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Variability of the Predicted Final Height in Idiopathic Short Stature Over Time

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Research Article

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Abstract

Background: Predicting the final height in children with idiopathic short stature is essential for starting growth hormone therapy. This study was conducted to assess final height estimation variability over time.

Materials and Methods: In this cross-sectional study, children with idiopathic short stature were examined. Bone age and final height were estimated through the Greulich-Pile and Bayley-Pinneau method. This process repeated in the later visits with at least six months, and the results were compared statistically. The patients were classified based on the changes in predicted final height (PFH).

Results: A total of 81 patients (46 boys, 35 girls) with a mean age of 11.09 years were enrolled. The calculated PFH in the first visit was 160.15±8.79 cm, which has decreased to 159.33±9.38 cm. Based on the second evaluation, 43 patients had few changes in PFH (±3 cm), 23 patients experienced a decrease in PFH of more than 3 cm, and 15 patients experienced an increase in PFH of more than 3 cm. A change in Tanner stage, weight gain, height velocity, target height, and the interval between the two evaluations were similar in all groups. Young under ten years had more decreasing in the PFH.

Conclusion: Depending on bone age velocity, predicting the final height can change over time. As bone age velocity increases, PFH decreases more. PFH is also less reliable at younger ages and requires monitoring of growth and puberty and repeating final estimations later in life.

Keywords: Idiopathic short stature; Final height; Bone age; PFH

Abbreviations: PFH: Predicted Final Height; SD: Standard Deviations; BP: Bayley-Pineau; SMR: Sexual Maturity Rate.

Introduction

Concern about short final height is one of the most common reasons to refer children to pediatric endocrinologists [1,2]. Short stature is defined as a height that is more than -2 standard deviations (SD) below the mean height for children of the same age and gender [3]. Some specialists recommend evaluating children shorter than the 10th percentile for children of the same age and gender [4-6]. Growing is typically one of the best indicators of a child's health. Failure to grow can be a sign of serious health problems, so linear monitoring growth is one of the most important tasks of a pediatrician [7,8]. Even if short stature raises concerns about the child's health, there are some normal growth variations in this group, such as short familial stature and constitutional growth delay [5]. To screen children who require more attention, endocrinologists determine the abnormality of growth velocity and the final height of short stature patients. Those with an estimated final height below the 3d percentile of adult height or below -2 SD of target height (based on their parents' height) need more assessment and treatment [9]. Because of that, careful estimation and the use of a reliable method in which its result is closer to real final height are essential in pediatric endocrine clinics. Bayley-Pineau (BP) method is a common way to estimate the final height of children [10,11]. In this study, we compared two estimated final heights of each child suffering from idiopathic short stature or have a concern to short final height to identify if it is changeable over time.

Materials and Methods

The Research and Ethics Committee approved this study of Kashan University of Medical Sciences. It was a cross-sectional study in children who had been referred to the pediatric endocrine clinic of Shahid Beheshti hospital. Idiopathic short stature diagnosis were done with clinical features and appropriate laboratory tests. Demographic data were recorded on a datasheet, and sexual maturity rate (SMR) was determined in all cases using the Tanner staging method. Preliminary screening tests such as complete blood count, creatinine, serum electrolytes, thyroid function tests, urine analysis, and GH stimulation test were performed in all participants. Still, specific tests (such as sweat tests, karyotype studying, etc.) were requested for some of them based on their history and physical examination to rule out specific causes of short stature. Children with genetic disorders and syndromes were excluded. Additionally, children with precocious puberty were excluded from the study because they were examined separately.

After two times measuring children's height in standing position and calculating their mean, using CDC growth charts, all children with a height below the 10th percentile for their age and sex that their bone age was above six years old were included. We also divided short stature pediatrics into three groups based on the number of PAH changes: group A (±3), group B (more than 3 cm increase), group C (more than 3 cm decrease). Short stature, defined as body height below the 10th percentile, is often a reason for referring children to the pediatric endocrinology department [5].

We examined the relationship between different indices of age, sex on PAH changes. After visiting by a pediatric endocrinologist, depending on their history and physical examination, patients with the following criteria were excluded: Systemic and chronic diseases, long term use of medicines, history of exposure with any types of sex steroids, precocious puberty, genetic syndromes, and patients who had treated with growth hormone or GNRH agonists or aromatase inhibitors between two evaluations.

The standard deviation index of the child (SDS) was also calculated using the relation SDS = XY / SD, where (x = actual height of the child), (Y = average height for age and sex) (SDS = standard deviation index).

The target height was calculated as follows: mean parental height minus 6.5 cm for girls, and plus 6.5 cm for boys. The height standard deviation score were calculated for each child.

An expert specialist estimated bone age by comparing the patient's left hand and wrist x-ray with Greulich-Pile atlas of bone age, and final height was predicted using the Bayley-Pinneau method. Height measurement, tanner stage evaluation, bone age determination, and predicted final height calculation was repeated at least six months later.

After collecting the study data, they were entered into the computer and analyzed by SPSS software version 16. First, PAH changes were calculated and based on that, children were divided into three groups, and then statistical comparison was performed using one-way analysis of variance and Tukey's test. Additionally, Kruskal-Wallis non-parametric test was used to compare quantitative variables with abnormal distributions or qualitative variables, and one-way ANOVA test was used to compare quantitative variables with normal distributions.

Results

By considering inclusion and exclusion criteria, 81 children enrolled during 55 months, including 46 male and 35 female. The mean interval between the two visits was 17.5±9.36 months. The children's mean age was 11.09 ± 1.91 years in the first evaluation. Their mean bone age was 9.56±2.09 years. In the last visit, these variables have

changed to a mean age of 12.54±1.78 years and a mean bone age of 11.61±1.68 years. The calculated predicted final height (PFH) in the first visit was 160.15±8.79 cm which has reached 159.33±9.38 cm in the second evaluation (P: 0.15) (Tables 1 & 2).

Variable	Total	Negligible change	Increased PAH	Decreased PAH	P-value
Number	81	53.1%)43)	%18.5)15)	%28.4)23)	
Age (year)	11.09 ± 1.91	11.35 ± 2	11.4 ± 1.75	10.39 ± 1.88	0.76
BMI SDS	.09±.78-	.15±.78-	.14±.78-	.03±.8	0.58
Height SDS	1.9±.53-	2±.57-	1.9±.5-	1.7±.43-	0.13
Growth velocity (cm/year)	1.5±6	1.7±6	1.3±6.3	1.1±5.7	0.57
bone age velocity (year /year)	1.43±.76	1.37±.82	1.02±.79	1.79±.41	0.0001
bone age velocity>1	69.1%)56)	65%)28)	42.9%)6)	95.7%)22)	0.002
PAH1(cm)	160.15±8.79	159.8±9.3	160.1±7.8	160.7±8.6	0.81
PAH2(cm)	159.3±9.38	159.9±9.5	164.8±7.9	154.9±8.4	0.002
PAH2- PAH1	-.66±4.2	.05±1.7	5.1±1.86	5.7±2.33-	0.0001

PAH: predicted adult height

Table 1: Comparison of three groups of PAH changes.

Variable	Total	Minor changes	Increased PAH	Decreased PAH	P-Value
Father's normal height	44 (72.1%)	26 (78.8%)	6(54.5%)	12(75%)	0.6
Mother's normal height	56 (71.8%)	30 (73.2%)	11(78.6%)	15(68.2%)	0.4
Familial Short stature	20 (25%)	11 (25.6%)	4(28.6%)	5(21.7%)	0.4
Constitutional growth delay	36 (45%)	18 (41.9%)	8(57.1%)	10(43.5%)	0.4
Delayed Bone Age	49 (60%)	18 (41.9%)	9(64.3%)	12(52.2%)	
Normal Bone Age	30 (37%)	15 (34.9%)	5(35.7%)	10(43.5%)	0.5

Table 2: Relationship of PAH changes with parental height and bone age status.

Changes in PFH has no significant relation with age at first visit (P:0.11), the interval between two bone age determination(P:0.14), first and second height-SDS(P:0.83 and P:0.43 respectively). According to changes of predicted final height, patients have classified into three groups: group A had less than 3 cm change in estimated final height (43 children), group B, who their estimated final height increased more than 3 cm (15 children), and group C who their estimated final height decreased more than 3 cm (23 children). The difference in age, sex (P: 0.52), mid-parental height (P: 0.66), and bone age(P:0.62) were not statistically significant between groups. Changing in tanner stage (P: 0.76) and weight gain and height velocity were similar in all groups. There was not any significant difference between groups in the interval between the two evaluations (P: 0.07). The mean bone age velocity (which shows the amount of increasing bone age per year) was greater in group C (P<0.001). When the groups were classified into three categories, based on their ages (<10years- 10 to12years- >12years), the analysis showed more changes in estimated final height in children younger than ten years old (P = 0.016) (Table 3).

Age > 12 year	27	15	7	5	
	-33%	-55.60%	-25.90%	-18.50%	
Age :10-12 year	31	19	6	6	
	-38%	-61.30%	-19.40%	-19.40%	
Age < 10 year	22	9	1	12	0.016
	-27%	-40.90%	-4.50%	-54.50%	

Table 3: Relation of age at first evaluation and PAH changes.

Discussion

All endocrinologists have experience treating children whose parents are anxious about their child's final height. The first step to managing these cases is to estimate final height using methods in which their results are closer to reality. In this study, we assessed the predicted final heights calculated in two separate visits, based on the Bayley-Pinneau method, with at least six months-interval to determine their variability. Our study predicted final height had changed more than 3 cm in about 47 percent of our patients. Topor's study compared three commonly used algorithms for height prediction: Bayley-Pineau (BP), Roche-Wainer-Thissen (RWT), and Khamis-Roche (KR). Unexpectedly overall agreement of the methods was poor in boys and negative in girls. In this study, the Bayley-Pinneau method predicted lower adult height than others [11]. Because in BP and RWT methods, bone age is essential for prediction, the reliability of the method used for bone age estimation can influence the result. We used Greulich and Pile standards to estimate the bone age. Moradi et al.' study investigated the reliability of the Greulich and Pile method in healthy Iranian adolescents. [12]. Although this study confirmed the reliability of this method for bone age determination in Iranian adolescents, other investigators believe that it may not be ideal [13]. Paxton found that the accuracy of Greulich and Pile standards is higher when it is used by an expert radiologist [14]. New methods for skeletal maturation assessment such as using an open compact MRI system, a pediatric hand MR scanner, and hand and wrist ultrasonography are under investigation [15,16]. A new height prediction algorithm using an automated bone age measurement is another option [17]. In this study, having a higher bone age velocity led to higher decreased bone age estimation. One of the essential causes of increasing bone age velocity is progressive puberty [18], but tanner stage progression was similar in groups. This may reflect that progressive puberty may not be responsible for this group's accelerated bone age velocity. As Chonchaiyaa mentioned in his study, another cause of advanced bone age in adolescents is obesity, but changes in weight in our groups were not statistically significant [19]. Racial difference in growth pattern has been approved in previous studies [13,20], so higher bone age velocity in some of our cases can be a reflection of this phenomenon. However, it needs to establish in future studies.

Even though the Bayley-Pinneau method is useable above six years old, we found that final height estimation is less accurate below ten years, which agrees with De Sanctis's study [21]. So in younger ages, we should be aware of this limitation in decision making.

While the predicted final height that is not within the normal range of adult height (160 cm for males and 150 cm for females) is one of the indications of growth hormone therapy in idiopathic short stature, finding an accurate method for estimating with the least error, is essential. If it is not available, close monitoring of growth pattern, multiple visits to assess sexual maturity rating, and calculating the estimated final height based on the wrist and hand X-rays through puberty will help make the best decision. This study showed variability in final height estimations through time. Thus, clinicians should pay attention to the limitations of each method of height prediction. If newer methods such as automated bone age measurements are more precise than traditional methods, our predictions would be nearer to the real final height and that may help reduce the cost of therapy.

Conclusion

The predicting of the final height by the Bayley-Pinneau method can vary over time, depending on bone age velocity. Higher bone age velocity leads to more decrease in PFH. Also, PFH is less reliable in younger ages and needs monitoring of growth and puberty and repeating final height estimation at later ages.

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