

The effects of adenoidectomy of serum insulin-like growth factor-1 (IGF-1) and ghrelin in hypertrophied adenoids in children with otitis media with effusion

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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ABSTRACT:

Aim: The aim of the current study was to assess the serum levels of insulin-like growth factor-1 (IGF-1) and ghrelin in hypertrophied adenoids in children suffering with or without otitis media with effusion before and after adenoidectomy.

Material and methods: Serum IGF-1 and ghrelin concentrations were measured with specific enzyme-linked immunoassay (ELISA) methods. The study was carried out in 20 children with otitis media with effusion. The reference group comprised 24 children with hypertrophied adenoid, while control group included 19 children.

Results: This mean values of IGF-1 in children with otitis media with effusion and children with hypertrophied adenoid before adenoidectomy were significantly lower than those found in healthy children. Serum levels of IGF-1 were higher after adenoidectomy. There was a significant difference of serum ghrelin levels between both examined groups and the control group.

Conclusion: Our results suggest that adenoidectomy in children with hypertrophied adenoids and in children with otitis media with effusion significantly increases the level of IGF-1 in serum compared to before surgery through the effect of the GH-IGF-1 axis, which could contribute to children's growth.

KEYWORDS:

ghrelin, hypertrophied adenoid, insulin-like growth factor-1 (IGF-1)

ABBREVIATIONS

BMI – body mass index

ELISA – enzyme-linked immunosorbent assay

GH – growth hormone

GH-IGF-1 – insulin-like growth factor-1

GHS-R – growth hormone secretagogue receptor

IGF-1 – concentration of insulin-like growth factor-1

INTRODUCTION

Adenoid hypertrophy is one of the most frequently found conditions in children otolaryngology [1]. The main reasons for this condition include recurring acute pharyngitis and tonsillitis, especially accompanying childhood diseases. Chronic antigen stimulation in the throat causes increased activity of immunological cells, which as a consequence may invoke hypertrophy of the pharyngeal lymphatic tissue [2, 3]. Adenoid hypertrophy is a factor conducive to the development of otitis media with effusion and could be one of the reasons for growth retardation in children [4, 5]. Growth hormone (GH) stimulates the synthesis of insulin-like growth factor (IGF-1)

in the liver and other target tissues [6]. In turn, IGF-1 is considered the main mediator stimulating GH secretion. The pathophysiology of retarded growth in children due to hypertrophied adenoid includes: low calorie intake, increased energy demand associated with breathing difficulties, hypoxemia and impaired growth hormone axis – insulin-like growth factor-1 (GH-IGF-1) [7].

Ghrelin, which is secreted from the stomach, constitutes a strong stimulus for GH release and takes part in induction of weight gain by stimulating food intake and at the same time reducing fat intake [8]. Chronic adenoid hypertrophy stimulates the secretion by lymphocytes of inflammatory cytokines which can affect the central nervous system and have negative repercussions on food intake and energy balance [9, 10].

PURPOSE

The purpose of this study was to determine serum (IGF-1) and ghrelin levels in children with adenoid hypertrophy, children with adenoid hypertrophy and otitis media with effusion before and after adenoidectomy, and healthy children with no signs of inflammation.

MATERIAL AND METHODS

The studied group consisted of 20 children (10 girls and 10 boys) aged 2 to 7 years (4.59 ± 1.40) with adenoid hypertrophy, patients with otitis media with effusion persisting over 3 months (SOM1, SOM2). Due to the lack of progress in pharmacotherapy, the children were qualified for adenoidectomy.

The reference group consisted of 24 children (14 girls and 10 boys) aged 3 to 8 years (4.95 ± 1.40) (HYP1, HYP2), all of whom had hypertrophic adenoids with no signs of otitis media with effusion.

The control group (C) consisted of 19 children aged 3 to 7 years (average age 5.09 ± 1.24) (10 girls and 9 boys) who did not show any signs of infection and have not undergone pharmacological treatment, including immunosuppression.

Patient qualification and adenoidectomy were performed at the Department of Paediatric Otolaryngology of the Medical University of Białystok. The research was approved by the Bioethical Committee of the UMB No. R-I-002/269/2019.

The study material was constituted by patients' blood taken from a vein into a collection tube in the absence of anticoagulant with a volume of 2.7 ml. The obtained serum was stored at 800C until further processing. The experimental material collected from children in the study group and in the control group was collected directly before adenoidectomy and six months after the procedure.

IGF-1 and ghrelin determination were performed using the ELISA method (enzyme-linked immunosorbent assay) with the use of IGF-1 and ghrelin antibody-coated plates. In the first stage, the wells were supplemented with patients' standards and sera and preincubation at room temperature was performed. The plates were then rinsed and each well was supplemented with enzyme-labeled polyclonal antibodies. The plates were incubated and washed once again. In the next stage of the study, substrate was added to the wells (H2O2 and tetramethylbenzidine) causing the formation of a colored product. The intensity of the color was measured spectrophotometrically at a wavelength of 450 and 630 nm. Sensitivity of the IGF-1 test was 0.091 ng/ml, and the measuring range was 0.09–1,050 ng/ml. Sensitivity of the ghrelin test was 49.5 pg/ml and the measuring range was 123.5–10,000 pg/ml.

Elements of descriptive statistics were used in the statistical analysis, and the obtained results were presented as mean values \pm standard deviation, median, P25 and P75. Due to the failure to meet the assumption about the normality of distribution, we used the nonparametric Mann-Whitney U test. $P < 0.05$ was considered statistically significant. The data was processed using the STATISTICA 12 PL software (StatSoft, Poland).

RESULTS

The average IGF-1 concentration in the HYP1 group was 155.11 ± 30.17 ng/ml and it was statistically significantly lower $p < 0.000000$ than in the HYP2 group 262.21 ± 65.88 ng/ml. In the control group,

IGF-1 concentration was statistically significantly higher than in the HYP1 group, $p < 0.000000$ and HYP2 $p < 0.019060$ (Fig. 1.). Statistical analysis revealed a statistically significant difference between IGF-1 concentration in the SOM1 group, which was 222.96 ± 60.25 ng/ml, and in the SOM2 group of 300.28 ± 98.01 ng/ml, $p < 0.00467$. In the control group, the average concentration was 305.45 ± 48.21 ng/ml and it was statistically significantly higher than in the SOM 1 group, $p < 0.000026$ (Fig. 2.). Statistical analysis did not show any relevant differences between ghrelin levels in both groups assessed and in the control group before and after the procedure (Figs. 3 and 4). Analyzing patient height, we obtained a statistically significant difference in the group of children with adenoid hypertrophy and in the group of children with adenoid hypertrophy and otitis media with effusion (Tab. I.).

DISCUSSION

Adenoid hypertrophy may give rise to growth retardation in children, which stems from a disorder of the axis: growth hormone – insulin-like growth factor-1 (GH-IGF-1) [11]. The biological functions of IGF-1 are mainly supported by the IGF-1R receptor [12] which shows hormonal, paracrine and autocrine activity. Furthermore, it stimulates the enzymatic systems of cells, encouraging their kariokinetic divisions conditioning the growth of soft tissues and bones. IGF-1 is a major mediating factor in the action of growth hormone (GH) on target cells, primarily chondrocytes, osteoblasts and endocrine glands [13]. As a natural ligand for growth hormone receptor (GHS-R), ghrelin encourages the release of growth hormone, prolactin and adrenocorticotrophic hormone [14].

In our previous studies we demonstrated a statistically significant difference in the concentration of IGF1 in the group of children with adenoid hypertrophy before surgery and in the group of children with adenoid hypertrophy and otitis media with effusion before and after surgery. However, no statistically significant differences were revealed between the assessed groups both before and after adenoidectomy.

The research of Bar et al. showed a statistically significant increase in the concentration of IGF-1 protein in a group of patients after adenotonsillectomy. These studies were conducted in a group of children with obstructive sleep apnea syndrome resulting from adenoid hypertrophy. The results may suggest that adenotonsillectomy could promote the proper functioning of the GH-IGF-1 axis by increasing the level of IGF in serum samples. At the same time, it leads to a faster growth rate compared to healthy peers [15]. Similar conclusions were also drawn by other authors who conducted a study in a group of children with sleep breathing disorders and adenoid hypertrophy. They found a significant increase in serum IGF-1 concentration as well as an increase in body weight and BMI after surgery [16].

Yilmaz et al. conducted a study in a group of children with adenoid hypertrophy. The levels of GH and IGF-1 were measured in patients before surgery and 3 to 6 months after surgery. In their study, the researchers found a statistically significant increase in IGF-1 concentration. Obstructive adenotonsillar hypertrophy can

Tab. I. Comparison of children's growth in the study group and the control group before and after adenoidectomy.

GROUP	CHILD'S HEIGHT (CM)		P
	BEFORE SURGERY	AFTER SURGERY	
Children with adenoid hypertrophy	78.21 ± 8.21	81.55 ± 7.25	p < 0.04
Children with adenoid hypertrophy and otitis media with effusion	70.13 ± 10.11	74.44 ± 8.10	p < 0.01

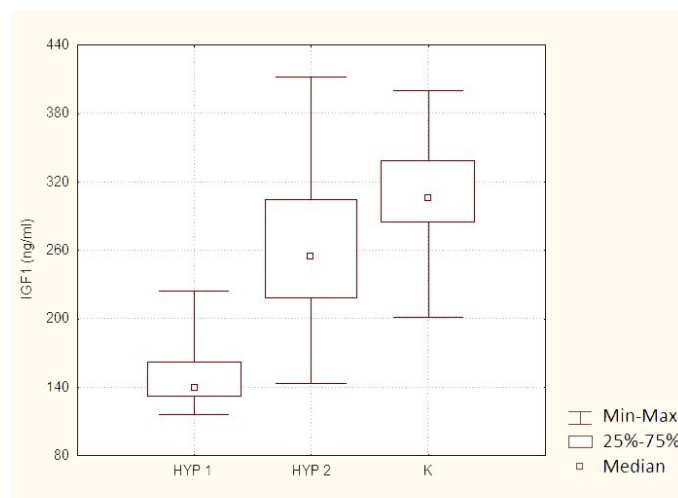
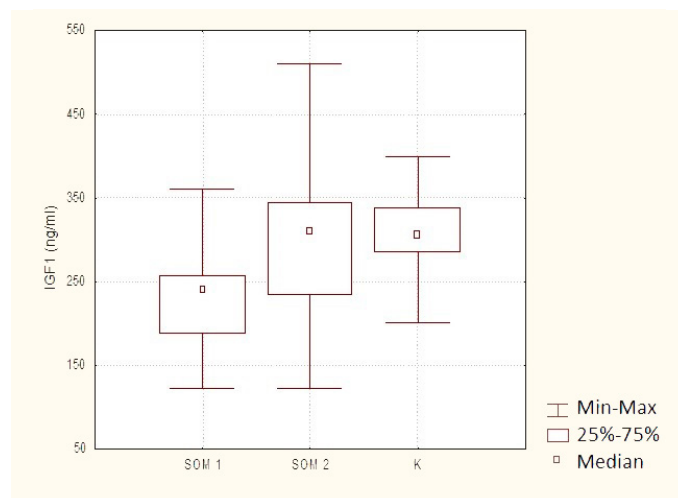
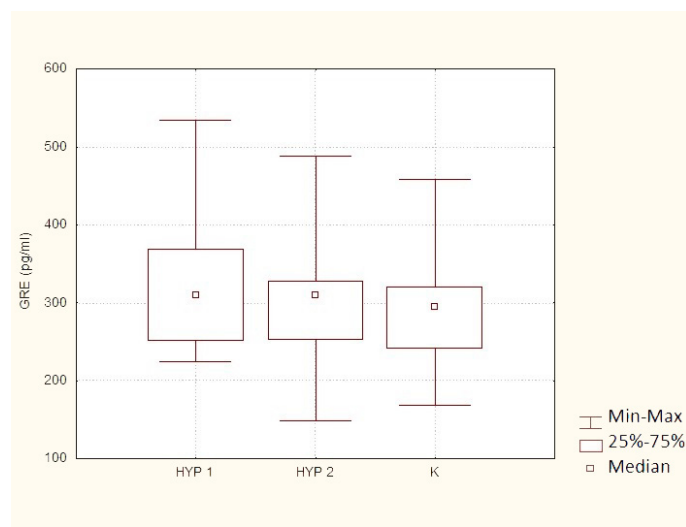
cause a reduction in serum IGF-1 levels by affecting the GH-IGF-1 axis, and tonsillectomy could be an effective therapeutic means in patients with adenoid hypertrophy [17].

Other authors [18] performed determinations in a group of children with obstructive adenoid hypertrophy and in the control group. In both groups, ghrelin as well as IGF-1 levels were measured in the morning. The results showed that the patients in the study group had lower levels of IGF-1 and ghrelin compared to the results of children in the control group. Lower levels of IGF-1 in the serum of children with adenoid hypertrophy may add to secondary deficiency of growth hormone stimulated by ghrelin [18]. Insufficient ghrelin levels in children with sleep apnea can be an important consideration for insufficient GH secretion, leading to reduced IGF-1 levels. It is possible that ghrelin is a new link between the GH/IGF-1 axis and the neuroendocrine regulation of energy balance [18, 19].

Koc et al. noted a substantial increase in body weight and BMI and a significant decrease in ghrelin levels in children after adenoidectomy due to adenoid hypertrophy. Their results suggest that the determination of ghrelin levels could be an important indicator for assessing a child's growth and development [20]. Gumussoy et al. measured the serum levels of IGF-1 and ghrelin in children with adenoid hypertrophy before and after surgery. The authors noted a substantial increase in IGF-1 concentration and a decrease in ghrelin levels after adenotonsillectomy. A rise in IGF-1 level may indicate an increase in daily secretion of growth hormone, while a reduced level of ghrelin reflects increased food intake in the post-surgical period [21].

Jabbari et al. conducted a study in a group of children with adenoid hypertrophy with sleep and breathing disorders who also showed growth retardation compared to other peers. The level of IGF-1 and ghrelin, assessed 12 months after surgery, increased substantially compared to the concentration of these hormones before surgery. An increase in body weight, BMI and height was also shown in the children [22].

Ghrelin affects eating habits, energy balance and patient growth. Chronic adenoid hypertrophy stimulates immune cells and promotes the inhibition of inflammatory cytokine secretion. When released from immune cells, these cytokines can affect the central nervous system. Although ghrelin does not directly affect the immune system at the site of functioning, some studies have shown that pro-inflammatory cytokines, e.g. IL-1 B, IL-6 and TNF- α , may produce such an effect [23, 24]. Ghrelin also increases the extraction of GHS-R (growth hormone secretagogue receptor) and inhibits the extraction of cytokines by leptin in T lymphocytes [24].

**Fig. 1.** IGF-1 concentrations in the group of children with adenoid hypertrophy before and after adenoidectomy and in the control group.**Fig. 2.** IGF-1 concentrations in the group of children with adenoid hypertrophy and otitis media with effusion before and after adenoidectomy and in the control group.**Fig. 3.** Ghrelin levels in the group of children with adenoid hypertrophy before and after adenoidectomy and in the control group.

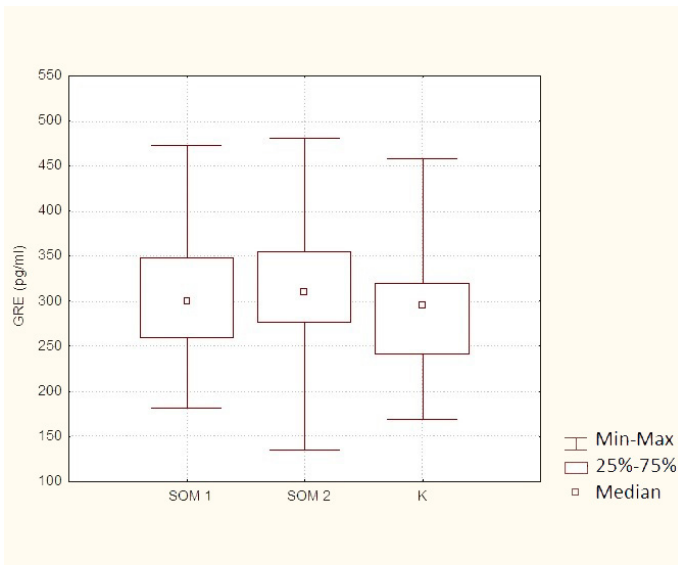


Fig. 4. Ghrelin levels in the group of children with adenoid hypertrophy and otitis media with effusion before and after adenoidectomy and in the control group.

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