of -1.8 cm/year, which was the non-inferiority margin met in the global Phase 3 study (n=224) with somatrogon (0.66 mg/kg/week) and Genotropin (0.034mg/kg/day) (ClinicalTrials.gov: NCT02968004). Most of the adverse events were mild to moderate in severity and somatrogon was generally well-tolerated with no notable difference in safety between the two treatment groups. Injection site pain was more common in the somatrogon group (somatrogon: 72.7%, Genotropin: 13.6%).
Conclusions: The Japanese Phase 3 trial in patients with pGHD demonstrated that once weekly somatrogon was comparable to daily Genotropin. The annual HV after 12 months of treatment was higher in the somatrogon group than the Genotropin group. Somatrogon administration was generally well tolerated in patients with pGHD. The results of this Japanese Phase 3 study are consistent with the results previously reported from the global Phase 3 study that met its primary endpoint of noninferiority to daily Genotropin.

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GROWTH AND GROWTH HORMONE

Pituitary Hypoplasia Is the Best MRI Predictor of the Severity and Type of Growth Hormone Deficiency in Children With Congenital Growth Hormone Deficiency

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Background and Objectives: Congenital idiopathic growth hormone deficiency(GHD) is associated with various MRI abnormalities, including both sellar anomalies such as pituitary hypoplasia, ectopic pituitary, empty sella and abnormalities of the pituitary stalk and extrasellar abnormalities such as Arnold Chiari malformation, corpus callosum agenesis, arachnoid cyst, septum pellucidum agenesis, enlarged ventricles, vermis dysplasia, and sphenoid cyst. However, it remains contentious whether MRI brain findings could provide an additional avenue for precisely predicting the differentiation of GHD based on severity(severe or partial) and type(isolated GHD or multiple pituitary hormone deficiency MPHD). This study aimed to ascertain the abnormality that is the best predictor of severe GHD and type of GHD amongst the different MRI findings. **Methods:** This was an analytical cross-sectional study conducted from 2018-2020. During the study period, we included a total of 100 subjects diagnosed to have idiopathic GHD after the exclusion of syndromic causes, system illness, presence of pituitary mass, and those with h/o cranial irradiation. Patients were divided into severe GHD and partial GHD based on peak stimulated GH of <5 ng/dl and ≥ 5 ng/dl respectively and into groups based on isolated GHD and MPHD. Patients were further divided into groups based on the presence of pituitary hypoplasia,extrasellar brain abnormalities (EBA), and presence of ectopic posterior pituitary and/or pituitary stalk abnormalities(EPP/PSA), respectively. Analyses were performed using SPSS version 24.0 software. **Results:** Amongst 100 subjects with idiopathic congenital GHD, 66 (66%) subjects had Isolated GHD while the remaining 34 (34%) had MPHD. 71 had severe GHD, and 29 had partial GHD. Amongst the MRI findings, pituitary hypoplasia was the most common finding observed in 53% of patients, while 23(23%) had EBA, and 25(25%) had EPP/PSA. Pituitary hypoplasia was observed to be the best predictor of severity of GHD with an odds ratio(OR) of 10.8 (95% CI 3.38-29.6) followed by ectopic posterior pituitary /pituitary stalk abnormalities (OR =2.8, 95% CI 1.5-9.5) while the presence of extrasellar abnormalities was the weakest predictor (OR =1.8, 95% CI 1.05-3.2). Pituitary hypoplasia was the only finding to significantly predict MPHD (OR=9.2). On ROC analysis, a Pituitary height SDS of -2.03 had a 73.2 % sensitivity and specificity of 79.3%(AUC =0.787,95% CI 0.7-0.873) for severe GHD and a sensitivity of 88.2 % and specificity of 66.7% (AUC =0.745, 95% CI 0.68-0.877) for MPHD. **Conclusion:** We observed Pituitary hypoplasia to be not only the most frequent MRI abnormality but also the best predictor of severe GHD and MPHD amongst various sellar and extrasellar abnormalities.

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Pituitary Volume Cutoffs as Another Tool for Determining Growth Hormone Treatment Eligibility

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Background: The GH stimulation test (GHST) is the gold standard for the diagnosis of GH deficiency (GHD), yet a significant number of short children fail to be diagnosed as GHD. We have speculated that pituitary volume (PV) could be used in conjunction with results from the GHST to diagnose GHD; however, cutoff values for low PVs need to be further explored.
Objective: To define a diagnostic cutoff value of PV for determining GH treatment eligibility for patients (PTs) with short stature.
Patients and Methods: The database of GHST results at a Pediatric Endocrinology center was queried for PTs aged 6-18 yrs who underwent a GHST, MRI, and blood work between 1/2018 - 6/2019. PTs with relevant comorbidities were excluded. Clonidine and L-dopa were used to induce GH secretion during the GHST. GHD was defined as a peak GH ≤ 10 ng/mL. MRIs were acquired on a Philips 1.5 or 3.0 T scanner (1mm slices) and PV was calculated using the ellipsoid formula (LxWxH/2). 144 PTs were the subjects of this study. ROC curve analysis was utilized to generate cutoff values. PV was used to predict GHD in prepubertal (age < 11 yrs) and pubertal (age > 11 yrs) children. The value with the greatest Youden index (J) was selected as the definitive cutoff.
Results: The mean (MN) and median (MD) ages of PTs were 12.2 ± 2.2 and 12.3, respectively. The MN and MD ages of prepubertal PTs (n=43) were 9.4 ± 1.1 and 9.7, respectively. The MN and MD ages of pubertal PTs (n=103) were 13.4 ± 1.4 and 13.2, respectively. Initially, 10 ng/mL was utilized as the cutoff for GHD. For predicting GHD from PV in

prepubertal PTs, sensitivity was 89.47% and specificity was 66.67%. The distance to corner was 0.3488, and the highest J was 0.5641, corresponding to a PV of 240.00 mm^3. The Area Under the Curve (AUC) was 0.6581 with a standard error (SE) of 0.2429 (p>0.05). For predicting GHD from PV in pubertal PTs, sensitivity was 72.94% and specificity was 81.25%. The distance to corner was 0.3292, and the highest J was 0.5419, corresponding to a PV of 275.00 mm^3. The AUC was 0.7901 with a SE of 0.0687 (p<0.05). Further analysis was done to explore the use of 7 ng/mL as the cutoff for GHD. For predicting GHD from PV in prepubertal PTs, sensitivity was 25.00% and specificity was 90.91%. The distance to corner was 0.7555, and the highest J was 0.1591, corresponding to a PV of 133.66 mm^3. The AUC was 0.4989 with a SE of 0.0931 (p>0.05). For predicting GHD from PV in pubertal PTs, sensitivity was 57.89% and specificity was 63.64%. The distance to corner was 0.5563, and the highest J was 0.2153, corresponding to a PV of 240.00 mm^3. The AUC was 0.6112 with a SE of 0.0584 (p<0.05).

Conclusion: PVs ≤ 275.00 mm^3 in pubertal PTs should be considered low; however, cutoffs for prepubertal PVs were not significant in this study. To our knowledge, we present the first study to generate a PV cutoff based on the GHST. Future studies including more PTs and tanner staging will further improve the accuracy of PV cutoffs for GHT eligibility.

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GROWTH AND GROWTH HORMONE

Pituitary Volume Is a Better Predictor of Growth During Growth Hormone Therapy Than the Growth Hormone Stimulation Test

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Background: Patients with diminished GH secretion are candidates for GH therapy (GHT). The GH stimulation test (GHST) is considered the gold standard for the diagnosis of GH deficiency (GHD), yet the cutoff of 10 ng/mL has not been well validated statistically. Another proposed method to define GHD has been to measure patients' pituitary volumes (PV), as the size of the gland may correlate with the amount of GH produced.

Objective: This study seeks to ascertain whether the GHST or PV is a better predictor of response to GHT, and determine which method can better define true GHD.

Patients and Methods: A database at a Pediatric Endocrinology center was queried for patients aged 6-18 yrs who underwent a GHST, MRI, and GHT between 1/2018 - 6/2019. Patients with relevant comorbidities, those with GHST peak ≥ 10.0 ng/mL, and patients that were non-adherent to their GHT were excluded. Clonidine and L-dopa were stimulants for the GHST. MRIs were acquired on a Philips 1.5 or 3.0 T scanner (1mm slices) and PV was calculated using the ellipsoid formula (LxWxH/2). 87 patients met these criteria for analysis. PV was converted to standard deviation scores (SDS) based on age and sex using the largest data set of pituitary volumes available in the literature. To account for sex-related growth rate differences by age, heights at the initial and subsequent time points were also converted to SDS based on age and sex using parameters provided by the National Center of Health Statistics. Response to treatment was defined as change in height SDS over the assessed time interval. The initial height was included as a covariate. R statistical software was utilized to analyze the correlation between response to GHT and GHST peak value, as well as response to GHT and PV. The relationship between GHST peak value and PV SDS was analyzed with a Spearman correlation.

Results: The GHST peak was not a significant predictor of growth response to treatment in both the first or second intervals (r= -0.01, p= 0.207 and r= 0.00, p= 0.815 respectively). GHST peak and PV SDS were not correlated (r=0.08, 95% CI: -0.14, 0.28). Lower SDS of PV significantly predicted growth response to therapy in the first 1 to 8.7 months of treatment (n= 87, model r^2=0.231, b=-0.05, SE=0.02, P=0.012). This association in the second interval between 7.8 and 17.4 months of treatment was neither as strong as the first interval nor was it statistically significant (n=62, model r^2=0.145, b=-0.05, SE=0.03, P=0.127). Within-person growth velocity was greater in the first interval (mean = 0.37, SD = 0.17) than in the second interval (mean = 0.20, SD = 0.16).

Conclusion: Our data indicates that PV can be a valuable tool in defining GHD and should be considered a criterion for determining eligibility for GHT. To our knowledge this is the first study to determine that PV is a better predictor of growth response to GHT than the GHST.

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GROWTH AND GROWTH HORMONE

Results From an Open-Label Extension of the Phase 2 Dose Finding Study of Once Weekly Somatrogon vs Daily Genotropin in Pediatric Patients With Growth Hormone Deficiency (GHD)

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Background: Somatrogon, a long-acting recombinant human growth hormone, is being developed as a once weekly treatment for pediatric patients (pts) with GHD. A phase 2, 12 month study (NCT01592500) in pts with GHD showed that weekly somatrogon at 0.66 mg/kg/week had similar efficacy and safety to daily Genotropin. Pts who