

RESEARCH

Evaluation of near final height in boys with constitutional delay in growth and puberty

Farzaneh Rohani^{1,2}, Mohammad Reza Alai², Sedighe Moradi³ and Davoud Amirkashani⁴

¹Pediatric Growth and Development Research Center, Iran University of Medical Sciences, Tehran, Iran

²Department of Pediatric Endocrinology and Metabolic Diseases, Mofid Children Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran

⁴Department of Pediatrics Endocrinology and Metabolism, Ali Asghar Children's Hospital, Iran University of Medical Sciences, Tehran, Iran

Correspondence should be addressed to F Rohani: rohani.f@iums.ac.ir

Abstract

Background: This study was conducted to find out whether boys with constitutional delay in growth and puberty (CDGP) could attain their target height and predicted adult height (PAH) in adulthood or not.

Methods: After measuring the height, weight, pubertal stage, parental height and bone age data of the patients at their first presentation were extracted from the files and their height and weight were measured at the end of the study, wrist X-Ray was performed in order to determine the bone age. PAH was calculated using Bayley–Pinneau method and target height was estimated by mid parental height. Final or near final heights of the patients were measured and compared with the target height and PAH.

Results: The mean age at presentation and the end of study was 15.2 ± 0.95 , 20 ± 0.75 years respectively. Mean of bone age at the beginning of study was 12.97 ± 1 years and at the end of study were 17.6 ± 0.58 years. Mean of delayed bone age was 2.2 ± 0.82 years. Mean of the primary measured heights was 150.16 ± 7 cm (138–160 cm). Mean of final or near final heights was 165.7 ± 2.89 cm (161–170.5 cm). Final or near final heights in our subjects were smaller than either their PAH (165.7 ± 2.89 vs 170.7 ± 5.17) (P value < 0.005) or target height (165.7 ± 2.89 vs 171.8 ± 4.65) (P value < 0.0001).

Conclusion: Most patients with CDGP do not reach their target height or predicted adult height; they are usually shorter than their parents and general population. Such patients need to be followed up until they reach their final height and, in some cases, adjunctive medical treatment might be indicated.

Key Words

- ▶ near final height
- ▶ boys
- ▶ constitutional delay
- ▶ growth
- ▶ puberty

Endocrine Connections
(2018) 7, 456–459

Introduction

Constitutional delay in growth and puberty (CDGP) is the most common cause of short stature and puberty delay in boys (1, 2, 3, 4). This condition is considered as a normal variation, and affected individuals typically have a slow pattern of growth during childhood and adolescence. The patients are identified with short stature, delay bone age and puberty. Their bone age lags behind

their chronological age, which is providing an indication of remaining the growth potential. According to some literature (5) and Butenandt (6) in most cases is expected to eventually grow their genetic potential height after puberty and attain normal adult height.

However, recent studies performed by Soliman *et al.* (7) and Poyrazoğlu *et al.* (8) indicate the final height (FH)

of these children are short related to parental height. They should be treated before puberty to reach to the target height (TH) and predicted adult height (PAH).

Soliman *et al.* (7) believed in children with CDGP height deficit at onset of puberty, shorter time between onset of puberty and pubertal growth spurt and attenuated peak growth velocity are correlated with final height. Therefore, many of them do not attain their target height or their predicted adult height.

CDGP may contribute to psychological difficulties, which can be improved with treatment. Based on the guidelines adopted by the U.S Food Administration, boys who have prediction final height of less than 160 cm, are candidates for treatment with growth hormone. Therefore, this study was conducted to find out whether boys with CDGP could attain their TH and PAH in adulthood or not.

Material and methods

Subjects and study design

The study was approved by Iran University of Medical Sciences, and consent has been obtained from each patient or subject after full explanation of the purpose and nature of all procedures used. The study was conducted in accordance with the guidelines on good clinical practice and with ethical standards for human experimentation established by the Declaration of Helsinki.

Study design and study population

In this cohort study, fifteen boys with CDGP who presented to Research Center of Endocrinology and Metabolism Tehran, Iran in a 7-year period were included. The average height of the patients at the beginning of the study was ≤ -2 SDS, and their puberty had not started until

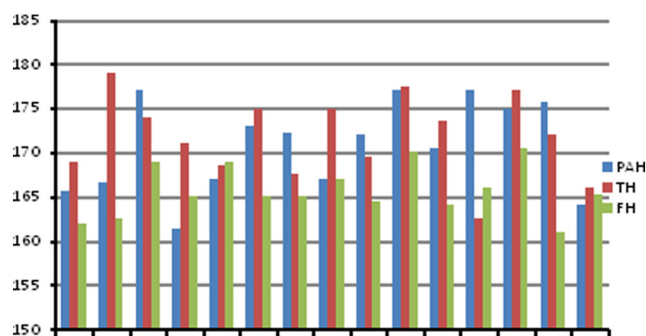


Figure 1 Comparison of final height (FH) with target height (TH) and predicted adult height (PAH).

the average age of 13.84 years; all patients had normal physical examination and their hormone profiles (growth and thyroid hormone) were normal. They did not have any skeletal abnormalities or systemic disease.

Measurements

The height, weight, pubertal stage, parental height and bone age data of the patients at their first presentation were extracted from the files and their height and weight were measured at the end of the study (bone age >17 years) and the patients' puberty stage was determined based on Tanner Staging (9). Simultaneous bone age was determined by wrist radiography based on Greulich and Pyle's radiographic atlas (10). PAH was calculated by Bayley–Pinneau method (11). The Bayley–Pinneau method uses a series of tables that provide the child's predicted percentage of adult height. TH in boys is calculated by parental heights using following formula: (12).

$$\text{Target Height} = \frac{\text{Mother's Height} + \text{Father's Height}}{2} + 6.5 \text{ cm}$$

Final height (height of boys after closure of the growth plates) skeletal abnormalities or near final height (bone age >16 years) of patients were compared with these two predicted adult heights and target height, statistical correlations of PAH and TH with final or near final height were evaluated (Fig. 1).

Statistical analysis

Data were analyzed using SPSS, version 16.0 software (SPSS). All data are expressed as mean \pm s.d. Kolmogorov–Smirnov test was performed to evaluate normal distribution of quantitative variables. Paired *T* test was used to compare the differences between the values of continuous variables at the end of the study. Linear regression analysis used to investigate the relationship (predictors) of near final and parental heights as independent variables. All two-sided *P* value less than 0.05 were regarded as being statistically significant.

Results

A total of 15 boys with CDGP were recruited in the current study. The mean ages at presentation and at the end of the study were 15.2 ± 0.95 and 20 ± 0.75 years respectively. Baseline characteristics of the patients with CDGP are given in Table 1. Near final or final height and

Table 1 Baseline demographic characteristic of patients.

Characteristics	Mean \pm s.d.	Range
Age (years)	15.2 \pm 0.95	14–16.5
Height (cm)	150.16 \pm 7.1	138.5–160
Height SDS	–2.9 \pm 0.77	
BMI (kg/m ²)	18.5 \pm 0.37	14.80–30
Bone age (years)	12.97 \pm 1	10–14.5
Bone age delay (years)	2.2 \pm 0.82	1–3.5

bone age at the end of the follow-up (17.6 \pm 0.58 year), predicted adult height and mid-parental height are shown in Table 2. As it is shown, final or near final height in subjects was smaller than their predicted adult height (165.7 \pm 2.89 vs 170.7 \pm 5.17) and target height (165.7 \pm 2.89 vs 171.8 \pm 4.65). Paired *T*-test analysis demonstrated that this difference was statistically significant (*P* value < 0.0001). There was no significant correlation between SDS of final or near final height and patient's baseline BMI (*P* > 0.05, *R* Spearman = 0.145). There was significant difference between SDS of height at the beginning of the study and SDS of final or near final height (*P* < 0.0002, *T* = –4.7). Correlations between final or near final height and all other parameters are shown in Table 3.

Discussion

Constitutional delay of growth and puberty is the most common cause of short stature in boys, entailing significant psychosocial implications. Our study showed that there is a significant difference between FH, TH and PAH. In addition, boys with CDGP would not reach their PAH or even their TH based on their genetic potential, and they would continue to be shorter than their peers of the same age, even after their puberty.

In parallel, Poyrazoglu *et al.* (8) investigated the clinical characteristics of 105 boys and 46 girls with CDGP in a retrospective study. Forty-one patients reached the final height. The average final height of these patients was less than their TH or their PAH. In another study

Table 2 Mean \pm s.d. of final or near final height, target height and predicted adult height.

Characteristics	Mean \pm s.d.	Range
Final or near final height (cm)	165.7 \pm 2.89	
SDS of final or near final height	–1.95 \pm 0.44	
Target height	171.8 \pm 4.65	162–179
SDS of target height (cm)	–0.87 \pm 0.77	
Predicted adult height	170.7 \pm 5.17	161.3–177
SDS of predicted adult height	–1.05 \pm 0.95	
Final bone age	17.16 \pm 0.58	16.5–18

Table 3 Correlation between final or near final height and all other parameters.

Parameters	<i>R</i>	<i>P</i> value
BMI	0.145	> 0.05
Target height	0.2	< 0.0001
Predicted adult height	0.32	< 0.0001

by Wehkalampi *et al.* (13) investigated the growth of 70 adult men with a history of CDGP among 21 had received testosterone and 31 had progressive height SD reduction between 3 and 9 years of age, but 39 lacked such a reduction. Final height of these patients was compared to their TH, and they concluded that those with early height SD reduction would not reach their FH in proportion to their potential genetic height, but those lacking this reduction would reach their TH. Moreover, Sperlich *et al.* (14) studied the growth of 49 boys with CDGP at two different age cross sections with average calendar age of 13.3 years and 22.9 years. In the first stage, the average bone age of the subjects was 11.1 years, and the average height was less than the 5th percentile for their calendar age. Average patients FH was 171.3 cm that was significantly less than their average TH of 173 cm. In addition, FH about 32.6% of the patients were more than 5 cm shorter than their PAH (By Bayley–Pinneau method).

On the other hand, in another study by Crown *et al.* (15), the growth of 43 boys with CDGP was followed, since their average calendar age of 14 years up to their FH. These patients' FH were –1.6 SDS. There was no significant difference between their FH and PAH, but a significant difference existed between FH and TH in these patients. Furthermore, some other studies revealed the different results in patients with CDGP reaching their TH and PAH. Salerno *et al.* (16) have evaluated final height in 20 patients with CDGP (11 boys and 9 girls); boys' average height in their pre-pubertal stage was –2.65 DS that improved to –1.3 in their adulthood. The average boys' final height was 166.4 cm, which was close to the TH (165.7 cm) and PAH (167.3 cm), respectively. Finally, they have suggested that patients with CDGP reach their PAH and TH even without medical treatment. The study sample (11 boys) and the average patients' final height (165.7 cm) were less than those in previous studies; however, the socio-economic state of the study group was unknown and patients' TH and FH were both at the lower limit of normal. In this study, the statistical significance or lack of significance between FH, TH and PAH has not been detailed. Curtis *et al.* (17) believe that boys with CDGP will finally reach their normal adult height of slightly less than predicted height calculated by parental height.

Conclusion

According to the results of this study and similar studies, most patients with CDGP do not reach their target height or predicted adult height; they are usually shorter than their parents and general population. Such patients need to be followed up until they reach their FH and in some cases, adjunctive medical treatment might be indicated.

Limitation of the study

The limitation of current study was small sample size because only 15 patients had inclusion criteria.

Declaration of interest

The authors declare no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Author contribution statement

F R and D A K conceived the study and participated in its design and coordination. S M and M R A helped to draft the manuscript and statistical analysis. All authors read and approved the final manuscript.

Acknowledgements

The authors are deeply indebted to MS Khodakarim for his statistical work conducted skillfully. They are also grateful to staff of the Oncology Department of the Ali Asghar Hospital for their assistance in planning and performing this study. This study was part of thesis in specialization courses in Pediatrics of Dr Samii approved by Iran University of Medical Sciences (IUMS).

References

- Xie C, Zhao Y, Gao L, Chen J, Cai D & Zhang Y. Elevated phthalates' exposure in children with constitutional delay of growth and puberty. *Molecular and Cellular Endocrinology* 2015 **407** 67–73. (<https://doi.org/10.1016/j.mce.2015.03.006>)
- Albanese A & Stanhope R. Predictive factors in the determination of final height in boys with constitutional delay of growth and puberty. *Journal of Pediatrics* 1995 **126** 545–550. ([https://doi.org/10.1016/S0022-3476\(95\)70347-0](https://doi.org/10.1016/S0022-3476(95)70347-0))
- Hero M, Wickman S & Dunkel L. Treatment with the aromatase inhibitor letrozole during adolescence increases near-final height in boys with constitutional delay of puberty. *Clinical Endocrinology* 2006 **64** 510–513. (<https://doi.org/10.1016/j.mce.2015.03.006>)
- Rohani F & Rashad A. Etiology of delayed puberty in the institute for endocrinology and metabolism. *Iranian Journal of Pediatrics* 2007 **17** 255–260. (available at: <http://ijp.tums.ac.ir/index.php/ijp/article/view/732>)
- Backeljauw PF & Cohen P. Disorders of growth hormone/insulin-like growth factor secretion and action. In *Sperling Textbook of Pediatric Endocrinology*, 4th ed., p 292–404. Ed MA Sperling. Philadelphia, PA, USA: WB Saunders, 2014.
- Butenandt O. For debate: constitutional and non-constitutional delay of growth and puberty. *Pediatric Endocrinology Reviews* 2017 **15** 132–135.
- Soliman AT & De Sanctis V. An approach to constitutional delay of growth and puberty. *Indian Journal of Endocrinology and Metabolism* 2012 **16** 698–705. (<https://doi.org/10.4103/2230-8210.100650>)
- Poyrazoğlu S, Günöz H, Darendeliler F, Saka N, Bundak R & Baş F. Constitutional delay of growth and puberty: from presentation to final height. *Journal of Pediatric Endocrinology and Metabolism* 2005 **18** 171–179. (<https://doi.org/10.1515/JPEM.2005.18.2.171>)
- Marshall WA & Tanner JM. Variations in the pattern of pubertal changes in boys. *Archives of Disease in Childhood* 1970 **45** 13–23. (<https://doi.org/10.1136/adc.45.239.13>)
- Greulich WW & Pyle SI. *Radiograph Atlas of Skeletal Development of the Hand and Wrist*. 2nd ed. Stanford, CA, USA: Stanford University Press, 1959.
- Bayley N & Pinneau SR. Tables for predicting adult height from skeletal age: revised for use with the Greulich-Pyle hand standards. *Journal of Pediatrics* 1952 **40** 423–441. ([https://doi.org/10.1016/S0022-3476\(52\)80205-7](https://doi.org/10.1016/S0022-3476(52)80205-7))
- Tanner JM, Goldstein H & Whitehouse RH. Standards for children's height at ages 2–9 years allowing for heights of parents. *Archives of Disease in Childhood* 1970 **45** 755–762. (<https://doi.org/10.1136/adc.45.244.755>)
- Wehkalampia K, Vangonena K, Lainea T & Dunkel L. Progressive reduction of relative height in childhood predicts adult stature below target height in boys with constitutional delay of growth and puberty. *Hormone Research* 2007 **68** 99–111. (<https://doi.org/10.1159/000101011>)
- Sperlich M, Butenandt O & Schwarz HP. Final height and predicted height in boys with untreated constitutional growth delay. *European Journal of Pediatrics* 1995 **154** 627–632. (<https://doi.org/10.1007/BF02079065>)
- Crowne EC, Shalet SM, Wallace WH, Eminson DM & Price DA. Final height in boys with untreated constitutional delay in growth and puberty. *Archives of Disease in Childhood* 1990 **65** 1109–1112. (<https://doi.org/10.1136/adc.65.10.1109>)
- Salerno M, De Filippo G & Di Maio S. Definitive body height in constitutional retardation of growth and puberty. *Journal of Pediatric Endocrinology and Metabolism* 2005 **18** 165–169. ([https://doi.org/10.1016/0929-693X\(96\)87574-9](https://doi.org/10.1016/0929-693X(96)87574-9))
- Curtis VA & Allen DB. Boosting the late-blooming boy, use of growth-promoting agents in the athlete with constitutional delay of growth and puberty. *Sports Health* 2011 **3** 32–40. (<https://doi.org/10.1177/1941738110386705>)

Received in final form 29 January 2018

Accepted 19 February 2018

Accepted Preprint published online 19 February 2018

