

Endokrynologia Polska/Polish Journal of Endocrinology Tom/Volume 61; Numer/Number 3/2010 ISSN 0423-104X

Aberrations in carbohydrate metabolism in patients with diagnosed acromegaly, hospitalized in the Endocrinology and Diabetology Department of *Collegium Medicum* University of Nicolaus Copernicus in Bydgoszcz in the years 2001–2009

Zaburzenia gospodarki węglowodanowej u pacjentów z akromegalią hospitalizowanych w Klinice Endokrynologii i Diabetologii *Collegium Medicum* Uniwersytetu im. Mikołaja Kopernika w Bydgoszczy w latach 2001–2009

Marcin Gierach, Joanna Gierach, Małgorzata Pujanek, Agnieszka Skowrońska, Emilia Rutkowska, Roman Junik

Department of Endocrinology and Diabetology, Nicolaus Copernicus University in Torun, Collegium Medicum, Bydgoszcz

Abstract

Introduction: The incidence rate of acromegaly is 50 to70 persons per one million people. It occurs twice as often in women than in men, especially in middle age. In the course of the disease, insulin resistance develops, which is connected with the hypersecretion of somatotropin. Type 2 diabetes mellitus occurs more frequently in patients with acromegaly than in the rest of the population. It is diagnosed in 13–56% of acromegaly sufferers; impaired glucose tolerance occurs in 16–46% of examined patients with acromegaly.

The aim of this study is to estimate disturbances of glycaemia in patients with diagnosed acromegaly, hospitalized in the Endocrinology and Diabetology Department of Collegium Medicum University of Nicolaus Copernicus in Bydgoszcz in the years 2001–2009.

Material and methods: The participants were a group of 70 patients with acromegaly diagnosed on the basis of clinical symptoms, high levels of somatotropin, and MRI imaging of the pituitary gland.

Results: Type 2 diabetes was diagnosed in 19 patients (27%); there were 11 cases (15%) of diagnosis of impaired fasting glycaemia (IFG) and imapired glucose tolerance (IGT) combined. Normoglycaemia was recognized in 57% of participants (40 patients). The average age of participants with concomitant type 2 diabetes was 56.1 years, whereas the average age of those without carbohydrate metabolism disturbances was 47.1 years.

Conclusions: In patients with acromegaly, the incidence rate of type 2 diabetes is 3–4-times higher than in the rest of the population and increases with age, especially after the age of 60. (Pol J Endocrinol 2010; 61 (3): 260–263)

Key words: acromegaly, diabetes, IFG, IGT

Streszczenie

Wstęp: Akromegalia występuje z częstością około 50–70 na milion osób, 2-krotnie częściej u kobiet niż u mężczyzn, szczególnie w średnim wieku. W przebiegu akromegalii dochodzi do wystąpienia insulinooporności związanej z nadmiernym wydzielaniem hormonu wzrostu. Cukrzyca typu 2 u pacjentów z akromegalią występuje częściej niż w populacji ogólnej. Stwierdza się ją u 13–56% pacjentów, natomiast upośledzona tolerancja glukozy występuje u 16–46% badanych osób z akromegalią.

Celem pracy była ocena zaburzeń gospodarki węglowodanowej u pacjentów z rozpoznaną akromegalią, hospitalizowanych w Klinice Endokrynologii i Diabetologii *Collegium Medicum* Uniwersytetu Mikołaja Kopernika w Bydgoszczy w latach 2001–2009.

Materiał i metody: W pracy przedstawiono 70 pacjentów z akromegalią rozpoznaną na podstawie podwyższonego stężenia hormonu wzrostu, obrazu klinicznego oraz badania MRI przysadki.

Wyniki: Cukrzycę typu 2 u osób z rozpoznaną akromegalią stwierdzono u 19 pacjentów (27%), natomiast nieprawidłową glikemię na czczo (IFG, *impaired fasting glycaemia*) i upośledzoną tolerancją glukozy (IGT, *impaired glucose tolerance*) łącznie u 11 z nich (15%). Pacjenci z normoglikemią stanowili w badanej populacji 57% (40 pacjentów). W grupie przebadanych 70 osób z rozpoznaną akromegalią, średni wiek osób z towarzyszącą cukrzycą typu 2 wynosił 56,1 lat w stosunku do osób bez zaburzeń gospodarki węglowodanowej — 47,1 lat.

Wnioski: U pacjentów z akromegalią częstość występowania cukrzycy typu 2 jest 3–4-krotnie większa niż w populacji ogólnej i rośnie wraz z wiekiem, szczególnie po 60. roku życia. (Endokrynol Pol 2010; 61 (3): 260–263)

Słowa kluczowe: akromegalia, cukrzyca, IFG, IGT



Marcin Gierach M.D., Department of Endocrinology and Diabetology of Ludwik Rydygier, *Collegium Medicum* in Bydgoszcz, University of Nicolaus Copernicus in Toruń, ul. M. Skłodowskiej-Curie 9, 85–094 Bydgoszcz, tel./fax: +48 52 585 42 40, e-mail: marcin_gierach@wp.pl

Introduction

The incidence rate of acromegaly is 50 to 70 persons per one million people. It occurs twice as often in women than in men, especially in middle age. In the course of the disease, insulin resistance develops, which is connected with the hypersecretion of somatotropin, which disturbs insulin activity both in the liver and peripheral tissues [1].

Somatotropin also increases lipolysis of adipose tissue, boosting the amount of free fatty acids in blood serum, and increasing insulin resistance, which results in aberrations in carbohydrate metabolism [2–4].

Type 2 diabetes mellitus occurs more frequently in patients with acromegaly than in the rest of the population [2, 5]. It is diagnosed in 13–56% of acromegaly sufferers; impaired glucose tolerance occurs in 16–46% of examined patients with acromegaly [2–4, 6–8].

However, impaired fasting glucose occurs in approximately 19% of patients with acromegaly [2].

The aim of this study was to examine the influence 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 2001–2009.

Material and methods

The study group consisted of 70 patients (44 women and 26 men; aged 19 to 76 years) with acromegaly diagnosed on the basis of clinical symptoms, high level of somatotropin, and MRI imaging 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 2001–2009.

Round-the-clock glucose profiles of the participants was marked; oral glucose tolerance tests were also conducted in cases of impaired fasting glucose (IFG) (> 100 mg/dL) or postprandial glucose (140–200 mg/dL).

Table I. Aberrations in carbohydrate metabolism in patients with acromegaly according as sex

Tabela I. Zaburzenia gospodarki węglowodanowej u pacjentów z akromegalią w zależności od płci

| Acromegaly | Normoglycaemia | IFG + IGT | Type 2 diabetes |
|--------------|----------------|-----------|--------------------|
| All (n = 70) | n = 40 | n = 11 | n = 19 |
| | (57%) | (15.7%) | (27%) |
| Female | n = 30 | n = 4 | n = 10 |
| (n = 44) | (68%) | (9%) | (22.7%) |
| Male | n = 10 | n = 7 | n = 9 |
| (n = 26) | (38.5%) | (26.9%) | (34.7%) |

Results

Type 2 diabetes was diagnosed in 19 patients (27%). There were 11 cases (15%) of diagnosis of IFG and impaired glucose tolerance (IGT) combined. Normoglycaemia was recognized in 57% of participants (40 patients) (Table I).

The average age of participants with concomitant type 2 diabetes was 56.1 years, whereas the average age of those without carbohydrate metabolism disturbances was 47.1 years. This difference was less in females than in males (F — 55 v. 50.8; M — 57.3 v. 36). The average age of patients with IFG and IGT was 49.6 years (Table II).

The participants were divided into four subgroups according to their age (20–30; 31–50; 51–60; >60). The group with the largest number of participants comprised the patients aged from 31 to 60, *i.e.* 54 patients (77%).

Aberrations of carbohydrate metabolism in cases of IFG, IGT, and type 2 diabetes mellitus occurred with similar frequency in all age subgroups except for the group of participants aged 60 and over, in which a significant increase of the percentage of patients with type 2 diabetes mellitus was observed, in comparison to those with normoglycaemia. Patients with IFG and IGT aged 60 years and over did not show changes compared with those under 60 (Table III).

Table II . Aberrations in carbohydrate metabolism in patients with acromegaly according as average age
Tabela II. Zaburzenia gospodarki węglowodanowej u pacjentów z akromegalią w zależności od średniego wieku

| Average age of patients with acromegaly | Normoglycaemia (years) | IFG + IGT (years) | Type 2 diabetes (years) | |
|---|---------------------------|----------------------|----------------------------|--|
| All (n = 70) | 47.1 | 49.6 | 56.1 | |
| Female (n = 44) | 50.8 | 49.2 | 55 | |
| Male (n = 26) | 36 | 49.8 | 57.3 | |

Table III. Occurrence of aberrations in carbohydrate metabolism in patients with acromegaly according of age
Tabela III. Występowanie zaburzeń gospodarki węglowodanowej u pacjentów z akromegalią w zależności od wieku

| Aged group (years) | Number of patients n = 70 | Normoglycaemia n = 40 | IFG + IGT n = 11 | Type 2 diabetes mellitus n = 19 |
|--------------------|---------------------------|--------------------------|---------------------|---------------------------------|
| 20–30 | 6 | 4 (66%) | 1 (16.6%) | 1 (16.6%) |
| 31–50 | 25 | 16 (64%) | 3 (12%) | 6 (24%) |
| 51–60 | 29 | 18 (62%) | 5 (17%) | 6 (20.6%) |
| > 60 | 10 | 2 (20%) | 2 (20%) | 6 (60%) |

Table IV. Average fasting, postprandial and twenty-four-hour glycaemia in patients with acromegaly and type 2 diabetes mellitus

Table IV. Średni poziom glikemii na czczo, poposiłkowej i dobowej u pacjentów z akromegalią i cukrzycą typu 2

| Patients with type 2 diabetes mellitus | Average fasting glucose | Average postprandial glycaemia | Average twenty-four-hour glycaemia |
|--|-------------------------|--------------------------------|------------------------------------|
| All (n = 19) | 128 mg/dL | 163 mg/dL | 158 mg/dL |
| Female (n = 10) | 126 mg/dL | 141 mg/dL | 149 mg/dL |
| Male (n = 9) | 130 mg/dL | 189 mg/dL | 169 mg/dL |

In patients with acromegaly and aberrations of carbohydrate metabolism such as type 2 diabetes mellitus, the average level of fasting glucose was 128 mg/dL. In these cases average postprandial glycaemia was 163 mg/dL, while average twenty-four-hour glycaemia was 158 mg/dL (Table IV).

Discussion

Acromegaly is an endocrinopathy which causes the development of insulin resistance. Therefore, there is a higher occurrence rate of aberrations in carbohydrate metabolism in patients with acromegaly.

In patients with diagnosed acromegaly, type 2 diabetes mellitus occurs 3.7 times more often than in the rest of the population ($20 \, v. \, 5.37\%$) [9, 10]. Stelmachowska-Banaś et al., who examined the Polish acromegaly population, found type 2 diabetes in 20% of patients, IGT in 15% of patients, and IFG in 19% of patients [9, 10].

In this study there were 70 patients with diagnosed acromegaly. In 43% of them aberrations in carbohydrate metabolism were observed. Type 2 diabetes was found in 27% of patients. This was approximately 7% more than in Stelmachowskaa-Banaś et al. study. Impaired fasting glucose and impaired glucose tolerance occurred in 15% of cases, whereas Stelmachowska observed it in 34% of cases.

Increased risk of aberrations in carbohydrate metabolism in patients with acromegaly was observed by

Resmini and his collaborators. They proved it was dependent on somatotropin concentration, duration of the disease, and the age of the patient. However, Stelmachowska et al. did not prove a statistically significant relationship between the levels of growth hormone (GH), insulin-like growth factor 1 (IGF-1), and disease duration in relation to aberrations in carbohydrate metabolism. Only the age of the patients proved to be statically significant (the older the patient, the more frequent the occurrence of aberrations in carbohydrate metabolism). Bierin et al. also assumed that the age of patients was a major risk factor in the development of aberrations in carbohydrate metabolism [11].

In this study a significant increase in the percentage of patients with type 2 diabetes in the age subgroup under 60 years of age was observed when compared to the ones with normoglycaemia ($60\% \ v.\ 20\%$). In patients under 60 years of age the proportions in each of the subgroups were reversed, i.e. the ratio of patients with normoglycaemia to the ones with type 2 diabetes was on average 64% to 21%.

There was a great number of studies in which it was observed that patients with type 2 diabetes coinciding with acromegaly were on average ten years older than the ones with acromegaly coinciding with normogly-caemia [2, 12].

In our study almost the same results were obtained. In the examined group of 70 patients with recognized acromegaly, the average age of patients with type 2 diabetes co-occurring was 56.1 years, whereas in those

without aberrations in carbohydrate metabolism it was 47.1 years of age. This difference seemed to be smaller in males than in females (F - 55 v. 50.8; M - 57.3 v. 36).

Conclusions

In patients with acromegaly the incidence rate of type 2 diabetes is 3–4 times higher than in the rest of the population and increases with age, especially in people aged 60 years and over.

References

- Coculescu M, Niculescu D, Lichiardopol R et al. Insulin resistance and insulin secretion in non-diabetic acromegalic patients. Exp Clin Endocrinol Diabetes 2007; 115: 308–316.
- Milaszewska K, Krętowski A. Zaburzenia gospodarki węglowodanowej w akromegalii. Przegląd Kardiodiabetologiczny 2009; 4: 90–93.
- Grzesiuk W, Szydlarska D, Jóźwik K. Insulinooporność w endokrynopatiach. Endokrynol., Otył. Zab. Przem. Mat. 2008; 5: 38–44.

- 4. Resmini E, Minuto F, Colao A et al. Secondary diabetes associated with principal endocrinopathies: the impact of new treatment modalities. Acta Diabetol 2009; 46: 85–95.
- Colao A, Ferone D, Marzullo P et al. Systemic complication of acromegaly: epidemiology, pathogenesis, and management. Endocr Rev 2004; 25: 102–152.
- Kreze A, Kreze-Spirova E, Mikulecky M. Risk factor for glucose intolerance in active acromegaly. Braz J Med Biol Res 2001; 34: 1429–1433.
- Szelachowska M, Górska M, Zonenberg A. Insulinooporność w wybranych endokrynopatiach. In: Kinalska I. (ed.). Patofizjologia i następstwa kliniczne insulinooporności. Wydawnictwo Kliniki Endokrynologii, Diabetologii i Chorób Wewnętrznych. W ramach działalności Polskiego Towarzystwa Kardiodiabetologicznego, Białystok 2005: 239–249.
- 8. Ezzat S, Forster MJ, Berchtold P et al. Acromegaly: clinical and biochemical features in 500 patients. Medicine 1994; 73: 233–240.
- Stelmachowska-Banaś M, Zdunowski P, Zgliczyński W. Abnormalities in glucose homeostasis in acromegaly. Does the prevalence of glucose intolerance depends on the level of activity of the disease and the duration of the symptoms? Endokrynol Pol 2009; 60: 20–24.
- Szybiński Z. Polskie wieloośrodkowe badanie nad epidemiologią cukrzycy (PWBEC 1998–2000). Pol Arch Med Wewn 2001; 106: 751.
- 11. Bierin H, Knapie G, Gerl H et al. Prevalence of diabetes in acromegaly and Cushing syndrome. Acta Med Austriaca 2000; 27: 27–31.
- Katz JR, Edwards R, Khan M et al. Acromegaly presenting with diabetic ketoacidosis. Postgrad Med J 1996; 72: 682–683.