Annals of Pediatric Endocrinology & Metabolism

apem

Final adult height in male patients with central precocious puberty after gonadotropin-releasing hormone agonist treatment

Kyoung Won Cho[1],
Youn Kyoung Kim[1],
Ji Eun Yoo[1],
Joon Young Kim[2],
Seo Jung Kim[1],
Sujin Kim[1],
Youngha Choi[2],
Kyungchul Song[2],
Eun Byeol Lee[3],
Hyun Wook Chae[2],
Junghwan Suh[1]

[1]Department of Pediatrics, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea
[2]Department of Pediatrics, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Pediatrics, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea

Purpose: We aimed to compare the final adult height (FAH) of male patients with central precocious puberty (CPP) after treatment with a gonadotropin-releasing hormone agonist (GnRHa). Specifically, we compared FAH with the target height (TH) and the predicted adult height (PAH) before and after GnRHa treatment to quantify height gain and identify predictive factors.
Methods: We retrospectively reviewed the medical records of 92 male patients with CPP and known FAH after GnRHa treatment at the Department of Pediatrics of Severance Children's Hospital between January 2000 and June 2024.
Results: The mean duration of GnRHa treatment was 2.7±1.3 years. A significant 1.1±0.9 years narrowing was observed in the difference between bone age (BA) and chronological age (CA) during treatment ($P<0.001$). TH was 172.4±3.4 cm. FAH was 173.6±6.4 cm. FAH was greater than TH by 1.2±5.9 cm ($P=0.047$). PAH before and after treatment was 179.9±8.1 and 181.2±7.4 cm, respectively. PAH was increased by 1.3±4.9 cm ($P=0.012$) after treatment. As the PAH standard deviation score (SDS) before GnRHa treatment increased, FAH tended to exceed TH. In contrast, higher testosterone levels before treatment are associated with FAH falling below TH. A longer duration of treatment and taller TH are associated with an FAH SDS greater than height SDS before treatment. Conversely, a greater weight SDS, BA–CA difference, and testis size before treatment are associated with FAH SDS being less than height SDS before GnRHa treatment.
Conclusion: GnRHa treatment improved FAH and inhibited bone maturation in male patients with CPP.

Keywords: Central precocious puberty, Gonadotropin-releasing hormone, Boys

Highlights

· The incidence of precocious puberty has increased along with the accelerated onset of puberty worldwide. GnRHa is a standard treatment for central precocious puberty in both boys and girls. Studies on the effectiveness of long-term GnRHa treatment and FAH in boys with CPP are rare and often limited in size. This study was conducted on a large scale to compare the FAH of male patients with CPP after GnRHa treatment.

Introduction

Central precocious puberty (CPP) is caused by premature activation of the hypothalamic-pituitary-gonadal axis and defined as the appearance of secondary sexual characteristics before the age of 9 years in boys [1]. The incidence of precocious puberty has recently increased along with the accelerated onset of puberty worldwide [2]. Although the underlying causes are not yet known, proposed contributors

include the increase in childhood obesity owing to poor dietary habits and insufficient physical activity, greater exposure to environmental hormones and endocrine disruption through environmental pollution, and increased use of medical facilities because social influences impact parental concern over child growth [3].

CPP can lead to premature osseous fusion, resulting in decreased final adult height (FAH) and psychosocial problems, requiring appropriate treatment [4]. Gonadotropin-releasing hormone agonists (GnRHa), which have been used as standard treatments for CPP for decades, suppress the secretion of sex hormones, inhibit rapid bone maturation, and extend the growth period, thereby improving FAH [1,4].

The prevalence of CPP in boys is approximately 10–15 times lower than in girls [5,6]. GnRHa treatment effectively improves FAH in children with CPP, with increased FAH in girls and long-term treatment allows most boys to reach their target height (TH) range [7]. Two Korean studies demonstrated that FAH was 3.3 and 1.0 cm greater than TH after GnRHa, respectively [8,9]. However, studies on the effectiveness of long-term GnRHa treatment and FAH in boys with CPP are rare and often limited in size [7-10].

Therefore, this study was conducted on a large scale to compare the FAH of male patients with CPP after GnRHa treatment with the TH and predicted adult height (PAH) before treatment, and to identify predictive factors.

Materials and methods

1. Study population

This study investigated 668 male patients diagnosed with CPP between January 2000 and June 2024 at the Severance Children's Hospital. After excluding 4 patients who did not receive treatment after diagnosis and 66 patients who were lost to follow-up during treatment, the total number of patients treated with GnRHa was 598. Of these, 253 patients were still undergoing treatment, 76 received concomitant growth hormone treatment, and 177 had not yet reached their final height. A total of 92 patients with known FAH were enrolled (Fig. 1).

2. Study design

CPP was diagnosed based on the following criteria: (1) objective testicular volume ≥4 mL, (2) advanced bone age (BA) beyond chronological age (CA), and (3) peak values of pubertal luteinizing hormone (LH) (cutoff value: ≥5 IU/L) achieved during a GnRH stimulation test. A brain magnetic resonance imaging was performed to rule out central nervous system tumors. FAH was defined as a BA height of 16 years or older, and the yearly growth rate was less than 1 cm/yr. The differences between FAH and TH and FAH and PAH before GnRHa treatment were evaluated for growth benefits. Height, weight, Tanner stage, BA, serum LH, follicle-stimulating hormone (FSH), and testosterone concentrations were evaluated every 6 months. GnRHa treatment was discontinued at a BA of approximately 13 years. We compared the differences between BA and CA at the beginning and end of the GnRHa treatment. In addition, we analyzed the correlation between FAH and factors such as Tanner stage, age at the start and end of treatment, treatment period, height, weight, body mass index (BMI), PAH, standard deviation score (SDS), BA at the beginning and end of treatment, and laboratory test results (LH, FSH,
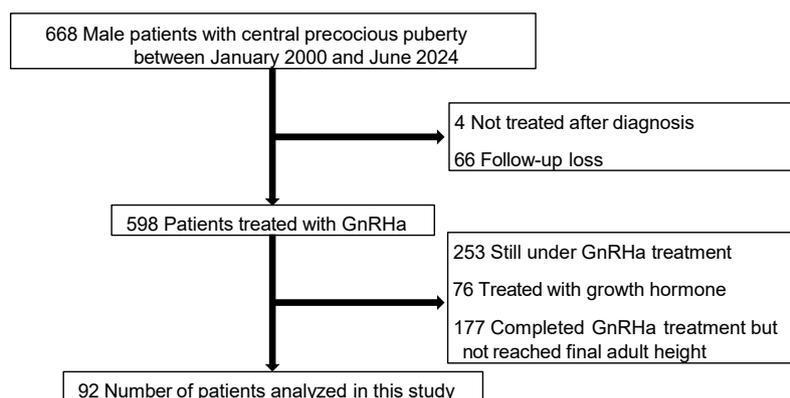

Fig. 1. Flow chart of the patient selection process. GnRHa, gonadotropin-releasing hormone agonist.

peak LH, and testosterone levels).

3. Parameters

Pubertal stage was evaluated by trained pediatric endocrinologists, and testicular volume was estimated using a Prader orchidometer. Tanner stage in boys was based on testicular volume using the following scale: T1, < 4; T2, 4–8; T3, 9–12; T4, 15–20; and T5, > 22 mL [11].

Trained nurses performed anthropometric measurements using a Harpenden stadiometer (Holtain, UK). As of 2018, the SDS values for height, weight, and BMI were calculated, and standard growth charts were used with 2 growth reference values for Korean children and adolescents in 2007 and 2017 provided by the Korean Academy of Pediatrics and the Centers for Disease Control and Prevention [12,13]. BA was measured using the Greulich-Pyle method with simple radiographs of the left hand and wrist [14]. PAH was calculated using the average and advanced tables in the Bayley-Pinneau (BP) method [15]. TH was defined as mid-parental height, which was calculated by adding 6.5 cm to the average parental height.

The GnRH stimulation test was performed using 0.1-mg gonadorelin or triptorelin acetate intravenously, and blood samples were taken at 0, 30, 60, 90, and 120 min to determine LH, FSH, and basal testosterone levels.

The standard treatment regimen was the subcutaneous administration of leuprolide and triptorelin, in either a 1 or 3-month formulation.

4. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics ver. 27.0 (IBM Co., USA). Statistical significance was set at $P<0.05$. The results are presented as mean±standard deviation unless indicated otherwise. We used a paired t-test to compare the FAH, TH, and PAH levels before GnRHa treatment and the differences between BA and CA at the beginning and end of treatment. To determine significant associations with height gain (FAH-TH, and PAH SDS-height SDS before GnRHa treatment), univariate analyses followed by multivariate linear regression analyses were performed with clinical factors.

5. Ethical statement

This study was conducted in accordance with the principles of the Declaration of Helsinki. Given that this was a retrospective study of data obtained during the general course of medical treatment, the need for informed consent was waived. This study was approved by the Institutional Review Board (IRB) of the Yonsei University Health System (IRB No. 4-2024-1574).

Results

1. Clinical characteristics before and after GnRHa treatment

The clinical and auxological factors according to the period of GnRHa treatment in the 92 male patients with CPP are shown in Table 1. The mean duration of GnRHa treatment was 2.7±1.3 years. The mean height, weight, and BMI before GnRHa treatment and their SDS values were 140.8±7.2 cm (1.00±1.09), 41.6±9.6 kg (1.08±0.87), and 20.8±3.5 kg/m² (0.86±0.90), respectively. The mean height, weight, and BMI after GnRHa treatment and their SDS values were 155.6±7.0 cm (0.76±1.16), 58.3±12.0 kg (1.17±0.90), and 23.9±3.8 kg/m² (1.10±0.83), respectively. Peak LH levels before GnRHa treatment were 13.2±6.8 mIU/mL and after they were 1.3±1.0 mIU/mL. Testosterone levels were 40.0±97.1 ng/dL before GnRHa treatment and 8.5±19.0 ng/dL after.

The BA and CA at the start of GnRHa treatment were 11.2±0.8 and 9.50±0.7 years, respectively. At the end of

Table 1. Clinical characteristics of patients before and after GnRHa treatment

Characteristic	Before treatment	After treatment
CA (yr)	9.5±0.7	12.2±1.0
BA (yr)	11.2±0.8	12.8±0.4
Testis size (cm³)	6.2±2.8	NA
Height (cm)	140.8±7.2	155.6±7.0
Height SDS	1.00±1.09	0.76±1.16
Height SDSBA	-3.92±0.95	-2.71±0.94
PAH (cm)	179.9±8.1	181.2±7.4
PAH SDS	0.80±1.29	1.01±1.19
Weight (kg)	41.6±9.6	58.3±12.0
Weight SDS	1.08±0.87	1.17±0.90
BMI (kg/m²)	20.8±3.5	23.9±3.8
BMI SDS	0.86±0.90	1.10±0.83
FSH (mIU/mL)	3.4±1.9	2.1±1.2
Peak LH (mIU/mL)	13.2±6.8	1.3±1.0
Testosterone (ng/dL)	40.0±97.1	8.5±19.0
Duration of GnRHa (yr)	-	2.7±1.23
TH (cm)	-	172.4±3.4
FAH (cm)	-	173.6±6.4
FAH-TH (cm)	-	1.2±5.9
PAH after – before GnRHa Tx (cm)	-	1.3±4.9

Values are presented as mean±standard deviation.
GnRHa, gonadotropin-releasing hormone agonist; CA, chronological age; BA, bone age; SDS, standard deviation score; PAH, predicted adult height; BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; FAH, final adult height; TH, target height; Tx, treatment; NA, not available.

GnRHa treatment, the BA and CA were 12.8±0.4 and 12.2±1.0 years. The difference between BA and CA was 1.7±0.6 years at the start of GnRHa treatment and 0.6±1.0 years at the end of treatment. A significant 1.1±0.9 years reduction in the difference between BA and CA was observed during GnRHa treatment ($P<0.001$) (Fig. 2).

TH was 172.4±3.4 cm, and FAH was 173.6±6.4 cm. FAH was significantly greater than TH by 1.2±5.9 cm ($P=0.047$) (Fig. 3). PAH before GnRHa treatment was 179.9±8.1 and after it was 181.2±7.4 cm. Following GnRHa treatment, there was a 1.3±4.9 cm ($P=0.012$) significant increase in the PAH (Fig. 4).

When 92 patients were categorized by age, 79 patients (85.9%) were over 9 years of age, and 13 patients (14.1%) were under 9 years. FAH-TH demonstrated no statisti-
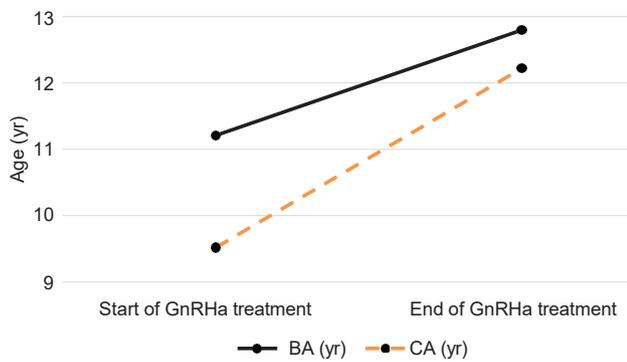
Fig. 2. Bone and chronological ages at the start and end of GnRHa treatment. The difference between BA and CA was 1.7±0.6 years at the start of GnRHa treatment and 0.6±1.0 years at the end of GnRHa treatment. A significant 1.1±0.9 years narrowing of the difference between BA and CA was observed during GnRHa treatment ($P<0.001$). GnRHa, gonadotropin-releasing hormone agonist; BA, bone age; CA, chronological age.
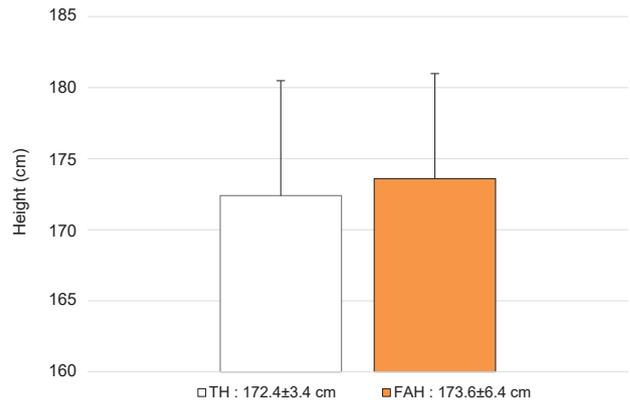
Fig. 3. Target height and final adult height in 92 male CPP patients. CPP, central precocious puberty; TH, target height; FAH, final adult height.
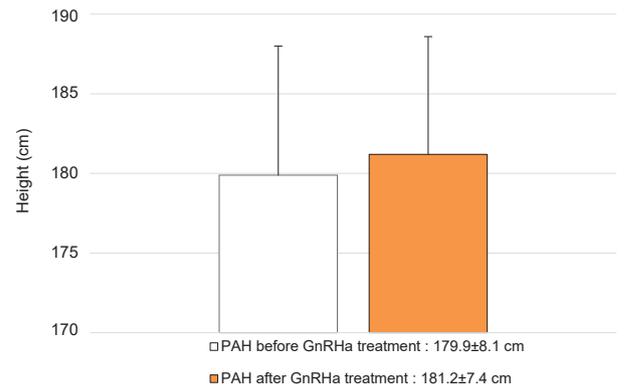
Fig. 4. Predicted adult height in 92 male CPP patients before and after GnRHa treatment. CPP, central precocious puberty; TH, target height; FAH, final adult height.

Table 2. Linear regression of variables significantly associated with FAH-TH

Variable	Univariate		Multivariate	
	B-coefficient	*P*-value	B-coefficient	*P*-value
Age before treatment (yr)	-2.262	0.766	-	-
Height SDS before treatment	3.345	<0.001	-	-
Height SDSBA before treatment	3.777	<0.001	-	-
Weight SDS before treatment	2.286	<0.001	-	-
BMI SDS before treatment	0.246	0.162	-	-
PAH SDS before treatment	0.625	<0.001	0.364	0.025
BA before treatment (yr)	-0.107	0.894	-	-
BA–CA before treatment (yr)	0.162	0.866	-	-
LH before treatment (mIU/mL)	-1.378	0.044	-	-
FSH before treatment (mIU/mL)	-0.603	0.067	-	-
Testosterone before treatment (ng/dL)	-0.019	<0.001	-0.250	0.010
Peak LH before treatment (mIU/mL)	-0.232	0.010	-	-
Testis size before treatment (cc)	-0.259	0.248	-	-
Treatment duration (yr)	0.127	0.796	-	-

FAH, final adult height; TH, target height; SDS, standard deviation score; BMI, body mass index; PAH, predicted adult height; BA, bone age; CA, chronological age; LH, luteinizing hormone; FSH, follicle-stimulating hormone.

cally significant difference between the 2 groups (mean difference, -1.3±2.7 cm; *P*=0.643). Furthermore, analysis of patients who initiated treatment before the age of 9 demonstrated a mean PAH increase of 4.2±1.4 cm, in contrast to patients who initiated treatment after the age of 9 (*P*=0.003).

In total, 92 patients were categorized according to their medications: 39 patients were treated with leuprolide acetate, of which 1 patient was on a 1-month formulation and 38 patients were on a 3-month formulation. The remaining 53 patients were treated with triptorelin acetate; 42 patients were on a 1-month formulation, and 11 patients were on a 3-month formulation. No significant differences were observed in height gain or reduction in the BA–CA difference between the triptorelin and leuprolide treatment groups after GnRHa treatment.

2. Factors associated with FAH

After the univariate linear regression analyses, a multivariate linear regression analysis was performed with significant factors. Before GnRHa treatment, PAH SDS had a significant positive correlation (*β*=0.364, *P*<0.05) with FAH-TH and testosterone level had a significant

negative correlation (*β*=-0.250, *P*<0.05) (Table 2). A positive correlation was identified between treatment duration, TH (*β*=0.254, 0.177, respectively, all *P*<0.05), and FAH SDS – height SDS before GnRHa treatment. Conversely, weight SDS, BA–CA difference, and testis size before GnRHa treatment had a negative correlation (*β*=-0.193, -0.432, and -0.278, respectively, all *P*<0.05) with FAH SDS – height SDS before GnRHa treatment (Table 3).

Discussion

A review of the literature revealed that studies on adult height gain and clinical factors after GnRHa treatment in male patients with CPP have been conducted in small patient populations, with fewer studies conducted in this patient group than in female patients. We analyzed the effects of GnRHa treatment on FAH and bone maturation and identified predictive factors. The BA–CA difference narrowed significantly during GnRHa treatment in male patients with CPP. The FAH was significantly taller than the TH. There was an increase in PAH after GnRHa treatment. A summary of previous studies involving height gain and suppression of bone maturation in male CPP patients with GnRHa treatment is shown in Table 4.

Table 3. Linear regression of variables significantly associated with FAH SDS – height SDS before treatment

Variable	Univariate		Multivariate	
	B-coefficient	*P*-value	B-coefficient	*P*-value
Age before treatment (yr)	-0.001	0.994	-	-
Weight SDS before treatment	-0.284	0.006	-0.193	0.040
BMI SDS before treatment	-0.146	0.165	-	-
PAH SDS before treatment	-0.130	0.217	-	-
BA before treatment (yr)	-0.384	<0.001	-	-
BA–CA before treatment (yr)	-0.457	<0.001	-0.432	<0.001
LH before treatment (mIU/mL)	-0.253	0.015	-	-
FSH before treatment (mIU/mL)	-0.171	0.084	-	-
Testosterone before treatment (ng/dL)	-0.267	0.010	-	-
Peak LH before treatment (mIU/mL)	-0.380	<0.001	-	-
Testis size before treatment (cc)	-0.446	<0.001	-0.278	0.012
Treatment duration (yr)	0.413	<0.001	0.254	0.042
TH (cm)	0.091	0.389	0.177	0.036

FAH, final adult height; PAH, predicted adult height; GnRHa, gonadotropin-releasing hormone agonist; BMI, body mass index; BA, bone age; CA, chronological age; LH, luteinizing hormone; FSH, follicle-stimulating hormone.

Table 4. A summary of previous studies in male CPP patients with GnRHa treatment

Study	Country	No.	Treatment duration (yr)	BA–CA before-after treatment (cm)	FAH (cm)	TH (cm)	FAH-TH (cm)	PAH before-after treatment (cm)
Cho et al., 2021 [8]	Korea	20	2.7±0.6	1.3	173.4±5.8	170.9±4.2	2.5	4.3
Shim et al., 2020 [9]	Korea	18	2.0±0.8	0.2	172.0±4.8	171.0±4.0	1.0	0.1
Ma et al., 2013 [10]	China	20	1.7±0.5	1.1	169.8±5.8	167.8±4.6	2.0	2.8
Rizzo et al., 2000 [16]	Italy	12	4.1±0.6	1.8	176.1±6.1	174.2±2.9	1.9	10.8
Lazar et al., 2001 [17]	Israel	11	3.4±0.8	1.5	172.3±7.0	170.6±4.5	1.6	1.0

Values are presented as mean±standard deviation unless otherwise indicated.
CPP, central precocious puberty; GnRHa, gonadotropin-releasing hormone agonist; BA, bone age; CA, chronological age; FAH, final adult height; TH, target height; PAH, predicted adult height.

Previous studies have indicated a reduction in BA–CA in patients with CPP during GnRHa treatment [8-10,15-18]. A Korean study reported a narrowing of the BA–CA difference by 1.3 years during a 2.9-year course of GnRHa treatment, administered to 20 male patients with CPP [9]. The present study also demonstrated that GnRHa treatment resulted in a 1.1-year delay in BA–CA, thereby substantiating the efficacy of GnRHa in inhibiting bone maturation in male patients with CPP. Inhibition of bone maturation and premature osseous fusion is beneficial for FAH because it extends the growth period.

In the present study, FAH was found to be taller by 1.2±5.9 cm compared to the TH. Two studies, each including 20 male CPP patients treated with GnRHa, found FAH values 2.5 cm and 2.0 cm greater than TH, respectively [9,10].

PAH was increased by 1.3±4.9 cm after GnRHa treatment in our study. A 4.3 cm and 2.8 cm increase in PAH was observed in 20 male CPP patients after GnRHa treatment in 2 studies [9,10]. An Israeli study of 11 male CPP patients treated with GnRHa for 3.4 years, found that PAH after GnRHa treatment was 1.0 cm greater than before [19]. In particular, the deviation of total height gain can depend on the method of height prediction (for example, the Bayley and Pinneau method), the retrospective nature of the study, regional differences in practices, the use of more liberal criteria to initiate GnRHa treatment, and different intervals between the onset of puberty and start of treatment in the participating countries [20]. In our study, PAH before and after GnRHa treatment was found to be greater when compared to FAH and TH. It is well known that when predicting adult heights via the BP method, the prediction may overestimate FAH in pediatric patients [21,22].

In this study, patients were grouped according to the age at which treatment was initiated, either before or after 9 years. Although there was no significant difference in FAH-TH, the posttreatment FAH in patients who started GnRHa before the age of 9 was increased by an average of 4.2 cm compared to those who started after 9. In a previous study [7], the boys who started treatment before the age of 6 years had a significantly better height gain in comparison with those who started after that age (12.5 cm vs. 2.3 cm), but final height was not significantly different between the 2 groups, and both reached their genetic target (174.1 cm vs. 171.8 cm). In a study by Paul et al. [17], male CPP patients treated with GnRHa were divided into groups before and after the age of 5 and compared. The results demonstrated that male CPP patients who initiated GnRHa treatment

before 5 years exhibited an increase in PAH of 11.1 cm after treatment, whereas those who began treatment after the age of 5 demonstrated a 6.0 cm increase in PAH. In a recent meta-analysis of female CPP patients treated with GnRHa, those with an average increase of 5.1 cm started treatment before the age of 8 years, but those with an average increase of 2.5 cm started treatment after the age of 8 years [23].

The synthetic GnRH analog, triptorelin, is characterized by the substitution of D-tryptophan for L-glycine at the sixth position. This alteration expands the plasma half-life and increases its effectiveness by improving resistance to enzymatic degradation and affinity for the pituitary receptor. Leuprolide is a synthetic nonapeptide analog of naturally occurring GnRH and is more potent than the natural hormone. There is a lack of comparative studies evaluating the effectiveness of various formulations, specifically concerning treatment completion [24]. No significant differences were observed between the triptorelin- and leuprolide-treated groups in the present study. The 2 analogs show similar effects in girls with CPP [24-26]. However, in another study involving girls with CPP, triptorelin treatment suppressed gonadotropins slightly more effectively than leuprolide acetate treatment and increased FAH to over the initial PAH [26].

The findings of this study indicate a positive correlation between PAH SDS before treatment with the FAH-TH. Conversely, a negative correlation was identified between the testosterone level before treatment and FAH-TH. When comparing FAH SDS – height SDS before treatment with multiple factors, treatment duration and TH were positively associated, whereas weight SDS, BA–CA difference, and testis size before GnRHa treatment were negatively correlated. PAH at the end of treatment and TH were factors influencing FAH in a previous Korean study with male patients with CPP [8,9]. Rizzo et al. [27] reported that factors influencing FAH after GnRHa treatment in boys identified TH and height at the end of treatment as important predictive factors. In a Japanese study [28], height gain was positively correlated with mean growth velocity and BA change during GnRHa treatment and negatively correlated with BA and CA before GnRHa treatment.

This study has some limitations. The single-country, single-center, and retrospective study design is a limitation. Another limitation is the absence of a control group of untreated patients. Nevertheless, this study had the largest number of patients compared to previous studies, and our study will inform future clinical applications for a growing number of male patients with

CPP.

In conclusion, GnRHa improved FAH and inhibited bone maturation in male patients with CPP. The greater PAH SDS before GnRHa treatment, TH, and longer GnRHa treatment duration were found to correspond with greater FAH. Conversely, the higher testosterone level, greater weight SDS, BA–CA difference, and testis size before GnRHa treatment were associated with smaller FAH.

Notes

Author contribution: Conceptualization: KWC, YKK, SJK, YC, KS, EBL, HWC, JS; Data curation: KWC, YKK, HWC, JS; Formal analysis: KWC, YKK, JEY, JYK, SJK, HWC, JS; Methodology: KWC, YKK, YC, KS, HWC, JS; Project administration: KWC, YKK, JEY, JYK, SJK, HWC, JS; Visualization: KWC, YKK, JEY, JYK, SJK, EBL, HWC, JS; Writing - original draft: KWC; Writing - review & editing: KWC, JS

ORCID
Kyoung Won Cho: 0000-0002-9881-0903
Youn Kyoung Kim: 0009-0004-5818-3054
Ji Eun Yoo: 0009-0009-7801-4625
Joon Young Kim: 0000-0001-9595-3610
Seo Jung Kim: 0000-0002-9799-0148
Sujin Kim: 0000-0003-0907-9213
Youngha Choi: 0000-0002-1607-6048
Kyungchul Song: 0000-0002-8497-5934
Eun Byeol Lee: 0009-0000-4981-2446
Hyun Wook Chae: 0000-0001-5016-8539
Junghwan Suh: 0000-0002-2092-2585

References

1. Cho AY, Shim YS, Lee HS, Hwang JS. Effect of gonadotropin-releasing hormone agonist monotherapy and combination therapy with growth hormone on final adult height in girls with central precocious puberty. Sci Rep 2023;13:1264.
2. Kim SJ, Kim JH, Hong YH, Chung IH, Lee EB, Kang E, et al. 2022 clinical practice guidelines for central precocious puberty of Korean children and adolescents. Ann Pediatr Endocrinol Metab 2023;28:168-77.
3. Shim KS, Kim JT. Therapy for idiopathic precocious puberty in children. J Korean Med Assoc 2011;54:953.
4. Kwon A. Commentary on "Effect of gonadotropin-releasing hormone agonist treatment on near final height in girls with central precocious puberty and early puberty". Ann Pediatr Endocrinol Metab 2023;28:3-4.
5. Teilmann G, Pedersen CB, Jensen TK, Skakkebaek NE, Juul A. Prevalence and incidence of precocious pubertal development in Denmark: an epidemiologic study based on national registries. Pediatrics 2005;116:1323-8.
6. Carel JC, Léger J. Clinical practice. Precocious puberty. N Engl J Med 2008;358:2366-77.
7. Bertelloni S, Mul D. Treatment of central precocious puberty by GnRH analogs: long-term outcome in men. Asian J Androl 2008;10:525-34.
8. Cho AY, Ko SY, Lee JH, Kim EY. Effects of gonadotropin-releasing hormone agonist treatment on final adult height in boys with idiopathic central precocious puberty. Ann Pediatr Endocrinol Metab 2021;26:259-65.
9. Shim YS, Lim KI, Lee HS, Hwang JS. Long-term outcomes after gonadotropin-releasing hormone agonist treatment in boys with central precocious puberty. PLoS One 2020;15: e0243212.
10. Ma H, Su Z, Chen Q, Li Y, Chen H, Du M. Final height outcome of boys with idiopathic central precocious puberty treated with gonadotropin-releasing hormone analogue. Int J Pediatr Endocrinol 2013;2013(Suppl 1):P75.
11. Sotos JF, Tokar NJ. Appraisal of testicular volumes: volumes matching ultrasound values referenced to stages of genital development. Int J Pediatr Endocrinol 2017;2017:7.
12. Kim JH, Yun S, Hwang SS, Shim JO, Chae HW, Lee YJ, et al. The 2017 Korean national growth charts for children and adolescents: development, improvement, and prospects. Korean J Pediatr 2018;61:135-49.
13. Moon JS, Lee SY, Nam CM, Choi J, Choe B, Seo J, et al. 2007 Korean National Growth Charts: review of developmental process and an outlook. Korean J Pediatr 2008;51:1.
14. Greulich WW, Pyle SI. Radiographic atlas of skeletal development of the hand and wrist. Calif Med 1959;91:53.
15. Bayley N, Pinneau SR. Tables for predicting adult height from skeletal age: revised for use with the Greulich-Pyle hand standards. J Pediatr 1952;40:423-41.
16. Bertelloni S, Baroncelli GI, Ferdeghini M, Menchini-Fabris F, Saggese G. Final height, gonadal function and bone mineral density of adolescent males with central precocious puberty after therapy with gonadotropin-releasing hormone analogues. Eur J Pediatr 2000;159:369-74.
17. Paul D, Conte FA, Grumbach MM, Kaplan SL. Long-term effect of gonadotropin-releasing hormone agonist therapy on final and near-final height in 26 children with true precocious puberty treated at a median age of less than 5 years. J Clin Endocrinol Metab 1995;80:546-51.
18. Oostdijk W, Rikken B, Schreuder S, Otten B, Odink R, Rouwé C, et al. Final height in central precocious puberty after long

term treatment with a slow release GnRH agonist. Arch Dis Child 1996;75:292-7.

19. Lazar L, Pertzelan A, Weintrob N, Phillip M, Kauli R. Sexual precocity in boys: accelerated versus slowly progressive puberty gonadotropin-suppressive therapy and final height. J Clin Endocrinol Metab 2001;86:4127-32.

20. Mul D, Bertelloni S, Carel JC, Saggese G, Chaussain JL, Oostdijk W. Effect of gonadotropin-releasing hormone agonist treatment in boys with central precocious puberty: final height results. Horm Res 2002;58:1-7.

21. Tarım O. Height predictions by Bayley-Pinneau method may misguide pediatric endocrinologists. Turk J Pediatr 2013;55: 485-92.

22. Blethen SL, Gaines S, Weldon V. Comparison of predicted and adult heights in short boys: effect of androgen therapy. Pediatr Res 1984;18:467-9.

23. Park HK, Choo MS, Shim YS. Adult height after gonadotropin-releasing hormone agonist treatment in girls with early puberty: a meta-analysis. Clin Endocrinol (Oxf) 2020;93:135-45.

24. Thaneetrakool T, Aroonparkmongkol S, Numsriskulrat N, Supornsilchai V, Wacharasindhu S, Srilanchakon K. Efficacy of leuprolide acetate versus triptorelin pamoate administe-

red every 3 months for treatment of central precocious puberty. Clin Exp Pediatr 2025;68:91-6.

25. Valenzise M, Nasso C, Scarfone A, Rottura M, Cafarella G, Pallio G, et al. Leuprolide and triptorelin treatment in children with idiopathic central precocious puberty: an efficacy/tolerability comparison study. Front Pediatr 2023;11:1170025.

26. Aka S, Abali S, Taskin A, Bengur FB, Semiz S. Comparison of two different GnRH analogs' impact on final height in girls with early puberty: triptorelin acetate vs. leuprolide acetate. Acta Endocrinol (Buchar) 2020;16:402-8.

27. Rizzo V, De Sanctis V, Corrias A, Fortini M, Galluzzi F, Bertelloni S, et al. Factors influencing final/near-final height in 12 boys with central precocious puberty treated with gonadotrophin-releasing hormone agonists. Italian Study Group of Physiopathology of puberty. J Pediatr Endocrinol Metab 2000;13 Suppl 1:781-6.

28. Tanaka T, Niimi H, Matsuo N, Fujieda K, Tachibana K, Ohyama K, et al. Results of long-term follow-up after treatment of central precocious puberty with leuprorelin acetate: evaluation of effectiveness of treatment and recovery of gonadal function. The TAP-144-SR Japanese Study Group on Central Precocious Puberty. J Clin Endocrinol Metab 2005;90:1371-6.