Effect of GnRHa 3.75 mg Subcutaneously Every6 weeks on Adult Height in Girls with Idiopathic Central Precocious Puberty

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Background

The the efficacy of GnRHa in suppressing hypothalamic-pituitary-gonadal axis has been accepted, there are still different opinions with respect to the dosage and medication cycle of GnRHa.
There is controversy on the relationship between GnRHa treatment and improvement in the final adult height.
At present, intramuscular or subcutaneous injection of GnRHa 3.75 mg every 4 weeks is generally applied.
From 2002, girls with ICPP in our hospital were treated with GnRHa 3.75 mg subcutaneously every 6 weeks. Good short-term efficacy was achieved, including effective suppression of sexual development, slowing bone maturation, and increasing predicted adult height.

Objective

To evaluate the long-term efficacy of triptorelin 3.75 mg subcutaneously every 6 weeks on final height in girls with ICPP.

Subjects and Methods

Forty females with ICPP were treated with GnRHa 3.75 mg subcutaneously every 6 weeks in our hospital, starting from 2002 to 2010 consecutively. All of them had already achieved final adult height. The whole follow-up lasted for 6-11 years. GnRHa therapy was discontinued at the BA of 12 years. During GnRHa treatment, if GV decreased below 4 cm/y, rhGH 0.15-0.175U/(kg·d) was used concomitantly.

Table 1: Auxological features of patients with ICPP before treatment

Parameters	**Group A** GnRHa alone	**Group B** GnRHa + rhGH	**P**
N	17	23	
CA	8.13±0.20	7.63±0.28	NS
CA at the onset of breast development	6.77±0.32	6.18±0.39	NS
BA	9.18±0.29	8.36±0.30	NS
Ht SDS-CA	0.62±0.19	0.15±0.17	NS
Ht SDS-BA	-0.50±0.14	-0.73±0.16	NS
Height (cm)	132.79±1.57	126.57±1.83	0.01
Weight(kg)	31.68 ±1.44	25.59±0.74	0.001
BMI(kg/m^2)	17.85±0.53	15.96±0.31	0.002
PAH	161.56±0.91	159.99±0.99	NS
THt(cm)	158.29±0.91	156.15±0.80	NS
GV(cm/yr)	7.57±0.36	7.25±0.29	NS
Breast stage(L)	2.29±0.14	2.22±0.14	NS
Breast stage(R)	2.29±0.17	2.26±0.13	NS
LH peak(mIU/ml)	9.60±1.76	6.32±0.87	NS
FSH peak(mIU/ml)	12.01±0.89	12.54±2.00	NS

CA：chronological age；BA：bone age；THt：target height；Ht SDS-CA：height SD score for CA；PAH：predicted adult height；Ht SDS-BA：height SD score for BA；GV：growth velocity;
NS：no significant difference (p＞0.05)

Statistical analysis

Data are expressed as mean ± standard error (SE). T tests were used to determine the significant difference of a variable in two groups. Factors affecting the final adult height were analyzed using linear regression with forward selection used to select variables so as to find an “optimal” regression equation. P ≤ 0.05 is considered statistically significant.

Results

1. Short-term effects

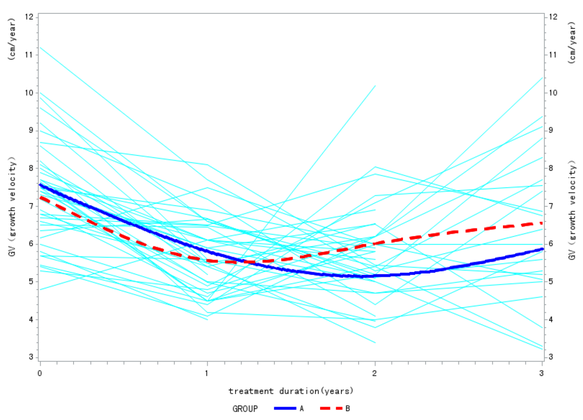

Fig. 1: Change in the GV of the Patients in the Two Groups after Treatment

Table 2. The changes of Ht SDS-BA before and after treatment

Parameters	Ht SDS Group A	Ht SDS Group B
N	17	23
Pre-treatment	-0.50 ±0.14	-0.73±0.16
1y post-treatment	-0.40±0.15	-0.69±0.19
2y post-treatment	-0.21±0.18	-0.64±0.17
3y post- treatment	0.07±0.30	-0.59±0.15

2. Long-term efficacy

Table 3. The relationship between the FAH and THt in the two groups

Parameters	Group A（n=17）	Group B（n=23）
FAH(cm)	159.81±1.20	161.01±1.02
THt(cm)	158.29±0.91	156.15±0.80*
FAH－THt (cm)	1.51±1.04	4.86±0.94#

* p<0.001(FAH and THt in group B)
# p<0.05 (the values of FAH-THt between the two groups)

Table 4. The relationship between FAH and PAH in two groups

Parameters	Group A（n=17）	Group B（n=23）
FAH(cm)	159.81±1.20	161.01±1.02
PAH pre- treatment (cm)	161.56±0.91	159.99±0.99
PAH post- treatment(cm)	162.04±1.23	159.57±1.04
FAH-PAH pre-treatment(cm)	-1.76±1.37	1.16±0.89
FAH-PAH post-treatment (cm)	-1.48±1.41	1.45±0.76#

# p<0.05 (the values of FAH-PAH post-treatment between the two groups)

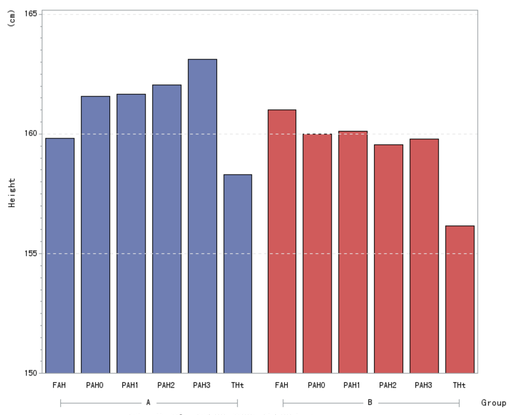

Fig. 2: The FAH, THt, PAH in two groups

Table 5. Relationship between FAH and Age at onset of Breast Development in the Two Groups

Parameters	FAH(cm) Group A	FAH(cm) Group B
Age at onset of breast development t≤6y	162.0±3.03	159.3 ±1.84
Age at onset of breast development＞6y	159.1 ±1.28	162.1± 1.15

Table 6. Change in the BMIs of Patients in Two Groups Before and After Treatment

Parameters	BMI Group A	BMI Group B
pre-treatment	17.85±0.53	15.96±0.31#
1y post-treatment	18.38±0.56	16.74±0.35#
2y post-treatment	19.14±0.57	17.34±0.37* #
end-of-treatment	18.61±1.02	17.83±0.48*

* p<0.001(BMI pre-treatment vs post-treatment in group B)
# p<0.05(BMI pre-treatment post-treatment between the two groups)

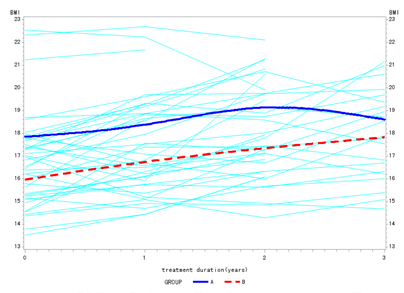

Fig. 3: Change in the BMIs of Patients in Two Groups pre- and post-Treatment

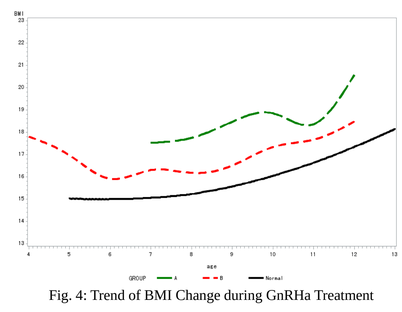

Fig. 4: Trend of BMI Change during GnRHa Treatment

Table 7. Age of Menarche and Time of Menarche from Discontinuation

Parameters	Group A	Group B
Age of Menarche(y)	11.74±0.16	12.18±0.15
Time of Menarche from Discontinuation(m)	17.41±1.69	14.71±1.04

Conclusion

The FAH was improved effectively by triptorelin 3.75 mg subcutaneously every 6 weeks, and more height gain could be achieved when rhGH was used concomitantly. BMI maintained steadily and ovarian function restored quickly after treatment discontinuation with the age of menarche similar to that of normal children. Neither significant side effect nor polycystic ovary syndrome was observed.

Acknowledgement

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