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Clinical Thyroidology

Metformin Prevents Goiter in Patients with Type 2 Diabetes

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Ittermann T, Markus MR, Schipf S, Derwahl M, Meisinger C, Völzke H. Metformin inhibits goitrogenous effects of type 2 diabetes. Eur J Endocrinol 2013;169:9-15.

SUMMARY

Background

The literature on the association between type 2 diabetes mellitus (T2DM) and thyroid volume is sparse. A recent experimental study demonstrated an inhibitory effect of metformin on the growth of human thyroid cells. According to the authors, no study on humans has investigated potentially modulating effects of metformin on the association between T2DM and thyroid volume. Their objective was to investigate these effects in a population-based cohort study.

Methods

The authors used data from the Study of Health in Pomerania (SHIP), a population-based cohort study conducted in West Pomerania, Germany. The population of the region had been iodine-deficient until the mid-1990s. Among older persons, the prevalence of goiter is still high. The study included 2570 individuals for cross-sectional and 1088 individuals for longitudinal analyses. T2DM was defined by physician-diagnosed self-report or by intake of antidiabetes medication. Age, sex, smoking status, drug intake, and T2DM were assessed by computer-assisted personal interviews. Initial examinations were performed between 1997 and 2001 and a follow up examination between 2002 and 2006 (1589 men and 1711 women, 83.5% of all eligible subjects). The median follow-up time was 5.0 years. Examinations at baseline and follow-up included anthropometry, thyroid ultrasonography, and laboratory measurements. For the longitudinal analyses, the authors considered sex, development of T2DM, and treatment with metformin or other antidiabetes drugs.

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Results

In the cross-sectional data, women with T2DM treated with antidiabetes medications other than metformin had a larger thyroid volume and a higher odds ratio (1.71) than women without T2DM. For men, no such association was detected. In women or men treated with metformin, T2DM was not associated with thyroid volume or goiter. In longitudinal analyses, incident T2DM not treated with metformin was significantly associated with a higher risk for incident goiter in the total population. Individuals with T2DM who changed from metformin to other antidiabetes agents during follow-up also had a higher risk for incident goiter than individuals without T2DM .

Conclusions

The authors demonstrate an inhibitory effect of metformin on prevalent and incident goiter and that the antigoitrogenic effect of metformin should be added to the general benefits of metformin treatment of T2DM.

ANALYSIS AND COMMENTARY

Patients diagnosed with T2DM and those with insulin resistance have been reported to have larger thyroid-gland volume as compared with control populations. In the present study, the authors followed a group of patients with T2DM and a control group, showing a significant decrease in the thyroid volume only in patients treated with metformin, versus those on diet alone or taking other antidiabetes agents; furthermore, in patients in the control group in whom diabetes developed, metformin prevented goiter. The relationship between metformin, thyroid function, and thyroid volume had been of interest to many investigators (1-4). A study by Cappelli et al. (4) (reviewed in Clinical Thyroidology [5]) confirmed the TSH-lowering effect of metformin in people with diabetes and hypothyroidism on L-T_4 treatment; in addition, the authors showed a significant reduction in serum TSH levels in euthyroid patients with higher baseline serum TSH levels independent of the presence of TPOAb. Metformin treatment was reported to reduce thyroid nodule size in a group of women diagnosed with the syndrome of insulin resistance (3). A recent study demonstrated an inhibitory effect of metformin on the growth of human thyroid cells, by activation of the adenosine monophosphate–activated protein kinase (AMPK)–mammalian target of rapamycin (mTOR) pathway and antagonism of the growth-stimulatory effect of insulin by inhibition of the mitogen-activated protein kinase (MAPK) pathway (6). A favorable metformin response to chemotherapy was reported in patients with breast cancer who had diabetes (7).

The above studies should be of clinical interest for practicing endocrinologists. Metformin is widely used in the management of prediabetes, metabolic syndrome, polycystic ovary syndrome, and T2DM. Recent studies of metformin's effect on thyroid function, beneficial action on thyroid volume, reduction in the size of thyroid nodules, and a possible potential effect on chemotherapeutic agents could bring exciting future alternative therapies for the benefit of our patients.

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