

Final adult height and bone mineral density of the children who were treated with gonadotropin releasing hormone analogues near the age eight

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Introduction

Precocious puberty starting at a very young age causes a severe loss in height potential and should be treated with gonadotropin releasing hormone agonists (GnRHa). However, there are controversial results about the benefit of the GnRHa treatment in girls whose CPP is initiated near the age 8. This study evaluated the effectiveness of GnRHa treatment on final height of 160 girls with CPP in this specific age group. Moreover, it has also been investigated if this therapy had any negative effect on bone health.

Methods

The girls who had any negative factor on growth (such as malnutrition, thyroid disease, other chronic diseases etc.) were excluded. Finally, this retrospective study was conducted on 117/160 girls with CPP who were diagnosed near the age 8 (7-9 years old) from October 2011 to March 2015. **The girls whose treatment were initiated between the ages 8-9 years (n=71) and 7-8 years (n=46) were included to the groups 1 and 2 respectively.** Predicted height (PAH), target height (TH) were calculated at the beginning of the therapy according to medical records and final adult heights (FAH) were obtained also from the same records. Age of onset of the treatment, the duration of GnRHa therapy, anthropometric measures of the children and bone mineral density z-scores (n=52) after the treatment were also recorded. Girls' PAH, TH and FAH were also compared between groups. Moreover, paired t test was performed to assess the difference between PAH and FAH.

Results

The mean age of the girls at the beginning of the treatment was 8.59 ± 0.27 in group 1 and 7.50 ± 0.47 in group 2. The durations of GnRHa therapy were 1.97 ± 0.54 and 2.91 ± 0.61 in group 1 and 2 respectively. The TH ($160,53 \pm 5,49$ vs $160,57 \pm 4,94$), PAH ($158,72 \pm 5,23$ vs $158,35 \pm 5,57$) and FAH ($162,42 \pm 5,32$ vs $162,14 \pm 5,70$) were not statistically different between the groups. Multiple regression analysis demonstrated that major determinant factor of the FAH was baseline height SDS (Beta: 0.572, $p < 0.001$). **However, FAH was improved approximately 4 cm from the PAH in both groups ($p < 0.001$).** There were not any girls with osteoporosis after the treatment. However, 4/52 girls had a BMD z-score between -1 and -2.

Table.1 Characteristics of the groups

| | Group 1 (n=71) | Group 2 (n=46) | p |
|--|-------------------|-------------------|--------|
| Age (years) | 8.59 ± 0.27 | 7.50 ± 0.47 | <0.001 |
| Bone age (years) | 10.40 ± 0.85 | 9.39 ± 1.03 | <0.001 |
| Height (cm) | 136.26 ± 5.66 | 130.08 ± 6.83 | <0.001 |
| Height SDS | 0.81 ± 0.78 | 0.76 ± 0.78 | 0.711 |
| Weight (kg) | 36.09 ± 7.01 | 30.56 ± 4.84 | <0.001 |
| Weight SDS | 1.12 ± 0.71 | 1.03 ± 0.58 | 0.470 |
| BMI (kg/m ²) (at baseline) | 19.32 ± 2.82 | 18.49 ± 3.04 | 0.136 |
| BMI SDS (at baseline) | 1.02 ± 0.67 | 0.90 ± 0.59 | 0.314 |
| Basal LH (mIU/ml) | 1.36 ± 2.25 | 0.40 ± 0.66 | 0.007 |
| Basal FSH (mIU/ml) | 4.51 ± 2.37 | 2.88 ± 1.45 | <0.001 |
| Basal E2 (pg/ml) | 29.01 ± 21.53 | 19.25 ± 10.78 | 0.005 |
| Stimulated LH peak (mIU/ml) | 15.74 ± 10.72 | 12.49 ± 10.2 | 0.156 |
| Stimulated FSH peak (mIU/ml) | 14.53 ± 4.35 | 17.57 ± 6.78 | 0.013 |
| Stimulated LH/FSH ratio | 1.05 ± 0.61 | 0.87 ± 0.71 | 0.210 |
| Duration of the treatment (years) | 1.97 ± 0.54 | 2.91 ± 0.61 | <0.001 |
| Age of menarche (years) | 11.72 ± 0.65 | 11.91 ± 0.70 | 0.176 |
| Target Height (cm) | 161.26 ± 4.39 | 160.53 ± 5.49 | 0.447 |
| Predicted adult height (cm) | 158.49 ± 5.30 | 158.19 ± 5.69 | 0.774 |
| Final Adult Height (cm) | 162.63 ± 5.20 | 162.12 ± 5.42 | 0.627 |

BMI: Body mass index, SDS: standard deviation score, LH: luteinizing hormone, FSH: follicle stimulating hormone, E2: estradiol

Conclusion: GnRHa may improve FAH even the treatment is delayed after the age of 8 without a serious negative effect on BMD. However, as this improvement is limited for this age group, the therapy option should be individualized and should not be considered for all children.