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Subclinical Hypothyroidism in Elderly People

M. M. Petrova and E. A. Pronina

Voyno-Yasenetskiy Krasnoyarsk State Medical University, ul. Partizana Zheleznyaka 1, Krasnoyarsk, 660022 Russia
e-mail: stk99@yandex.ru

Abstract—The article describes clinical manifestations of subclinical hypothyroidism in the elderly, as well as the current diagnostic criteria and approaches to its treatment in the patients of the elderly age group.

Keywords: subclinical hypothyroidism, elderly people

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Demographic changes in contemporary society are characterized by longer adult lifespans and a higher proportion of elderly people in the total population. Subclinical hypothyroidism is one of the most frequently diagnosed thyroid diseases in the elderly and the older age group of patients. The progressive aging of the population will lead in the future to higher occurrence rates and more frequent new cases of hypothyroidism and other thyroid-related pathologies.

Subclinical hypothyroidism (SH) is a laboratory phenomenon in which a normal level of thyroid hormones is diagnosed in combination with moderately elevated thyroid hormone (TTH) levels. This is due to the fact that even a small decrease in the level of free T4 leads to a multifold increase in the level of TTH (by the feedback principle) [11, 13]. SH is encountered more frequently than the manifest hypothyroidism in both the general population and the elderly [22]. D.A. Bemben et al. [19] detected SH in 14.6% of females and in 15.4% of males aged 60–97.

In the absence of treatment for one year, in 5–15% of persones SH transitions into real hypothyroidism, and this occurs especially faster in the presence of antithyroid antibodies (4 years in 80% of persons aged over 65) [6]. In some cases, SH may be of a transient character in elderly patients, and the TTH level may spontaneously normalize in 37.4% of cases [24]. If SH is diagnosed, analysis of the TTH level is repeated in 3–6 months to exclude the transient character of changes or a laboratory error.

The causes for SH in the elderly are the same as for manifest hypothyroidism. Those are mainly autoimmune thyroidism (AIT) and surgeries on the thyroid or radiotherapy. The increasing trend in the occurrence of hypothyroidism with aging is usually explained by the argument that AIT leads to the destruction of the thyroid many years after its onset [13]. The development of SH in the elderly may also be caused by the administration of various preparations with antithyroid action (amiodarone, lithium preparations, interferon-α, et al.).

Diagnostics

Certain shifts take place in the thyroid status during the physiological conditions of aging. T4 secretion decreases with aging, and its metabolism and clearance simultaneously slow down; finally, the serum concentration of T4 does not change significantly. The T3 level gradually decreases in some older patients; however, there are grounds to associate this fact with the development of a different nonthyroid pathology (the low T3 syndrome) rather than with thyroid hypofunction. It is only at older ages that the T3 level naturally decreases, which is probably due to the arrest of peripheral conversion of iodine thyrodines. The described changes are, against expectations, unaccompanied by an elevation in the TTH content; moreover, even the opposite trend can be observed, although the average TTH level does not fall outside the reference range. Thus, the standard criteria for the functional state of the thyroid can also be considered to be informative in the elderly.

Laboratory investigations of the blood serum levels of TTH and thyroid hormones are the main tests in the diagnostics of thyroid hypofunction. The main focus is placed on testing TTH by high-sensitive methods and free T4. The tests for total T4 have no diagnostic value, since its level depends on the content of transporter proteins. It is also inexpedient to test the T3 level, since the peripheral conversion of T4 to T3 is accelerated in hypothyroidism and the T3 serum level may be normal due to this circumstance [1, 10].

Clinical Picture

The term "subclinical" presupposes the absence of clinical manifestations. Nevertheless, SH may be

accompanied by a group of changes characteristic of manifest hypothyroidism.

The brain is very sensitive to a thyroid hormone deficiency. Despite the absence of clinical signs of hypothyroidism in SH, the emotional sphere is susceptible since the levels of intellectual workability and attention decrease [7, 11, 17]. Intellectual disorders and anxious-depressive syndrome are the earliest manifestations of SH in patients with AIT, which are undistinguishable from those in manifest hypothyroidism. Mental disorders, sometimes reaching a state of expressed depression, are observed in nearly 50% of SH patients [29, 30]. As has been shown in a study, SH was diagnosed in 50% of cases in patients with refractory depression [32]. The mechanisms underlying the effect of thyroid hormones on the psychological status have not so far been studied. Many authors believe that SH is not so much an independent cause of the development of depression as a factor able to decrease the threshold for developing depressive states.

A group of neurological symptoms may be more expressed in SH patients than in those with more severe forms of the disease. Nonspecific manifestations, such as a headache, neurosis-like syndrome, and mild levels of irritability are encountered in patients with SH more frequently. Despite their mild course, neurological disorders may worsen the quality of life in patients [9].

The anxious-depressive state cannot always be removed by substitutive therapy with L-thyroxin. Disorders in the emotional state persist in one-third of patients with SH and manifest hypothyroidism, despite reaching a normal TTH level [12].

SH may lead to the development of nonobvious and predominantly sensitive polyneuropathy, primarily, with the affection of upper limbs with signs of tunnel syndromes. The clinical picture may include pains, paresthesia, and numbness that is more expressed in hands [9].

At the same time, some studies have shown that SH does not lead to disorders in everyday activity or the development of cognitive disturbances and depression in elderly people aged over 65 [23, 34].

The effect of thyroid hormones on the activity of the cardiovascular system is very high. Triiodothyronine (T3) decreases the total peripheral vascular resistance, which produces reflective positive chronotropic and inotropic effects. As a result of its direct relaxing action on smooth muscle cells and the increase in the nitric oxide synthesis in endothelial cells, the average blood pressure (BP) and diastolic blood pressure (DBP) decrease (after loading the left ventricle [20]. Thus, T3 increases cardiac output, as a result of a significant decrease (reaching even 50% of the initial level) in the peripheral vascular resistance, on the one hand, and an increase in the venous outflow towards the heart, on the other hand. The cardiac output may decrease and the vascular resistance may increase in hypothyroidism, leading to elevated DBP [2, 3].

The association of SH and arterial hypertension (AH) has been shown in a series of studies [39]. We should note that some studies described in the literature have failed to report any associations between the presence of SH in patients and AH [25]. Nevertheless, the meta-analysis of seven crossover studies by Chinese researchers in 2010 on the effect of SH on BP has demonstrated that SH is associated with elevated levels of both systolic BP and DBP [21]. Two Norwegian (Tromso and HUNT) studies have revealed that an increase in the TTH level even within the normal values is associated with elevated BP [16, 31].

The age of patients may probably affect the expressiveness of SH-characteristic cardiovascular shifts. In young women (20–40 years of age) SH is associated with disorders in the global and segmented diastolic function and elasticity of arteries. Cardiovascular and metabolic disorders in persons of older ages (40–50 years) are less frequently manifested, and the role of SH as a factor of cardiovascular risk seems less significant [8].

Dyslipidemia in SH has an atherogenic nature. Major studies have shown that dyslipoproteinemia associated with hypothyroidism increases the risk of developing atherosclerosis, ischemic heart disease (IHD), and myocardial infarction [16, 40].

SH in patients with IHD and a stable stenocardia of tension is associated with a more severe course of the disease and is manifested in a significantly higher DBP, occurrences of episodes with painful and painless ischemia with a long decrease in the ST segment and the number of episodes of painful ischemia with a long decrease in the ST segment, and a longer duration of episodes with painful and painless ischemia with a decrease in the ST segment, as well as with reliably lower left ventricle ejection fraction and tolerance for physical loads [14].

Elevated TTH levels, as compared to the reference values, are more frequently recorded in patients with severe multivascular lesions of coronary arteries [4].

A series of studies have demonstrated that the tolerance for physical loads in the group of patients with IHD and SH decreases. Levothyroxine therapy in patients with an initial TTH level exceeding or equal to 10 IU/L resulted in a 26.7% decrease in the objective manifestations of dyspnea during a 6-minute test of walking and more frequent ECG criteria for ischemia in the left ventricular myocardium (by 6.8%) [15]. A presence of SH in patients with diabetes mellitus II serves as an additional factor for the risk of endothelial dysfunction [5].

Major studies have demonstrated that SH is associated with an increased risk of developing IHD, myocardial infarction, and chronic cardiac insufficiency (CCI) [35].

At the same time, SH in very old patients (85–89 years) is unaccompanied by cognitive disorders, depression,

and decrease in everyday physical activity. Moreover, SH in this age category of patients was associated with a lower level of mortality [28, 37]. G. Atzmon et al. (2009) showed that a higher level of TTH is recorded in long-livers and suggested that longevity was associated with an elevated TTH level [18]; R.T. de Jongh et al. have also shown in their work that SH was unaccompanied by a mortality increase among elderly patients [23]. Therefore, physicians should probably avoid prescribing a substitutive therapy with levothyroxine for patients aged over 85 years in whom the TTH level is within the interval of 4–10 μU/mL [27].

Thus, hypothyroidism may affect the formation and development of cardiovascular diseases already at its early (subclinical stage). However, the expediency of treatment of SH in elderly patients has so far remained a controversial topic, especially if the level of TTH does not exceed 10 IU/L. It is not completely clear, on the one hand, whether this expediency may distort the distant prognosis for patients with an already realized risk of IHD, but, on the other hand, whether clinically significant hypothyroidism can develop in elderly patients (in particular, aged over 70) with SH without IHD during their remaining lifetime [13].

The results of reviewed randomized placebo-controlled studies dedicated to the assessment of the efficiency demonstrated by substitutive therapy with thyroxine in SH patients have shown that levothyroxine therapy did not produce any significant effect on the symptoms of hypothyroidism, the quality of life, the lipid content in the blood serum in such patients, or their cardiovascular morbidity and mortality, as compared with patients from the group taking a placebo. At the same time, the authors performing the analysis noted that there were confirmations that some parameters of diastolic function in the SH patients taking the substitutive levothyroxine therapy improved [26, 33, 38].

The discovered associations of SH and IHD in the elderly should be interpreted rather as an argument in favor of a substitutive therapy for SH in younger ages to counteract the development of atherosclerosis. For example, recent studies have shown that, whereas levothyroxine therapy in patients aged 40–70 with SH characterized by a mildly elevated TTH level decreases the risk of developing cardiovascular diseases, such data have not been confirmed for patients aged over 70 [36].

Treatment

Thus, the decision about substitutive levothyroxine therapy should be taken individually for elderly patients with TTH outside the reference values and below 10 IU/L. The requirement for levothyroxine in patients with SH is significantly lower and usually accounts for 25–75 μg, depending on the initial TTH level. When the decision about a substitutive therapy is made, a full dose should not be prescribed immediately, but titration should be started with a dose of 12.5–25 μg/day [10]. We should also remember that, apart from a potential hazard of worsening the course of IHD, an overdose of L-4 may also lead to a reduction in the mineral density of bone tissue, an increased risk of fractures, and the development of atrial fibrillations [10]. In practice, the question of SH treatment in elderly patients with a TTH level of 4–10 IU/L is answered in a majority of cases rather negatively [13].

CONCLUSION

Subclinical hypothyroidism is frequently encountered in the elderly. The data on its pathological significance, screening expediency, and substitutive levothyroxine therapy in the elderly are controversial. It is necessary to include many additional factors, such as concurrent cardiovascular diseases, in prescribing any therapies for the treatment of subclinical hypothyroidism in elderly patients.

REFERENCES

1. Abdulkhabirova, F.M., Principles of modern diagnostics and treatment of hypothyroidism, *Eff. Farmakoter.*, 2010, no. 36, pp. 68–73.
2. Blankova, Z.N., Ageev, F.T., Seredenina, E.M., et al., Hypothyroidism and cardiovascular diseases, *Russ. Med. Zh.*, 2014, vol. 22, no. 13, pp. 980–986.
3. Demidova, T.Yu. and Galieva, O.R., Hypothyroidism, obesity, and heart ischemia, *Ozhirenie Metab.*, 2007, no. 2, pp. 9–13.
4. Duisheeva, G., Leont'eva, N.S., Satkynalieva, Z.T., and Kaliev, R.R., Analysis of thyroid status and results of coronary arteriography of the coronary heart disease, *Vestn. Kyrgyz. Gos. Med. Akad. im. I.K. Akhunbaeva*, 2013, vol. 1, no. 4, pp. 46–50.
5. Kasatkina, S.G. and Panova, T.N., The influence of substitutive therapy on subclinical hypothyroidism in the patients with type II pancreatic diabetes on risk markers of development cardiovascular complications, *Ter. Arkh.*, 2012, vol. 84, no. 11, pp. 47–50.
6. Kulikova, V.V., *Disfunktsiya shchitovidnoi zhelezy u pozhilykh* (Dysfunction of Thyroid Gland in Elderly People), Nizhny Novgorod: Nizhegorod. Gos. Med. Akad., 2007.
7. Mozerov, S.A. and Erkenova, L.D., Hypothyroidism and mental health, *Byull. Med. Internet Conf.*, 2011, vol. 1, no. 7, pp. 29–31.
8. Nekrasova, T.A., Ledentsova, O.V., Strongin, L.G., Kazakova, L.V., and Lukushkina, A.Yu., Specific features of hemodynamics in the patients of different age groups with autoimmune thyroiditis and subclinical hypothyroidism, *Probl. Endokrinol.*, 2011, vol. 57, no. 3, pp. 21–24.
9. Nikanorova, T.Yu., Spirin, N.N., Kasatkina, E.L., and Aleksandrov, Yu.K., Subclinical hypothyroidism in practice of neurologists, *Nevrol. Revmatol.*, 2008, no. 2, pp. 35–39.
10. Petunina, N.A. and Trukhina, L.V., The hypothyroidism, *Russ. Med. Zh.*, 2013, vol. 21, no. 12, pp. 664–666.

11. Podzolkov, A.V. and Fadeev, V.V., The hypothyroidism, subclinical hypothyroidism, and highly normal level of thyroid-stimulating hormone (TSH), *Klin. Eksp. Tireoidol.*, 2009, vol. 5, no. 2, pp. 5–15.
12. Tereshchenko, I.V. and Kayusheva, N.V., Subclinical hypothyroidism and mental dysfunctions in the patients with autoimmune thyroiditis, *Psikhofarmakol. Biol. Narkol.*, 2008, vol. 8, no. 1–2–2, p. 2378.
13. Fadeev, V.V., Clinical aspects of thyroid gland diseases in elderly people, *Thyroid Int.*, 2007, no. 3, pp. 1–16.
14. Fes'kova, A.A. and Kaverzina, M.Yu., Specific clinical course, instrumental parameters, and life quality in patients with subclinical hypothyroidism and cardiovascular pathology, *Molodoi Uchenyi*, 2014, no. 17, pp. 210–213.
15. Shiryaeva, A.V. and Popova, M.A., Physical activity of patients with heart ischemia and subclinical hypothyroidism, *Fundam. Issled.*, 2014, no. 10, pp. 1205–1209.
16. Asvold, B.O., Bjøro, T., Nilsen, T.I., et al., Thyrotropin levels and risk of fatal coronary heart disease: the HUNT study, *Arch. Int. Med.*, 2008, vol. 168, no. 8, pp. 855–860.
17. Aszalós, Z., Some neurological and psychiatric complications in the disorders of the thyroid gland, *Orv. Hetil.*, 2007, vol. 148, no. 7, pp. 303–310.
18. Atzmon, G., Barzilai, N., Hollowell, J.G., et al., Extreme longevity is associated with increased serum thyrotropin, *J. Clin. Endocrinol. Metab.*, 2009, vol. 94, pp. 1251–1254.
19. Bemben, D.A., Hamm, R.M., Morgan, L., et al., Thyroid disease in the elderly, *J. Fam. Pract.*, 1994, vol. 38, pp. 583–588.
20. Biondi, B., Palmieri, E., Lombardi, G., et al., Effects of thyroid hormone on cardiac function: the relative importance of heart rate, loading conditions, and myocardial contractility in the regulation of cardiac performance in human hyperthyroidism, *J. Clin. Endocrinol. Metab.*, 2002, vol. 87, p. 968.
21. Cai, Y., Ren, Y., and Shi, J., Blood pressure levels in patients with subclinical thyroid dysfunction: a meta-analysis of cross-sectional data, *Hypertens. Res.*, 2011, vol. 34, no. 10, pp. 1098–1105.
22. Canaris, G.J., Manowitz, N.R., Mayor, G., and Ridgway, E.C., The Colorado thyroid disease prevalence study, *Arch. Int. Med.*, 2000, vol. 160, pp. 526–534.
23. De Jongh, R.T., Lips, P., van Schoor, N.M., et al., Endogenous subclinical thyroid disorders, physical and cognitive function, depression, and mortality in older individuals, *Eur. J. Endocrinol.*, 2011, vol. 165, pp. 545–554.
24. Diez, J. and Iglesias, P., Spontaneous subclinical hypothyroidism in patients older than 55 years: an analysis of natural course and risk factors for the development of overt thyroid failure, *J. Clin. Endocrinol. Metab.*, 2004, vol. 89, pp. 4890–4897.
25. Duan, Y., Peng, W., Wang, X., et al., Community-based study of the association of subclinical thyroid dysfunction with blood pressure, *Endocrine*, 2009, vol. 35, pp. 136–142.
26. Fadeyev, V.V., Sytch, J., Kalashnikov, V., et al., Levothyroxine replacement therapy in patients with subclinical hypothyroidism and coronary artery disease, *Endocrinol. Pract.*, 2006, vol. 12, pp. 5–17.
27. Gesing, A., Lewiński, A., and Karbownik-Lewińska, M., The thyroid gland and the process of aging; what is new?, *Thyroid Res.*, 2012, vol. 5, p. 16.
28. Gussekloo, J., van Exel, E., De Craen, A.J., et al., Thyroid status, disability and cognitive function, and survival in old age, *JAMA, J. Am. Med. Assoc.*, 2004, vol. 292, pp. 2591–2599.
29. Haggerty, J.J., Stern, R.A., Mason, G.A., et al., Subclinical hypothyroidism: a modifiable risk factor for depression?, *Am. J. Psychol.*, 1993, vol. 150, no. 3, pp. 508–510.
30. Howland, R.H., Thyroid dysfunction in refractory depression: implications for pathophysiology and treatment, *J. Clin. Psychiatry*, 1993, vol. 54, no. 2, pp. 47–54.
31. Iqbal, A., Figenschau, Y., and Jorde, R., Blood pressure in relation to serum thyrotropin: the Tromso study, *J. Hum. Hypertens.*, 2006, vol. 20, pp. 932–936.
32. Jensovsky, J., Ruzicka, E., Spackova, N., and Hejdukova, B., Changes of event related potential and cognitive processes in patients with subclinical hypothyroidism after thyroxin treatment, *Endocrinol. Regul.*, 2002, vol. 36, no. 3, pp. 115–122.
33. Ladenson, P.W., Singer, P.A., Ain, K.B., et al., American Thyroid Association guidelines for detection of thyroid dysfunction, *Arch. Int. Med.*, 2000, vol. 160, no. 11, pp. 1573–1575.
34. Park, Y.J., Lee, E.J., Lee, Y.J., et al., Subclinical hypothyroidism (SCH) is not associated with metabolic derangement, cognitive impairment, depression or poor quality of life (QoL) in elderly subjects, *Arch. Gerontol. Geriatr.*, 2010, vol. 50, pp. 68–73.
35. Rodondi, N., Den Elzen, W.P., and Bauer, D.C., Subclinical hypothyroidism and the risk of coronary heart disease and mortality, *JAMA, J. Am. Med. Assoc.*, 2010, vol. 304, no. 12, pp. 1365–1374.
36. Rosario, P.W. and Calsolari, M.R., How selective are the new guidelines for treatment of subclinical hypothyroidism for patients with thyrotropin levels at or below 10 mIU/L?, *Thyroid*, 2013, vol. 23, no. 5, pp. 562–565.
37. van den Beld, A.W., Visser, T.J., Feelders, R.A., et al., Thy roid hormone concentrations, disease, physical function, and mortality in elderly men, *J. Clin. Endocrinol. Metab.*, 2005, vol. 90, pp. 6403–6409.
38. Villar, H.C., Saconato, H., Valente, O., and Atallah, A.N., Thyroid hormone replacement for subclinical hypothyroidism, *Cochrane Database Syst. Rev.*, 2007, vol. 3, no. CD003419.
39. Velkoska Nakova, V., Krstevska, B., Bosevski, M., et al., Dyslipidaemia and hypertension in patients with subclinical hypothyroidism, *Prilozi*, 2009, vol. 30, no. 2, pp. 93–102.
40. Walsh, J.P., Bremner, A.P., Bulsara, M.K., et al., Subclinical thyroid dysfunction as a risk factor for cardiovascular disease, *Arch. Int. Med.*, 2005, vol. 165, pp. 2467–2472.

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