

PREVALENCE AND CORRELATES OF ADHERENCE IN CHILDREN AND ADOLESCENTS TREATED WITH GROWTH HORMONE: A MULTICENTER ITALIAN STUDY

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ABSTRACT

Objective: To evaluate the self-reported prevalence of poor adherence to recombinant human growth hormone (rhGH) therapy in a large, representative sample of Italian children and adolescents and to assess treatment and patient level correlates of poor adherence.

Methods: The study was conducted in 46 pediatric centers throughout Italy. A questionnaire was administered to consecutive children/adolescents treated with rhGH or their parents. Eligible patients were represented by subjects aged between 6 and 16 years, of both sexes, on rhGH treatment for at least 6 months. The questionnaire was administered to the person in charge of preparing the injection. Multivariable logistic regression analysis was performed to identify factors independently associated with adherence.

Results: Overall, 1,007 children/adolescents were involved, of whom 24.4% missed 1 or more injections during a typical week and were thus considered as nonadherent. The most frequently reported reasons for missing a dose were being away from home (33.3%), forgetfulness (24.7%), not feeling well (12.9%), and pain (10.3%).

Multivariable analysis indicated association between poor adherence and adolescence, low level of parent education, longer duration of treatment, need to convince the child to inject, and low level of awareness of the consequences of not properly following treatment. The likelihood of adherence markedly increased with higher levels of perceived device convenience.

Conclusion: Poor adherence is still a major problem in the treatment of growth disorders. Increasing awareness and reassessment of treatment adherence on an annual basis should be part of clinical practice of pediatric endocrinologists involved with rhGH treatment.

Abbreviations:

CI = confidence interval; GH = growth hormone; rhGH = recombinant human growth hormone

INTRODUCTION

From 1985, the availability of the recombinant growth hormone (rhGH) has increased the possibility of treating a larger number of children and adolescents with a wide range of different conditions, with the aim of normalizing linear growth as quickly as possible and attain a “normal adult height,” while minimizing risks and cost (1). The achievement of an optimal growth response during rhGH therapy is influenced by several factors such as age at treatment start, diagnosis, GH dose, duration of treatment and specifically by adherence to the prescribed GH dose (2-4). There is no unequivocal definition of adherence; according to the World Health Organization, adherence is defined as the extent to which a person’s behavior with regard to taking medication corresponds with agreed recommendations from a healthcare professional (5). Drug adherence in pediatrics is unique because of the involvement

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of a third party (i.e., the parent/guardian) and because the child is often unaware of the purpose of the medication and is reluctant to take it (6). Depending on the definition and methods used, suboptimal adherence to GH treatment has been reported to vary between 18 and 95% (7). In one study, 66% of the patients had missed more than 1 injection per week, based on the number of GH vials returned (8). In another study, 23% of the patients had missed more than 2 doses per week, based on documented GH usage versus amount prescribed (3).

Barriers to GH therapy adherence in pediatric patients may include medication factors (e.g., apparent ineffectiveness, inadequate supply, and side effects), scheduling factors (social convenience), logistics of portability of the device, and cognitive/emotional problems (e.g., forgetfulness, concerns, low level of understanding of the disorder, lack of symptoms, fear of needles, poor tolerability, and inadequate family support) (7). Additional barriers in adolescence may include denial, peer pressure, and reluctance to seek medical advice (9-12). Many of these factors have been found to be associated with poor adherence in some studies but not others.

Starting from these premises, aim of this study was to evaluate the prevalence of nonadherence to rhGH therapy in a large, representative sample of Italian children and adolescents and to assess treatment- and patient-level correlates of poor adherence using a questionnaire.

METHODS

The study was conducted in 46 pediatric centers affiliated with the Italian Society for Pediatric Endocrinology and Diabetes (SIEDP/ISPED). Centers were uniformly distributed throughout Italy. In the period from November 2015 to May 2016, 1 questionnaire per person was provided to consecutive children/adolescents treated with any rhGH or their parents. Eligible patients were represented by subjects aged between 6 and 16 years, of both sexes, on rhGH treatment for at least 6 months.

The questionnaire was provided to the person in charge of preparing the injection, either the child/adolescent or the parent during a follow-up visit; self-reported answers by the person filling the questionnaire were then analyzed. It included 27 items investigating demographics, treatment type and duration, adherence (injections missed), reasons for missing an injection (more than one allowed), ease of use and reliability of the device used, satisfaction with therapy, levels of understanding of the disease and the importance of therapy, and how often the parent needed to convince the child to inject (never, sometimes, often, always) (Appendix 1). Pain during the injection was assessed through a visual analogue scale, ranging from 1 (absence of pain) to 10 (severe pain). Adherence was arbitrarily defined as no injection missed over a typical week, while nonadherence as ≥ 1 injection missed over a typical

week during the last 12 months of rhGH; a “typical week” was defined as a week during school time in the last 12 months of rhGH treatment. When parents had different levels of school education, the highest level was considered. The questionnaire was self-administered during a routine follow-up visit and was completely anonymous: no patient-specific information was requested including data on demographics, disease specificity, or rhGH brand, so informed consent was not needed.

Statistical Methods

Descriptive statistics are reported in terms of absolute frequencies and percentages for qualitative data, and the Pearson χ^2 test or Fisher exact test, if appropriate, were applied to compare proportions. Quantitative data are described in terms of median values and interquartile range (IQR) values due to their nonnormal (Gaussian) distribution. Accordingly, comparisons between groups were performed by the nonparametric Mann-Whitney *U* test. Bivariate analysis of study variables for comparison between adherent and nonadherent subjects was applied, excluding missing data.

Multivariable logistic regression analysis was performed to identify factors independently associated with adherence. Variables significantly and independently associated with adherence at bivariate analysis or possible confounders were entered in the model: age, highest level of parent education, duration of GH therapy, device convenience, how often the parent has to convince his child to inject, and awareness of the consequences of not properly following treatment. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. To measure the global effect of each predictor on the outcome, the likelihood ratio test and test for trend (considering variables as continuous) were applied. All tests were 2 tailed, and $P < .05$ was considered significant. Analyses were performed with Stata software version 11.0 (Stata Corp, College Station, TX).

RESULTS

Overall, 1,007 children/adolescents treated with rhGH were involved. The questionnaire was filled in by 771 (76.6%) parents and 221 (21.9%) patients; for 15 (1.5%) additional questionnaires, the person filling in the questionnaire was not known.

Patient characteristics and descriptive statistics of the answers to the questionnaire are reported in Table 1. All age classes were well represented. The duration of rhGH therapy exceeded 3 years in almost half of the sample, while the duration of use of the current device was over 12 months in 70.3% of participants. The injection was prepared by the parent in 76.8% of the cases. The median time for the preparation of the injection was 5 minutes (IQR 2-10) with great variability (<1 to 30 minutes) among subjects. We found that 1 in 3 children/adolescents

injected rhGH alone, with the proportion increasing with the age of participants (12.8%, 25.0%, 40.9%, and 52.2% for age classes 8-9, 10-11, 12-13, and 14-15, respectively; $P < .001$). When the child/adolescent self-injected rhGH, a parent was always present in 45.7% of the cases, while in only 12.7% of the cases they were never present. Injection was associated with no or little pain for most of the participants (86.9%), and 60.8% of them considered important/very important having a device covering the needle while injecting. Almost one-third of the children/adolescents were reluctant in getting the injection, and parents needed to convince them at least in some instances. The vast majority of participants felt confident regarding the dose administered, considered the device convenient, and were satisfied with it. Also, over 90% of the participants reported a moderate to high degree of knowledge of their condition, considered rhGH therapy important, and were aware of the benefits and consequences of not properly following the therapy. The level of satisfaction with the treatment and the time dedicated to the child by the healthcare team were generally high.

Overall, 72.1% of participants reported they never missed an injection during a typical week, 22.4% missed 1 injection, 2.0% missed 2 or more injections, and 3.5% did not answer this question. Poor adherence, defined as missing at least 1 injection during the week, was reported by 24.4% (246) of participants that were further asked about the most frequent reasons for missing a dose with multiple answers being allowed. A total of 348 answers were received by the 246 nonadherent subjects, and the most frequently reported were being away from home (33.3%), forgetfulness (24.7%), not feeling well (12.9%), and pain (10.3%) (Fig. 1).

Characteristics of children/adolescents and parents according to adherence are reported in Table 2. Nonadherence increased with the age of children/adolescents, although this was not statistically significant. Adherent patients were more likely to have a parent with a high level of school education; they also showed a shorter duration of GH treatment and a shorter duration of use of the current device. Greater adherence was associated with administration of the injection by the parent and less pain. The level of confidence regarding the dose administered, convenience of the device, and overall satisfaction with it were also associated with adherence. Nonadherence was most common when the parent had to convince the child to inject, and when the importance of GH therapy and the consequences of not properly following it were not fully understood. Finally, adherence was significantly associated with overall treatment satisfaction and time dedicated to the child by the healthcare team.

Multivariable analysis confirmed that several factors are associated with level of adherence (Table 3). In particular, adolescents aged 14 to 15 years were 63% less likely than children aged 6 to 7 years to be adherent to GH

therapy. The likelihood of adherence increased with parent education level: children having a parent with a high school degree were 1.6-fold more likely to be adherent, and those with a college-educated parent were about 2-fold more likely to be adherent compared to children having a parent with a primary school education. Adherence decreased with increasing treatment duration; compared to a duration of less than one year, the likelihood of adherence decreased by 50%, 73%, and 61% for treatment durations of 1 to 3 years, 3.1 to 5 years, and >5 years, respectively. The likelihood of adherence markedly increased with greater levels of device convenience: perceiving the device as “very convenient” was associated with a 4 times greater likelihood of being adherent compared to considering the device as “not convenient at all.” On the other hand, the frequent need to convince the child to inject was associated with a substantial reduction in the likelihood to be adherent. Finally, the level of awareness of the consequences of not following treatment properly was independently associated with the likelihood of poor adherence.

DISCUSSION

The prevalence of poor adherence to GH therapy on growth has been reported in several studies (3,8,13,14), but only few were large enough to allow analysis of the combined effect of different risk factors. The importance of maintaining rhGH without interruption has been emphasized by clinical practice guidelines issued by the American Association of Clinical Endocrinologists (15) and the Endocrine Society (16). One of the largest cohort reported on 217 naïve patients across 6 pediatric endocrinology centers showed that good adherence to therapy was associated with greater height velocity (17). Our study involved 46 pediatric clinics and a very large number of children/adolescents treated with rhGH, representing almost one-tenth of all patients in Italy. The study showed that 1 in 4 participants missed at least 1 injection a week, thus confirming that poor adherence is still a major problem in the treatment of growth disorders. Poor adherence was associated with increasing patient age, low parent level of school education, and with longer treatment duration. The frequent need to convince the child to inject was also associated with suboptimal adherence. On the other hand, perceiving the device as convenient markedly increased the likelihood of GH therapy adherence. Major reasons for missing a dose were reported to be scheduling issues (being away from home), forgetfulness, intercurrent illness, and pain. Some of the former factors may be improved by using long-acting GH compounds that represent a novel treatment approach of growth disorders not yet commercially available (18). Thus, the impact of long-acting GH treatment on adherence needs to be proven.

Comparison with current literature is made difficult by the different definitions of nonadherence. In a study on 75

Table 1		
Patient/Parent Characteristics and Answers to the Questionnaire (N = 1,007)		
Characteristic	n	%
Age of child/adolescent, n (%)		
6-7	95	9.4
8-9	135	13.4
10-11	209	20.8
12-13	216	21.5
14-15	263	26.1
Missing	89	8.8
Highest level of education of the parent, n (%)		
Primary school	221	22.0
High school	481	47.8
Graduated	286	28.4
Missing	19	1.8
Duration of GH therapy, n (%)		
6-11 months	160	15.9
1-3 years	373	37.0
3.1-5 years	231	22.9
>5 years	229	22.7
Missing	14	1.4
Duration of use of current device, n (%)		
<6 months	67	6.7
6-12 months	200	19.9
>12 months	708	70.3
Missing	32	3.2
Number of injections missed in a typical week, n (%)		
None	726	72.1
1	226	22.4
≥2	20	2.0
Missing	35	3.5
GH injection performed by, n (%)		
Parent	675	67.0
Child/adolescent	324	32.2
Missing	8	0.8
GH injection prepared by, n (%)		
Parent	773	76.8
Child/adolescent	224	22.2
Missing	10	1.0
Time for the preparation of the injection (minutes), median (IQR)	5	2-10
Pain during injection, n (%)		
No pain	445	44.2
Little pain	430	42.7
Pain	91	9.7
A lot of pain	17	1.0
Excruciating pain	6	0.6
Missing	18	1.8
Importance of having a device that covers the needle during injection, n (%)		
Not important	259	25.7
Of little importance	103	10.2
Important	278	27.6
Very important	334	33.2
Missing	33	3.3

Table 1 Continued		
Confident of having administered the right dose, n (%)		
Not at all	2	0.2
Uncertain	35	3.5
Confident	383	38.0
Absolutely confident	578	57.4
Missing	9	0.9
Convenience of the device, n (%)		
Not convenient at all	34	3.4
Inconvenient	115	11.4
Convenient enough	472	46.9
Very convenient	354	35.2
Missing	32	3.2
Satisfaction with the device, n (%)		
Not satisfied at all	5	0.5
Unsatisfied	23	2.3
Satisfied enough	411	40.8
Very satisfied	533	52.9
Missing	35	3.5
How often the parent has to convince their child to inject, n (%)		
Never	663	65.8
Sometimes	169	16.8
Often	88	8.7
Always	50	5.0
Missing	37	3.7
Degree of knowledge of the disease, n (%)		
None	7	0.7
Low	39	3.9
Moderate	518	51.4
High	404	40.1
Missing	39	3.9
Importance of GH therapy for the child's health, n (%)		
Not important	0	0.0
Of little importance	6	0.6
Important enough	176	17.5
Very important	791	78.6
Missing	34	3.4
Awareness of the consequences of not following treatment properly, n (%)		
Unaware	30	3.0
Little awareness	43	4.3
Aware enough	301	29.9
Fully aware	587	58.3
Missing	46	4.6
Treatment satisfaction, n (%)		
Not satisfied at all	0	0.0
Unsatisfied	16	1.6
Satisfied enough	293	29.1
Very satisfied	663	65.8
Missing	35	3.5
Satisfaction with the time dedicated to the child by healthcare team, n (%)		
Not satisfied at all	0	0.0
Unsatisfied	8	0.8
Satisfied enough	233	23.1
Very satisfied	732	72.7
Missing	34	3.4

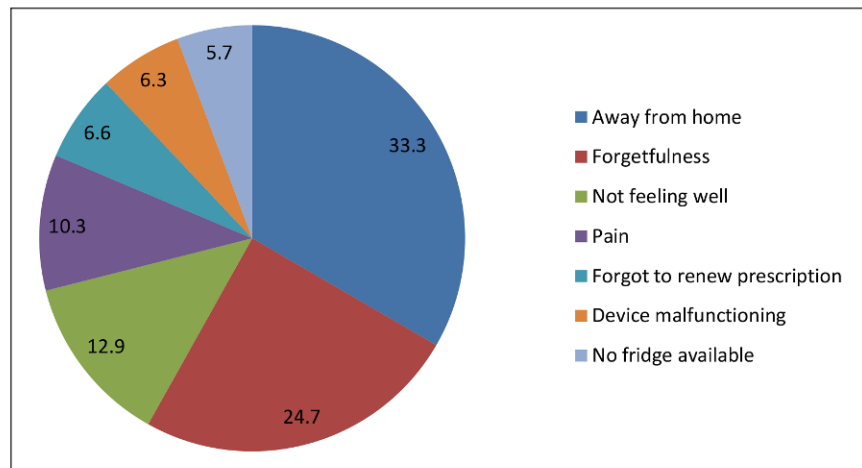


Fig. 1. Frequencies (%) of the most frequent reasons for missing a recombinant human growth hormone dose.

patients in UK, 39% had missed >1 injections per week, and 24% had missed >2 injections (3). In another study involving 175 patients in New Zealand, 34% had missed >1 injection per week (8). In a larger study on 631 patients in North America (13), the proportion of patients missing ≥ 3 injections per month ranged between 15 and 24%. Overall, our data suggest slightly better adherence to rhGH therapy in Italy, with 22.4% of participants missing 1 injection and 2% missing 2 or more injections during one week.

As for correlates of poor adherence, in agreement with previous studies we found that adolescence is associated with higher levels of non-compliance (10,19,20). These findings call for education, empowerment, and support of the child and his/her family, particularly when the responsibility for managing the therapy is assigned to the adolescent.

In our study, the likelihood of poor adherence decreased with increasing levels of school education of the parent. School education can be considered as a proxy of socio-economic status, and an association between low socio-economic level, low levels of education, and poor adherence to rhGH therapy has been previously documented (14,21). Low education can also be associated with poor understanding of the disease and its treatment, suggesting that modalities and frequency of education and training for parents should be tailored to their specific needs and characteristics. In line with previous studies (3,22), we also found that the likelihood of being adherent decreased as rhGH therapy duration increased.

The need for a long-term commitment to daily subcutaneous injections has major implications for the child and their family. Reinforcing education and motivation, providing regular feedback about treatment efficacy, addressing specific barriers to adherence from the points of view of the child and his/her parents, and eliciting their preferences can help maintain adherence over time. In this respect, device choice can play an important role, and a recent study

showed that an injection-recording device could enhance the ability of physicians to monitor adherence (23). In our study, 17.2% of nonadherent children/adolescents versus 8.4% of adherent ones reported injection-associated pain. Indeed, puberty and self-administration of medication have been shown to be negative predictors of adherence to GH therapy, illustrating the importance of re-engaging with patients, parents, and caregivers on a regular basis (24).

The frequent need to convince the child to inject represented an independent correlate of nonadherence. These findings suggest that increasing device acceptability can improve adherence. Along the same line, we found that 1 in 5 nonadherent participants did not consider the device they were using to be convenient. Multivariate analysis showed perception of convenience of the device was by far the most important correlate of adherence. Offering patients different options of rhGH injection devices, preferably based on personalized characteristics (indications, formulations, waste, age, socio-economic status, simplicity) thus represents an important aspect, and restrictions of this choice for financial reasons may have negative effects on patient outcomes and potentially undermine longer-term health-economic benefits (7).

The study has limitations. First, adherence was defined arbitrarily and was self-reported, so the real frequency of injections may have been overestimated. Secondly, the study was conducted in current users, so no information on treatment dropouts was available. Finally, perceptions of parents can differ from those of children. Nevertheless, the results provide a realistic picture of the problems faced by the person in charge of preparing the injection, being it the parent or the child/adolescent.

CONCLUSION

Although adherence to GH therapy is difficult to assess reliably, the results of our survey in a large cohort

Table 2
Probability of Adherence to rhGH Therapy by Demographic,
Clinical, and Behavioral Risk Factors Based on Univariate Analysis

Characteristic, n (%)	Adherent n = 726^a	Nonadherent n = 246^a	P^b
Age of child/adolescent			.10
6-7	71 (10.6)	16(7.3)	
8-9	98 (14.7)	33 (15.1)	
10-11	161 (24.1)	45 (20.6)	
12-13	162 (24.3)	48 (21.9)	
14-15	175 (26.2)	77 (35.1)	
Highest level of education of the parent			.002
Primary school	139 (19.4)	71 (30.0)	
High school	358 (50.0)	108 (45.6)	
Graduated	219 (30.6)	58 (24.4)	
Duration of GH therapy			.001
6-11 months	135 (18.7)	22 (9.0)	
1-3 years	273 (37.9)	90 (36.7)	
3.1-5 years	149 (20.7)	73 (29.8)	
>5 years	164 (22.8)	60 (24.5)	
Duration of use of current device			.01
<6 months	54 (7.6)	11 (4.7)	
6-12 months	161 (22.6)	36 (15.3)	
>12 months	499 (69.9)	188 (80.0)	
GH injection performed by			.04
Parent	503 (69.4)	153 (62.2)	
Child/adolescent	222 (30.6)	93 (37.8)	
GH injection prepared by			.10
Parent	571(78.9)	182(74.0)	
Child/adolescent	152(21.1)	64(26.0)	
Pain during injection			.004
No pain	335 (46.7)	99 (40.6)	
Little pain	318 (44.3)	102 (41.8)	
Pain	51 (7.1)	34 (13.9)	
A lot of pain	9 (1.3)	8 (3.3)	
Severe pain	5 (0.7)	1 (0.4)	
Importance of having a device that covers the needle during injection			.27
Not important	195 (27.6)	60 (25.1)	
Of little importance	70 (9.9)	31 (13.0)	
Important	189 (26.7)	73 (30.5)	
Very important	253 (35.8)	75 (31.4)	
Confident of having administered the right dose			<.0001
Not at all	0 (0.0)	2 (0.8)	
Uncertain	21 (2.9)	13 (5.3)	
Confident	258 (35.6)	113 (46.1)	
Absolutely confident	446 (61.5)	117 (47.8)	
Convenience of the device			<.0001
Not convenient at all	17 (2.4)	17 (7.1)	
Inconvenient	80 (11.3)	33 (13.8)	
Convenient enough	334 (47.2)	123 (51.5)	
Very convenient	277 (39.1)	66 (27.6)	
Satisfaction with the device			.006
Not satisfied at all	5 (0.7)	0 (0.0)	
Unsatisfied	13 (1.9)	10 (4.2)	
Satisfied enough	280 (39.9)	115 (48.7)	
Very satisfied	404 (57.6)	111 (47.0)	

Table 2 Continued			
How often the parent has to convince their child to inject			<.0001
	Never	534 (76.1)	107 (45.5)
	Sometimes	100 (14.3)	64 (27.2)
	Often	43 (6.1)	40 (17.0)
	Always	25 (3.6)	23 (10.2)
Degree of knowledge of the disease			.62
	None	5 (0.7)	1 (0.4)
	Low	25 (3.6)	12 (5.1)
	Moderate	366 (52.4)	129 (54.7)
	High	302 (43.3)	94 (39.8)
Importance of GH therapy for the child's health			.04
	Not important	0 (0.0)	0 (0.0)
	Of little importance	3 (0.4)	3 (1.3)
	Important enough	116 (16.5)	52 (21.9)
	Very important	583 (83.1)	182 (76.8)
Awareness of the consequences of not properly following treatment			.001
	Unaware	23 (3.3)	7 (3.0)
	Little awareness	24 (3.5)	19 (8.1)
	Aware enough	201 (29.1)	89 (37.7)
	Fully aware	443 (64.1)	121 (51.3)
Treatment satisfaction			<.0001
	Not satisfied at all	0 (0.0)	0 (0.0)
	Unsatisfied	9 (1.3)	7 (2.9)
	Satisfied enough	187 (26.7)	91 (38.2)
	Very satisfied	504 (72.0)	149 (58.8)
Satisfaction with the time dedicated to the child by healthcare team			.007
	Not satisfied at all	0 (0.0)	0 (0.0)
	Unsatisfied	4 (0.5)	3 (1.3)
	Satisfied enough	151 (21.5)	72 (30.5)
	Very satisfied	548 (78.0)	161 (68.2)
^a Missing data were excluded from the analysis			
^b χ^2 test or Fisher exact test			

of children and adolescents show that the great majority of Italian patients treated with rhGH have good adherence to the scheduled treatment. The target for intervention should be focused on adolescents, patients treated for longer times, and those with parents with low education. Moreover, good device convenience could further increase treatment adherence. Increasing awareness and reassessment of treatment adherence should be part of clinical practice of pediatric endocrinologists involved with rhGH treatment, and future studies are needed to correlate clinical outcomes in terms of how adherence impacts height gain and metabolic consequences.

There is a need for multifactorial and effective interventions to improve adherence by combining risk-assessment and screening of poor adherent patients. Device choice, training family and patients, perception of parents and patient's behavior, and their support are determinant factors. Increasing awareness and reassessment of treatment adherence on an annual basis should be part of the clinical practice of pediatric endocrinologists involved with rhGH treatment.

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Table 3 Logistic Regression Results of Independent Variables Associated with Adherence		
	OR (95% CI)	P
Age of child/adolescent, years	0.83 (0.72-0.95)	.008 ^a
6-7	<i>ref.</i>	
8-9	0.55 (0.26-1.17)	
10-11	0.82 (0.40-1.70)	.0089 ^b
12-13	0.62 (0.30-1.27)	
14-15	0.37 (0.18-0.75)	
Highest level of education of the parent	1.35 (1.06-1.72)	.013 ^a
	<i>ref.</i>	
Primary school	1.62 (1.05-2.49)	.0216 ^b
High school	1.92 (1.19-3.11)	
Graduated		
Duration of GH therapy	0.74 (0.62-0.88)	.001 ^a
	<i>ref.</i>	
6-11 months		
1-3 years	0.50 (0.26-0.94)	.0004 ^b
3.1-5 years	0.27 (0.14-0.52)	
>5 years	0.39 (0.20-0.77)	
Convenience of the device	1.44 (1.16-1.79)	.001 ^a
	<i>ref.</i>	
Not convenient at all		
Inconvenient	2.30 (0.92-5.77)	.0098 ^b
Convenient enough	2.69 (1.19-6.06)	
Very convenient	3.91 (1.69-9.05)	
How often the parent has to convince their child to inject	0.49 (0.41-0.58)	<.001 ^a
	<i>ref.</i>	
Never	0.36 (0.23-0.56)	<.001 ^b
Sometimes	0.17 (0.10-0.30)	
Often	0.16 (0.08-0.32)	
Always		
Awareness of the consequences of not properly following treatment	1.37 (1.09-1.73)	.007 ^a
	<i>ref.</i>	
Unaware	0.51 (0.14-1.93)	.0249 ^b
Little awareness	0.82 (0.27-2.55)	
Aware enough	1.33 (0.43-4.06)	
Fully aware		

Abbreviations: CI = confidence interval; GH = growth hormone; OR = odds ratio.
^a Test for trend
^b Likelihood ratio test

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Appendix 1 Survey on GH Therapy Adherence

Center: _____

Type: University Center: Hospital Center:

Is available a dedicated nurse to GH therapy:
Yes No

Date of filling out the questionnaire: [][]/[][]/[][][][]

DEMOGRAPHIC DATA

Region of residence: _____

Person filling out the questionnaire:

Parent Child/Adolescent:

Age of child/adolescent:

- A. >6 years <8 years
- B. >8 years <10 years
- C. >10 years <12 years
- D. >12 years <14 years
- E. >14 years <16 years

1. The highest qualification or level of schooling of the father:

- A. Primary school
- B. High school
- C. Graduation
- D. Other

2. The highest qualification or level of schooling of the mother:

- A. Primary school
- B. High school
- C. Graduation
- D. Other

3. How long has the child/adolescent been treated with GH?

- A. 6-12 months
- B. 1-3 years
- C. >3 years
- D. >5 years

4. How long has the child/adolescent been using the current device?

- A. <6 months
- B. 6-12 months
- C. >12 months

5. Is the GH injection is performed by the child/adolescent?

- Yes No

6. If Yes, is the parent always present to control that the GH injection is being correctly performed?

- A. Yes, 7 days/7 days
- B. Yes, ≥ 5 days/7 days
- C. Not always, <5 days/7 days
- D. Never

7. Who is in charge of preparing the GH injection?

- A. Parent
- B. Child/adolescent

8. How long does it takes the preparation of the GH injection?

_____Minutes

(Please consider also the time needed before the preparation, after having retrieved the drug from the fridge)

9. Does it happen in a typical week during the last 12 months of GH therapy to miss an injection?

- A. Never
- B. Yes, once a week
- C. Yes, twice a week
- D. Yes, more than twice a week

10. For what reasons the child/adolescent might miss a GH injection in a typical week?

(number the reasons from 1-7 in order of importance: 1 is the most important)

- Forgetfulness
- Forgot to renew the prescription
- Pain during injection
- Not feeling well
- Away from home
- No fridge available
- Malfunctioning of the device

11. How do you define the level of pain that the child feels during the GH injection? (on a VAS scale)

1	2	3	4	5	6	7	8	9	10
No pain		Little pain		Pain		A lot of pain		Excruciating pain	

12. How important it is for the parent or his child to have a device that would cover the needle during the GH injection?

- A. Not important
- B. Of little importance
- C. Important
- D. Very important

13. The child/parent feels confident of having administered the right dose?

- A. Not at all
- B. Uncertain
- C. Confident
- D. Absolutely confident

14. How much does the parent believe that the device that the child is now using is convenient to be taken outside?

- A. Not convenient at all
- B. Inconvenient
- C. Convenient enough
- D. Very convenient

15. Overall, how much is the parent satisfied with the device now being used by the child?

- A. Not satisfied at all
- B. Unsatisfied
- C. Satisfied enough
- D. Very satisfied

16. How often does the parent have to convince the child to have the injection?

- A. Never: 0/7 days
- B. Sometimes: <5/7 days
- C. Often: ≥5/7 days
- D. Always: 7/7 days

17. How much is in your opinion the degree of knowledge about the child's disease?

- A. None
- B. Low
- C. Moderate
- D. High

18. How much does the parent believes that the GH therapy is important for the child's health?

- A. Not important
- B. Of little importance
- C. Important enough
- D. Very important

19. How much the parent is aware of the consequences of NOT properly following the prescribed schedule?

- A. Unaware
- B. Little awareness
- C. Aware enough
- D. Fully aware

20. Overall, is the parent satisfied with the prescribed therapy?

- A. Not satisfied at all
- B. Unsatisfied
- C. Satisfied enough
- D. Very satisfied

21. How much the parent is satisfied with the time that the medical team usually dedicate to him/her and to the child?

- A. Not satisfied at all
- B. Unsatisfied
- C. Satisfied enough
- D. Very satisfied

Abbreviations: GH = growth hormone; VAS = visual analogue scale.

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