EP700

Quality of Life (QoL) and IGF-I Status in Adults with Severe Growth Hormone Deficiency (GHD)

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Background In adult patients with pituitary disease no relationship has been established between the biochemical severity of GHD, measured by stimulated GH or IGF-I SDS, and the degree of QoL impairment, measured by QoL-AGHDA score (range 0-25, higher values denoting poorer QoL).

- Country-specific differences are noted, necessitating detailed normative data

	General population	GHD
Sweden	**3.9** (SEM 0.1)	**8.1** (SEM 0.3)
UK	**6.7** (SEM 0.2)	**15.8** (SEM 0.2)

- Reasons for lack of correlation may include heterogeneity of underlying pathologies and related therapies
- Severe QoL impairment (QoL-AGHDA >11) is the sole criterion for GH reimbursement in the UK but not elsewhere

Methods KIMS, the Pfizer International Metabolic Database, was used to focus solely on patients with non-functioning pituitary adenomas (NFPA) and prolactinomas treated by surgery alone.

- Entry criteria include peak GH of less than 3 µg/L to an insulin tolerance test and at least 2 other pituitary hormone deficits (severe GHD).
- IGF-I was measured centrally and IGF-I SDS calculated using normal range for age and gender.
- Health-related QoL was measured using QoL-AGHDA, a disease-specific validated questionnaire (1).

Objective 1

• To investigate whether a relationship exists between GHD severity and QoL status.

• By selecting patients with a specific pathology, treated in a uniform way, resulting in a well-defined and homogeneous group, thereby reducing confounding variables to a minimum.

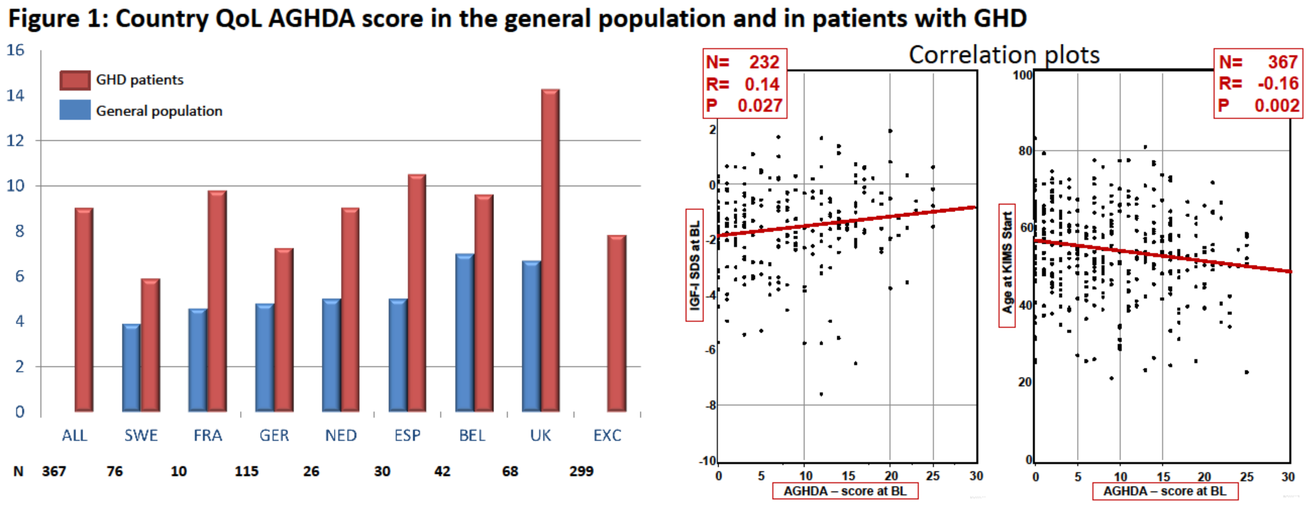
Inclusion and Exclusion Criteria

- Only countries with normative QoL-AGHDA data
- Only NFPA and prolactinoma of adult-onset
- Pituitary surgery >6 months before baseline, but no radiotherapy
- Severe GHD + ≥ 2 additional hormone deficiencies on conventional replacement, no diabetes insipidus
- Naïve to GH replacement
- Separate analysis of UK

Table 1: Descriptive analysis of factors to explain QoL

(± SD)	ALL minus UK n=299	UK n=68	p
Gender (M : F)	1.3 ± 0.5	1.3 ± 0.5	ns
Pituitary diagnosis → GH start (years)	5.7 ± 6.6	7.0 ± 7.0	0.0234
GHD diagnosis → GH start (years)	1.8 ± 3.1	2.7 ± 3.8	0.0009
Age at KIMS start (years)	54.4 ± 11.8	53.1 ± 11.3	ns
Additional pituitary deficiencies (n)	2.7 ± 0.5	2.5 ± 0.5	0.0197
GH peak by ITT (µg/L)	0.7 ± 1.0	0.8 ± 0.9	ns
IGF-I SDS	-1.7 ± 1.6	-1.0 ± 1.3	0.0042
QoL-AGHDA (score)	7.8 ± 6.5	14.3 ± 6.7	<0.0001

Figure 1: Country QoL AGHDA score in the general population and in patients with GHD



Objective 2

- To investigate whether, in the similar well-defined and homogeneous group, a relationship exists between the severity of GHD (measured by baseline IGF-I SDS) and the changes in QoL-AGHDA during 1 year GH replacement or the adequacy of GH replacement (measured by on-treatment IGF-I SDS)

Figure 2: Country QoL-AGHDA score at baseline and Δ during GH replacement (Y1)

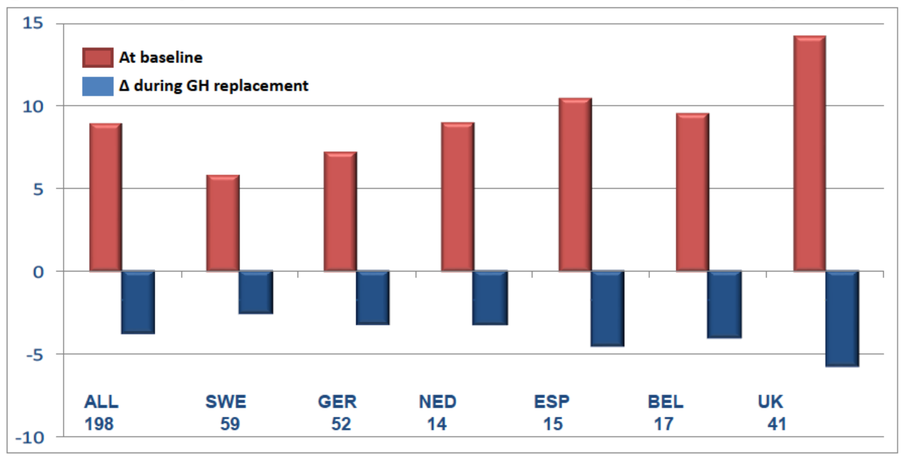


Table 2: Analyses based on IGF-I SDS groups at baseline and at Y1 of GH replacement

(±SD)		IGF-I SDS groups at baseline			IGF-I SDS groups first year of GH replacement		
IGF-I SDS	All	① < -2	② -2 to -1	③ > -1	④ > 1	⑤ 0 – 1	⑥ < 0
n	162	52	53	57	62	51	49
IGF-I SDS	-1.7 ± 1.6	-3.5 ± 1.3	-1.5 ± 0.3	-0.2 ± 0.7	-1.0 ± 1.1	-1.7 ± 1.7	-2.5 ± 1.6
+ 1Y GH	0.5 ± 1.4	-0.1 ± 1.7	0.6 ± 1.1	1.1 ± 1.0	1.8 ± 0.6	0.5 ± 0.3	-1.1 ± 1.0
QoL-AGHDA	8.2 ± 7.0	7.1 ± 5.8	7.8 ± 7.6	9.6 ± 7.2	8.2 ± 7.3	8.7 ± 7.3	7.7 ± 6.3
+GH Δ	-3.4 ± 4.9	-3.2 ± 4.3	-3.8 ± 5.6	-3.4 ± 4.9	-3.9 ± 5.0	-2.8 ± 5.1	-3.6 ± 4.7

- **No significant differences between groups ①②③ for:**
- Age of diagnosis, start GH, BMI, waist, lipids, glycaemia, QoL-AGHDA, + effect of GH on all parameters, except for baseline IGF-I SDS and waist ①-②.
- **Significant within group changes for:** IGF-I SDS and Δ QoL-AGHDA.

- **No significant differences between groups ④⑤⑥ for:**
- Age of diagnosis, start GH, BMI, waist, lipids, glycaemia, QoL-AGHDA, + effect of GH on all parameters, except for baseline IGF-I SDS.
- **Significant within group changes for:** IGF-I SDS and Δ QoL-AGHDA.

Results 1 The analysis was performed separately for UK data versus the collective other European countries (Belgium, Germany, Sweden, France, Holland, Spain) data. Median AGHDA score at baseline for UK (n=68) was 15.5 and for Europe (n=299) 7.0 (p<0.0001) whilst median IGF-I SDS for UK (n=54) was -0.87 and for Europe (n=178) -1.53 (p=0.0042). The UK cohort had much greater impairment of QoL and were less severely GHD than the Europe cohort, implying that a significant component of impaired QoL in the UK cohort is unrelated to their GH status.

- There is no correlation between GHD severity (assessed by peak GH response or IGF-I SDS) and degree of QoL impairment.
- The decision criterion to treat GHD patients in the UK differs from the approach in the rest of the EU because QoL in the UK is the sole endpoint on which selection for GH replacement is based.
- In the UK, QoL-AGHDA is positively influenced by marital status, independent of educational level or type of employment, but adversely affected by the need of assistance with daily life activities
- Other generic measures of QoL, like the Nottingham Health Profile (NHP) and the Psychological General Well-Being (PGWB) scores, reflect the QoL-AGHDA score.

Results 2

- At baseline the severity of GHD, measured by IGF-I SDS, is unrelated to the degree of impairment of QoL, while normalization of IGF-I SDS by GH replacement induces a comparable and significant amelioration of QoL irrespective of baseline IGF-I status.
- The adequacy of GH replacement, defined by on-treatment IGF-I SDS, is unrelated to the degree of improvement of QoL.

Conclusions

1. The literature indicates that QoL improves significantly in UK GHD adults in response to GH replacement. However, our results question a treatment strategy focused on QoL alone, a medical endpoint not shown to be related to the degree of GHD, and affected by multiple factors. As for all other endocrine deficits, the classical approach is to treat those with biochemical evidence of the severest deficit first.
2. GH replacement therapy induces a profound and comparable favorable effect on QoL independent of the severity of GHD and depends rather on a substantial increase in IGF-I SDS than in strict normalization.

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