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Association between subclinical hypothyroidism and depression: an updated systematic review and meta-analysis

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Abstract

Background: Although depression is associated with changes in the hypothalamic-pituitary-thyroid axis, its relationship with subclinical hypothyroidism (SCH) is controversial. To date, there is a lack of data on the improvement of depressive symptoms with levothyroxine therapy among individuals with coexistent SCH.

Methods: We conducted a meta-analysis to evaluate the association between SCH and depression including 1) the prevalence of depression in SCH (with a sub-analysis of the geriatric cohort), 2) thyroid stimulating hormone (TSH) level among patients with depression and 3) the effect of levothyroxine therapy among patients with SCH and coexistent depression.

Results: In a pooled analysis of 12,315 individuals, those with SCH had higher risk of depression than euthyroid controls (relative risk 2.35, 95% confidence intervals [CI], 1.84 to 3.02; $p < 0.001$). Geriatric cohort with SCH had a 1.7-fold higher risk of depression compared with healthy controls (odds ratio 1.72, CI, 1.10 to 2.70; $p = 0.020$). There was no difference in the mean TSH level between individuals with depression and healthy controls (2.30 ± 1.18 vs. 2.13 ± 0.72 mIU/L, $p = 0.513$). In individuals with SCH and coexistent depression, levothyroxine therapy was neither associated with improvement in the Beck Depression Inventory scoring (pooled d + = − 1.05, CI -2.72 to 0.61; $p = 0.215$) nor Hamilton Depression Rating Scale (pooled d + = − 2.38, CI -4.86 to 0.10; $p = 0.060$).

Conclusion: SCH has a negative impact on depression. Early and routine screening of depression is essential to prevent morbidity and mortality. However, the use of levothyroxine among patients with SCH and coexistent depression needs to be individualized.

Keywords: Subclinical hypothyroidism, Depression, Thyroid stimulating hormone, Levothyroxine

Background

Neuropsychiatric disorders account for approximately 14% of the global burden of disease [1]. Depression, being one of the common chronically disabling disorders, can lead to poor quality of life [1, 2]. On the other hand, thyroid hormones (free triiodothyronine [fT3] and free thyroxine [fT4]) which are widely distributed in the central nervous system, regulate the neuronal growth and form synapses between neurons [3]. Given that depression is known to be associated with changes in the hypothalamic-pituitary-thyroid (HPT) axis [4], studies have reported its positive correlation with overt hypothyroidism [5]. However, its relationship with subclinical hypothyroidism (SCH) is not well established [6].

SCH is defined as an elevated thyroid stimulating hormone (TSH) with normal fT4 and fT3 levels. It affects 3 to 8.5% of the general population with a female preponderance, and a higher rate up to 20% among elderly people [7, 8]. This diagnosis is often overlooked especially when laboratory tests are not readily available, as these individuals with SCH tend to present with subtle

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