Growth Hormone (GH) Retesting and Final Adult Height in Childhood-Onset GH Deficiency (CO-GHD): Experiences from King Chulalongkorn Memorial Hospital, Thailand

Suttipong Wacharasindhu MRCPCH*, Suphab Aroonparkmongkol BSc*,
Taninee Sahakitrungrueng MD*, Vichit Supornsilchai MD, PhD*

** Division of Endocrinology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, & Growth and Growth Monitoring Center, Pediatric Out-Patient Unit, King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

Objective: *Evaluate GH status in CO-GHD subjects after completion of linear growth, and report the auxological outcomes of rhGH treatment.*

Material and Method: *Twenty-four CO-GHD subjects (14 with IGHD and 10 with MPHD), treated with rhGH for a period of 6.6±3.1 years were re-evaluated for their capacity of GH secretion by performing insulin tolerance test (ITT). Ht SDS at final height was compared with Ht SDS at the start of the treatment and MPH SDS.*

Results: *Thirty-eight percent (9 in 24) of CO-GHD subjects had normal GH secretion on retesting. All subjects were diagnosed as isolated GHD during childhood. In contrast, all MPHD subjects during childhood period had GH insufficiency on retesting. GH insufficient subjects had higher total cholesterol level than those with GH sufficiency (214±51 vs. 174±36 mg/mL, p = 0.03). rhGH treatment significantly increased Ht SDS of -2.0±1.1 at the start of the treatment to -0.6±1.3 at the end of the treatment (p<0.01) and -0.8±1.2 at GH retesting (p<0.01).*

Conclusion: *GH retesting is recommended in subjects with IGHD during the childhood period. However, rhGH treatment can enhance the final height in both GH sufficient and insufficient subjects on retesting.*

Keywords: *Growth hormone deficiency (GHD), childhood onset GHD (CO-GHD), isolated GHD (IGHD), multiple pituitary hormone deficiency (MPHD), GH retesting*

J Med Assoc Thai 2015; 98 (6): 542-8
Full text. e-Journal: *http://www.jmatonline.com*

Recombinant human GH (rhGH) treatment has been widely accepted to improve final adult height in children with various growth disorders especially in those with GHD. Diagnosis of childhood-onset growth hormone deficiency (CO-GHD) depends on auxological data and subnormal growth hormone (GH) response during various GH provocative tests. Previous studies have shown that a large number of patients with CO-GHD progress to have normal GH secretion on GH retesting when they reached their final adult height; they probably needed no GH treatment[1-3]. The percentage of having normal GH secretion depends on the cut-off level of the GH applied during the GH provocative test in each study. During the transitional period, which is usually a period from mid to late adolescence until six to seven years after the achievement of the final height, GH secretion is physiologically declining. However, once the diagnosis of GHD is confirmed, replacement with GH may be needed throughout the adult life. In the present study, we aimed to describe the GH status and final height outcome of GH treatment in CO-GHD subjects who had been treated with rhGH until they reached their final adult height.

Correspondence to:
Wacharasindhu S, Department of Pediatrics, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Rama IV, Bangkok 10330, Thailand.
Phone: +66-2-2564951, Fax: +66-2-2564911
E-mail: Wacharasindhu@yahoo.com

Material and Method

This retrospective study recruited all CO-GHD subjects who were treated with rhGH until they reached their final height at the Endocrine Unit, Department of Pediatrics, Chulalongkorn University, Bangkok, Thailand. Clinical and auxological data of all subjects at the start of the treatment and their final heights were retrieved from medical record. CO-GHD subjects were diagnosed by pediatric criteria of peak GH that was lower than 10 ng/mL in two standard GH provocative tests [insulin tolerance test (ITT) and clonidine test]. Persisting GHD at the final height was diagnosed according to the consensus statements on the management of GH-treated adolescent in the transition to adulthood by the cutoff point of 5 ng/mL

during ITT[4]. The height was transformed to height standard deviation score (Ht SDS), using the National Growth Data of Thai Children. Mid parental height (MPH) was calculated, using the formula of (father height + mother height + 13)/2 for boys and (father height + mother height - 13)/2 for girls. The final adult height was determined when the height velocity was less than 2 cm/year or the bone age was more than 14 in girls, and more than 17 in boys. Ht gain was a difference between final HtSDS and Ht SDS at the start of the treatment. Serum GH, insulin-like growth factor (IGF)-I, and IGF binding protein (IGFBP)-3 levels were measured by the enzyme-linked immunosorbent assay (ELISA), Immulite 1000, Siemens, USA. Intra and interassay coefficient variations are 6% and 5.8% for GH assay, 3.6% and 6.6% for IGF-I assay and 4.2% and 8.6% for IGFBP-3 assay. Lipid profile was sent to the Central Laboratory of King Chulalongkorn Memorial Hospital. The results were presented as mean ± SD. T-test was used in this study and a statistical significant was considered if p-value <0.05.

The present study had been approved by the Ethic Committee, the Faculty of Medicine, Chulalongkorn University. This study was performed without any sources of fund.

Results

Twenty-four subjects (15 males, 9 females), who were diagnosed as having CO-GHD at a mean age of 8.9±2.9 years and had been treated with rhGH subcutaneous injection (25-30 µg/kg/day, 6 days/week) for a mean period of 6.6±3.1 years, were recruited into this study. GH retesting was evaluated in all subjects after discontinuation rhGH treatment and reaching their final adult height.

At time of start rhGH treatment

Fourteen subjects had isolated GH deficiency (IGHD), and 10 had multiple pituitary hormone deficiencies (MPHD). In the IGHD group, five had idiopathic causes, two had small pituitary gland, two had GHD after surgery for tumor removal, and five had no MRI performed on. In the MPHD group, five were due to post-surgical tumor removal, one was due to post tuberculosis meningitis, two were due to small pituitary gland with ectopic posterior pituitary (EP), one was due to EP, and one had no imaging performed. GHD was diagnosed by two GH provocative tests (insulin tolerance test and clonidine test). Peak GH during ITT was 2.7±2.6 ng/ml and during clonidine test was 4.1±2.7 ng/mL (Fig. 1). Clinical and auxological data of these subjects are demonstrated in Table 1. A mean age of GH discontinuation was 16.2±1.9 years in male and 14.3±0.9 years in female. After GH discontinuation, all subjects were followed-up until reaching their final adult height; then the GH status was re-evaluated.

GH retesting

The capacity of GH secretion by GH retesting was re-evaluated at the mean of 17.6±2.9 years by performing ITT. A mean peak GH at retesting was 8.4±12.3 ng/mL (Fig. 1). According to consensus statements on the management of GH-treated adolescents in the transition to adulthood, nine subjects (38%) had normal GH secretion on retesting. Fifteen of them (62%) remained GH insufficient. Among the GH sufficient subjects, all were isolated CO-GHD. Ten in 15 subjects (67%) who remained GH insufficient were in MPHD at the childhood onset. Among isolated CO-GHD children, five (36%) remained GH insufficient, two were due to idiopathic causes, two were due to post-surgical tumor removal, and one had no MRI performed on. In addition, all subjects with MPHD at CO-GHD remained GH insufficient on

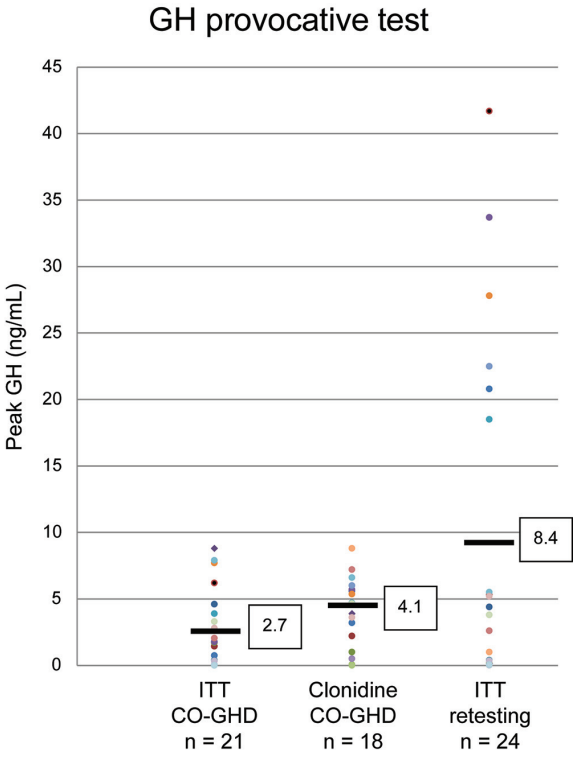

Fig. 1 Mean of peak GH during provocative test at CO-GHD and at retesting.

Table 1. Clinical and auxological data of isolated growth hormone deficiency (IGHD) and multiple pituitary hormone deficiency (MPHD) subjects at the start of the treatment with recombinant human GH (rhGH)

	Total (n = 24)	IGHD (n = 14)	MPHD (n = 10)
Sex (male:female)	15:9	9:5	6:4
Age at start rhGH (year) (mean ± SD)	8.9±2.9	8.3±3.1	9.7±3.0
MRI pituitary		5 normal pit. MRI 2 small pit. 2 post-op tumor removal 5 not performed	5 post-op tumor removal 2 small pit with EP 1 EP 1 post TB meningitis 1 not performed
Ht SDS at start rhGH (mean ± SD)	-2.0±1.1	-2.1±1.1	-1.9±1.6
Body mass index (BMI) (kg/m^2) (mean ± SD)	17.6±4.8	17.1±4.1	18.3±5.1
MPH SDS (mean ± SD)	-0.1±0.9	-0.4±0.8	0.3±1.1
Peak GH (ITT) (ng/mL) (mean ± SD)	2.7±2.7	3.6±2.6	0.9±1.0
Peak GH (clonidine) (ng/mL) (mean ± SD)	4.1±2.7	4.9±1.5	2.1±3.4

Ht SDS = height standard deviation score; MPH = mid parental height; ITT = insulin tolerance test; pit. = pituitary; MRI = magnetic resonance imaging; EP = ectopic pituitary, TB = tuberculosis

Table 2. Clinical and auxological data in growth hormone (GH) sufficient and GH insufficient subjects on retesting

	GH sufficient group peak GH ≥ 5 ng/ml (n = 9)	GH insufficient group peak GH <5 ng/mL (n = 15)	*p*-value
Age at retesting (year)	17.0±1.4	18.1±3.2	
CO-GHD			
IGHD	9 (100%) Normal pit MRI = 3 Small pit = 2 Not performed = 4	5 (33%) Normal pit MRI = 2 Post-op tumor = 2 Not performed = 1	
MPHD	0 (0%)	10 (67%) Post-op tumor = 5 EP = 1 Small pit with EP = 2 Post TB meningitis = 1 Not performed = 1	
Ht SDS at start rhGH	-2.0±1.0	-2.1±1.4	NS
Ht SDS at stop rhGH	-0.7±0.8	-0.5±1.7	NS
Ht SDS at retesting	-1.7±0.7	-0.5±1.6	NS
MPH SDS	-0.4±0.9	0.0±1.0	NS
Ht gain SDS	1.0±0.7	1.5±1.3	0.04
Total cholesterol (mg/dL)	174±36	214±51	0.03
Triglyceride (mg/dL)	79±18	132±99	NS
HDL-cholesterol (mg/dL)	59±9	60±14	NS
LDL-cholesterol (mg/dL)	113±30	136±45	NS
IGF-I (ng/mL)	349±175	182±186	0.025
IGFBP-3 (ng/mL)	5,555±631	4,342±1,830	NS

CO-GHD = childhood onset GHD; HDL = high-density lipoprotein; LDL = low-density lipoprotein; IGF-I = insulin-like growth factor I; IGFBP-3 = IGF binding protein 3; NS = not significant

Table 3. Ht SDS in IGHD (n = 14), MPHD (n = 10), and total (n = 24) at start, stop rhGH treatment and at retesting of GH status

	Ht SDS at start treatment mean ± SD	Ht SDS at stop treatment mean ± SD	Ht SDS at retesting mean ± SD	MPH SDS mean ± SD
Total	-2.0±1.1	-0.6±1.3 (p<0.01)	-0.8±1.2 (p<0.01)	-0.1±0.9 (p = 0.01)
IGHD	-2.1±1.1	-0.8±1.0 (p<0.01)	-1.3±0.7 (p = 0.04)	-0.4±0.8 (p<0.01)
MPHD	-1.9±1.6	-0.2±1.9 (p<0.01)	0.2±1.4 (p<0.01)	0.3±1.0 (p<0.01)

retesting (Table 2). Height gain was significantly higher in GH insufficient subjects on retesting. However, the subjects who remained GH insufficient had significantly higher cholesterol level and lower IGF level than those with normal retesting GH.

Outcome of rhGH on height (Table 3)

Treatment with rhGH can significantly improve HtSDS in both IGHD and MPHD subjects as demonstrated in Table 3. In addition, BMI significantly increased from 17.6±4.8 at diagnosis to 21.3 ±3.4 at the stop of the treatment (p<0.1) and 22.2 ±4.5 kg/m^2 on retesting (p<0.1).

Discussion

Benefits of rhGH in terms of final adult height have been wildly accepted. However, some of them develop normal GH secretion upon reaching the adult height. Many factors determine the percentage of persisting GHD of CO-GHD in adult life such as the presence of pituitary MRI abnormalities, the severity of GHD, and the cutoff criteria applied in various studies. A previous study by Maghnie et al[5] suggests that subjects with CO-GHD due to congenital hypothalamic-pituitary abnormalities do not require further investigation of GH secretion but subjects with isolated GHD due to normal or small pituitary gland should receive GH reassessment. In addition, they reported that more than three quarters of partial GHD subjects and one quarter of the complete GHD subjects had normal GH response on retesting. Using the pediatric criteria, persisting GHD at final height varies from 12 to 86%[1,6-8]. ITT is considered a gold standard of the diagnosis of GHD in adulthood. However, a combined arginine/GH-releasing hormone test or glucagon test may work as an alternative test if ITT is contraindicated[9]. Our study demonstrates that 62% of the subjects still have GHD after their final height achievement if we use the cutoff point at 5 ng/mL according to the consensus[4]. The arbitrary cutoff point to differentiate between GH sufficient and insufficient subjects is still a subject of debate. Physiological secretion of GH declines after achievement of full adult maturation. According to the consensus statements, the cutoff GH level lower than 5 ug/L[4] during the transition period and less than 3 ug/L[9] in adults is suggestive of GHD diagnosis. However, a cutoff at 1 ug/L was suggested for diagnosis of GHD in overweight/obese adult[10]. In isolated CO-GHD subjects who became GH sufficient at retesting, two of them had small pituitary gland, three had normal pituitary MRI, and four had no MRI performed on and had no clinical and laboratory evidences of other pituitary hormones deficiency. In the IGHD subjects, 60% (3 in 5) of subjects with normal pituitary MRI and all subjects with small pituitary gland had normal GH secretion on the retesting. A similar result was demonstrated by Thomas et al who suggested that isolated GHD children with normal or small pituitary gland should have GH retesting[8].

The number of pituitary hormone deficiency may predict the outcome of persisting GHD in the adulthood because MPHD subjects have a higher proportion of persisting GHD than isolated GHD subjects as found in our study. This shows that all MPHD became GH insufficiency at the final height. A previous study also reported that the severity of GHD in adults is related to the number of additional pituitary hormone deficiencies[11].

The syndrome of GHD in adults has already been established[12,13]. The etiology of GHD in adulthood may be due to previous hypothalamo-pituitary diseases occurring during either adulthood or childhood. A significant number of CO GHD became having normal GH secretion on retesting and this condition was postulated as "transient GH deficiency". Therefore, some of them may not need GH replacement in their adult life. Nevertheless, one with persisting GHD during the adulthood may need a continuation of GH replacement in order to correct metabolic disturbances, which may occur[14,15]. GHD in the adulthood affects both the body composition and lipid metabolism. Typically, they are likely to have lean body mass and increased fat mass accumulating around the visceral

tissues and the abdomen. Dyslipidemia leading to a cardiovascular morbidity and mortality can be demonstrated in this condition such as premature atherosclerosis, hypertension, and abnormal cardiac function. Elevated total cholesterol, low-density lipoprotein cholesterol, and triglyceride with low HDL cholesterol manifest in adults with GHD. GH treatment has been reported to reverse all these abnormal lipid profiles[13,16]. Our study demonstrated that a trend of dyslipidemia predicting the risk of cardiovascular morbidity could occur in persisting GHD in the transition period.

The outcome of GH treatment, in terms of the final adult height, was similar between GH sufficient and insufficient groups on retesting. Although rhGH has been reported in many studies including our study to improve the final height in subjects with normal GH status in retesting, no one can clearly explain why they became normal GH status on retesting. A condition of transient GH deficiency may reflect inappropriate low level of sex hormones in the childhood period. A previous study by Thomas et al[8] showed that although HtSDS is small in the start of rhGH treatment in persisting GHD in adult height but the final adult height was comparable between normal and persisting GHD groups on retesting. Tauber et al[7] also demonstrated that height gain was not different between those who normalized their test and those who did not.

In conclusion, from the present study, 38% of childhood-onset GHD became normal GH on retesting during the transition period. Organic causes of GHD and MPHD subjects had higher percentage of persisting GHD in the adult life. All isolated CO-GHD children are strongly recommended to have GH retesting when reaching the final height. GH treatment benefits the final adult height in both subjects with GH sufficiency and those with GH insufficiency at retesting and this has no impact on the effectiveness of GH treatment at childhood-onset GHD. However, abnormal lipid metabolism, which may predict a cardiovascular morbidity, is demonstrated in persisting GHD. The number of subjects in this study was so limited; therefore, further study to recruit more subject may clarify this.

What is already known on this topic?

The percentage of GHD children becoming normal GH secretion after rhGH treatment and reaching final adult height varies in previous studies depending on the etiology and cut-off value of GH provocative test. The number of pituitary hormone deficiency and severity of GH deficiency may predict outcome of persistent GH in adult period. However, the consensus statement on the management of the GH-treated adolescent in the transition to adult care recommends to use the Cutoff GH level lower than 5 ug/L for diagnosing of GHD.

What this study adds?

The findings in our study suggested that 38% of CO-GHD became normal GH secretion on retesting which was similar to other previous studies. To avoid unnecessary GH treatment in adult life, GH retesting should be performed in all isolated CO-GHD when reaching final adult height.

Potential conflicts of interest

None.

References

1. Clayton PE, Price DA, Shalet SM. Growth hormone state after completion of treatment with growth hormone. Arch Dis Child 1987; 62: 222-6.
2. Longobardi S, Merola B, Pivonello R, Di Rella F, Di Somma C, Colao A, et al. Reevaluation of growth hormone (GH) secretion in 69 adults diagnosed as GH-deficient patients during childhood. J Clin Endocrinol Metab 1996; 81: 1244-7.
3. Juul A, Kastrup KW, Pedersen SA, Skakkebaek NE. Growth hormone (GH) provocative retesting of 108 young adults with childhood-onset GH deficiency and the diagnostic value of insulin-like growth factor I (IGF-I) and IGF-binding protein-3. J Clin Endocrinol Metab 1997; 82: 1195-201.
4. Clayton PE, Cuneo RC, Juul A, Monson JP, Shalet SM, Tauber M. Consensus statement on the management of the GH-treated adolescent in the transition to adult care. Eur J Endocrinol 2005; 152: 165-70.
5. Maghnie M, Strigazzi C, Tinelli C, Autelli M, Cisternino M, Loche S, et al. Growth hormone (GH) deficiency (GHD) of childhood onset: reassessment of GH status and evaluation of the predictive criteria for permanent GHD in young adults. J Clin Endocrinol Metab 1999; 84: 1324-8.
6. Wacharasindhu S, Cotterill AM, Camacho-Hubner C, Besser GM, Savage MO. Normal growth hormone secretion in growth hormone insufficient children retested after completion of linear growth. Clin Endocrinol (Oxf) 1996; 45: 553-6.
7. Tauber M, Moulin P, Pienkowski C, Jouret B,

Rochiccioli P. Growth hormone (GH) retesting and auxological data in 131 GH-deficient patients after completion of treatment. J Clin Endocrinol Metab 1997; 82: 352-6.
8. Thomas M, Massa G, Maes M, Beckers D, Craen M, Francois I, et al. Growth hormone (GH) secretion in patients with childhood-onset GH deficiency: retesting after one year of therapy and at final height. Horm Res 2003; 59: 7-15.
9. Ho KK. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia. Eur J Endocrinol 2007; 157: 695-700.
10. Dichtel LE, Yuen KC, Bredella MA, Gerweck AV, Russell BM, Riccio AD, et al. Overweight/obese adults with pituitary disorders require lower peak growth hormone cutoff values on glucagon stimulation testing to avoid overdiagnosis of growth hormone deficiency. J Clin Endocrinol Metab 2014; 99: 4712-9.
11. Toogood AA, Beardwell CG, Shalet SM. The severity of growth hormone deficiency in adults with pituitary disease is related to the degree of hypopituitarism. Clin Endocrinol (Oxf) 1994; 41: 511-6.
12. de Boer H, Blok GJ, Van der Veen EA. Clinical aspects of growth hormone deficiency in adults. Endocr Rev 1995; 16: 63-86.
13. Newmann CB, Kleinberg DL. Adult growth hormone deficiency. Endocrinologist 1998; 8: 178-86.
14. Pfeifer M, Verhovec R, Zizek B, Prezelj J, Poredos P, Clayton RN. Growth hormone (GH) treatment reverses early atherosclerotic changes in GH-deficient adults. J Clin Endocrinol Metab 1999; 84: 453-7.
15. Molitch ME, Clemmons DR, Malozowski S, Merriam GR, Shalet SM, Vance ML, et al. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2006; 91: 1621-34.
16. Jorgensen JO, Pedersen SA, Thuesen L, Jorgensen J, Ingemann-Hansen T, Skakkebaek NE, et al. Beneficial effects of growth hormone treatment in GH-deficient adults. Lancet 1989; 1: 1221-5.

การประเมินการหลั่งฮอร์โมนเจริญเติบโตซ้ำและความสูงสุดท้ายในเด็กที่มีภาวะขาดฮอร์โมนเจริญเติบโต: ประสบการณ์ในโรงพยาบาลจุฬาลงกรณ์

สุทธิพงศ์ วัชรสินธุ, สุภาพ อรุณภาคมงคล, ธนินี สหกิจรุ่งเรือง, วิชิต สุพรศิลป์ชัย

วัตถุประสงค์: *เพื่อประเมินการหลั่งของฮอร์โมนเจริญเติบโตในเด็กที่ได้รับการวินิจฉัยว่ามีภาวะขาดฮอร์โมนเจริญเติบโตและได้รับการรักษาจนถึงความสูงสุดท้ายรวมทั้งผลของการรักษาในด้านความสูง*

วัสดุและวิธีการ: *เด็กที่ได้รับการวินิจฉัยว่ามีภาวะขาดฮอร์โมนเจริญเติบโตในวัยเด็กจำนวน 24 ราย (14 ราย ขาดฮอร์โมนเจริญเติบโตอย่างเดียว, 10 ราย ขาดฮอร์โมนเจริญเติบโตร่วมกับฮอร์โมนอื่นจากต่อมใต้สมอง) ที่ได้รับการรักษาด้วยฮอร์โมนเจริญเติบโตชนิดสังเคราะห์เป็นระยะเวลาเฉลี่ย 6.6±3.1 ปี จะได้รับการประเมินการหลั่งฮอร์โมนเจริญเติบโตด้วยวิธี insulin tolerance test (ITT) เมื่อหยุดให้การรักษา ความสูงสุดท้ายจะนำมาเปรียบเทียบกับความสูงก่อนการรักษาและความสูงตามพันธุกรรม*

ผลการศึกษา: *ร้อยละ 38 (9 ใน 24 ราย) ของเด็กที่ขาดฮอร์โมนเจริญเติบโตในวัยเด็กพบว่าความสามารถในการหลั่งฮอร์โมนเจริญเติบโตกลับมาเป็นปกติ และในผู้ป่วยที่มีการหลั่งฮอร์โมนเจริญเติบโตกลับมาเป็นปกติทั้งหมดเป็นเด็กที่ได้รับการวินิจฉัยว่ามีภาวะขาดฮอร์โมนเจริญเติบโตอย่างเดียวในวัยเด็ก ในส่วนของเด็กที่ขาดฮอร์โมนเจริญเติบโตร่วมกับฮอร์โมนอื่นจากต่อมใต้สมองทั้งหมดมีระดับการหลั่งของฮอร์โมนเจริญเติบโตต่ำกว่าปกติเมื่อมาตรวจประเมินซ้ำ ผู้ป่วยที่ยังคงมีการหลั่งฮอร์โมนเจริญเติบโตต่ำมีระดับไขมันโคเรสเตอรอลสูงกว่าในผู้ป่วยที่มีการหลั่งฮอร์โมนเจริญเติบโตกลับมาเป็นปกติ (214±51 vs. 174±36 มก/ดล., p = 0.03) ฮอร์โมนเจริญเติบโตชนิดสังเคราะห์สามารถเพิ่มความสูง Ht SDS จาก -2.0±1.1 เมื่อก่อนให้การรักษา ขึ้นมาเป็น -0.6±1.3 เมื่อหยุดให้การรักษา (p<0.01) และ -0.8±1.2 ในเวลาที่ประเมินการหลั่งของฮอร์โมนเจริญเติบโตซ้ำ (p<0.01)*

สรุป: *ผู้ป่วยเด็กทุกรายที่มีภาวะขาดฮอร์โมนเจริญเติบโตอย่างเดียวในวัยเด็กและได้รับการรักษาด้วยฮอร์โมนเจริญเติบโตชนิดสังเคราะห์ ควรได้รับการประเมินการหลั่งของฮอร์โมนเจริญเติบโตซ้ำเมื่อหยุดให้การรักษา อย่างไรก็ตามการรักษาดังกล่าวพบว่ามีประสิทธิภาพในการเพิ่มความสูงได้ไม่ว่าผลการประเมินซ้ำจะพบว่ามีการหลั่งฮอร์โมนเจริญเติบโตเป็นปกติหรือไม่*