firmed PWS in the first months of GH therapy (GHT). Case 1: This boy died at the age of 3.8 years. He was born at term from an uneventful pregnancy. His birth weight was 3,180 g and lenght was 51 cm. GHT was started at the age of 3.3 years (0.33 mg/d), when the patient was at 180% of his ideal body weight (ibw): 27 kg, 96.5 cm. 6 months later (175% of ideal bw) he was found dead in the morning in his bed. He was well the night before his death. Case 2: This 3.9-year-old girl was born at term by cesarean section due to breech presentation. Birth weight was 3,450 g. GHT was started at the age of 3.5 years (0.76 mg/d), when the patient was at 130% of her ibw (16.3 kg, 84.7 cm). Hypertrophy of adenoids was previously demonstrated. Snoring and sleep apnea were present before GHT, and did not increase during therapy. Four months later she died at home suddendly in the morning. Case 3: This patient was a 6.3-year-old boy. At the age of 6 years his weight was at 144% of his ibw. GHT was started with a dosage of 0.75 mg/d. Two months later, adenoidectomy+tonsillectomy were performed to improve respiratory function. Three weeks after surgery, he died at home in the morning following an acute crisis of apnea. The parents have previously noticed recurrent episodes of nocturnal apnea. Our data seem to confirm that some children with PWS are at risk for a sudden death at the beginning of GHT. It may be suggested that during the first months of GHT increased awareness for its possible side effects is necessary in order to avoid fatalities as described.

**P2-620** GH Treatment

## Improvement of Quality of Life in Adolescents Born Small for Gestational Age (SGA)

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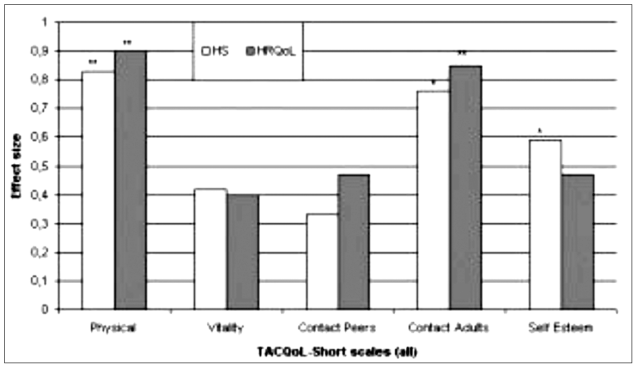
We evaluated whether long-term growth hormone therapy (GHRx) in children born SGA, which results in a normal childhood and adult height, is accompanied by a better quality of life (QoL). 2 Groups of adolescents born SGA (GH-treated and an untreated group (U)) were analysed and compared with references. Table: data expressed as mean(SD).

| | GH group n=44 | Untreated group n=28 |
|---|---|---|
| BASELINE: | | |
| Height sds | -3.1(0.7) | -2.3(0.7) |
| AT QOL EVALUATION: | | |
| age(yrs) | 15.8(2.1) | 15.8(2.1) |
| Height sds | -0.6(1.2) | -1.8(0.8) |
| Duration of GHRx (yrs) | 8.8(1.7) | - |

**Methods:** A generic child health questionnaire (CHQ) and a condition specific questionnaire, the TNO-AZL Childrens QoL-Short Stature(TACQOL-S).

**Results:** CHQ: GH-group had better effect sizes [(mean GH-mean ref.)/highest SD] on 'social-behavior', 'behavior', 'mental health' and 'self esteem' compared to references, however without reaching significant differences. The U-group showed on all the scales of the CHQ lower effect sizes than the GH-group and the references. There were no sign. differences between the GH and the U-group. TACQOL-S: Effect size=[(mean GH-mean U)/highest SD]. Fig. shows effect sizes of the differences between the GH-group and the U-group, indicating that the QoL in the GH-group was better on all scales with a moderate to large effect. Health status: quantity of problems (HS); Health related QoL: emotional impact of the problems (HRQOL). Effect size is small if <0.5; moderate if 0.5-0.8 and large if ≥0.8. Difference GH compared to U-group: *p<0.05, **p<0.01.




**Conclusions:** Our study shows that children born SGA, treated with long-term GHRx, show significantly better QoL in physical abilities and contact with adults than untreated children born SGA, when measured with the condition specific TACQOL-S. In addition, positive effect sizes are shown on all scales of the specific TACQOL-S and the generic CHQ compared to the U-group. Our study also indicates that evalutation of QoL in short children and the effect of GHRx on QoL should be performed with a condition specific questionnaire.

**P2-621** GH Treatment

## Two Years Follow–Up of Growth Hormone (GH) Therapy in Short Stature Children with Reduced GH Bioactivity

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**Introduction:** Biologically inactive growth hormone (GH) due to genetic mutations is a rare cause of short stature, characterized by the lack of GH action despite its normal immunoreactivity. Commercial GH measurements provide no information on the biologic activity of the hormone, but the Nb2 cell bioassay does. The diagnosis of GH bioinactivity should be confirmed by a marked catch-up growth after exogenous GH administration.

**Patients/Methods:** We studied 8 boys (aged 9.60±2.78 yr., 23.1±7.6 kg, BMI 15.35±1.92 kg/m$^2$ and bone age 7.65±2.75 yr.) with short stature, reduced growth velocity (GV) and discordant GH responses to standard provocative tests. On the basis of the reduced GH bioactivity, demonstrated by Nb2 bioassay, all children were treated with GH (0.24mg/kg/week). Aim of our study was to evaluate the effect of GH therapy in these children.

**Results:** All results (table) are reported as the mean±SDS. Student's t test for paired samples was used for comparison of data between before and after 12 and 24 months of therapy (* p<0.05).

| GH therapy | 0 (# 8) | 12 mo. (# 8) | 24 mo. (# 8) |
|---|---|---|---|
| Height (cm) | 121.23±14.03 | 129.37±13.52* | 135.66±14.29* |
| Height (SDS) | -2.26±0.47 | -1.84±0.47* | -1.63±0.35* |
| GV (cm/yr.) | 4.07±0.72 | 7.82±1.59* | 6.40±0.95* |
| GV (SDS) | -2.26±0.94 | 3.05±2.21* | 2.24±1.95* |
| IGF–1 (ng/ml) | 111.43±31.11 | 216.92±71.75* | 294.82±64.54* |
| IGF–1 (SDS) | -1.57±0.81 | -0.37±1.31* | 0.05±0.62* |

**Conclusions:** GH treatment significantly improves auxological and laboratory data of our patients such as treated GHD subjects. The positive effect obtained during the first year of therapy persists in the second year. The results of this study confirm that the Nb2 cell bioassay is a useful tool to clarify the diagnosis of short stature due to GH bioinactivity that is, moreover, confirmed by the persistent significant catch-up growth following GH therapy.

**P2-622** GH Treatment

## The Combined Treatment with Growth Hormone and GnRH Analogue for the Short Stature Occuring in Leri-Weill Syndrome gives Encouraging Results

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**Introduction:** Dyschondrosteosis, also known as LWS is an autosomal dominant disorder characterized by disproportionate short stature attributable to mesomelic shorteness of the limbs, forearm deformity (Madelung), and Turner syndrome-like symptoms. Haploinsufficiency of gene SHOX (on the short arm of chromosome X) is considered to be responsible for short stature in both Turner syndrome and LWS. Increased height velocity during growth hormone (GH) treatment has been reported, but the number of patients was limited. The aim of this study was to evaluate the effect of GH treatment in a larger cohort of LWS.

**Patients and results:** We report 29 patients with short stature, clinically and/or radiologically confirmed LWS. Karyotype was performed in order to eliminate Turner syndrome. GH therapy was started before or during puberty. Age at onset