Growth Pattern of Childhood Thyrotoxicosis: Longitudinal Follow-Up to Final Height

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Objective: *To study the growth pattern of children affected with thyrotoxicosis.*
Material and Method: *A retrospective study of growth data of 40 patients with thyrotoxicosis diagnosed at prepuberty or at early puberty was conducted. All patients were evaluated for height and weight every 3-6 months. Height and weight were transformed to standard deviation score (SDS) to account for differences of age and sex.*
Results: *At the time of diagnosis, the patients were slightly underweight for height (weight SDS -0.27 1.24, height SDS -0.06 1.26). After 1 year of treatment, the average weight gain of the patients was 4.9 3.1 kg, resulting in becoming relatively overweight for height (weight SDS +0.32 1.42, height SDS +0.02 1.32). At the time of reaching their final height, the patients had an appropriate weight for height (weight SDS +0.06 0.21, height SDS -0.04 1.01). The average final height SDS of the patients was -0.04 1.01. This was at the average of the general population, but was +0.57 0.48 SDS or +2.85 1.0 cm greater than their target height (p <0.01).*
Conclusion: *Growth of patients with thyrotoxicosis showed the same pattern as in the general population. The final height of thyrotoxicosis patients was averagely +0.57 SDS or +2.85 cm greater than their genetic potential. This could be from the result of secular trend in the general population rather than being the effect of thyrotoxicosis.*

Keywords: *Graves disease, growth, thyrotoxicosis*

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Thyrotoxicosis or Graves disease is an uncommon disease in children and adolescents with an overall incidence of 0.1-3.0/100,000[1,2]. Thyroid hormones are known to be essential for normal bone growth. The presence of excess circulating thyroid hormones has been recognized to cause acceleration of bone maturation resulting in accelerated growth velocity along with advanced bone age. To date, there have been only a limited number of reports on the effect of hyper-thyroidism on final height[3-6], and a few that found the final heights of thyrotoxicosis children had exceeded their target heights by +0.35 to +0.67 SDS[5,6].

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The present study was undertaken to examine the effect of thyrotoxicosis on growth of the affected children beginning from the time of diagnosis, during the longitudinal follow-up, till reaching their final height, and to compare their final heights to their target heights.

Material and Method

The data of pediatric patients diagnosed as thyrotoxicosis and follow-up at Songklanagarind Hospital from January 1992 to December 2004 were retrospectively reviewed. The diagnosis of thyrotoxicosis was made on the bases of the clinical criteria and confirmed by elevated serum free thyroxine (FT_4), suppressed thyrotropin (TSH) and the presence of thyroid antibodies (either anti-thyroglobulin antibody > 1:10 or anti-microsomal antibody > 1:100, or both).

From January 1992 to December 2004, there were 56 patients with thyrotoxicosis[7]. Seven were excluded due to having associated diseases affecting growth from either the disease itself (3 patients with Down syndrome) or from therapy with glucocorticoid (2 patients with myasthenia gravis and 2 patients with systemic lupus erythematosus). Nine patients were excluded due to having reached their final height at the time of diagnosis. Therefore, 40 children (10 boys and 30 girls) were included for evaluation of growth status in the present study. The average age at diagnosis was 10.3 $\pm$ 1.8 years (range 8.3-12.5). Eight patients were prepuberty and 32 patients were in early or midpuberty.

All patients were followed-up every 3-6 months. Height and weight measurements were done in the standing position using a stadiometer and beam-balanced scale. To account for age and sex differences and to allow comparison between children, the measured height and weight were transformed to standard deviation score (SDS) using the reference growth data of Thai children[8]. Final height (FH) was considered reached when height velocity of the preceding year was less than 0.5 cm/year. The heights of the patient's parents were measured at the clinic. Mid-parental height was considered as target height and was transformed to SDS to compare with the final height of the patients. For girls, the onset of menarche was recorded.

For statistical analysis, analysis of variance (ANOVA) was used to compare between growth (height, weight) at the time of diagnosis, each year of follow-up, and at the time of final height, and student's t test to compare between final height and target height. A p-value of less than 0.05 was considered statistically significant.

Results

The average height and weight SDS of the patients at the time of diagnosis, at the time of annual follow-up, and at final height are shown in Fig. 1. The average height SDS at the time of diagnosis was -0.06 $\pm$ 1.26 SDS and showed no difference to the general population. The average heights at the annual follow-up were along the average height of the general population. Of the total 40 patients, 36 patients (90%) achieved their final heights. The average final height SDS was -0.04 $\pm$ 1.01 and was at the average of the general population. However, the average final height of the patients was +0.57 $\pm$ 0.48 SDS or 2.85 $\pm$ 1.0 cm greater than their target height (-0.61 $\pm$ 0.59) and was statistically significant ($p < 0.01$).

The average weight SDS at the time of diagnosis was -0.27 $\pm$ 1.24, slightly lower than the general population. When this is compared to the patient's height, it shows that the patients were slightly underweight for height. After 1 year of treatment with antithyroid drugs, the weight SDS increased to +0.32 $\pm$ 1.42, showing significant weight gain ($p < 0.01$). The average weight gain in the first year of treatment was

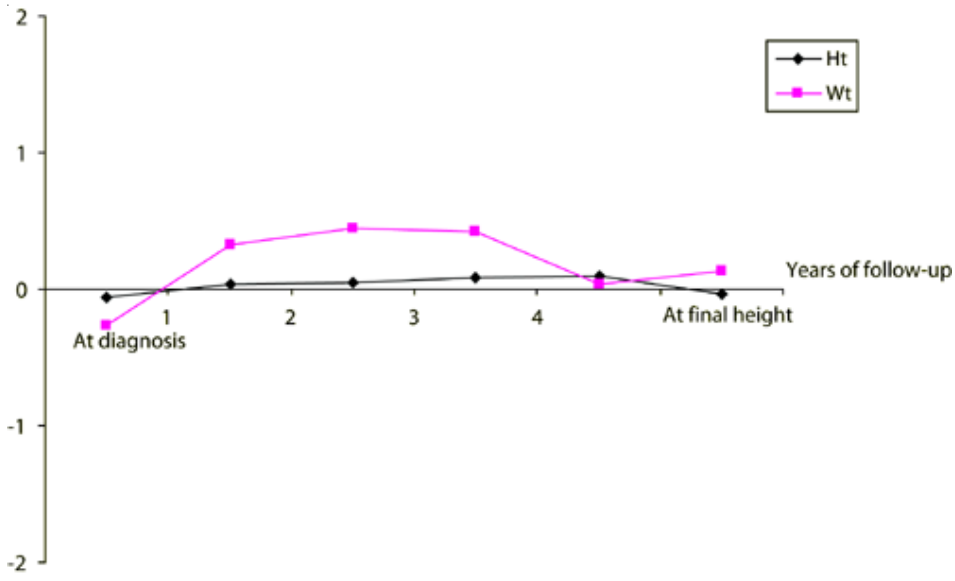

Fig. 1 The average height and weight SDS of the patients at the time of diagnosis, during the follow-up period, and at final height

Table 1. The details of growth data of the patients at the time of diagnosis, during treatment, and at the time of final height compared to the target height

	$\bar{X} \pm SD$	Range
Age at diagnosis (yr)	10.3 ± 1.8	8.3-12.5
Duration of follow-up (yr)	5.7 ± 2.4	3.4-10.0
Weight SDS at diagnosis	-0.27 ± 1.24	(-2.35)-(+2.16)
Height SDS at diagnosis	-0.06 ± 1.26	(-1.67)-(+2.34)
Weight gain after 1 year of treatment		
in SDS	0.59 ± 1.42	0-(+2.64)
in kg	4.9 ± 3.1	0-8.6
Target height (TH) SDS	-0.62 ± 1.21	(-1.96)-(+0.64)
Boys (cm)	167.1 ± 1.8	165-171
Girls (cm)	153.3 ± 2.9	148-160
Final height (FH) SDS	-0.04 ± 1.01	(-1.85)-(+2.31)
Boys (cm)	168.1 ± 2.7	165-173
Girls (cm)	156.7 ± 2.9	151-164
FH-TH		
in SDS	+0.57 ± 0.48	(-0.05)-(+2.14)
in cm	+2.85 ± 1.0	(-0.50)-(+6.20)

+0.59 ± 1.42 SDS or +4.9 ± 3.1 kg, slightly overweight for height. After the first year of treatment, the weight gain continued at the same rate as in the general population, resulting in a persistent condition of being overweight for height during the time of follow-up. At 5 years of follow-up, most patients had reached their final heights. The average body weight was the same as in the general population resulting in appropriate weight for height. In girls, the mean age at menarche was 11.9 ± 0.85 years, slightly younger than in the general population (12.4 ± 1.1 years)[9], but not statistically different.

The details of the patients, growth at the time of diagnosis and at final height compared to their target heights are summarized in Table 1.

Discussion

The present study demonstrated that the growth of children with thyrotoxicosis at the time of diagnosis was at the average of the general population with relatively underweight for height. The underweight for height could be the result of weight loss from excessive metabolic rate despite the increased appetite of the patients. After euthyroidism was achieved with antithyroid treatment, most of the patients gained body weight and became overweight for height. This could be explained by the decreased metabolic rate while the patients consumed the same amount of dietary intake. However, when the patients reached their final height, they could control their intake and showed no further weight gain resulting in the appropriate weight for height.

Although the final height of the patients in the present study was at the average as in the general population, their average height was +0.57 SDS or 2.85 cm greater than their genetic potential and that was statistically significant. This finding is in agreement with previous reports that found final heights of +0.35 to +0.67 SDS over target heights[5,6]. Other previous studies have shown that an excess of thyroid hormones has resulted in accelerated height thus, children with thyrotoxicosis were tall for their age at the time of diagnosis[3,5,6]. The accelerated growth was proportionately associated with bone maturation and the ratio of bone age to height age was close to 1. In the present study, bone age was not performed since it is not a routine investigation and is not indicated in children growing along the normal growth curve.

Compared to the target height, the children with thyrotoxicosis were significantly taller than their genetic potential. However, the 1999 national growth study in the Thai children[8] showed the secular trend of 2-3 cm increase of height in Thai population compared to the 1987 national growth study[10]. Therefore, the +0.57 SDS or 2.85 cm greater final height of the thyrotoxicosis patients than their genetic potential could be a natural occurrence of the secular trend as occurred in the general population rather than being the result of thyrotoxicosis. The average age at menarche of female thyrotoxicosis patients was slightly

earlier than in the general population, but was not statistically different. Again, the earlier age at menarche was probably from the result of the secular trend that is occurring in the general Thai population[9].

In conclusion, the growth of children with thyrotoxicosis was the same pattern as in the general population. The final height was on average, 2.85 cm taller than their genetic potential and this would be the result of secular trend rather than being the effect of thyrotoxicosis.

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การเจริญเติบโตในผู้ป่วยเด็กไทรอยด์เป็นพิษ: การติดตามระยะยาวจนถึงความสูงสุดท้ายในวัยผู้ใหญ่

สมจิตร์ จารุรัตนศิริกุล, หัชชา ศรีปลั่ง

วัตถุประสงค์*: เพื่อศึกษาแบบแผนการเจริญเติบโตของผู้ป่วยเด็กไทรอยด์เป็นพิษ*

วัสดุและวิธีการ*: เป็นการศึกษาย้อนหลังในผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่าเป็นโรคไทรอยด์เป็นพิษ ตั้งแต่มกราคม พ.ศ. 2535 ถึง ธันวาคม พ.ศ. 2547 จำนวน 40 คนที่ได้ทำการศึกษาในเรื่องของความสูงและน้ำหนัก น้ำหนักและความสูงที่วัดได้จะถูกนำมาเปลี่ยนเป็น standard deviation score (SDS) เพื่อนำมาใช้เปรียบเทียบได้ในกรณีที่ผู้ป่วยมีความแตกต่างของอายุและเพศ ผู้ป่วยทุกรายได้รับการติดตามวัดน้ำหนักและความสูงทุก 3-6 เดือน*

ผลการศึกษา*: ขณะได้รับการวินิจฉัย ผู้ป่วยจะมีน้ำหนักค่อนข้างน้อยเมื่อเทียบกับความสูง หลังการรักษา 1 ปี ผู้ป่วยมีน้ำหนักเพิ่มขึ้น 4.9 $\pm$ 3.1 กก. ทำให้น้ำหนักค่อนข้างมากเมื่อเทียบกับความสูง ขณะที่ถึงความสูงสุดท้าย ผู้ป่วยมีน้ำหนักปกติเมื่อเทียบกับความสูง ความสูงสุดท้ายเฉลี่ยของผู้ป่วยคือ -0.04 $\pm$ 1.01 SDS ซึ่งสูงเท่ากับประชากรทั่วไป แต่เมื่อเทียบกับความสูงเป้าหมายซึ่งเป็นความสูงที่เป็นผลจากพันธุกรรมแล้ว ผู้ป่วยมีความสูงสุดท้ายมากกว่าความสูงเป้าหมาย +0.57 $\pm$ 0.48 SDS หรือเท่ากับ 2.85 $\pm$ 1.0 ซม.*

สรุป*: การเจริญเติบโตในผู้ป่วยเด็กไทรอยด์เป็นพิษ มีแบบแผนเช่นเดียวกับในประชากรทั่วไป ความสูงสุดท้ายของผู้ป่วยจะมากกว่าความสูงที่เป็นผลจากพันธุกรรมโดยเฉลี่ย +0.57 SDS หรือ 2.85 ซม. ซึ่งน่าจะอธิบายจากความสูงที่เปลี่ยนแปลงตาม secular trend เช่นเดียวกับที่พบในประชากรทั่วไป*
