THE PREVALENCE OF MELANOCORTIN-4 RECEPTOR GENE MUTATIONS IN TURKISH OBESE CHILDREN AND ADOLESCENTS

Selma TUNÇ 1, Korcan DEMİR 2, F. Ajlan TÜKÜN3, Cihan Topal4, Filiz HAZAN5, Burcu Salgamlı6, Özlem NALBANTOĞLU7, Melek YILDIZ8, Behzat ÖZKAN9

1Clinics of Pediatric Endocrinology, Behçet Uz Children’s Hospital, İzmir, Turkey
2Division of Pediatric Endocrinology, Dokuz Eylül University of Medicine, İzmir, Turkey
3Department of Genetics, Ankara University of Medicine, Ankara, Turkey
4Clinics of Pediatrics, Behçet Uz Children’s Hospital, İzmir, Turkey
5Department of Genetics, Dr. Behçet Uz Children’s Hospital, İzmir, Turkey
6Division of Genetic Diagnosis Center, Duzen Laboratory, Ankara

BACKGROUND

• Melanocortin-4 receptor (MC4R) mutations are the most common known cause of monogenic obesity (1).
• Prevalence of MC4R mutations in children with severe obesity varies from 0.3% up to 6.3% (2).
• >150 different mutations have been reported (1).

OBJECTIVE

• To establish the prevalence of MC4R mutations in a group of Turkish obese children and adolescents with morbid obesity.

METHODS and SUBJECTS

MC4R gene was sequenced in 47 morbid non-syndromic obese children and adolescents (28 girls and 19 boys) aged 1-18 years. Body weight, height and Body mass index (BMI), weight z-score, height z-scores and BMI z-scores were recorded using Turkish national anthropometric references (3).

Cases were included if BMI was ≥120 percent of the 95th percentile values or ≥35 kg/m² (whichever is lower). This corresponds to approximately the 99th percentile or BMI Z-score ≥2.33

RESULTS

• Mean age was 13.2±4.1 years, mean age at onset of obesity 5.1±2.1 years, mean height SD score 1.21±0.93, mean BMI 40.0±8.8 and BMI SD score 2.72±0.37.
• In four cases (8.5%), we detected three mutations one of which was novel (c.870delG) (Table 1).
• In addition, screening of family members revealed six more cases (one child, five adults) with a MC4R mutation.

<table>
<thead>
<tr>
<th>Case</th>
<th>Genotype</th>
<th>Age (years)</th>
<th>Gender</th>
<th>BMI SDS</th>
<th>Height SDS</th>
<th>Age at onset of obesity (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>c.496 G&gt;A</td>
<td>Heterozygous</td>
<td>16</td>
<td>F</td>
<td>2.47</td>
<td>1.36</td>
</tr>
<tr>
<td>2</td>
<td>c.496 G&gt;A</td>
<td>Heterozygous</td>
<td>8</td>
<td>M</td>
<td>3.05</td>
<td>3.4</td>
</tr>
<tr>
<td>3</td>
<td>c.870delG</td>
<td>Heterozygous</td>
<td>6</td>
<td>M</td>
<td>3.01</td>
<td>1.94</td>
</tr>
<tr>
<td>4</td>
<td>c.346_347delAG</td>
<td>Homozygous</td>
<td>10</td>
<td>F</td>
<td>3.07</td>
<td>1.06</td>
</tr>
</tbody>
</table>

Table 1. Genotypes and phenotype characteristics of mutation carriers

• No differences were present regarding the anthropometric (BMI, height, and weight SD scores) and biochemical (fasting blood glucose, lipids and fasting blood insulin levels) between mutation carriers and noncarriers.

CONCLUSIONS

There is no published study regarding MC4R mutations in Turkish children and adolescents with morbid obesity. In the present study, prevalence of MC4R mutations was found to be 8.5%. We speculate that MC4R gene mutations are an important cause of morbid obesity with early onset in the Turkish children and adolescents as well.

REFERENCES