



Final adult height in girls with idiopathic central precocious puberty treated with monthly leuprorelin acetate VS triptorelin acetate



Voraluck Phatarakijirund¹, Nawaporn Numbenjapon¹, Chula Kooanantkul², Phairuch Chaiyakul¹, Kurusart Phowang¹

¹Division of Endocrinology, Department of Pediatrics, Phramongkutklao Hospital and College of Medicine, ²Kids Center, Vejthani Hospital

Background

- Gonadotropin-releasing hormone analogs (GnRHa) are the standard treatment of central precocious puberty (CPP).
- Many studies demonstrate the effects of GnRHa on preserved final adult height. However, data compares the efficacy of different GnRHa on growth outcome and gonadotropin suppression in girl with CPP was limit.

Objectives

Evaluate the effect of 2 different GnRHa on final adult height (FAH) and gonadotropin suppression in girl with idiopathic CPP.

Method

Design: Retrospective study.

Setting: Department of Pediatric, Phramongkutklao Hospital.

Subjects: Girls with idiopathic CPP who had been treated with GnRHa, either 3.75 mg depot leuprorelin acetate (Enantone®, Takeda, Japan) or triptorelin acetate (Decapeptyl®, Ferring, Switzerland), intramuscular injection every 4 weeks for at least one year and reach their FAH between January 1st, 1997 and December 31th, 2017.

Study protocol:

- Data was collected from the medical records and laboratory database.
- Final adult height determine by growth velocity during the preceding year was less than 1 cm and/or a bone age of 16 years.
- BA was assessed according to Greulich and Pyle.
- Target adult height (TAH) = (father's height + mother's height -13)/2.
- Both accelerated (AcPAH) and average predicted adult height (AvPAH) were calculated in all girls by using method of Bayley and Pinneau.
- LH, FSH and estradiol (E₂) levels were analyzed by automated chemiluminescence assay using Cobas® e801 autoanalyzer.
- Suppression of hypothalamic-pituitary-gonadal (HPG) axis was determined by measuring LH level 2 hours after depot GnRHa injection. LH level of less than 5 IU/L was considered adequate HPG axis suppression.

Outcome: FAH and height gain (FAH-AcPAH and FAH-AvPAH)

Statistical Analysis: Data are expressed as mean ± SD. Comparisons of the results were analyzed by using independent T-test. Analyses were performed using the IBM SPSS statistics version 22 and p < 0.05 was considered statistically significant.

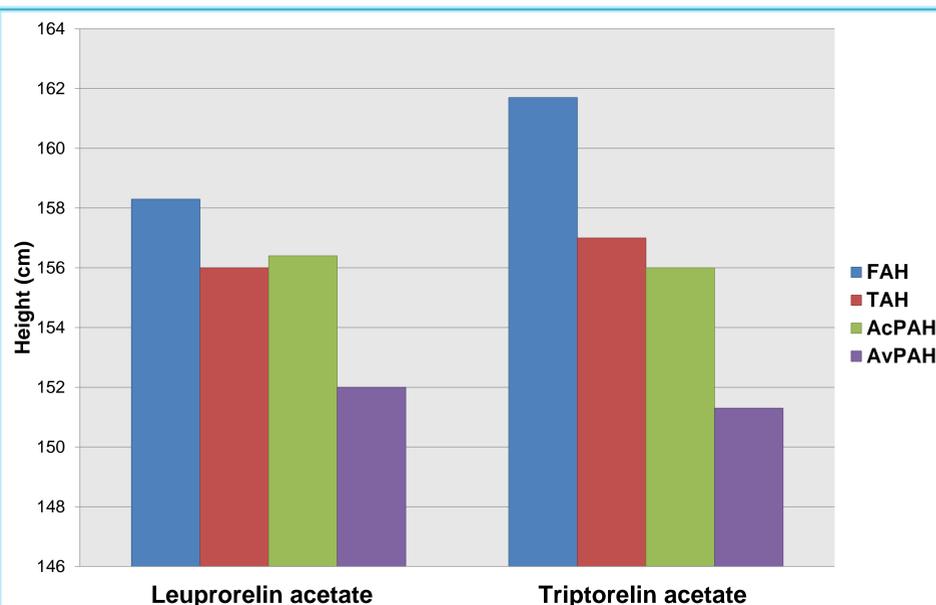


Figure 1: Final, target and predicted adult height (cm) in girl with idiopathic CPP treated with 2 different GnRHa.

Results

- Thirty-five girls, 20 treated with leuprorelin acetate (LA group) and 15 with triptorelin acetate (TA group), were enrolled.
- There were no different in age, height SDS, weight SDS, BMI SDS, bone age, PAH, dose of GnRHa at the time of diagnosis and TAH between the groups. However, the duration of treatment in TA group was significantly longer than LA group (p 0.001) and they were discontinued treatment at older age (p 0.002). (Table 1)
- In both groups, FAH were comparable with to TAH. The height gain from PAH (FAH-AcPAH and FAH-AvPAH) was significantly higher in TA group compare with LA group. (Table 2, Figure 1)
- After using a one-way ANCOVA controlling for duration of treatment and age of discontinue treatment, no significant different in FAH-AcPAH and FAH-AvPAH between 2 groups were found (p 0.4 and 0.3, respectively).
- At 6 month after GnRHa treatment, 16.7% in LA group reveals inadequate gonadotropin suppression and peak LH was significantly higher in LA compare to TA group (p 0.03). (Table 3)

Table 1: Characteristics of 35 girls with idiopathic CPP

Parameters	All (N = 35)	Leuprorelin acetate (N = 20)	Triptorelin acetate (N = 15)	p-value*
At start of treatment				
Chronological age (yr)	8.3 ± 0.6	8.4 ± 0.8	8.2 ± 0.4	0.31
Height (cm)	135.9 ± 7.6	136.7 ± 9.0	134.9 ± 5.5	0.51
Height SDS	1.8 ± 1.1	1.8 ± 1.4	1.8 ± 0.8	0.88
Weight SDS	1.6 ± 1.2	1.6 ± 1.0	1.6 ± 1.5	0.98
BMI SDS	1.3 ± 1.5	1.3 ± 1.0	1.3 ± 2.1	0.94
BA (yr)	10.9 ± 1.2	11.1 ± 1.4	10.7 ± 1.0	0.38
BA-CA (yr)	2.6 ± 1.0	2.7 ± 1.1	2.6 ± 0.9	0.64
TAH (cm)	156.4 ± 5.5	156.0 ± 6.8	157.0 ± 3.3	0.62
TAH SDS	-0.1 ± 1.1	-0.2 ± 1.4	0.02 ± 0.7	0.62
AcPAH (cm)	156.3 ± 7.5	156.4 ± 8.3	156.0 ± 6.7	0.88
AvPAH (cm)	151.7 ± 6.9	152.0 ± 7.7	151.3 ± 6.0	0.78
AcPAH-TAH (cm)	-0.2 ± 6.8	0.4 ± 8.0	-1.0 ± 4.8	0.54
AvPAH-TAH (cm)	-4.7 ± 5.9	-4.0 ± 7.0	-5.7 ± 4.2	0.40
Dose (mcg/kg)	113.7 ± 24.0	111.3 ± 22.7	116.9 ± 26.0	0.50
At the end of treatment				
Chronological age (yr)	11.1 ± 0.8	10.8 ± 0.8	11.6 ± 0.5	<0.01
Duration of treatment (yr)	2.8 ± 0.9	2.4 ± 0.9	3.4 ± 0.6	<0.01
Height (cm)	149.2 ± 6.0	147.9 ± 6.6	150.8 ± 4.7	0.16
Height SDS	1.0 ± 1.1	1.1 ± 1.3	0.8 ± 0.9	0.52
Weight SDS	1.7 ± 1.2	1.8 ± 1.0	1.5 ± 1.4	0.47
BMI SDS	1.6 ± 1.4	1.8 ± 1.1	1.3 ± 1.6	0.36
Dose (mcg/kg)	81.0 ± 14.6	80.9 ± 13.2	81.0 ± 16.7	0.98

Table 2: Height outcomes in both groups

Parameters	All (N = 35)	Leuprorelin acetate (N = 20)	Triptorelin acetate (N = 15)	p-value*
Chronological age (yr)	17.1 ± 2.9	16.7 ± 3.4	17.5 ± 2.3	0.42
Height (cm)	159.8 ± 7.1	158.3 ± 7.7	161.7 ± 5.8	0.16
Height SDS	0.7 ± 1.4	0.5 ± 1.6	1.0 ± 1.2	0.26
FAH-MPH (cm)	3.3 ± 6.1	2.3 ± 6.6	4.7 ± 5.2	0.25
FAH-AcPAH (cm)	3.5 ± 4.9	1.9 ± 4.9	5.7 ± 4.2	<0.05
FAH-AvPAH (cm)	8.1 ± 4.6	6.3 ± 4.4	10.4 ± 3.8	<0.01

Table 3: Hormonal data at 6 months of treatment in both groups

Parameters	Leuprorelin acetate (N = 12)	Triptorelin acetate (N = 7)	p-value*
LH (IU/L)	2.6 ± 2.4	0.8 ± 0.4	<0.05
FSH (IU/L)	7.5 ± 0.5	2.0 ± 0.7	0.07
Estradiol (pg/mL)	7.3 ± 3.8	5.5 ± 1.2	0.14

*p-value compared between 2 different GnRHa.

Conclusion

Girls with idiopathic CPP treated with GnRHa reach their FAH comparable with PAH and TAH. No different in FAH and FH increase over PAH between LA and TA. LH suppression was more pronounced in TA group.

