Does Pituitary Volume Based on Bone Age Have the Diagnostic Value on Growth Hormone Deficiency and Prognostic Value on the Response to Growth Hormone Therapy?

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Objectives

Pituitary gland imaging is conventionally done after the diagnosis of growth hormone (GH) deficiency (GHD) was established, to ascertain the cause of GHD. Pituitary hypoplasia is the most frequent pituitary abnormality in the children with GHD (1). In clinical practices, it has not been exactly known how pituitary volume (PV) should be evaluated on which basis of chronological age (CA), height age (HA) or bone age (BA) in the GH-deficient patients. Because delayed HA and BA in the GH deficient patients is well known. We aimed to investigate the most accurate diagnostic tool for defining pituitary hypoplasia, and determine the differantial diagnostic value of pituitary volume (PV) based on BA on GHD, and effect of PV on responses to GH therapy.

Methods

This retrospective study was conducted on 152 GH-deficient patients and 46 patients with idiopathic short stature (ISS). Patients with SGA birth (n=23), Turner syndrome (n=24), pycnodysostosis (n=2), multiple pituitary hormone deficiency (n=2), and poor compliance to GH therapy (n=4) were excluded. Seven children with SGA in ISS group were also dropped off the study. Any patients had history/clinical evidence of any chronic diseases, or other endocrine abnormalities, head injury, craniospinal irradiation and neuropsychiatric disorder. The patients were classified into following groups

- According to GH peak value (the highest response to two different stimulation tests)

1) Severe GHD: Peak GH level <7 ng/ml, (26 females, 31 males)
2) Mild GHD: Peak GH level 7-10 ng/ml, (23 females, 17 males)
3) ISS: Peak GH level >10 ng/ml, (16 females, 23 males)

- According to PV the patients with GHD were divided into two groups [PV was calculated according to formula: height x width x length x 0.52, and compared with the age and gender related national normative data (2)]

1) Patients with pituitary hypoplasia
2) Patients with normal PV.

All the patients with GHD had been treated with recombinant GH with the mean dose of 31 µg/kg/d ± 5 µg/kg/d, at least 2 years. The efficacy of GH therapy was evaluated as an increase in height velocity and the increment in height SDS.

Table 1. Pituitary measurements of patients with severe and partial growth hormone deficiency and idiopathic short stature

	Severe GHD (n=57)	Partial GHD (n=40)	ISS (n=39)	p value
Pituitary height, mm	3.8 ± 1.5	4.2 ± 1.4	4.5 ± 1.2	>0.05
Pituitary width, mm	8 ± 1.5	7.5 ± 1.14	8.3 ± 1	>0.05
Pituitary lenght, mm	12.2 ± 2	12.3 ± 1.6	12.6 ± 1.8	>0.05
Pituitary volume, mm^3	192 ± 89	209 ± 96	252 ± 107	0.004*
Pituitary infundibulum, mm	1.3 ± 0.4	1.3 ± 0.5	1.3 ± 0.5	>0.05

*** Statistically significance was observed between severe GHD and ISS groups.**
GHD: Growth hormone deficiency
ISS: İdiopathic short stature

Table 2. The diagnostic value of pituitary volume and pituitary height on the different basis for the diagnosis of GHD

	Sensitivity,%	Specificity,%	Positive predictive value,%	Negative predictive value,%
Pituitary volume				
On the basis of CA	22	92	88	32
On the basis of HA	10	95	90	30
On the basis of BA	17	98	94	39
Pituitary height				
On the basis of CA	50	66	79	35
On the basis of HA	32	89	88	34
On the basis of BA	36	89	90	35

BA: Bone age, CA: Chronological age, HA: Height age

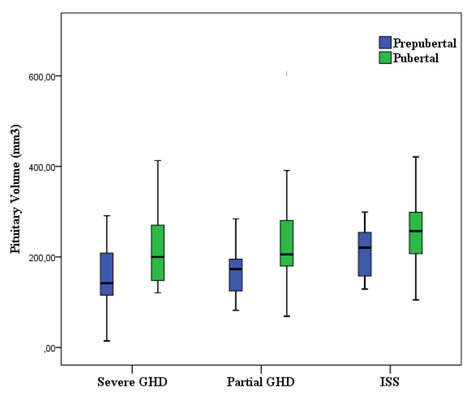

Figure 1. Pituitary volumes in the goups created according to peak GH response to provocative testing. Patients with ISS had larger pituitary volume compared with the patients with severe GHD during puberty (p=0.004).

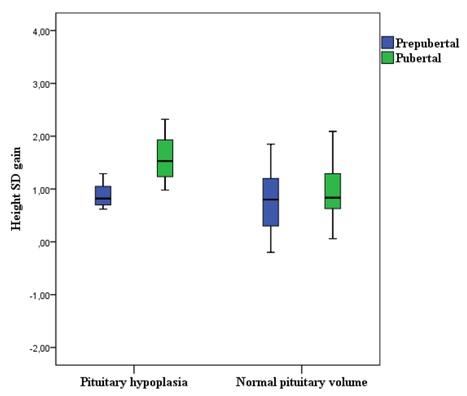

Figure 2. Height SD gain in the patients with pituitary hypoplasia and normal pituitary volume in GHD group. Pubertal patients with GHD had higher height SD gain compared with pubertal patients with normal PV (p= 0.03).

Results

- The mean ages of patients with severe GHD, partial GHD and ISS at the diagnosis were 11.4 ± 2 years, 11 ± 2 years and 12 ± 2 years, respectively (p>0.05). HA, BA were also similar in all groups. Tanner staging at baseline showed pubertal development for 49% of patients with severe GHD, 57% of patients with partial GHD and 69% of patients with ISS. Gender distribution was similar in the groups.

- The mean PV was significantly larger in the patients with ISS compared to the patients with severe GHD (p=0.004). Other pituitary measurements did not differ between the groups (Figure 1)(Table 1).

- BA-based pituitary volume to tend to be able to discriminate ISS from GHD better than the other methods (Sensitivity:16.49%, specificity: 97.3, positive predictive value: 94.12%, negative predictive value: 30.77%) (Table 2).
- On the basis of PV respect to BA, 17% of patients with GHD and 2.6% of patients with ISS had pituitary hypoplasia. (11 patients had severe and 5 patients had partial GHD).

- Before GH therapy HV was similar between the groups. After recombinant GH therapy, whereas height SD gain was completely similar in the prepubertal GH-deficient children with pituitary hypoplasia and normal PV, pubertal GH-deficient patients with pituitary hypoplasia were found to have significantly higher height SD gain compared with the patients with normal PV (1.6 ± 1, 0.8 ± 0.6, respectively, p=0.03). (Figure 2).

Conclusions

PV based on BA does not contribute to diagnose GHD, but to be able to discriminate ISS from GHD, as well as might be beneficial predicting response to GH therapy in the patients with GHD. Even if discrimination of the patients with ISS could be possible with the method we offered, there might be still pituitary hypoplasia in the children with ISS, although the secretion of GH is normal. Thus, the mechanisms underlying these findings require further researches.

References

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