Thyroid Volume in Type 2 Diabetics: Relationship to Patients' Weight and Type of Treatment

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Abstract

Diabetes mellitus and thyroid diseases are closely connected, and 11% of patients with diabetes have thyroid diseases. The data is the same for type 1 and type 2 patients with diabetes mellitus; women face the disease two times more frequently than men. The latest researches have proved that metformin has lowered the level of TSH and thyroid volume.

The aim of the research is to prove the correlation between thyroid volume and the changes of weight in connection with type 2 diabetes, by analysing patients' medical situation, maintaining laboratory and clinical data, and therapy.

The research information (138 case histories) was divided into three groups: the first – 76 patients with type 2 diabetes and obesity who use metformin, the second control group – 39 patients with type 2 diabetes and obesity who are cured with insulin but do not use metformin, and the third – 23 patients with normal body mass index. The results of the research have been processed with the SPSS for Windows 22.0.

The correlation appraisal between body mass index and thyroid volume correlation was proved (r_s = 0.23; p = 0.006), and the results are statistically significant. It was proved that the patients with metabolic syndrome and insulin resistance have bigger thyroid volumes.

Thyroid volumes for patients with type 2 diabetes and obesity using metformin are nearly the same as for patients with type 2 diabetes and obesity who do not use metformin, (p = 0.857), and there is no significant statistical difference between these two groups.

TSH level for the first group is 1.67 ± 0.84 mU/L, for the second – 1.8 ± 0.81 mU/L, but for the third – 1.47 ± 0.86 mU/L (p = 0.443). The average TSH level for the first group compared to the second group is lower. The data proves that metformin may lower the TSH level.

Keywords: diabetes mellitus, thyroid volume, TSH, metformin.

Introduction

There are about 60 million people with diabetes in the European Region – about 10.3% of men and 9.6% of women aged 25 years and over. Prevalence of diabetes is increasing among all ages in the European Region, mostly due to increase in overweight and obesity, unhealthy diet and physical inactivity. Furthermore, high blood glucose kills about 3.4 million people worldwide annually. Almost 80% of these deaths occur in low- and middle-income countries, and almost half are people aged less than 70 years. WHO predicts that deaths due to diabetes will double between 2005 and 2030 [21].

Prevalence of diabetes is increasing in Latvia too. In 2007, the number of patients who were diagnosed with the second type of diabetes (T2DM) was 54 305; in the 2012, this number rose to 73 680 [1].

Diabetes mellitus and thyroid disease appear to be closely linked. A recent meta-analysis of 10 920 patients with diabetes mellitus revealed a mean frequency of thyroid disease of 11%. The data in type 1 diabetes mellitus did not differ from those in type 2 diabetes mellitus, but the prevalence in women was consistently more than twofold compared to men. There was a wide variability of the prevalence reported in different studies varying between 4.8% and 31.4%, partly explained by the different definitions used for the diagnosis of diabetes mellitus and thyroid disorders [5; 8].

Thyroid disease and type 1 and type 2 diabetes mellitus are strongly associated, and this has important clinical implications for insulin sensitivity and treatment requirements. Hyper- and hypothyroidism have been associated with insulin resistance, which has been reported to be the major cause of impaired glucose metabolism in T2DM. The state-of-art evidence suggests a pivotal role of insulin resistance in underlining the relation between T2DM and thyroid dysfunction [15; 19]. The pathophysiological basis of this association has only recently been better elucidated. The pathophysiological mechanisms underlying this linked regulation are increasingly being unravelled. They are exemplified in the regulation of 5´ adenosine monophosphate-activated protein kinase (AMPK), a central target not only for the modulation of insulin sensitivity but also for the feedback of thyroid hormones on appetite and energy expenditure. The present review will discuss these concepts and their consequences for the clinical care of patients with diabetes mellitus and thyroid disorders. Moreover, it refers to the added effect of metformin in suppressing thyroid stimulating hormone (TSH) [7; 8; 13; 14].

Aim

The aim of the research is to prove the correlation between thyroid volume and changes in weight in connection to the second type of diabetes, analysing patients' medical situation, maintaining laboratory and clinical data, therapy.

Material and methods

The research information about 138 case histories were divided into three groups: the first – 76 patients with type 2 diabetes and obesity who use metformin, the second control group – 39 patients with type 2 diabetes and obesity who are cured with insulin but do not use metformin, and the third – 23 patients with normal body mass index.

Patients were divided into three groups in order to compare patients with type 2 diabetes and obesity, metformin users, in patients with type 2 diabetes mellitus and obesity, and those not taking metformin, to determine how metformin is able to influence TSH levels and thyroid volume in patients who use metformin. The third control group was set up to explore overweight effects on the thyroid volume.

The first and the second group were examined by looking at the duration of diabetes, glicated hemoglobin, and C-peptide, all groups took into account the patient's age, sex, BMI, smoking, and smoking pack years, antibodies to TPO, TSH and free thyroxin, thyroid volume, and the number of nodes.

The results of the research have been processed with the SPSS for Windows 22.0 (Statistical Package for the Social Sciences).

Results

By assessing variability of age, the average age of the group is 41.41 years ± 11.796. Evaluation of groups was divided according to sexes – in the first group were 44 women (57.9%) and 32 men (42.1%), in the second group were 22 women (56.4%) and 17 men (43.6%), p = 0.879 between the first two groups, and in the third group were 17 women and 6 men.

In the first and second group, the medium duration of diabetes was 10.08 ± 8.46 years, but glicated hemoglobin (HbA1c) medium value was 9.2945 ± 1.7624%, which is significantly higher than in the normal range from 4.8 to 5.9% and the target glycemia. However, when comparing the first and second groups, the difference was not statistically significant: for the first group the median HbA1c level was 9.3 ± 1.77% (min 5.9%, max 14.9%), while the second – 9.27 ± 1.77% (min 5.9%, max 12.5%). On the other hand, the mean thyroid volume in all groups was 14.1934 ± 6.7282 mL. The first and the second group did not differ in the C-peptide level – 2.52 ± 1.27 ng/mL and 2.52 ± 2.62 ng/mL, respectively (min 0.54 ng/mL, max 6.18 ng/mL and min 0.1 ng/mL, max 12.1 ng/mL, respectively).

The average BMI was 33.7 ± 8.604 kg/m^2. Comparing the first and second groups of women, the first group of women had a higher BMI, 34.32 and 31.86 kg/m^2, respectively. Thyroid volume was 14.1934 ± 6.7282 mL (95% CI 13.06 to 15.32). After evaluating the correlation between BMI and thyroid volume in general population, it was statistically significant (r_s = 0.23; p = 0.006).

Comparing the thyroid volume in the first and second group, there was no statistically significant difference (p = 0.857). Comparing the thyroid volume between the first and second groups of women and men, there was not statistically significant difference (p = 0.989 and p = 0.9, respectively). This means that patients with type 2 diabetes and obesity receiving metformin have thyroid volume almost as high as patients have with type 2 diabetes and obesity not using metformin. Comparing the first to the third group of thyroid volume, there was a statistically significant difference (p < 0.001). Knowing that the first group has patients with type 2 diabetes mellitus and obesity, and the third one – patients with a normal weight, it can be concluded that the volume of the thyroid gland was bigger in first group (type 2 diabetes and metformin users) than third group (people with normal BMI).

When analysing the data, a reliable correlation between thyroid volume and TSH levels (r_s = −0.194, p = 0.024). The average TSH levels in all groups were 1.67 ± 0.84 mU/L (95% CI 1.53 to 1.81). The first group's TSH level was 1.67 ± 0.84 mU/L (min 0.48, max 4.1), for the second it was 1.8 ± 0.81 mU/L (min 0.5 max 3.5) and in the third it was 1.47 ± 0.86 mU/L (min 0.25, max 3.2) (p = 0.443). The average level of TSH in the first group was statistically significantly lower than in the second one, suggesting that perhaps metformin is able to reduce TSH levels.

Discussion

The study did not prove metformin's ability to reduce thyroid volume, which may be associated with a relatively small population. To further explore this topic, there is a need for a larger percentage of patients as well as patient questionnaires to find out how long and if metformin is used regularly. Hence, a large part of the study was based on the fact that metformin was administered for at least six months.

Following this study, it is interesting to compare patients with type 2 diabetes mellitus and obesity who use metformin, with patients with type 2 diabetes mellitus and normal weight who also are metformin users, to evaluate in which case metformin is able to reduce the volume of the thyroid gland.

A recent study included 2570 individuals for cross-sectional and 1088 individuals for longitudinal analyses. In cross-sectional data, females with T2DM were treated with anti-diabetic medication other than metformin and had a larger thyroid volume (β = 4.69; 95% CI 1.87 to 7.50) and a higher odds ratio (OR) for goitre (OR = 1.71; 95% CI 1.05 to 2.79) than females without T2DM. For males, no such association was detected. Females or males treated with metformin, T2DM were not associated with thyroid volume or goitre. In longitudinal analyses, incident T2DM not treated with metformin was significantly associated with a higher risk for incident goitre in the total population (incidence rate ratio (IRR) = 1.70; 95% CI 1.10 to 2.91). Individuals with T2DM having changed from metformin to other anti-diabetic agents during follow-up also had a higher risk for incident goitre than individuals without T2DM had (IRR = 2.71; 95% CI 1.74 to 4.20) [10].

Another result of the study was mean TSH level in the diabetes group (1.9 ± 0.9 mIU/L) was higher than in the control group (1.4 ± 0.8 mIU/L) and the pre-diabetes group (1.5 ± 0.8 mIU/L) (p < 0.0001 for both). Mean thyroid volume was higher in the pre-diabetes (18.2 ± 9.2 mL) and diabetes (20.0 ± 8.2 mL)

groups than in controls (11.4 ± 3.8 mL) ($p < 0.0001$ for both). Percentage of patients with thyroid nodules was also higher in the pre-diabetes (51.3%) and diabetes groups (61.8%) than in controls (23.7%) ($p < 0.0001$ for both) [2].

In conclusion, we would like to explore the effect of metformin on thyroid nodes that were not taken into account in this study because most of the thyroid USG descriptions did not accurately describe thyroid nodules number and size.

The recent study results suggest that patients with metabolic syndrome have significantly increased thyroid volume and nodule prevalence. Multivariate regression analysis model demonstrated that the presence of insulin resistance contributed substantially to this increased risk. Data provided the first evidence that insulin resistance is an independent risk factor for nodule formation in an iodine-deficient environment [3].

Conclusions

1. When analysing the results of the Latvian patients it was not proved that the metformin is capable of statistically significant reduction in thyroid volume compared to patients with type 2 diabetes mellitus and obesity using metformin and type 2 diabetes mellitus patients with obesity injecting insulin and who do not use metformin ($p = 0.857$).
2. It was possible to prove that patient's weight affects the thyroid volume, evaluating the weak correlation between average BMI and average capacity of thyroid volume ($r_s = 0.23$; $p < 0.006$).
3. Comparing the average TSH value between the groups (medium TSH volume in the first group is 1.67 ± 0.84 mU/L, but in second – 1.8 ± 0.81 mU/L, which may indicate a possible effect of metformin on TSH levels ($p = 0.443$)). It is possible that metformin is able to reduce TSH level, as well as statistically significant correlation between TSH level and thyroid volume ($r_s = -0.194$; $p = 0.024$).

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