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Letter to the Editor

Herbal medicine (Jogyongseongjang decoction) for precocious puberty girls: a retrospective study



Precocious puberty (PP) is generally defined as the onset of secondary sexual characteristics before eight years of age in girls and nine in boys. PP promotes sexual development and bone maturation and results in a shorter final height.¹

Gonadotropin-releasing hormone agonist (GnRHa) treatment has been widely used for PP since the 1980s, but some GnRHa-treated patients have shown decreased growth rates and have not reached their target heights.² Recently, GnRHa treatment in parallel with growth hormones has been proposed for children with short predicted adult heights.³ However, the effectiveness of this parallel therapy is controversial, and the associated medical costs are high.

As an alternative treatment for PP, herbal medicines have been used to promote growth and delay the development of puberty in children with PP. Although experimental and clinical studies have revealed the effectiveness of herbal medicine, research on the effectiveness and safety of long-term herbal treatment is insufficient. The authors, therefore, conducted this study.

We included 22 girls with idiopathic central precocious puberty (ICPP) who visited the H Korean Medical Clinic in Seoul from May 30, 2009, to February 10, 2018. The inclusion criteria were that the girls had continued treatment for more than 24 months and underwent hormone tests (e.g., estradiol, follicle-stimulating hormone, or luteinizing hormone) every six months. We only included girls who had ICPP and no organic diseases, such as central nervous system tumors. All participants had received no previous treatment for ICPP, and no other treatments, including GnRHa, were taken during the study period. Both the girls and their caregivers gave their approval for the girls to participate in this study and receive herbal treatment for ICPP. All the girls were treated with herbal medicine, specifically a Jogyongseongjang decoction. The composition of this prescription is shown in Supplementary Table S1.

Height and weight were measured during the first and last visits and at menarche. Liver function tests, such as AST and ALT, were performed on the last visit.

The average age of the girls was 8.21 ± 0.50 years at the first visit and 11.83 ± 0.98 years at the last visit. The latter is the expected age in the third stage of the Tanner scale.^{4,5} The level of sex hormones are listed in Table 1. After 36 months of treatment, E2 and FSH

were below the expected basal hormone levels for Tanner stage III (i.e., 133.9 ± 12.1 pg/ml for E2, 5.41 ± 0.30 mIU/ml for FSH, and 4.49 ± 0.34 mIU/ml for LH).⁶ These results suggest that the sex hormone levels (E2 and FSH) in girls who received the herbal medicine slowly increased.

The average period from breast development to menarche was 39.95 ± 10.58 months, which is much longer than the typical 24–30 months.^{7,8} This indicates that girls who received herbal medicine experienced a delay in puberty.

The average growth between breast development and menarche was 25.19 ± 4.15 cm, with an average growth rate of 7.80 ± 1.28 cm/yr. This indicates that the growth rate of girls treated with the herbal medicine was better than that of girls treated only with GnRHa.⁹ The observed growth rate was similar to the 6.8 ± 2.8 cm/yr that is the growth rate at the twelfth month of treatment for patients who received GnRHa and growth hormone parallel therapy.¹⁰

Liver function test results in girls receiving herbal medicine treatment for more than 24 months showed normal levels. This is evidence that herbal medicine is safe in children, as it does not cause liver function abnormalities even after long-term administration.

The limitations of this study include the absence of a control group and follow-up, and a small number of participants. In the future, more systematic and diverse clinical research is necessary to provide additional evidence.

Even so, this study is meaningful in that it evaluated the objective effects of long-term Korean herbal medicinal treatment on 22 ICPP girls. In order to successfully treat PP, it is important that patients and caregivers trust their medical doctors and receive long-term treatment. In this regard, we hope that this paper will serve as a testament to the efficacy and safety of herbal medicine for PP.

Author contributions

Conceptualization: SCP and HLL. Methodology: SCP and HLL. Formal Analysis: SBS and HLL. Investigation: SCP, KYC, SYL, JLL, and MSB. Writing - original draft: SBS and HLL. Writing - review & editing: JAL, SCP, and HLL. Funding acquisition: ICJ and YCP.

Conflict of interest

The authors have no conflicts of interest to declare.

Table 1
The Sex Hormone Levels (E2, FSH, and LH) According to Treatment Months.

	First visit	6 months	12 months	18 months	24 months	30 months	36 months
E2 (pg/ml)	14.96 ± 6.50	10.97 ± 4.79	14.79 ± 5.69	20.22 ± 12.08	28.25 ± 13.62	36.58 ± 21.04	43.71 ± 24.40
FSH (mIU/ml)	2.35 ± 0.89	2.39 ± 0.85	2.66 ± 1.32	3.67 ± 1.47	4.02 ± 1.34	4.29 ± 1.25	4.81 ± 1.33
LH (mIU/ml)	0.17 ± 0.09	0.29 ± 0.37	0.96 ± 1.10	1.69 ± 1.02	2.66 ± 1.41	3.15 ± 1.86	4.89 ± 2.74

E2, Estradiol; FSH, Follicle stimulating hormone; LH, Luteinizing hormone.

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Ethical statement

This study has been approved by the Institutional Review Board (IRB) of Gachon Oriental Medicine Hospital (IRB File No. 2018-18-105).

Data availability

Data will be made available upon request.

Supplementary material

Supplement Table S1. List of medicinal plants in Jogyeseongjang decoction and their effects can be found in the online version at doi:[10.1016/j.imr.2020.02.001](https://doi.org/10.1016/j.imr.2020.02.001).

References

- Berberoglu M. Precocious puberty and normal variant puberty: definition, etiology, diagnosis and current management. *J Clin Res Pediatr Endocrinol* 2009;1:164–74.
- Carel J, Leger J. Precocious puberty. *N Engl J Med* 2008;358:2366–77.
- Hayward C, Killen JD, Wilson DM, Hammer LD, Litt IF, Kraemer HC, et al. Psychiatric risk associated with early puberty in adolescent girls. *J Am Acad Child Adolesc Psychiatry* 1997;36:255–62.
- Neely EK, Hintz RL, Wilson DM, Lee PA, Gautier T, Argente J, et al. Normal ranges for immunochemiluminometric gonadotropin assays. *J Pediatr* 1995;127:40–6.
- Bidlingmaier F, Barnack MW, Butenandt O, Knorr D. Plasma estrogens in childhood and puberty under physiologic and pathologic conditions. *Pediatr Res* 1973;7:901–7.
- Chada M, Průsa R, Bronský J, Pechová M, Kotaska K, Lisá L. Inhibin B, follicle stimulating hormone, luteinizing hormone, and estradiol and their relationship to the regulation of follicle development in girls during childhood and puberty. *Physiol Res* 2003;52:341–6.
- Dixon S, Stein M. *Encounters with children*. 4th, editor: Mosby; 2005.
- Rosenfeld RG. Evaluation of growth and maturation in adolescence. *Pediatr Rev* 1982;4:175–83.
- Ahn SY, Yoo JH, Shin CH, Yang SW. The effects of gonadotropin-releasing hormone agonists on final height and its related factors in patients with true precocious puberty. *Korean J Pediatr* 2004;47:647–55.

- Chae HW, Koh H, Rhie YJ, Kim HS, Kim DH. Effect of gonadotropin releasing hormone agonist on growth and sex hormone in girls with early puberty. *J Korean Soc Pediatr Endocrinol* 2006;11:162–9.

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