Assessment of Parental Satisfaction with the Treatment of Human Recombinant Growth Hormone in Children with Hypopituitarism

Ocena satysfakcji rodziców z leczenia ludzkim rekombinowanym hormonem wzrostu dzieci z somatotropinową niedoczynnością przysadki

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Abstract

Introduction. Growth depends on genetic, metabolic and also hormonal factors. Growth depends on health, the supply of nutrients and a properly functioning nervous system. Growth hormone deficiency is a disorder that does not cause typical somatic symptoms, but has a negative impact on a child's life and functioning in society.
Aim. The aim of the study was to evaluate the satisfaction of parents with the treatment with human recombinant growth hormone in children with somatropin-induced pituitary insufficiency.
Material and Methods. The studies were conducted among parents of children with somatropin-induced pituitary insufficiency treated with human recombinant growth hormone in the Provincial Complex Hospital of Rydygier in Toruń at the Department of Paediatrics, Endocrinology, Diabetology and Paediatric Neurology, from 1.12.2019 to 1.02.2020. 69 parents of children treated with recombinant growth hormone were included in the study. The mean age of parents of children participating in the study was 11.77±3.53 years. The research tools were: a record, self-questionnaires and the standardized KIDSCREEN-52 health questionnaire for children and adolescents in the version for parents.
Results. The highest mean values of the standardized KIDSCREEN-52 scale in the version for parents were shown for the following areas: moods and emotions (84.55±12.73), relationships with parents and home (81.83±10.88) and social acceptance (89.86±12.86). It was found that the higher the quality of the area of physical well-being and health, the lower the need for mental preparation of the child for hospital visits in connection with treatment — r_S=0.254, p=0.035. The analyses showed that the higher the quality of the area of social support and colleagues, the smaller the difficulty resulting from the treatment-related visits to the hospital ward — r_S=0.266, p=0.027, there was also a lower need to mentally prepare the child for hospital visits — r_S=0.261, p=0.030.
Conclusions. Satisfaction with treatment with recombinant growth hormone depends on the duration of treatment and the growth results achieved. Parents of children with hypopituitarism are satisfied with the treatment with recombinant growth hormone and assess the treatment positively. **(JNNN 2021;10(3):120–125)**
Key Words: children, growth hormone, hypopituitarism, satisfaction of treatment

Streszczenie

Wstęp. Wzrastanie jest zależne od czynników genetycznych, metabolicznych a także hormonalnych. Wzrost jest uwarunkowany stanem zdrowia, dostarczeniem składników odżywczych i prawidłowo działającego układu nerwowego. Niedobór hormonu wzrostu to zaburzenie, które nie powoduje typowych objawów somatycznych, natomiast w sposób negatywny wpływa na życie dziecka i funkcjonowanie w społeczeństwie.

Cel. Celem prowadzonego badana była ocena satysfakcji rodziców z leczenia ludzkim rekombinowanym hormonem wzrostu dzieci z somatotropinową niedoczynnością przysadki.

Materiał i metody. Badania prowadzone były wśród rodziców dzieci z somatotropinową niedoczynnością przysadki leczonych ludzkim rekombinowanym hormonem wzrostu w Wojewódzkim Szpitalu Zespolonym im. Rydygiera w Toruniu na oddziale Pediatrii, Endokrynologii, Diabetologii i Neurologii Dziecięcej, w terminie od 1.12.2019 do 1.02.2020 r. Do badania włączono 69 rodziców dzieci leczonych rekombinowanym hormonem wzrostu. Średni wiek rodziców dzieci biorących udział w badaniu, wynosił 11,77±3,53 lat. Narzędziem badawczym były: metryczka, kwestionariusze ankiety własnej oraz standaryzowany kwestionariusz zdrowotny dla dzieci i młodzieży KIDSCREEN-52 w wersji dla rodziców.

Wyniki. Najwyższe średnie wartości, standaryzowanej skali KIDSCREEN-52 w wersji dla rodziców wykazano dla obszarów: nastroje i emocje (84,55±12,73), relacje z rodzicami i dom (81,83±10,88) oraz akceptacja społeczna (89,86±12,86). Stwierdzono, że im wyższa jakość obszaru samopoczucia fizycznego i zdrowia, tym mniejsza potrzeba przygotowania psychicznego dziecka do wizyt w szpitalu w związku z leczeniem — r_S=0,254, p=0,035. Analizy wykazały, że im wyższa jakość obszaru wsparcia społecznego i kolegów, tym mniejsze utrudnienie wynikające z wizyt na oddziale szpitalnym związanych z leczeniem — r_S=0,266, p=0,027, również obserwowano mniejszą potrzebę przygotowania psychicznego dziecka do wizyt w szpitalu — r_S=0,261, p=0,030.

Wnioski. Satysfakcja z leczenia rekombinowanym hormonem wzrostu jest zależna od czasu trwania kuracji i osiągniętych rezultatów wzrostowych. Rodzice dzieci z somatotropinową niedoczynnością przysadki są usatysfakcjonowani z leczenia rekombinowanym hormonem wzrostu i oceniają kuracje pozytywnie. **(PNN 2021;10(3):120–125)**

Słowa kluczowe: dzieci, hormon wzrostu, niedoczynność przysadki, satysfakcja leczenia

Introduction

The pituitary gland is an endocrine gland. It is located in the Turkish saddle in the centre fossa of the skull. Hypopituitarism is associated with the insufficient secretion of pituitary hormones. Pituitary cells produce hormones that stimulate, among others, the endocrine glands (thyroid, adrenal glands, gonads) to synthesize and release hormones necessary for the proper functioning of the body [1,2].

Somatotropic hypopituitarism (SNP) results from impaired growth hormone secretion by pituitary somatotropic cells during the developmental period, resulting in impaired growth rate. SNP may occur as an isolated disease, and in the absence of the secretion of other pituitary hormones, multi-hormonal pituitary insufficiency (CIS) occurs [2,3].

Growth hormone (GH) called somatotropin is produced by the cells of the anterior pituitary gland. GH molecules consist of 191 amino acids in a polypeptide chain. The GH gene is found on the arm of chromosome 17. In the blood plasma, GH circulates with binding proteins. The concentration of the hormone in the blood rises in short intervals. GH synthesis occurs in somatotropic cells, which are located laterally in the anterior pituitary gland. A healthy person secretes about 400 mg GH daily, during adolescence this amount is twice as high. The secretion of the hormone is pulsating during the day and at night. A much larger part of the hormone is released at night (70–80%) during sleep. The greatest secretion occurs 1–2 hours after falling asleep in the deep sleep phase [2–5].

The role of the growth hormone is to stimulate growth processes. Cellular processes are stimulated. The hormone released from the pituitary gland affects all cells of the body. Ultimately, these are liver cells. When the signal is received by the receptor, insulin-like growth factor IGF-1 is synthesized, which acts directly on target cells, triggering cell division [2,4,5].

Short stature is defined as the condition of a child's height below two standard deviations (SD) from the norm for gender and age, and when the child's height is below the 3rd percentile on the grid. In practice, the actual child's height is compared with the percentile grids for a given population, e.g. for Polish children. Short stature affects 3% of the population (<3 percentile) to 1.5% (<–2 SD) [6–8].

The diagnosis of short stature and the necessity to enter the treatment program causes moral dilemmas in parents about the correctness of the treatment, doubts whether their children will grow up. The disease and the related treatment method require the involvement of the whole family in the therapeutic process. The family must be trained in the administration of growth hormone, its storage and dosing. Currently, in Poland, treatment with recombinant human growth hormone is reimbursed under the Drug Programs of the National Health Fund. The treatment covers children with Somatotropin Hypopituitarism (SNP), Chronic Renal Failure (CRF), Turner Syndrome (TS), Prader-Willie Syndrome (PWS) and children with low birth weight in relation to the duration of pregnancy (SGA). While growth hormone treatment is safe, it requires strict adherence to therapy monitoring. Administering the hormone in the form of daily infections is burdensome and very stressful for younger children. The multidirectional action of GH improves the quality of life of young patients, and thus positively influences their development in the peer group. Initially, when the child grows a lot, the parents perceive the therapy positively. With time, doubts arise as to the

effectiveness of the therapy when the growth gain is much smaller. Control visits to the ward every 3 months disrupt everyday life, parents must be free from work. Treatment affects the quality of life for the whole family. Children with (SNP) treated with a natural hormone achieve good growth results [9,10].

The aim of the study was to assess the satisfaction of parents with the treatment of human recombinant growth hormone in children with pituitary somatotropin insufficiency.

Material and Methods

The author's own research was conducted among parents of children with somatotropin pituitary insufficiency treated with human recombinant growth hormone in the Provincial Complex Hospital of Rydygier in Toruń at the Department of Paediatrics, Endocrinology, Diabetology and Paediatric Neurology, from 1.12.2019 to 1.02.2020. 69 patients were included in the study. The characteristics of the study group are included in Table 1.

The mean age of the children of the parents participating in the study was 11.77±3.53 years. The

Table 1. Characteristics of the study group

Variable	N	%
Gender		
Women	53	77
Men	16	23
Age of the surveyed parent		
Under 25 year	2	3
25–35 years	39	56
Over 35 years	28	41
Child's gender		
Boy	48	70
Girl	21	30
Place of residence		
City	42	61
Village	27	39
Professionally active parent		
No	20	29
Yes	49	71
Distance from the place of residence to the hospital		
Up to 5 km	13	19
5–10 km	21	30
Over 20 km	35	51

youngest child was one year old, and the oldest was 18 years old. The median age of the children was 12 years. The mean height of the children at the beginning of the treatment was 121.11±17.37 cm. The minimum height of the child at the beginning of treatment was 90.00 cm, while the maximum height was 160.00 cm, the median was 120 cm. The average height of the child at the time of filling in the questionnaires by the parents was 142.41±19.24 cm. The average increase in height from the beginning of treatment to the completion of the questionnaires was 20.87±11.45 cm, the minimum increase was 2.40 cm and the maximum was 49 cm, while the median was 20 cm. The mean period of child treatment up to the time of study of the respondents was 32.75±19.36 months, the median was 30 months, with a minimum period of 6 months and a maximum period of 88 months.

The research tools were: a record and questionnaires, which were used to implement the selected research technique. Patterns of the questionnaires used in the own research are presented in the Annex to this work.

The record sheet consisted of 12 single-choice closed questions, in which it was possible to obtain basic socio-demographic data about the parents and the child.

The questionnaire consisted of 12 single-choice closed questions, in which it was possible to obtain information on the assessment of parents' satisfaction with the treatment of children with somatotropin hypopituitarism, human recombinant growth hormone.

The study also used the standardized health questionnaire for children and adolescents KIDSCREEN-52 in the version for parents, which is used to study 10 dimensions of quality of life: physical well-being (W1), mental well-being (W2), moods and emotions (W3), self-image (W4), independence (W5), relationships with parents and home (W6), financial resources (W7), social support, colleagues (W8), school environment (W9) and social acceptance (W10). The questionnaire contained 52 single-choice questions on a 5-point Likert scale. The categories were frequency (never, rarely, quite often, often, always) or intensity (not at all, little, medium, very, hugely). Only in the first question about the state of health, it was necessary to indicate the answer according to other categories, defining health as: excellent, very good, good, so-so or bad. 14 questions in the questionnaire had a negative orientation, which was re-coded during the analyses. After recoding, all analysed indexes of the questionnaire had a positive orientation, high scores meant a good quality of life [11].

Results

The statistical analysis of individual areas of the KIDSCREEN-52 health questionnaire for children and adolescents in the version for parents was performed. The highest mean values of the standardized scale were found for the following areas: moods and emotions (84.55±12.73), relations with parents and home (81.83±10.88) and social acceptance (89.86±12.86). The results showed a high level of quality of life in these areas. The lowest average values, indicating a low level of quality of life, were presented by the following areas: financial resources (70.14±17.44), social support and colleagues (65.51±16.60) and school environment (67.34±15.78).

The relationship between individual areas of treatment assessment/parental satisfaction and the areas of children's quality of life was analysed. For this purpose, the Spearman rank correlation coefficient was used. Statistically significant relationships were observed for six pairs of variables. It was found that the higher the quality of the area of physical well-being and health, the lower the need for mental preparation of the child for hospital visits in connection with treatment — the r_S coefficient was 0.254, p=0.035. The analyses showed that the higher the quality of the area of social support and colleagues, the smaller the difficulty resulting from the treatment-related visits to the hospital ward — the

r_S coefficient was 0.266, p=0.027, and there was also a lower need to prepare the child mentally for hospital visits — the r_S coefficient was 0.261, p=0.030. The higher level of financial resources was significantly associated with a smaller increase in the child's self-esteem as a result of the treatment used — the r_S coefficient =0.275, p=0.22, and a lower effect of treatment on a more positive perception of the child in the peer group — the r_S coefficient =0.264, p=0.028. It was found that the higher the quality of the area of the school environment, the less the impact of treatment on a more positive perception of the child in the peer group — the r_S coefficient was 0.277, p=0.021 (Table 2).

A correlation analysis of individual areas of treatment evaluation and the length of the treatment period was performed. A statistically significant relationship was observed for the difficulty associated with visits to the ward during the treatment. The coefficient r_S=0.279 at the level of p=0.020 meant that with the lengthening of the treatment time, visits to the ward became less of a difficulty. The second statistically significant relationship was observed for the compliance of the treatment effect with the parents' expectations. The r_S coefficient =−0.406 at p=0.001 meant that the longer the treatment lasted, the treatment effect was more in line with the parents' expectations. Moreover, a correlation analysis of individual areas of treatment assessment and the achieved child growth was performed. A statistically significant

Table 2. Correlations of individual areas of assessment of treatment/parental satisfaction with the indicators of the KIDSCREEN-52 questionnaire of the version for parents

Treatment assessment area		W1	W2	W3	W4	W5	W6	W7	W8	W9	W10
		Quality of life area (indicator)									
Difficulty related to visiting the ward during the treatment (every 3 months)	p	0.433	0.067	0.192	0.982	0.806	0.076	0.773	0.027	0.986	0.934
	r_S	0.096	0.221	−0.159	0.003	0.030	0.215	−0.035	0.266	0.002	0.010
The need for mental preparation of a child for hospital visits during treatment	p	0.035	0.307	0.670	0.724	0.258	0.338	0.192	0.030	0.375	0.090
	r_S	0.254	0.125	0.052	0.043	0.138	0.117	0.159	0.261	0.108	0.205
Child's fear of check-up during the stay in the ward	p	0.171	0.915	0.133	0.917	0.921	0.493	0.228	0.505	0.382	0.194
	r_S	0.167	−0.013	0.183	−0.013	−0.012	−0.084	0.147	0.082	−0.107	0.158
Problems with storing growth hormone during trips	p	0.210	0.248	0.690	0.359	0.280	0.486	0.920	0.219	0.887	0.376
	r_S	0.153	0.141	0.049	−0.112	−0.132	0.085	−0.012	0.150	−0.017	0.108
Increased child's self-esteem as a result of treatment	p	0.589	0.485	0.907	0.489	0.587	0.838	0.022	0.206	0.021	0.840
	r_S	−0.066	0.086	0.014	0.085	0.067	−0.025	0.275	0.154	0.277	0.025
Effect of treatment on the perception of a child in the peer group	p	0.531	0.999	0.809	0.374	0.882	0.753	0.028	0.862	0.194	0.708
	r_S	−0.077	0.000	−0.030	0.109	−0.018	−0.039	0.264	0.021	0.158	−0.046
Child's stress related to hormone administration	p	0.133	0.692	0.470	0.486	0.217	0.667	0.958	0.149	0.360	0.096
	r_S	0.183	−0.049	0.088	0.085	−0.150	−0.053	0.007	0.176	−0.112	0.202
Compliance of treatment effects with parents' expectations	p	0.669	0.097	0.783	0.764	0.179	0.426	0.157	0.138	0.101	0.541
	r_S	0.052	0.201	−0.034	−0.037	−0.164	0.097	0.172	0.181	0.199	−0.075
Assessment of quality of life during treatment	p	0.236	0.536	0.560	0.187	0.945	0.943	0.300	0.476	0.341	0.691
	r_S	−0.145	0.076	0.071	0.161	−0.009	−0.009	0.126	0.087	0.116	−0.049

Table 3. Correlations between individual areas of treatment assessment/parental satisfaction and the length of the treatment period and the achieved increment

Treatment assessment area	Length of the treatment period		Achieved gain (cm)	
	p-value	r_S	p-value	r_S
Difficulty related to visiting the ward during the treatment (every 3 months)	0.020	0.279	0.042	0.249
Mental preparation of the child for hospital visits during treatment	0.122	0.188	0.470	0.090
Child's fear of check-ups during the stay in the ward	0.308	0.125	0.769	0.037
Problems with storing growth hormone during trips	0.120	–0.189	0.032	–0.263
Increased child's self-esteem as a result of treatment	0.462	–0.090	0.054	–0.236
Effect of treatment on the child's perception in the peer group	0.229	–0.147	0.062	–0.229
Child's stress related to hormone application	0.163	0.170	0.781	0.035
Compliance of treatment effects with parents' expectations	0.001	–0.406	0.000	–0.458
Assessment of quality of life during treatment	0.395	–0.104	0.187	–0.163

r_S — Spearman's rank correlation coefficient

relationship was observed for the difficulty associated with visits to the ward during the treatment. The coefficient r_S=0.249 at the level of p=0.042 meant that with the greater achieved growth, visits to the ward became less of a difficulty. The second statistically significant relationship was observed for the problem of storing growth hormone during trips/holidays. The coefficient r_S=–0.263 at the level of p=0.032 meant that the longer the treatment lasted, the problem of storing the hormone during the trips increased. The analyses also showed that the achieved increase in the child's height correlated with the compliance of the treatment effect with the parents' expectations. The coefficient r_S=–0.458 at p=0.000 meant that the greater the increase, the treatment effect was more in line with the parents' expectations (Table 3).

Discussion

Growth hormone therapy is being promoted around the world. The advancement of medicine allows you to achieve a height that is satisfactory for both the child and the parents. Children with growth failure are perceived as younger, often isolated in the peer group. In these children, depression and anxiety disorders can be observed. Concerns about short stature lead parents to explain the causes of short stature and possibly treat them. The use of therapeutic methods that allow for treatment causes many parents to visit their GP, and then an endocrinologist. It was found that short stature is related to anxiety of parents and the child. Initially, when the child does not pay attention to his height, a visit to the endocrinologist and the signal that he will be treated gives the child a feeling that the parent does not accept his appearance. The child builds a self-image and self-esteem on the basis of how it is perceived by relatives and parents. Parents want their child to be included in the treatment program at all costs. This allows you to reassure your conscience and feel that everything was done to facilitate the start of your child. Identification of short stature usually occurs in early school age, where the children themselves notice differences in height. Early and proper diagnosis helps to protect children from irreversible consequences, and also gives the opportunity to explain to parents the causes of growth disorders. Bielecka-Jesiocha et al. observed that low stature is burdened with numerous negative beliefs and stereotypes concerning, in particular, the characteristics, social relations, and educational and professional achievements of a short person. Similarly, short children have been described as less privileged in many spheres [12–14].

The conducted own studies on parental satisfaction with SNP treatment assume that the level of parental satisfaction with treatment can be assessed by evaluating the quality of life of children with short stature during treatment. The parent, who highly appreciates the quality of the child's life during the hormone treatment, positively assesses the entire treatment. He is satisfied with the entire therapy program. Quitmann et al. [15] showed that human growth hormone treatment increased the quality of life in the physical, social and emotional spheres. In turn, among untreated patients there was a decrease in the above-mentioned domains. Moreover, a statistically significant increase in body height was observed in patients treated with growth hormone. Moreover, Lee et al. [16] showed high effectiveness of growth hormone treatment after two years. The change in height in the standard deviations scale was greater in

born small for gestational age and smaller in patients with idiopathic short stature ISS compared to those with isolated growth hormone deficiency. The obtained differences may be due to the nature of the disease or to other confounding factors, such as age. Height gain was greatest among pre-adolescent children. This shows that starting treatment early optimizes growth results and is most effective.

Conclusions

Finally, parents of children with somatotropic hypopituitarism are satisfied with the treatment with recombinant growth hormone and evaluate the treatment positively. Satisfaction with treatment with recombinant growth hormone depends on the duration of treatment and the growth results achieved. The treatment effect is in line with the parents' expectations. Moreover, the conducted research and the obtained results suggest the necessity to conduct further such research during growth hormone therapy.

Implications for Nursing Practice

An important role of the nurse in caring for a child with somatotropic hypopituitarism is to educate both the child and parents. It is important to ensure that growth hormone is considered safe, it requires adherence to established principles of therapy monitoring, which include clinical evaluation and laboratory results. Treatment with recombinant growth hormone should be initiated as soon as possible. It is also important to provide information about the possibility of side effects and complications. The side effects are usually temporary and do not have any health consequences.

References

[1] Lecka-Ambroziak A., Walczak M., Szalecki M. Leczenie ludzkim rekombinowanym hormonem wzrostu dzieci niskorosłych w ramach programów lekowych NFZ. *Pediatr Dypl*. 2012;16(5):26–32.

[2] Bednarczuk T. (Red.), *Podstawy endokrynologii*. ITEM Publishing, Warszawa 2017.

[3] Pyrżak B., Walczak M. (Red.), *Endokrynologia wieku rozwojowego*. PZWL, Warszawa 2019.

[4] Oświęcimska J. Niedobór hormonu wzrostu u dzieci młodych i dorosłych. *Postepy Hig Med Dosw*. 2016;70:928–937.

[5] Pilch T., Bauman T. Zasady badań pedagogicznych. *Strategie ilościowe i jakościowe*. Wydawnictwo Akademickie „Żak", Warszawa 2010.

[6] Beń-Skowronek I. Leczenie niskorosłości u dzieci. *Forum Pediatrii Praktycznej*. 2016;11:6–16.

[7] Zhou E., Hauser B.R., Jee Y.H. Genetic evaluation in children with short stature. *Curr Opin Pediatr*. 2021; 33(4):458–463.

[8] Yadav S., Dabas A. Approach to short stature. *Indian J Pediatr*. 2015;82(5):462–470.

[9] Lewiński A., Smyczyńska J., Stawerska R. i wsp. Ogólnopolski Program Leczenia Ciężkiego Niedoboru Hormonu Wzrostu u Osób Dorosłych oraz u Młodzieży po Zakończeniu Terapii Promującej Wzrastanie. *Endokrynol Pol*. 2018;69(5):497–524.

[10] Zubkiewicz-Kucharska A., Lasota W., Tumilewicz U., Matula A., Seifert M., Noczyńska A. Wpływ wybranych czynników na skuteczność leczenia rhGH u dzieci z somatotropinową niedoczynnością przysadki. *Endokrynol Pediatr*. 13/2014;4(49):19–26.

[11] The Kidscreen Group Europe. *The KIDSCREEN questionnaires. Quality of life questionnaires for children and adolescents*. Pabst Science Publishers, Lengerich–Berlin–Bremen–Miami–Riga–Viernheim–Wien–Zagreb 2006.

[12] Bielecka-Jasiocha J., Rymkiewicz-Kluczyńska B. Psychospołeczne funkcjonowanie dzieci niskorosłych. *Endokrynol Pediatr*. 7/2008;1(22):71–80.

[13] Marini M.G., Chesi P., Mazzanti L. et al. Stories of experiences of care for growth hormone deficiency: the CRESCERE project. *Future Sci OA*. 2016;2(1):FSO82.

[14] Graham S., Auyeung V., Weinman J. Exploring Potentially Modifiable Factors That Influence Treatment Non-Adherence Amongst Pediatric Growth Hormone Deficiency: A Qualitative Study. *Patient Prefer Adherence*. 2020;14:1889–1899.

[15] Quitmann J., Bloemeke J., Silva N. et al. Quality of Life of Short-Statured Children Born Small for Gestational Age or Idiopathic Growth Hormone Deficiency Within 1 Year of Growth Hormone Treatment. *Front Pediatr*. 2019;7:164.

[16] Lee P.A., Sävendahl L., Oliver I. et al. Comparison of response to 2-years' growth hormone treatment in children with isolated growth hormone deficiency, born small for gestational age, idiopathic short stature, or multiple pituitary hormone deficiency: combined results from two large observational studies. *Int J Pediatr Endocrinol*. 2012;2012(1):22.

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