



The strategies of orthodontic treatment in children with growth hormone deficiency

Elżbieta Pels^{1,A-F}, Szymon Krzewski^{2,A-F}, Aleksandra Krzewska^{3,B,C,E},
Iwona Beń-Skowronek^{3,A,B,C,E}, Joanna Wawer^{4,D}, Michał Łobacz^{5,E-F}✉

¹ Chair and Department of Developmental Dentistry, Medical University of Lublin, Poland

² Stankowscy&Białach Dentistry, Lublin, Poland

³ Department and Clinic of Pediatric Endocrinology, Medical University of Lublin, Poland

⁴ Department of Experimental Immunology, Medical University of Lublin, Poland

⁵ Chair and Department of Oral Surgery, Medical University, Lublin, Poland

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Abstract

Introduction and objective. Growth hormone (GH) is crucial for body growth and affects parameters such as bone development. Malocclusions, resulting from discrepancies between the dental arches of the maxilla and mandible, are common in children with growth hormone deficiency (GHD). The study aimed to assess the frequency of malocclusions and dental irregularities in children treated for GHD and evaluate discrepancies between their skeletal, chronological, and dental ages.

Material and methods. The study included 43 children aged 7–17 years undergoing recombinant growth hormone therapy for GHD. A control group comprised 46 healthy children with similar socio-demographic conditions. Clinical dental examinations, alginate impressions, and panoramic X-rays were performed. Orthodontic analyses were conducted using OrtoBajt Ortoncja 9.1.1m software, and skeletal age was assessed through radiographic imaging.

Results. Children with GHD exhibited a significantly higher prevalence of malocclusions compared to the control group. Common issues included crowding, delayed skeletal age, and narrow palates. Recombinant growth hormone therapy positively influenced craniofacial development, particularly mandibular growth, enhancing the potential for orthodontic treatment.

Conclusions. Orthodontic treatment strategies should focus on periods of increased bone plasticity during rhGH therapy. Regular monitoring is essential to promptly address developmental changes and optimize orthodontic outcomes in children with GHD.

Keywords

growth hormone, growth hormone deficiency, Malocclusions

INTRODUCTION AND OBJECTIVE

The stomatognathic system comprises dental arches, jawbones, soft tissues, muscles, and the temporomandibular joint. Disorders occurring within this system can also affect the entire body. Hormones such as growth hormone, thyroid hormones, parathyroid hormone, vitamin D3 involved in bone metabolism, as well as sex hormones influence the cessation of bone growth, and play a significant role in the development of the human masticatory organ [1, 2].

Growth hormone deficiency (GHD) is a rare disease, with an incidence ranging from 1 in 4000 to 1 in 10000 births. The symptoms of the disease stem from a deficiency of somatotropin – growth hormone (GH). Most commonly, the occurrence of GHD has an idiopathic basis, but it can be caused by genetic mutations, pituitary and central nervous system defects, pituitary disorders (especially tumors, hemorrhages) [3–8].

The GH is primarily responsible for body growth, but it also influences the metabolism of fats, carbohydrates, and the increase in body mass, especially bone growth.

It stimulates cell growth and division, promoting bone elongation. GH affects bone and other tissue growth both directly and through the production of insulin-like growth factor (IGF1) [9, 10].

Currently, there is no standardized diagnostic criterion for GHD worldwide. Failure to initiate GH deficiency treatment can lead to extreme short stature – dwarfism, significantly diminishing the quality of life for patients, often rendering them unable to work and disrupting social relationships. The classical form of GHD is diagnosed through a stimulation test based on reduced GH secretion. Upon diagnosis, the preferred course of action is the prompt initiation of treatment with recombinant human growth hormone (rhGH) [6, 11]. This treatment is substitutive in nature. The metabolic effects induced by rhGH in the body are identical to those of natural GH. The therapy yields favorable effects and is safe. The initiation of recombinant human growth hormone (rhGH) therapy stimulates proportional linear growth and skeletal development. This treatment continues until growth is complete or the target height is achieved. Significant adverse effects associated with rhGH therapy are reported very rarely [4, 6, 12].

Studies have shown that in children with limited somatic growth, cranial structures tend to be smaller than normative

✉ Address for correspondence: Michał Łobacz, Chair and Department of Oral Surgery, Medical University, Chodźki 6, 20-093 Lublin, Poland
E-mail: michallobacz@tlen.pl

values [13–15]. The process of craniofacial development is regulated by a combination of genetic, epigenetic, hormonal, and environmental factors, including nutritional habits [13, 16]. Furthermore, improper craniofacial development can lead to malocclusions, which refer to discrepancies in the alignment of the maxillary and mandibular dental arches [17]. According to the World Health Organization (WHO), malocclusions, dental caries, and periodontal diseases are among the three most prevalent oral health issues worldwide [18, 19].

The classification of malocclusions was first introduced by E.H. Angle in 1899. Malocclusions can result from irregularities in the bones, teeth, or a combination of both [20–22]. A 2018 global analysis reported the following prevalence of Angle's malocclusion classes: Class I – 74.7% (Fig. 1), Class II – 19.56% (Fig. 2a, Fig. 2b), and Class III – 5.93% (Fig. 3) [18]. In Poland, the prevalence of malocclusions varies between 60.6% and 71.2% depending on the source.

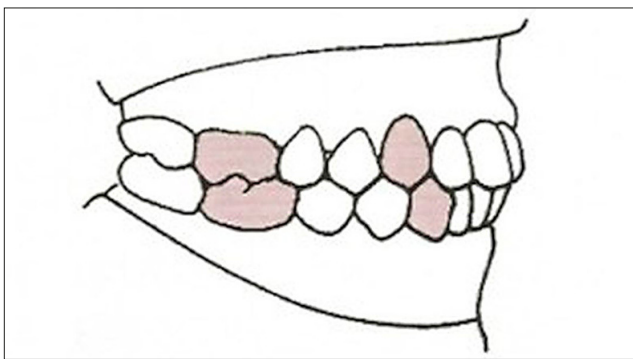


Figure 1. Angle class I and canine class

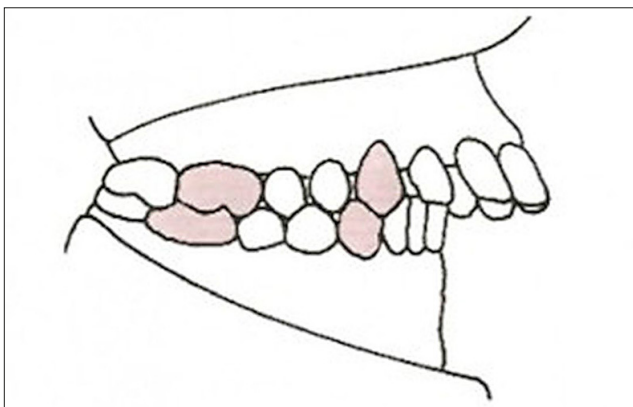


Figure 2a. Angle class IIa and canine class II

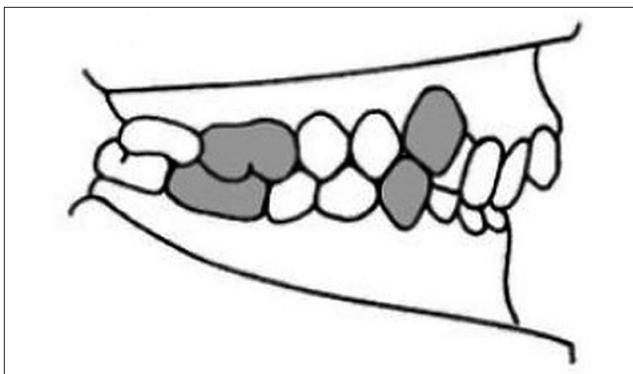


Figure 2b. Angle class IIb and canine class II

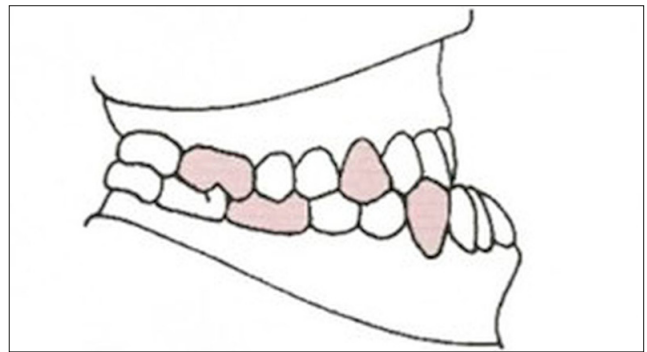


Figure 3. Angle class III and canine class III

Among these, posterior crossbites are the most frequently observed [18].

The classification of malocclusions is based on their occurrence in three spatial planes: sagittal, frontal, and transverse. Additionally, dental irregularities such as abnormal structure, number, position, and eruption timing of teeth can contribute to the development of malocclusions [23–26].

Research suggests that growth hormone deficiency (GHD) significantly impacts the development of jawbones. The mandible appears to be more affected than the maxilla, often presenting with retrognathia. Moreover, parameters such as width, length, and the angle of inclination between the maxilla and mandible are frequently altered in affected individuals [5, 13, 16, 25, 26]. Literature data indicate that children with GHD exhibit a significantly higher prevalence of malocclusions—up to 40% more—compared to healthy children [4, 16, 27].

The assessment of a child's biological age can be conducted through skeletal and dental age evaluations. One of the most commonly used methods for tooth development assessment is Demirjian's method (1973) [28, 29]. In clinical settings, children with GHD often undergo skeletal age assessment, which reflects their physiological development rather than chronological age [27]. Björk introduced an approach that identifies eight stages of hand-skeletal maturity, allowing for the determination of skeletal growth phases in individual patients. The Greulich-Pyle atlas is also widely used for skeletal age assessment.

Currently, no standardized orthodontic treatment guidelines exist for children undergoing rhGH therapy, making this an important topic for discussion among orthodontic specialists and pediatric endocrinologists. Further research is required to establish evidence-based orthodontic management strategies for patients with short stature, with long-term follow-ups needed to evaluate treatment outcomes. Therefore, close interdisciplinary collaboration between dentists, orthodontists, and pediatric endocrinologists is essential.

The aim of this study was to assess the frequency of malocclusions and dental irregularities in children undergoing treatment for GHD and to evaluate discrepancies between skeletal, chronological, and dental age in this patient group.

MATERIAL AND METHODS

The study was conducted at the Chair and Department of Developmental Dentistry in collaboration with the Department of Pediatric Endocrinology and Diabetology and

the Endocrinological-Metabolic Laboratory at the Medical University of Lublin between 2018 and 2022.

A total of 92 children (n=92) undergoing recombinant human growth hormone (rhGH) therapy for growth hormone deficiency (GHD) were initially considered for inclusion. Of these, 43 patients (n=43) formed the study group, while 49 patients (n=49) were excluded due to ongoing or completed orthodontic treatment.

The final study cohort consisted of 43 children (48.31%) aged 7 to 17 years, all of whom were receiving rhGH therapy for GHD and provided informed consent to participate in the study.

The selection of the control group took into account similar socio-demographic conditions as the study group. The control group (n=46) consisted of healthy children from the same geographical region, attending the same dental institutions—the Department of Developmental Dentistry at the Medical University of Lublin and the NeoDent Clinic in Lublin. The selection of participants considered similar environmental conditions, minimizing the impact of external factors on the study results. Comparative analysis showed no statistically significant differences in terms of age and gender between the study and control groups.

A total of 89 children participated in the follow-up study. No statistically significant differences were observed in terms of age or gender between the study and control groups.

Following data collection through patient interviews, a comprehensive dental examination was performed. Alginate impressions were taken, and digital intraoral photographs were captured. Plaster models were cast on the same day and subsequently digitized using an iTero digital scanner. Each participant was also asked to complete a questionnaire.

After the initial examination, referrals were issued for panoramic X-rays. The collected dental models were then analyzed using OrtoBajt Ortodoncja 9.1.1m software to assess orthodontic parameters. Additionally, panoramic X-rays and digital photographs were analyzed.

Skeletal age data were obtained from the Imaging Diagnostics Department at the University Children's Hospital in Lublin, while laboratory test results were provided by the Department of Pediatric Endocrinology and Diabetology with the Endocrinological-Metabolic Laboratory at the Medical University of Lublin.

The obtained results were subjected to statistical analysis. The characteristics of the studied measurable parameters were presented using the mean, median, minimum, and maximum values, as well as the standard deviation. The Mann-Whitney U test was used to compare two independent groups. To assess the relationship between two quantitative variables, Spearman's rank correlation test was applied. To compare dependent groups, Wilcoxon's signed-rank test was used. The statistical analysis was conducted using the STATISTICA 12.0 software, assuming a significance level of $p < 0.05$.

The research project obtained a positive opinion from the Bioethics Committee of the Medical University of Lublin, decision number: KE-0254/315/2017.

RESULTS

Children undergoing hormonal substitution therapy did not exhibit differences in dental habits compared to

healthy children. Statistical analysis revealed no significant differences between the study groups in terms of DT (decayed tooth), MT (missing tooth), FT (filled tooth), and DMTF (sum of decayed, missing due to caries, and filled teeth in permanent dentition). The caries prevalence in the examined group was 86.05%.

A statistically significant association was observed between malocclusions and single nucleotide polymorphisms (SNPs). The total cohort (n=92) included both study group participants (n=43) and patients excluded due to ongoing or completed orthodontic treatment (n=49). Notably, malocclusions occurred significantly more frequently in children with GHD compared to their healthy peers, with a prevalence of 69.57% (Table 1).

Table 1. Occurrence of malocclusions in both groups

occurrence of malocclusion	study group	control	statistical analysis
	with GHD	group	
yes	n=64	n=16	test Chi ² Pearson=15.23; p=0.0001
	69.57%	34.78%	
no	n=28	n=30	
	30.43%	65.22%	

The most common malocclusions were located in the posterior region, accounting for 21.95% of defects in the study group, while anterior malocclusions were observed in 14.64% of cases (Table 2). Dental crowding was also significantly more prevalent among short-statured children, occurring in 70% of participants in the upper arch and 30.43% in the lower arch. The Tonn index in the study group indicated an excess of dental material, with Moyers (Table 3), Lundström (Table 4), and Little's indices (Tables 5 and 6) further confirming the presence of moderate crowding, which was more frequently observed in female participants.

Table 2. Angle's classification in both groups

class	study group with GHD	control group	statistical analysis
I	n=26	n=26	Chi ² Pearson test=0.47; p=0.93
	63.41%	61.90%	
II a	n=8	n=9	
	19.51%	21.43%	
II b	n=1	n=2	
	2.44%	4.76%	
III	n=6	n=5	
	14.63%	11.90%	

Analysis using McNamara's palatal width index demonstrated that patients in the study group had statistically narrower palates compared to healthy children. A weak positive correlation was observed between the duration of substitution therapy and palatal width, indicating that longer therapy durations resulted in index values approaching the accepted norm.

An assessment based on the McNamara index was conducted on digital scans, where the distance between points defined by McNamara was measured. These points are located at the junction of the palatal groove of the upper first permanent molar and the gingival margin.

Table 3. Moyers index values in both groups

Moyers index	group						statistical analysis	
	study			control			Z	p
	M	Me	SD	M	Me	SD		
width of the lower permanent teeth (32–42)	22.7	22.5	1.48	21.95	21.7	1.47	2.30	0.02
expected width of the lower permanent teeth	22.3	21.9	1.29	21.68	21.4	1.05	2.27	0.02
width of the upper permanent teeth (32–42)	30.0	29.9	2.52	28.60	29.2	2.75	2.08	0.037
expected width of the upper permanent teeth	25.6	25.9	0.57	25.19	25.9	1.03	2.35	0.02

Table 4. Lundström index in the upper arch in both groups

Lundström index (upper arch)	group		statistical analysis
	Study	control	
crowding	12 27.91%	5 10.87%	Chi ² Pearson test=6.17 p=0.046
gaps	12 27.91%	16 34.78%	
without crowding and gaps	19 44.19%	25 54.35%	

Table 5. Little's index in the upper arch in both groups

Little's index (upper arch)	group		statistical analysis
	study	control	
without crowding	13 30.23%	19 41.3%	Chi ² NW test=4.54; p=0.32
small	0 0%	2 4.35%	
medium	13 30.23%	9 19.57%	
big	10 23.26%	7 15.22%	
very big	7 16.28%	9 19.57%	

Table 6. Little's index in the lower arch in both groups

Little's index (lower arch)	group		statistical analysis
	study	control	
without crowding	8 18.60%	18 39.13%	Chi ² NW test=11.18 p=0.03
small	4 9.3%	8 17.39%	
medium	20 46.51%	16 34.78%	
big	8 18.6%	4 8.7%	
very big	3 6.98%	0 0%	

Table 7. Results of the analysis on diagnostic models according to the McNamara index

Examined parameters	Study group			Control group			Statistical analysis	
	M	Me	SD	M	Me	SD	Z	p
McNamara index	34.58	34.40	2.53	35.59	35.35	3.13	2.16	0.04

The McNamara index results are presented in the tab. 7.

The McNamara index has significantly lower values in the study group compared to the control group ($p < 0.05$).

No statistically significant differences in McNamara index values were found between girls and boys in both analyzed groups ($p > 0.05$).

In the group of short-statured children, tooth agenesis occurred significantly more frequently (11.6%). In the control group, this abnormality was observed in only one person. A supernumerary tooth was observed in one patient.

The dental age in patients with single nucleotide polymorphism (SNP) showed no statistically significant differences compared to the chronological age. However, the skeletal age was delayed by an average of 8 months and 23 days.

Patients not included in the study underwent orthodontic treatment for an average of 2 years using removable appliances. The most common reasons for starting treatment were persistent deciduous teeth, delayed eruption of permanent teeth, and existing crowding.

DISCUSSION

The majority patients had been treated using removable orthodontic appliances, while two individuals were treated with fixed appliances. The average treatment time was two years. The most common reason for seeking treatment was a referral from a general dentist. Parents' concerns primarily revolved around current crowding of teeth, retained primary teeth, and a lack of permanent successors in the oral cavity. Following the completion of therapy in the retention phase, patients were provided with removable retainers – to be worn at night.

Early initiation of orthodontic treatment can prevent the occurrence and exacerbation of malocclusions in adulthood [19]. The best effects of orthodontic appliances are observed when they are applied during the period of intensive facial growth. The most favorable period to start treatment is before or during the peak growth spurt. Before commencing orthodontic treatment, the treating doctor must understand the characteristics of the craniofacial complex in patients with a deficiency in rhGH. Differences in chronological and skeletal age may influence the timing and method of orthodontic treatment [29, 30].

When commencing treatment, attention should be paid to the following aspects:

rhGH therapy has a greater impact on the development of the mandible than on the development of the maxilla.

The pattern of jawbone development during hormonal substitution therapy is not entirely predictable. rhGH therapy rarely affects the process of tooth maturation [11, 29–33].

In recent years, several attempts have been made to treat skeletal abnormalities correlated with GH deficiency [29,

34, 35]. It is believed that hormonal substitution therapy mainly influences regions of bone growth through cartilage, particularly in the mandibular region. [30, 36, 37] In the diagnostic process of children with short stature, special attention should also be paid to the breathing pattern. Compensatory mechanisms related to oral breathing observed among the study group may hinder orthodontic treatment [38].

The most observed malocclusions in children treated with rhGH were Class II malocclusions according to Angle's classification. In such cases, a basic treatment scheme for early Class II malocclusion intervention can be applied, modifying it throughout the treatment depending on the growth pattern that occurs. This approach involves intervention using removable appliances during the mixed dentition stage (Phase I) and, if necessary, treatment with fixed appliances during adolescence (Phase II) [35]. Phase I treatment aims to restore normal growth and development of the jawbones, potentially eliminating the need for Phase II treatment in the future. If emerging orthodontic issues in children with growth hormone deficiency stem solely from inadequate jawbone dimensions, directing their development using removable appliances might prove to be sufficient therapy. This assumption is supported by patients who were disqualified from the study. Most of them exclusively used removable appliances during therapy, which proved to be adequate. During substitution therapy, the orthodontist can anticipate ongoing growth in patients.

The study observed a positive effect of rhGH treatment on the development of the masticatory system, therefore orthodontic treatment strategy should be based on the use of orthodontic appliances when the child is treated with rhGH, as then the bones are the most plastic.

The topic of treatment should be subjected to further long-term studies involving a large group of patients.

CONCLUSIONS

The oral health status of children with growth hormone deficiency (GHD) undergoing recombinant growth hormone (rhGH) therapy does not significantly differ from that of generally healthy children in terms of dental caries prevalence and oral hygiene. However, dental irregularities and malocclusions occur significantly more frequently in children diagnosed with GHD and treated with rhGH compared to their healthy peers.

GHD has a notable impact on skeletal age, causing a delay relative to chronological age. Nevertheless, the duration of rhGH therapy significantly improves these parameters, reducing the discrepancy over time. In contrast, GHD does not affect dental age in relation to chronological age, indicating that tooth development progresses independently of growth hormone deficiency.

Given these findings, children with short stature should receive systematic dental care, with a particular emphasis on orthodontic monitoring. The rhGH treatment period represents a critical window of accelerated bone growth, which can be leveraged to enhance the effectiveness of orthodontic therapy. Consequently, orthodontic treatment strategies should prioritize faster interventions, particularly focusing on mandibular developmental processes to optimize outcomes.

Throughout orthodontic therapy, continuous specialized monitoring is essential to facilitate timely orthognathic interventions, ensuring that emerging skeletal and dental changes during endocrinological treatment are promptly addressed. A multidisciplinary approach, integrating endocrinologists, orthodontists, and dentists, is crucial to maximizing the benefits of rhGH therapy and achieving optimal craniofacial development in affected children.

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