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ORIGINAL ARTICLE

Quality of life in transition phase in adolescents and young adults with severe and partial growth hormone deficiency

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Abstract

BACKGROUND: Transition is a term used to describe the period of adolescence after which the final adult height during growth hormone (GH) treatment is achieved. According to re-evaluation results in insulin tolerance test (ITT) patients with severe and partial growth hormone deficiency (GHD) may be distinguished.
OBJECTIVES: The aim of the study was to assess QoL in patients with different degrees of GHD in transition phase.
METHODS: QoL was evaluated in 76 subjects aged 16–25 years with severe (SGHD, n=26), partial GHD (PGHD, n=22) and normal GH secretion (NGH, n=28) using SF-36 v.2™ Health Survey and the Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) questionnaires.
RESULTS: Physical Component Score (PCS), Physical Functioning (PF) and General Health (GH) results were significantly lower in patients with SGHD than in NGH group. SF-36 v.2™ Health Survey scores in PGHD were similar as in NGH patients. There were no statistically significant differences in QoL-AGHDA scores between the examined groups. We found positive correlations between peak GH in ITT and PF (r=0.29; p=0.02) or Role Emotional (r=0.37; p=0.002) scores.
CONCLUSIONS: We demonstrated that the QoL in adolescents and young adults with severe GHD in transition period is disturbed mainly in terms of physical health and emotions. These changes were detected only by generic SF-36, but not by disease-specific QoL-AGHDA questionnaire. Therefore AGHDA-QoL assessment may not be applicable in GHD patients in transition period. QoL in the patients with partial GHD is unchanged in comparison to growth hormone sufficient subjects.

INTRODUCTION

Transition is a term used to describe the period of adolescence after which the final adult height being the primary goal of growth hormone (GH) treatment is achieved, and the major goals of GH replacement become normalization of metabolism and quality of life (Leong & Johannsson 2003; Rosenfeld & Nicodemus 2003). It has been arbitrarily defined as the period extending from late puberty to full adult maturity (i.e., from mid to late teenage years until 6–7 years after achievement of final height) (Clayton *et al.* 2005). This period represents a crucial time for the reassessment children's GH secretion and deciding whether GH therapy should be continued throughout life (Clayton *et al.* 2005; Radovick & DiVall 2007; Inzaghi *et al.* 2013).

Evidence-based guidelines for diagnosis and treatment of growth hormone deficient children during transition are lacking. It is suggested, that after the final height has been achieved, the patient should be re-evaluated and further indications for reinstitute GH treatment should be established (Clayton *et al.* 2005; Ho 2007; Cook *et al.* 2009). However, there is no general agreement according to the choice of the stimulation test and the cut-off values to be used to discriminate between normal and abnormal GH response in patients during the transition phase. Insulin tolerance test (ITT) is considered „the gold standard" for the diagnosis of GHD in adults, but the cut-off values in the transition phase are suggested to be increased up to 5.0 ng/ml (Bonfig *et al.* 2008) or even 6.1 ng/ml (Maghnie *et al.* 2005).

Therefore, there is some population of adolescents that are not severely GH deficient, according to the above mentioned criteria, but fail to attain normal GH status (peak GH on ITT >10 ng/ml) on re-evaluation. This condition is defined as partial growth hormone deficiency (Taubert *et al.* 2003; Clayton *et al.* 2005; Shalet 2010).

Childhood onset growth hormone deficiency (CO-GHD) in the adolescents after the treatment with recombinant growth hormone has been stopped is associated with reduced muscle mass and strength (Rutherford *et al.* 1991; Hulthen *et al.* 2001; Koranyi *et al.* 2001), lower bone mass (Boot *et al.* 2009), increased visceral adiposity (Colle *et al.* 1993; Johannsson *et al.* 1999), abnormal lipid profile (Capaldo *et al.* 1997; Johannsson *et al.* 1999; Mukherjee *et al.* 2004; Follin *et al.* 2006), cardiac impairment (Colao *et al.* 2002; Follin *et al.* 2006) and increased cardiovascular risk (Colao *et al.* 2002; Follin *et al.* 2006)

The data on metabolic balance and body proportions in adults with partial growth hormone deficiency during transition period are scarce. It has been confirmed that severity of growth hormone deficiency (GHD) in the adults is correlated with the degree of abnormality of lipid profile, bone loss, body composition and cardiac impairment (Shalet 2010). The study by Taubert *et al.* (2003) revealed significant disturbances of body composition (increased total body fat and decreased lean body mass) in adolescents with the partial GHD group. Moreover, these alterations worsened after 1 year without GH treatment. These findings suggest that long-term follow-up for these adolescents should be pursued with sequential GH retesting and careful evaluation.

Quality of life (QoL) has been defined by the World Health Organization as "the state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO 1947). This parameter, although complex and difficult to evaluate permits for cost-benefit analysis and may be helpful in establishing indications for continuation relatively expensive GH treatment from childhood to adulthood.

The transition period is not only the process of somatic maturation but also the time frame when a significant psychosocial adjustment takes place. Therefore, CO-GHD may influence some aspects of QoL in adolescents (Dean *et al.* 1985; Takano *et al.* 1994; Sandberg et al.1998; Keselman *et al.* 2000; Attanasio *et al.* 2005).

Studies on adult QoL outcome after paediatric GH treatment have shown essentially normal psychosocial adjustment and educational attainment (Takano *et al.* 1994; Attanasio *et al.* 2005), but higher rates of unemployment or underemployment, reduced marital rates and impaired general health perception (Dean *et al.* 1985; Sandberg *et al.* 1998; Keselman *et al.* 2000). QoL scoring in adolescents with severe CO-GHD although not overtly compromised, but has been observed to be slightly poorer in terms of depression, general health and anxiety. In these patients some dimensions related to age-specific behavioural patterns and psychological issues are affected as a function of the achieved developmental status (Leong & Johannsson 2003; Attanasio *et al.* 2005).

GHD may affect QoL via neurological mechanisms, but also as result of metabolic, cardiovascular, reproductive and immune disturbances (Hull *et al.* 2003). Therefore, it can be suspected that in partial CO-GHD in adolescents QoL may be disturbed, however to a lesser extent than in its severe form.

Unfortunately, to the best of our knowledge, there is no data according the quality of life in adolescents with partial growth hormone deficiency. Therefore, the aim of this study was to assess and compare the QoL in adolescents with severe and partial GHD using generic and disease-specific surveys.

MATERIAL AND METHODS

Subjects

The study involved 76 participants aged 16–25 years (39 females and 83 males) who had stopped the treatment with recombinant growth hormone due to CO-GHD at least 6 months before. According to the results of insulin tolerance test (ITT) the subjects were included to the one of three studied groups: 1) severe growth hormone deficiency (SGHD) (26 subjects – 8 females, 18 males);

2) partial growth hormone deficiency (PGHD) (22 subjects – 7 females, 15 males); 3) normal growth hormone status (NGH) (28 subjects – 9 females, 19 males).

The exclusion criteria were: Turner syndrome or other chromosomal aberrations, skeletal dysplasia, chronic diseases of the heart, liver, kidney, cystic fibrosis, coeliac disease, arterial hypertension, hyperlipidemia), type 1 or 2 diabetes, primary hypothyroidism, Addison's disease or hypergonadotrophic hypogonadism, insufficient treatment of multihormonal pituitary deficiency (pituitary hypothyroidism, adrenal insufficiency, hypogonadism or diabetes insipidus), low birth weight, pregnancy in women.

The adequacy of the treatment of multihormonal pituitary insufficiency was assessed on the basis of medical history, physical examination and laboratory tests (serum fT_4, cortisol, serum and urine osmolality, estradiol in women or testosterone in men).

There were 16 patients with multihormonal pituitary insufficiency in SGHD group and 1 – in PGHD group. All subjects with current normal growth hormone secretion had idiopathic growth hormone deficiency in childhood. No subject had neoplasm or neurosurgery in the past history.

The insulin tolerance test was performed according to Biller *et al.* (2002) and the peak GH cut-off levels for SGHD group was <5.0 ng/ml and >10.0 ng/ml for NGH (Clayton *et al.* 2005; Bonfig *et al.* 2008). The patients with results between these values were included to the PGHD group.

The clinical characteristics of the examined groups are given in Table 1.

This study was approved by the Bioethics Committee at the Medical University of Silesia in Katowice, Poland (no. L. dz. KNW-6501-63/I/08) and written informed consent was obtained from all examined participants and their parents or legal guardians if the participant is younger than 18 years of age before their involvement.

Anthropometric measurements

Anthropometric parameters were measured in all participants in the morning between 7:00 AM and 8:30 AM after a 12-hour fast and passing urine. The body weight was measured on medical scales and height using Harpander type anthropometer. In all participants BMI (body weight [kg]/height [m^2]) was calculated.

Laboratory tests

Serum growth hormone concentrations in the samples obtained during the ITT were performed using IRMA *(immunoradiometric assay)* method (BioSource Europe, Nivelles, Belgium). The limit of detection for the kit was 0.12 ng/ml. The intra- and inter-assay coefficients of variation were 4.4% and 8.17%, respectively.

Serum insulin growth factor-1 concentrations were evaluated in serum samples obtained between 7:00 AM and 8:30 AM after a 12-hour fast using ELISA *(enzyme-linked immunosorbent assay)* kit (Bio-Line, Brussels, Belgium) with the limit of detection 1.1 ng/ml. The intra- and inter-assay coefficients of variation were 5.6% and 11.5%, respectively.

Assessment of QoL

QoL was evaluated using licensed and validated Polish versions of SF-36 v.2™ Health Survey (licence to D.R.) and Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA) (Karbownik-Lewinska *et al.* 2008) (permission from prof. M. Karbownik-Lewińska).

SF-36 v.2™ Health Survey is a generic health survey from the patient's point of view, while QoL-AGHDA is a disease-specific questionnaire.

The theoretical model of the SF-36 assumes that the Physical Functioning (10 items), Bodily Pain (2 items), and Role Physical (4 items) scales correlate strongly with the Physical Component and its summary measure (PCS). In turn, the Mental Health (5 items), Role Emotional (3 items), and Social Functioning (2 items) scales correlate more strongly with the Mental Component and its summary measure (MCS). The Vitality (4 items), General Health (5 items) and Social Functioning (2 items) scales should correlate with both components (Ware *et al.* 2000).

The procedures for item recoding, summing the responses for each of the variables that make up the scale, transforming the scales into scores ranging from 0 to 100, and standardisation and normalisation, in which average values vary around value 50 with a dispersion factor of 10, followed the recommendations of the SF-36 v.2™ developers for calculating the domains (Ware *et al.* 2000).

QoL-AGHDA measure is constructed of 25 items that evoke yes/no answers, acknowledging or denying certain problems. The QoL-AGHDA score is computed by summing a number of recognized problems i.e. each "yes" answer is assigned a score of 1, and therefore a high numerical QoL-AGHDA score denotes poor QoL (McKenna *et al.* 1999).

Statistical analysis

The database was prepared using Excel 2000 (Microsoft Corporation). Statistical analysis was carried out with Statistica 6.0 software (StatSoft Inc., Tulsa, Oklahoma, USA). Results are presented as means ± standard deviation (SD).

Normal data distribution was assessed using the Shapiro-Wilk test; the homogeneity of variance was computed using Levene's test.. Comparisons between the examined groups were performed using the analysis of variance (ANOVA) and *post-hoc* RIR Tukey's multiple comparison test for different sample sizes or Kruskal-Wallis test if data distribution was not normal. Correlations were analyzed by Pearson's linear correlation test or Spearman's test if data distribution was not normal. All results were considered statistically significant at $p<0.05$.

RESULTS

There were no significant differences between the examined groups according age, body weight, height, BMI and time from the end of GH treatment. The duration of the treatment was the longest in the SGHD group (Table 1).

Peak serum GH during ITT as well as IGF-1 concentrations were significantly lower in SGHD group than in NGH. These values in PGHD subjects were significantly higher than in SGHD, but decreased when compared to NGH (Table 1).

Quality of life evaluated by SF-36 v.2™ Health Survey revealed that Physical Component Score (PCS) was significantly lower in patients with SGHD than in NGH group. Patients with severe CO-GHD considered their Physical Functioning (PF) worse than those with normal GH secretion (NGH). Their General Health (GH) score was also lower in comparison to NGH as well as PGHD subjects (Table 2).

We did not observed significant differences between the examined groups in Mental Component Score (MCS), however Role Emotional (RE) score was lower in SGHD than in NGH group (Table 2).

SF-36 v.2™ Health Survey scores in PGHD were similar as in NGH patients (Table 2).

There were no statistically significant differences between the examined groups in QoL-AGHDA scores (Figure 1).

We found positive Spearman's correlations between peak GH in ITT and PF (r=0.29; p=0.03) (Figure 2) or RE (r=0.37; p=0.001) (Figure 3). Treatment duration correlated positively with QoL-AGHDA score (r=0.25; p=0.03) and negatively with Social Functioning score

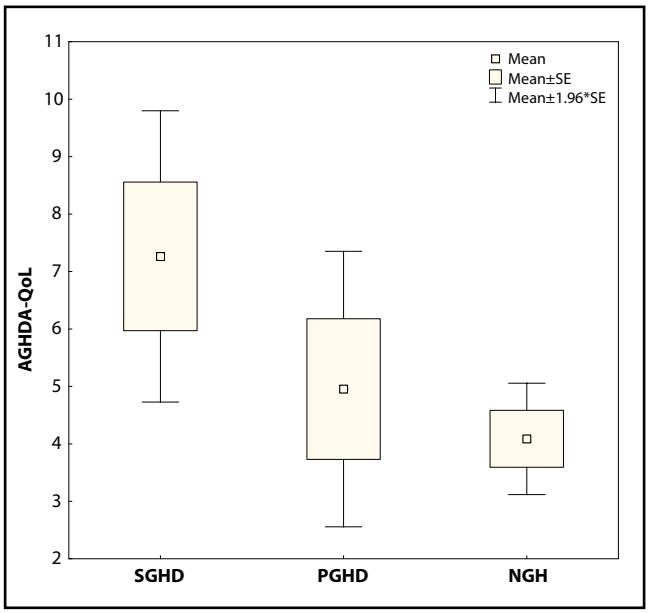

Fig. 1. Results of AGHDA-QoL in examined patients with childhood-onset growth hormone deficiency. SGHD – severe growth hormone deficiency; PGHD – partial growth hormone deficiency; NGH – normal growth hormone status.

Tab. 1. Clinical characteristics of examined patients with childhood-onset growth hormone deficiency.

	mean ± SEM (range)		
	SGHD (n=26; F=8; M=18)	**PGHD** (n=22; F=7; M=15)	**NGH** (n=28; F=9; M=19)
Age [years]	20.93±0.54 (16.7–25.1)	19.05±0.43 (17.1–24.8)	20.01±0.49 (15.6–25.0)
Body weight [kg]	62.77±4.05 (31.8–105.2)	57.76±1.98 (33.2–79.3)	57.85±1.78 (41.4–75.2)
Height [cm]	164.89±2.44 (149.3–184.2)	163.01±1.79 (141.30–175.30)	166.48±1.39 (149.40–176.70)
BMI [kg/m^2]	22.55±0.78 (13.76–33.58)	21.74±0.73 (16.63–30.84)	20.82±0.53 (16.03–27.15)
Duration of GH treatment [months]	56.73±9.77[a] (12.4–170.4)	37.13±5.72 (12.9–143.1)	27.15±3.26 (3.4–67.8)
Time from the end of GH treatment [months]	57.38±8.89 (7.1–136.2)	46.77±4.60 (6.3–78.6)	41.87±4.35 (13.1–86.4)
Peak GH in ITT [ng/ml]	1.37±0.27[a.b] (0.19–4.98)	7.79±0.34[a] (5.15–9.98)	15.82±0.45 (11.91–20.13)
IGF-1 [ng/ml]	75.68±15.60[a.b] (12.53–287.92)	157.93±11.88[a] (54.13–239.34)	135.24±9.84 (69.38–225.67)

[a] p<0.05 in comparison to NGH group; [b] p<0.05 in comparison to PGHD group
F – female; M – male; SGHD – severe growth hormone deficiency; PGHD – partial growth hormone deficiency; NGH – normal growth hormone status; GH – growth hormone; ITT – insulin tolerance test; IGF-1 – insulin growth factor 1; SEM – standard error of the mean

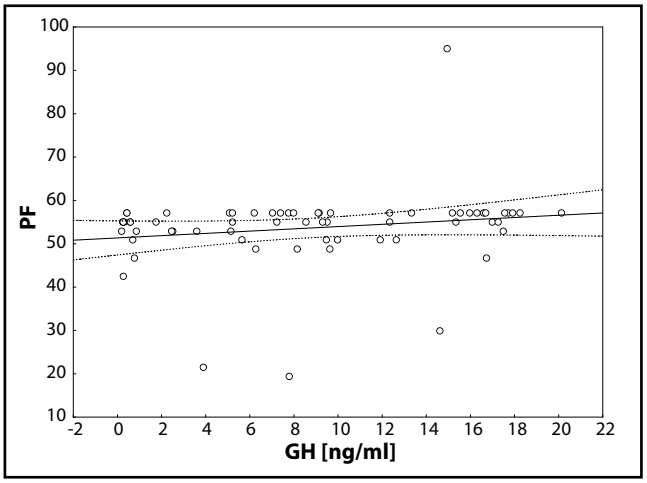

Fig. 2. Spearman`s correlation between peak GH obtained in insulin tolerance test [ng/ml] and Physical Functioning (PF) score in SF-36 v.2™ Health Survey (r=0.29; *p*=0.02).

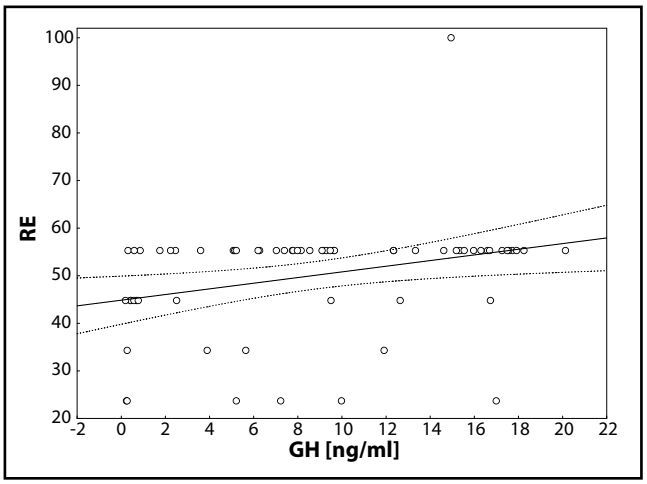

Fig. 3. Spearman`s correlation between peak GH obtained in insulin tolerance test [ng/ml] and Role Emotional (RE) score in SF-36 v.2™ Health Survey (r=0.29; *p*=0.02).

Tab. 2. Results of SF-36 v.2™ Health Survey in examined patients with childhood-onset growth hormone deficiency.

	mean ± SEM (range)		
	SGHD (n=26; F=8; M=18)	**PGHD** (n=22; F=7; M=15)	**NGH** (n=28; F=9; M=19)
PF	51.81±3.68[a] (21.50–57.10)	52.74±3.37 (19.40–57.10)	56.03±4.23 (29.90–95.00)
RP	52.13±2.43 (42.10–56.20)	53.32±3.10 (28.00–56.20)	52.89±5.37 (35.00–100.00)
BP	53.24±4.19 (37.50–62.70)	56.19±3.78 (62.80–64.00)	53.65±4.39 (28.50–62.70)
GH	45.89±5.21[a.b] (26.50–60.30)	51.91±3.32 (36.80–64.00)	50.97±3.12 (33.6–64.00)
VT	52.32±5.41 (27.80–70.40)	54.99±4.47 (30.10–70.40)	56.03±5.86 (23.00–70.40)
SF	48.84±4.39 (30.00–57.10)	48.74±4.29 (24.60–57.10)	51.20±5.86 (24.60–100.00)
RE	45.89±4.70[a] (23.70–55.30)	49.56±4.84 (23.70–55.30)	54.04±5.23 (23.70–100.00)
MH	48.28±3.96 (27.70–59.50)	51.37±3.10 (36.80–64.10)	51.06±3.27 (36.80–64.10)
PCS	50.94±2.74[a] (34.60–61.50)	53.02±3.00 (32.80–60.40)	51.34±2.25 (39.10–58.60)
MCS	47.15±5.39 (19.80–59.80)	49.98±4.10 (26.80–66.50)	51.09±3.35 (29.50–63.00)

[a] $p<0.05$ in comparison to NGH group; [b] $p<0.05$ in comparison to PGHD group
F – female; M – male; SGHD – severe growth hormone deficiency; PGHD – partial growth hormone deficiency; NGH – normal growth hormone status; SEM – standard error of the mean; PF – Physical Functioning; RP – Role Physical; BP – Bodily Pain; GH – General Health; VT – Vitality; SF – Social Functioning; RE – Role Emotional; MH – Mental Health; PCS – Physical Component Score; MCS – Mental Component Score

(r=–0.25; *p*=0.03). There were no correlations between anthropometric and clinical parameters (age, sex, body weight, height, BMI, time from the end of GH treatment, serum IGF-1) and the results of performed QoL surveys.

DISCUSSION

In this study we demonstrated that in adolescents and young adults with severe and partial growth hormone deficiency quality of life measured by disease-specific score (QoL-AGHDA) is similar than in participants who were treated with recombinant growth hormone in the past due to growth hormone deficiency, but at present have normal growth hormone secretion. However, when assessment was performed using generic scale (SF-36 v.2), the severe growth hormone deficient patients showed lower results according to their physical and general health as well as emotions which correlated with the degree of growth hormone deficiency (defined as peak GH concentration in ITT).

QoL-AGHDA questionnaire was constructed based on in-depth interviews with adult patients with GH deficiency (McKenna *et al.* 1999). Almost all patients were dissatisfied with their body image and complained of lack of energy (94% and 91%, respectively), 83% had problems with memory and concentration, 71% described themselves as being short-tempered and easily irritated, 66% suffered from lack of strength and stamina, 63% experienced reduced physical and mental drive and 57% had difficulties coping with stressful situations and avoided external stimulation (Holmes *et al.* 1995).

The QoL-AGHDA is an unusual scale. Although it was developed to measure the quality of life of adults with GHD, in fact it contains no terms specific only to those patients or to that condition. Thus, healthy normal people are able to complete it, and they do not

find its questions to be inappropriate or inapplicable (Wirén *et al.* 2000)

So far, this instrument was used predominantly in the patients with adult onset growth hormone deficiency (AO-GHD) or in mixed (AO- and CO-GHD) groups of subjects (Abs *et al.* 1999; Sanmartí *et al.* 1999; Murray *et al.* 1999; Malilk *et al.* 2003; Kołtowska-Häggström *et al.* 2008). In the majority of studies QoL-AGHDA scores in adults with growth hormone deficiency are elevated in comparison to general population (Sanmartí *et al.* 1999; Barkan 2001; Malik *et al.* 2003; Moock *et al.* 2011) and the improvement after recombinant growth hormone treatment was noted (Abs *et al.* 1999; Murray *et al.* 1999; Kołtowska-Häggström *et al.* 2008).

There is, however some data, that QoL in patients with growth hormone deficiency is influenced by the age of the disease onset and adult onset patients express the greater distress (Murray *et al.* 1999; Attanasio *et al.* 1997). Therefore the above mentioned results cannot be simply extrapolated on adolescents and young adults with the onset of the disease in childhood, but the studies limited to CO-GHD subjects are scarce.

Sandberg *et al.* (1998) found only minor differences between the patients and same sex siblings in the SF-36 score. However, their GH status was not reassessed after completion of childhood GH therapy, thus the majority of those labelled as isolated GHD, and hence the cohort overall, would turn out to be normal subjects if re-tested (Murray *et al.* 1999).

In the other study, scoring of QoL using generic Nottingham Health Profile questionnaire in adolescents with GHD was normal. However, these patients had slightly poorer scoring in terms of depression, general health and anxiety (Wirén *et al.* 2001).

Also in the study by Attanasio *et al.* (2005) using disease-specific questionnaire (QLS-H), the overall QoL assessment in CO-GHD was similar as the average of the general population. On the other hand, they showed significant differences for the ability to become sexually aroused, ability to tolerate stress, body shape, concentration, physical stamina and self confidence.

Stheneur *et al.* (2011) suggest that some psychological impacts among patients treated with GH during childhood, may persist in late adolescence. Although their social adjustment and quality of life is similar to the general population despite lower-than-average final height, a negative impact on sexuality and relationships with members of the opposite sex is noted.

About half of the GHD patients, especially those in whom GH treatment was started after the age of 12 years, complained of retrospective difficulties with self-confidence and social contact, and about one-quarter of the patients had current difficulties with self-confidence, social contact, contact with the opposite sex and with emotional life. The educational level of patients with a height deficit < –3 SDS at start of GH therapy was lower than in patients with a height deficit > –3 SDS. Parents of GHD patients frequently expect difficulties in finding a job, leaving home or in having a stable relationship (Lagrou *et al.* 2001).

It should be noted here, that in this study despite no significant differences in Social Functioning (SF) between examined groups were found, this score correlated negatively with treatment duration which was significantly longer in SGHD patients.

Some authors speculate that even small differences caused by GHD in such domains as memory function, energy, drive, and confidence as well as reduced illness and absenteeism in early adulthood could have major long-term effects. These subjects may be more prone to social difficulties, ill health and neuroses (Wirén *et al.* 2001). Therefore, it has been suggested that patients with severe GHD apart from GH replacement therapy should be given other interventions such as psychological counselling, exercise programmes, relaxation techniques and pharmacological interventions (Malik *et al.* 2003).

To explain the difference in self-reported QOL between AO- and CO-GHD patients it has been proposed that CO-GHD patients, who were born with, or have developed GHD early in life, had grown up with any problems it created, and therefore had little experience with which to contrast their current feelings (Hunt 1994). Moreover, currently available methods for measuring QoL in the transition period are limited and the marked mismatch between the perceived QoL of subjects with GHD and their affect, behaviour, and social and economic achievements in the eyes of others has been observed (Wirén *et al.* 2001). Self-rating questionnaires may thus underestimate the true impairment of QoL in CO-GHD adults (Murray *et al.* 1999). It is also not clear if in adult patients with persistent CO-GHD impaired QoL results from long-term consequences of paediatric GHD, the actual adult GHD syndrome or combination of these two components (Attanasio *et al.* 2005).

Unfortunately, in the available literature there is no study comparing QoL-AGHDA scores in young adults with CO-GHD and healthy controls to which we would be able to compare our results.

Bülow and Erfurth (1998) in a small group of young adults (aged 21–28 years) with childhood-onset growth hormone deficiency (idiopathic or multiple pituitary deficiencies) demonstrated high QoL-AGHDA (that means poor quality of life), which markedly improved after 9 months of treatment with recombinant growth hormone. Similar results were obtained by Hilczer *et al.* (2008) in Polish population of young adults (aged 17.6±1.5 years) with CO-GHD. The mean QoL-AGHDA score in their study was higher than obtained by us, however they examined also subjects after neurosurgery due to *craniopharyngioma*, whereas none of our patients had neoplasm or neurosurgery in the past history.

To our knowledge, we are the first reporting that QoL in patients with partial growth hormone deficiency is similar than that with normal GH secretion. These data are not surprising considering PGHD sub-

jects shortly after growth hormone therapy was stopped do not present any significant differences according to their height and IGF-1 concentrations in comparison to patients with idiopathic short stature with normal growth hormone secretion (Smyczyńska *et al.* 2007). However, it is possible, that QoL in PGHD may deteriorate in time analogously to the appearance of metabolic, body composition and cardiac abnormalities (Taubert *et al.* 2003; Shalet 2010). This hypothesis may be supported by the fact that AGHDA-QoL scores correlate with age (Moock *et al.* 2011), although further prospective studies to elucidate this question are needed.

Our findings also indicate that generic health surveys are more sensitive in recognizing impaired QoL in adolescents and young adults with CO-GHD. This may result from discrete changes in some aspects of their physical or emotional health (Hunt 1994; Attanasio *et al.* 2005), which is supported by significant correlations of PF and RE components of SF-36 v.2 with peak GH in ITT.

Interestingly, Suzukamo *et al.* (2006) demonstrated that some subscales of the SF-36 (General Health and Role Physical) were better for discriminating GHD patients from controls than disease-specific QoL-AGHDA survey. They concluded that QoL-AGHDA scores may be good indicators of mental and psychosocial status, but not of the effects of physical problems. Considering the fact, that the QoL-AGHDA cannot differentiate the effects of too much growth hormone from the effects of too little (Barkan *et al.* 2001) the content validity of the QoL-AGHDA may therefore need to be re-evaluated.

In conclusion, our study demonstrated that the QoL in adolescents and young adults with severe GHD in transition period is disturbed mainly in terms of physical health and emotions. The disease-specific QoL-AGHDA score is insufficient to detect these changes which are revealed only by generic SF-36 questionnaire. This raises the question if AGHDA-QoL assessment is applicable in GHD patients in transition period. QoL in transition phase of adolescents and young adults with partial GHD is unchanged in comparison to growth hormone sufficient subjects.

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