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GLUCOSE AND LIPID ABNORMALITIES IN NEWLY DIAGNOSED ACROMEGALIC PATIENTS

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Abstract

Background and Aims. *Acromegaly is frequently associated with abnormalities of glucose and lipid metabolism. The aim of our study was to analyze the prevalence of glucose and lipid metabolism abnormalities in newly diagnosed acromegaly patients.* ***Material and Methods.*** *This retrospective study included 14 patients (F/M=10/4), mean age 49.5 ± 10.6 years, registered with acromegaly between January and December 2013. In all the cases the values of blood glucose (fasting and during the oral glucose tolerance test), total cholesterol and triglycerides were analyzed. The glucose disorders were classified according to the current criteria of the American Diabetes Association. Regarding the lipid metabolism, the cases were classified as having normal cholesterol, normal triglycerides, high cholesterol and high triglycerides.* ***Results.*** *A number of 7 patients (50%) presented abnormalities of glucose metabolism. The prevalence of diabetes mellitus (14.3%) was lower compared to that reported by other studies (15.5%-56%). Abnormalities of lipid metabolism were present in 8 patients (57.2%): high cholesterol was detected in 2 cases and 6 cases presented increased values for both cholesterol and triglycerides. Only 4/14 cases (28.6%) presented normal values for all glucose and lipid metabolisms parameters.* ***Conclusions.*** *Abnormalities of glucose and lipid metabolisms are very common in acromegalic patients.*

key words: *acromegaly, glucose metabolism abnormalities, lipid disorders*

Background and Aims

Acromegaly is a pituitary disease characterized by an excess of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). In most of the cases the pathologic condition is induced by a GH-secreting pituitary adenoma [1]. The clinical features of acromegaly were first described in 1886 by Pierre Marie and consist in specific changes induced by skeletal, tissue and internal organs growth. Excess GH and IGF-1 interacts also with metabolic regulations [2]. In most cases, GH hypersecretion induces hepatic and peripheral insulin resistance. A number of patients develop alterations of glucose metabolism, from

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prediabetes to secondary diabetes mellitus (DM) [3].

The reported prevalence of DM ranges from 15.5% to 56% in different studies [4,5], this variability being explained by differences in patients' characteristics and even by variation in the criteria used for the diagnosis of DM. The prevalence of mild abnormalities of glucose metabolism, as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), range from 16 to 46% in different studies [4].

Acromegaly is associated also with abnormalities of lipid metabolism, too. The reported incidence of hypercholesterolemia in acromegalic patients was similar to that of general population, whereas hypertriglyceridemia was three times more frequent than in controls [6].

In this study we intended to evaluate the prevalence of glucose and lipid metabolisms abnormalities at diagnosis of acromegaly in cases registered and followed-up in our department.

Material and Methods

Patients

This was a retrospective study that included all the patients registered between January and December 2013 with the diagnosis of acromegaly, in the Department of Endocrinology, County Emergency Hospital Timișoara.

Data collection

The following data were collected from the medical records of these patients: age, gender, weight, height, blood glucose values (fasting and during oral glucose tolerance test) measured at the time of diagnosis, value for basal GH, IGF-1, cholesterol, triglycerides, the presence of associated pituitary insufficiency and treatment for DM and/or dyslipidemia. Two cases with insufficient data in the medical records were excluded.

Because all the cases were investigated in our department, all the determinations for GH and IGF-1 were performed in the same laboratory, by using a chemi-luminescent immunoassay method.

Normal range for GH is 0-10 ng/ml for women and <5 ng/ml for men. Normal range for IGF-1 is 101-267 ng/ml.

Since the present study was a retrospective medical record-based study and the subjects were de-identified, the Local Ethics Committee waived the need for written consent from the patients. The study followed the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Patient classification

Glucose metabolism abnormalities in patients were classified according to the current criteria of the American Diabetes Association [7] into the following subgroups: 1 – cases with normal glucose tolerance, defined as fasting plasma glucose <100 mg/dL (5.6 mmol/L) and 2h post-load blood glucose <140 mg/dL (7.8 mmol/L); 2 – patients with IFG and/or IGT, meaning that fasting plasma glucose was 100-125 mg/dL (5.6-6.9 mmol/L) and/or 2h post-load plasma glucose was 140-199 mg/dL (7.8-11.0 mmol/L); 3 – patients with DM (defined as fasting blood glucose ≥126 mg/dL and/or 2h post-load plasma glucose ≥200 mg/dL).

For lipid metabolism abnormalities patients were classified as presenting hypercholesterolemia when cholesterol values were >200 mg/dL and hypertriglyceridemia when triglycerides values were >150 mg/dL.

Statistical analysis

Data was collected and analyzed using SPSS v.17 (SPSS Inc. Chicago, IL, USA) statistical package. Hormonal and biochemical

determinations were stored in numerical variables and had a Gaussian distribution, so their results are presented as mean and standard deviation. To assess the statistical significance of the differences between groups we used the following statistical tests: unpaired t-student and one-way ANOVA (Gaussian distributed, numerical variables). Continuous variables distributions were tested for normality with Shapiro-Wilk test and for equality of variances with Levene's test. A "p" value lower than 0.05 was considered statistical significant.

Results

The study-group included 14 patients, 10 females (71.4%) with a mean age of 49.5 ± 10.6 years (range 35 – 64 years). All the patients were Caucasians (Table 1).

Table 2 presents the distribution of the patients according to glucose metabolism parameters in the moment of diagnosis. We could observe that 50% of the cases from our study group had different types of glucose metabolism abnormalities, but only two patients (14.3%) had secondary DM.

Table 1. Characteristics of the studied acromegaly patients

Parameter	**Value**
Patients (n)	14
Age (years)	49.5 ± 10.6
Women (n, %)	10 (71.4%)
Weight (kg)	79.4 ± 14.9
Body mass index (kg/m^2)	28.1 ± 4.8

Table 2. Study subgroups based on the presence of abnormalities in glucose metabolism.

Study subgroups	Glucose tolerance	Number of cases (%)
Subgroup 1 (7 cases)	Normal glucose tolerance	7 (50%)
Subgroup 2 (5 cases)	IFG/IGT	5 (35.7%)
Subgroup 3 (2 cases)	DM	2 (14.3%)

Table 3 presents the values of the body mass index (BMI) in the study groups.

Table 3. BMI and weight in acromegalic patients with normal or abnormal glucose tolerance.

Study groups	Total (14 cases)	Subgroup 1 (7 cases)	Subgroup 2 (5 cases)	Subgroup 3 (2 cases)	p*
Obese/Overweight (% from total)	4/3 (50%)	1/1 (28.6%)	2/1 (60%)	1/1 (100%)	0.17
BMI (kg/m^2)	28.1 ± 4.8	26.3 ± 3.7	29 ± 5.2	32 ± 7	0.32
Weight (kg)	79.4 ± 14.8	74.7 ± 14.1	83 ± 17.6	87 ± 9.9	0.51

Legend: *: p reflects the differences between the 3 subgroups.

The values of GH and IGF-1 were higher in cases with abnormalities of glucose metabolism as shown in Table 4.

Table 4. GH and IGF-1 levels in the studied patients.

Study groups	Total (14 cases)	Subgroup 1 (7 cases)	Subgroups 2 and 3 (7 cases)	p*
GH (ng/ml)	20 ± 13.2	17 ± 13.2	24.2 ± 20.3	0.47
IGF-1 (ng/ml)	727.8 ± 406.8	580.3 ± 265.6	934.3 ± 508	0.07

Legend: *: p reflects the differences between subgroup 1 and subgroups 2 and 3.

Two patients were diagnosed as having with hypercholesterolemia at the time of diagnosis and 6 as having combined dyslipidemia (both hypercholesterolemia and hypertriglyceridemia). As shown in Figure 1, only 6 cases (42.8%) had normal lipid parameters.

By analyzing the cases with and without lipid disorders we found that weight, BMI and GH values were higher, and IGF-1 level was lower, in patients with dyslipidemia, as shown in Table 5.

Only 4 out of the 14 studied cases (28.6%) presented normal values for all glucose and lipid metabolisms parameters when acromegaly was diagnosed.

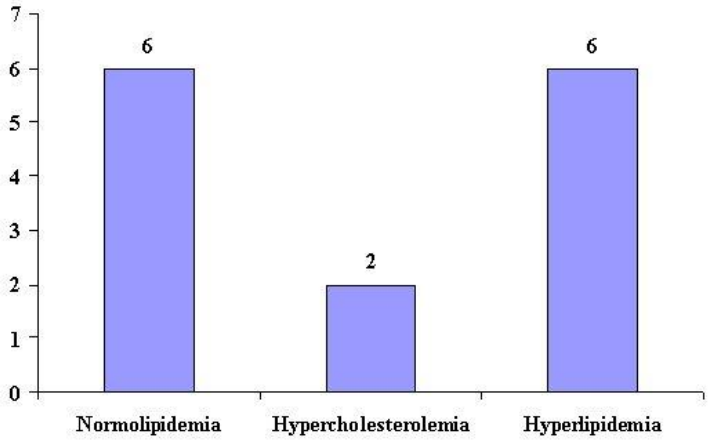

Figure 1. *Lipid abnormalities at diagnosis in the acromegalic patients.*

Table 5. GH, IGF-1, weight and BMI in acromegalic patients with and without abnormalities of lipid metabolism.

Study groups	Total (14 cases)	Normal lipids (6 cases)	Lipid abnormalities (8 cases)	p
BMI (kg/m^2)	28.1 ± 4.8	27.3 ± 6.3	28.7 ± 3.6	0.61
Weight (kg)	79.4 ± 14.8	76.7 ± 18.1	81.5 ± 12.8	0.57
GH (ng/ml)	20 ± 16.1	10.5 ± 4.6	24.8 ± 17.9	0.15
IGF-1 (ng/ml)	727.8 ± 406.8	870.8 ± 578.8	625.6 ± 225.6	0.33

Legend: *: p reflects the differences between patients with normal and those with abnormal lipid values.

Discussions

Untreated acromegaly is associated with a significant morbidity and mortality, mainly due to prolonged exposure to high levels of GH and IGF-1. It is well known that GH has influences both on glucose and lipid metabolisms.

Secondary DM and IGT are frequently associated with active acromegaly, but their prevalence differs widely among studies. In our patients, 50% (7 cases) presented abnormalities of glucose metabolism: DM was present in 2 patients (14.3%), IFG was revealed in 4 cases (28.6%) and IGT in one (7.1%).

In a recent study published in 2014 [4], using the same criteria for glucose abnormalities proposed by the American Diabetes Association, 28.5% of the patients had DM and 26.5% had IFG or IGT. Glucose abnormalities were present in 55% of their cases, a result that is comparable with ours. Even so, in our study the prevalence of DM (14.3%) was slightly lower than the minimum one reported by other studies as shown in Table 6.

Table 6. Prevalence of DM in different series of acromegalic patients in the most important studies.

Authors	Study group (n)	Prevalence (%)
Mestron et al. [8]	1219	37.6
Biering et al. [9]	206	32
Vitale et al. [5]	200	15.5
Bengtsson et al. [10]	166	27
Nabarro [11]	256	18.8
Gordon et al. [12]	100	18
Ronchi et al. [13]	208	18
Bex et al. [14]	415	25.3
Fieffe et al. [3]	519	22.3
Alexopoulou et al. [4]	148	28.5

In the present study, GH and IGF-1 mean values were higher in the patients with IFG/IGT or DM, but the differences did not reach the threshold for statistical significance due to the small number of cases. The weight and BMI were also higher in acromegalic patients with abnormalities of glucose metabolism, too. These results suggest that increased GH and IGF-I are

associated with the development of glucose metabolism abnormalities, but genetic and environmental factors are involved, as well.

Abnormalities of lipid metabolism were present in most cases (57.2%): high cholesterol level was detected in 2 cases and 6 cases presented increased values for both cholesterol and triglycerides.

From the whole group of acromegalic patients only 28.6% presented normal values for all glucose and lipid parameters.

In our opinion the strengths of our study is that all the cases were diagnosed and followed in the same department, using the same diagnostic criteria and laboratory investigations. The limitations of this study are the lack of data regarding cholesterol fractions (HDL, LDL) and the reduced number of the cases, which determined the nonsignificant statistic differences. Efforts to include other cases are forthcoming.

Conclusions

The results of this study indicate that abnormalities of glucose and lipid metabolism are very common in acromegalic patients, at the moment of acromegaly diagnosis. Even so, the prevalence of DM is lower than those reported in other studies.

Conflict of interest statement. The authors declare that they don't have any conflict of interest.

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