our samples, but other authors have reported variations in leptin values according to LEP G-2548A genotypes and alleles [6,10,11,16].

Conclusions

The LEP G-2548A polymorphism has been associated with obesity and breast cancer risk in several ethnic populations. However, this study does not support an association between the LEP G-2548A polymorphism and breast cancer risk in western Mexican women.

Competing Interests

The author(s) declare that they have no competing interests.

References