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Aberrations in carbohydrate metabolism in patients with diagnosed acromegaly — observational study

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Abstract

Introduction: Acromegaly is characterized by excessive secretion of growth hormone (GH). The incidence rate of acromegaly is 40 to 70 persons per one million people. Carbohydrate disorders often accompany the above pathology. The aim of this study was to examine the influence of high levels of somatotropin on aberrations in glycaemia in patients with acromegaly, and then a 5-year observation.

Material and methods: The study group consisted of 86 patients (48 females and 38 males) with acromegaly diagnosed on the basis of clinical features, elevated insulin-like growth factor 1 (IGF-1) levels, and/or no inhibition of GH ≤ 1 $\mu\text{g/L}$ secretion during 2 hours after an oral glucose load.

Results: In the study group type 2 diabetes mellitus (T2DM) was diagnosed in 21 patients (24.4%). There were also 14 cases (16.3%) of the diagnosis of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) combined. The mean age of participants with concomitant T2DM was 52.1 years, while the mean age of those without carbohydrate metabolism disturbances was 46.1 years. During a 5-year observation, we noticed an increase level of glycated haemoglobin (HbA_{1c}) and new cases of pre-diabetes and T2DM.

Conclusion: In patients with acromegaly the incidence rate of T2DM is 3–4 times higher than in the rest of the population, and it increases with age, especially after the patient reaches 55 years old. (*Endokrynol Pol* 2022; 73 (4): 743–744)

Key words: acromegaly; T2DM; IGT; IGF-1

Introduction

Acromegaly is characterized by excessive secretion of growth hormone (GH) [1]. The incidence rate of acromegaly is 40 to 70 persons per one million people. Chronic exposure to GH and insulin-like growth factor 1 (IGF-1) hypersecretion leads to soft tissue swelling of the tongue, heart, kidney, colon, and vocal cords. Elevated levels of the hormone prolactin (PRL) are also observed in approximately 30% of patients [2]. Additionally, carbohydrate disorders often accompany the above pathology. Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) occurs in approximately 60–70% and type 2 diabetes mellitus (T2DM) in 13–30% of patients [3, 4].

The aim of this study was to examine the influence of high levels of somatotropin on aberrations in glycaemia in patients with (active/diagnosed) acromegaly, hospitalized in the Endocrinology and Diabetology Department of Collegium Medicum University of Nicolaus Copernicus in Bydgoszcz in the years 2008–2015, and then a 5-year observation.

Material and methods

The study group consisted of 86 patients (48 females and 38 males; aged 35 to 66 years) with acromegaly diagnosed on the basis of

clinical features, elevated IGF-1 levels, and/or no inhibition of GH ≤ 1 $\mu\text{g/L}$ secretion during 2 hours after an oral glucose load (75 g) and additionally magnetic resonance imaging (MRI) of the pituitary gland. All patients were hospitalized in the Endocrinology and Diabetology Department of Collegium Medicum University of Nicolaus Copernicus in Bydgoszcz in the years 2008–2015. Round-the-clock glucose profiles of the participants were marked; an oral glucose tolerance test (OGTT) was also conducted in the cases of impaired fasting glucose (> 100 mg/dL) or postprandial glucose (140–200 mg/dL). T2DM, IFG, and IGT were diagnosed based on the American Diabetes Association criteria, followed by a 5-year observation period, during which glucose and glycated haemoglobin (HbA_{1c}) were measured every 6 months.

Results

The characteristics of the study group are presented in Tables 1 and 2.

During 5-year observation we noticed an increase in the level of HbA_{1c} and increased prevalence of pre-diabetes and T2DM (Supplementary File — Fig. 1–3).

Discussion

Acromegaly is an endocrinopathy that causes the development of insulin resistance [5]. The degree of disorder of carbohydrate metabolism is greater in the active form of the disease and correlates with the dura-



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Table 1. The characteristics of the study group at the time of diagnosis

Acromegaly (n)	Normoglycaemia		IFG + IGT		T2DM	
	Average age	%(n)	Average age	%(n)	Average age	%(n)
All (86)	46.1	59.3% (51)	49.3	16.3% (14)	52.1	24.4% (21)
Females (48)	45.6	60.4% (29)	48.9	14.6% (7)	51.1	25.0% (12)
Males (38)	46.8	57.9% (22)	49.7	18.4% (7)	53.2	23.7% (9)

IFG — impaired fasting glucose; IGT — impaired glucose tolerance; T2DM — type 2 diabetes mellitus

Table 2. The participants were divided into 3 subgroups according to their age

Aged group [years]	Number of patients	Normoglycaemia	IFG + IGT	T2DM
The study group at the time of diagnosis				
35–44	16	14 (87.5%)	1 (6.2%)	1 (6.2%)
45–54	49	35 (71.4%)	8 (16.3%)	6 (12.2%)
55–66	21	2 (9.5%)	5 (23.8%)	14 (66.6%)
p		< 0.001	< 0.001	< 0.001
The study group after 5-year observation				
35–44	16	7 (43.7%)	6 (37.5%)	3 (18.7%)
45–54	49	24 (49%)	14 (28.6%)	11 (22.4%)
55–66	21	1 (4.8%)	4 (19%)	16 (76.2%)
p		< 0.001	< 0.001	< 0.001

IFG — impaired fasting glucose; IGT — impaired glucose tolerance; T2DM — type 2 diabetes mellitus

tion of acromegaly, age, concentration of GH, IGF-1, and IGF-binding protein (IGFBP-3, insulin-like growth factor-3-binding protein) [4, 6]. The pathomechanism of insulin resistance in acromegaly is complex. Long-term supraphysiological GH concentration interferes with both insulin action in the liver and the other peripheral tissues. This leads to enhanced production of glucose by the liver and decreased utilisation of glucose in peripheral tissues. This is probably due to disturbances in the production and action of a second messenger in the insulin receptor. In addition, growth hormone increases lipolysis of adipose tissue, and increased concentration and oxidation of fatty acids enhances insulin resistance [7]. In our study, we observed 24.4% of patients with T2DM and another 16.3% with pre-diabetes. Stelmachowska et al. [8], who examined a Polish acromegaly population, found T2DM in 20% of patients, IGT in 15% of patients, and IFG in 19% of patients. Biering et al. also assumed that the age of patients was a major risk factor in the development of aberrations in carbohydrate metabolism [3]. In our study, we observed that in the course of acromegaly, new cases of T2DM appeared during the 5-year follow-up [21] (24.4%)

vs. 30 (34.8%). The limitations of our study were as follows: we did not include therapeutic procedures; all of the subjects were treated with only the first-generation somatostatin analogues, but we know that acromegaly treatment by adenectomy results in improved glucose tolerance, decreasing insulin resistance, and hyperinsulinism. However, Yun et al. [9] found in their study that the treatment group, according to the treatment modality, demonstrated that the incidence of diabetes in each group showed no significant difference.

In patients with acromegaly the incidence rate of T2DM and pre-diabetes is 3–4 times higher than in the rest of the population, and it increases with age, especially in people aged 55 years and over [10].

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