MKRN3 levels in girls with central precocious puberty during GnRHa treatment: a longitudinal study.

Anna Grandone1, Grazia Cirillo1, Marcella Sasso1, Gianluca Tornese2, Caterina Luongo1, Adalgisa Festa1, Pierluigi Marzuillo1, Emanuele Miraglia del Giudice1

1Department of Woman, Child, General and Specialized Surgery, Università degli Studi della Campania “Luigi Vanvitelli”, Naples, Italy
2Institute for Maternal and Child Health - IRCCS “Burlo Garofolo” – Trieste, Italy

Background

Recently, mutations of makorin RING-finger protein 3 (MKRN3) have been identified in familial central precocious puberty (CPP). Serum levels of this protein decline before the pubertal onset in healthy girls and boys and are lower in patients with CPP compared to prepubertal matched pairs. The aim of our study was to investigate longitudinal changes in MKRN3 circulating levels in patients with CPP before and during GnRHa treatment.

Methods

We performed a longitudinal prospective study. We enrolled 15 patients with CPP aged 7.2 years (range: 2-8 years) with age at breast development onset <8 years and 12 control girls matched for time from puberty onset (mean age 11.8±1.2 years). Serum values of MKRN3, gonadotropins, (17)estradiol were evaluated before and during treatment with GnRHa (at 6 and 12 months). MKRN3 gene was genotyped in CPP patients. Only basal levels were analyzed in control girls.

Results

No MKRN3 mutations were found among CPP patients. MKRN3 levels declined significantly form baseline to 6 months of GnRHa treatment (p: 0.0007) and from 6 to 12 months of treatment (p: 0.003); MKRN3 levels at six months were significantly lower than in control girls (p<0.001).

<table>
<thead>
<tr>
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<th>At diagnosis</th>
<th>After 6 months of GnRHa treatment</th>
<th>After 12 months of GnRHa treatment</th>
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<tbody>
<tr>
<td>BMI Z-score</td>
<td>0.1±0.42</td>
<td>-0.25±0.73</td>
<td>-0.14±0.41</td>
</tr>
<tr>
<td>LH (IU/L)</td>
<td>1.6±1.8</td>
<td>0.3±0.2</td>
<td>0.3±0.1</td>
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<tr>
<td>FSH (IU/L)</td>
<td>5.02±2.63</td>
<td>1.66±1.45</td>
<td>2.46±0.97</td>
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<tr>
<td>17-β-Estradiol (pg/mL)</td>
<td>21.03±13.93</td>
<td>&lt;5</td>
<td>&lt;5</td>
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<tr>
<td>MKRN3 (pg/mL)</td>
<td>612.67±764.54</td>
<td>117.9±119.47</td>
<td>54.19±39.03</td>
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<tr>
<td>MKRN3 (pg/mL) median (IQR)</td>
<td>590.25 (136.83-1012.64)</td>
<td>68.04 (39.32-141.48)</td>
<td>49.3 (31.2-72.8)</td>
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</tbody>
</table>

Conclusion

We showed that girls with CPP had a decline in peripheral levels of MKRN3 during GnRHa treatment. Our data suggest a suppression of MKRN3 by pharmacological continuous administration of GnRHa. Further longitudinal studies on patients treated by long-acting GnRHa for different purposes (i.e. breast cancer or endometriosis) or in different ages could help to better understand the interplay among GnRH, gonadotropins, sexual hormones and MKRN3.

References


No conflict of interest to declare