

Med Princ Pract 2017;26:199–200
DOI: 10.1159/000452955

Comment on “Metformin Decreases Thyroid Volume and Nodule Size in Subjects with Insulin Resistance: A Preliminary Study”

Umit Cintosun, Mehmet Ilkin Naharci, Huseyin Doruk

Department of Geriatrics, Gulhane School of Medicine, Ankara, Turkey

Dear Editor,

The study by Anil et al. [1] deserves attention for investigating 2 common health problems: insulin resistance and thyroid nodules. From a geriatric perspective it is more remarkable because of the high incidence of these 2 conditions.

Firstly, it is understood that choosing an upper limit of TSH 4.0 mU/L may not be appropriate for older adults. Aging by itself is associated with elevated TSH, and keeping treatment targets tight

as in a younger population could be harmful to the adults [2]. Secondly, using only body mass index (BMI) in such a heterogeneous group could lead to false results. Sarcopenic obesity which accelerates insulin resistance is a common condition in elderly population; therefore, BMI should be supported by additional measurements [3]. A third matter is that a hypocaloric diet, weight loss, and lifestyle changes are also well-known factors that affect thyroid nodules [4]. These factors also have to be ruled out to reveal the separate effect of metformin treatment on thyroid volume and nodule.

References

- 1 Anil C, Kut A, Atesagaoglu B, et al: Metformin decreases thyroid volume and nodule size in subjects with insulin resistance: a preliminary study. *Med Princ Pract* 2016;25:233–236.
- 2 Atzmon G, Barzilai N, Hollowell, JG, et al: Extreme longevity is associated with increased serum thyrotropin. *J Clin Endocrinol Metab* 2009; 94:1251–1254.
- 3 Wells JCK: *The Evolutionary Biology of Human Fatness*. Cambridge, Cambridge University Press, 2009.
- 4 Hua J, Yongfeng T, Wenhua Y, et al: The prevalence of thyroid nodules and an analysis of related lifestyle factors in Beijing Communities. *Int J Environ Res Public Health* 2016;13:442.

Reply

Cuneyd Anil^a, Altug Kut^b, Berna Atesagaoglu^a, Asli Nar^a, Neslihan Bascil Tutuncu^a, Alptekin Gursoy^a

Departments of ^aEndocrinology and Metabolism, and ^bFamily Medicine, Baskent University Faculty of Medicine, Ankara, Turkey

Dear Editor,

We have examined the comments of Cintosun et al. on our published manuscript entitled “Metformin Decreases Thyroid Volume and Nodule Size in Subjects with Insulin Resistance: A Preliminary Study” [1].

The first issue was about the reference range of TSH in a geriatric population. We agree that target TSH should be set higher in this population, but the target reference range of TSH levels has not been strictly defined in recent endocrine guidelines and endocrine textbooks [2, 3]. However, this is generally valid for (sub-clinical) hypothyroidism cases who are on levothyroxine therapy, which was not a subject of our study. No randomized controlled trial of LT₄ treatment in elderly patients with hypothyroidism compared to different TSH target values are available [2]. In one up-to-date guideline regarding hypothyroidism published by the American Thyroid Association [2], it has been finally reported that based on the current evidence it is reasonable to raise the target

serum TSH to 4–6 mIU/L in persons older 70–80 years. Therefore, using the upper limit of normal for TSH level as 4 IU/mL, in a study population aged maximum 75 years, seems reasonable.

As to the second issue, we are aware that sarcopenic obesity, a common pathology in aging population, is closely associated with metabolic syndrome and related conditions [4]. This condition might have contributed to the development of insulin resistance (IR) in this small subgroup of our study population of early geriatric age. We studied some possible outcomes of IR such as thyroid morphology and function, not the etiology or its mechanisms. Besides, diagnostic measures of sarcopenic obesity require different methods and instruments (including muscle mass, muscle strength, and physical performance) [4]. However, a universal consensus for a standard, objective, and unique parameter of sarcopenic obesity has not been reported yet, as far as we know. Thus, universally well-known and scientifically accepted parameters such as BMI and waist circumference are commonly and favorably used in research

like ours [1, 5]. In a previous study by our group, which helped to form the basis for the present study, the study population also included cases from early geriatric age (e.g., up to 75 years) [5]. An analysis we performed has revealed that the level of significance of the findings did not change when we excluded cases older than 65 years.

Concerning the third issue, we think that omission of the effect of lifestyle factors in such intervention studies is only possible with inclusion of a control group. Otherwise, leaving the cases without a standard diet would probably affect the outcomes unpredictably. Lack of a control group has been expressed as a limitation of this unique work, which was preliminary. Our ongoing prospective study with a higher number of cases, longer follow-up period, and including a control group will probably address these concerns. In any case, as the authors have cited, the effects and the mechanisms of those effects of lifestyle changes on the thyroid gland have not been prospectively reported, and merely depend on epidemiological and prevalence data. Lifestyle changes probably act mainly through weight loss, which decreases IR; some other factors may be operative. We may all appreciate that lifestyle factors probably did not predominate the effect of losing such weight and decreasing IR in a time span of 6 months.

References

- 1 Anil C, Kut A, Atesagaoglu B, et al: Metformin decreases thyroid volume and nodule size in subjects with insulin resistance: a preliminary study. *Med Princ Pract* 2016;25:233–236.
- 2 Jonklaas J, Bianco AC, Bauer AJ, et al; American Thyroid Association Task Force on Thyroid Hormone Replacemen: Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. *Thyroid* 2014;24:1670–1751.
- 3 Brent GA, Weetman AP: Hypothyroidism and Thyroiditis; in Melmed S, Polonsky KS, et al. (eds): *Williams Textbook of Endocrinology*. Philadelphia, Elsevier, 2016, pp 416–448.
- 4 Lim S, Kim JH, Yoon JW, et al: Sarcopenic obesity: prevalence and association with metabolic syndrome in the Korean Longitudinal Study on Health and Aging (KLoSHA). *Diabetes Care* 2010;33:1652–1654.
- 5 Ayturk S, Gursoy A, Kut A, et al: Metabolic syndrome and its components are associated with increased thyroid volume and nodule prevalence in a mild-to-moderate iodine-deficient area. *Eur J Endocrinol* 2009;161:599–605.

Cuneyd Anil
Department of Endocrinology and Metabolism
Baskent University Faculty of Medicine
5. Sokak No. 48, TR-06490 Bahcelievler, Ankara (Turkey)
E-Mail cuneydanil@yahoo.com