

Cognition Deficit and Hypothyroidism in a Population-Based Study of Iranian Women

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Abstract

Background: There are some evidences on adverse effects of reducing thyroid hormones levels on appearing cognition. The present study aimed to assess cognitive function in patients with hypothyroidism under-treated with routine hormone replacement therapy compared to healthy euthyroid individuals.

Methods: Thirty consecutive hypothyroid female patients aged 25 to 40 years who referred to endocrinology and metabolism clinic at Rasoul-e-Akram hospital in Tehran within a four-year period in 2015 were assessed. Also, thirty healthy euthyroid subjects matched for sex, age, and educational level were selected as the control. For assessment of cognitive function status, the Mini Mental Status Exam (MMSE) was used.

Results: The study showed lower mean cognitive score in hypothyroid patients when compared to euthyroid ones (25.33 ± 3.90 versus 29.40 ± 1.80 , $p = 0.010$). Regarding association between cognition deficit and patients' baseline characteristics, except for educational level that was positively associated with cognition score ($p < 0.001$), no significant association was revealed between mean cognition score and other parameters including age ($p = 0.569$), occupation status ($p = 0.631$), and marital status ($p = 0.859$). According to the Bonferroni correction analysis, lower cognitive function was revealed in those with primary educational levels than those who with college degrees.

Conclusion: Clinical hypothyroidism is potentially association with cognition deficit especially in those with lower educational level.

Keywords: cognition; hypothyroidism; education; mini mental status exam

Introduction

The development of cognition ability is directly associated with normal functional status of metabolic systems such as thyroid function throughout life. In fact, the association between thyroid hormones deficiency and deterioration of cognitive disorders has been recently proposed. Some pathophysiological basis of this association has been well described [1]. It has been shown that hypothyroidism may lead to inadequate sustaining the glucose consumption that is necessary for memory enhancement, synthesis of neurotransmitters, as well as improve high brain function. These neural abnormalities caused by low brain uptake of energy can finally deteriorate cognition and cause Alzheimer's disease [2]. These changes considerably occurred by increasing age in parallel with progressive cognitive decline. Some studies could show adverse effects of reducing thyroid hormones levels on appearing cognitive deficits in attention, memory, learning, and psychomotor speed

[3-13]. It has been also suggested a direct association between the severity and duration of hypothyroidism and degree of cognitive dysfunction. However, the association between treatment of hypothyroidism and improvement of cognitive deficits has not been well clarified. So, it has been shown that by treating hypothyroidism even for one year, cognition deficits still remain and the recovery of cognitive functioning has not been fully achieved. As shown by Wekking et al [14], although the treatment of hypothyroidism for a period of 5.5 years led to normalization of TSH, but some aspects of cognitive deficits such as memory deficits remained persistent following this adequate hormone replacement. It seems that the brain in advanced ages may become more susceptible to thyroid dysfunction as shown by Capet and his colleagues [15]. As similarly shown by Osterweil et al [3], improvement in cognitive function following thyroid hormones replacement was more revealed in younger patients than in those who aged more than 75 years. Thus, increase of age

is associated with increased vulnerability on cognitive in background of hypothyroidism [15].

The present study aimed to assess cognitive function in patients with hypothyroidism under-treated with routine hormone replacement therapy compared to healthy euthyroid individuals.

Materials and Methods

Study population:

Thirty consecutive hypothyroid female patients aged 25 to 40 years who referred to endocrinology and metabolism clinic at Rasoul-e-Akram hospital in Tehran within a four-year period in 2015 were assessed. The included patients had no risk factors for psychological disorders and were regularly treated with levothyroxine within the last six months with normal serum TSH level. Also, thirty healthy euthyroid subjects matched for sex, age, and educational level were selected as the control. These controls had no history of thyroid disorders, diabetes mellitus, hyperlipidemia, anemia or other major risk factors for psychological disorders. For removing confounding effect of sex and age factors, all female patients aged 25 to 40 years were included into the study. The study protocol was approved by the ethics committee at Iran University of Medical Sciences and written informed consents were taken from all subjects.

Study measurement:

For assessment of cognitive function status, the Mini Mental Status Exam (MMSE) was used. The MMSE was originally developed by Marshall and Susan Folstein as a tool to quickly assess cognitive function in the elderly hospitalized population [16]. Originally, the MMSE was tested on a mere 206 patients before Folstein declared that this exam could accurately determine one's cognitive abilities. The MMSE is composed of 11 major items; temporal orientation (5 points), spatial orientation (5 points), immediate memory (3 points), attention/concentration (5 points), delayed recall (3 points), naming (2 points), verbal repetition (1 points), verbal comprehension (3 points), writing (1 points), reading a sentence (1 points), and constructional praxis (1 points). The MMSE has maximum score of 30, with five different domains of cognition analyzed: (1) Orientation, contributing a maximum of 10 points, (2) Memory, contributing a maximum of 6 points, (3) Attention and calculation, as a measure of working memory, contributing a maximum of 5 points, (4) Language, contributing a maximum of 8 points, and (5) Design copying, contributing a maximum of 1 point [17]. A score of, or close to, 30 is indicative of normal cognitive function. The lower the score indicates the higher the level of impairment. In total, the score higher than 25 was considered as normal cognitive function, 20 to 25 as the possibility of cognitive deficit, and lower than 20 as definitive cognitive damage [17]. In a study by Seyedian et al [18], the Farsi version of MMSE obtained a good reliability with the Cronbach's alpha coefficient 0.81. Also, in their study and using ROC curve, a cut-off point of 22 showed a sensitivity of 90 and specificity of 93.6 percent. Internal consistency in the present study was explored for MMSE, and Cronbach's alpha coefficients was adequate as 0.81. In the present study, first, the objectives of the study were described briefly to participants. Then, baseline characteristics and clinical data of study subjects were collected by interviewing. Then all women in both case and control groups were invited to complete the questionnaire under the supervision of the researcher.

Statistical analysis:

Results were presented as mean \pm standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann-Whitney U test. For the statistical

analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

Results

Compared to euthyroid group, the patients with hypothyroid were older as well as had lower educational level (table 1). Also, students and employed ones were more categorized in euthyroid group, while housewives were more observed in hypothyroid group. There was no difference in marital status between hypothyroid and euthyroid groups. The study showed lower mean cognitive score in hypothyroid patients when compared to euthyroid ones (25.33 ± 3.90 versus 29.40 ± 1.80 , $p = 0.010$). Regarding association between cognition deficit status and patients' baseline characteristics (table 2), except for educational level that was positively associated with cognition score ($p < 0.001$), no significant association was revealed between mean cognition score and other parameters including age ($p = 0.569$), occupation status ($p = 0.631$), and marital status ($p = 0.859$). According to the Bonferroni correction analysis (table 3), lower cognitive function was revealed in those with primary educational levels than those who with college degrees.

Discussion

As the first finding, we could show significant cognition deficit in hypothyroid patients when assessed by a common tool for assessing cognitive condition named as MMSE. In fact, lower mean MMSE cognition score was expected in those who suffered hypothyroidism in comparison with normal thyroid subjects. This evidence was similarly obtained in some previous studies. Some authors such as Burmeister et al [19] emphasized on mainly deficit in memory following stabilization and progression of hypothyroidism. They could show that hypothyroidism was associated with a decrease in retrieval from memory, but was not related to other components of cognition including affect immediate recall, verbal learning, inhibitory efficiency, information processing speed, or attention switching. In another study emphasizing cognitive dysfunction in older hypothyroid patients [20], prose Memory Test score resulted significantly lower in subjects with subclinical hypothyroidism and also TSH was negatively correlated with MMSE score, however in their study, other aspects of cognition such as selective attention was also less evident. Despite discovering a strong association between overt hypothyroidism and cognitive deficit in various populations, the association between subclinical hypothyroidism and cognition deficit has remained uncertain. So in some recent population-based studies [21, 22], no association was revealed between hypothyroidism indicated by lowering thyroxin and cognitive deficit especially in the elderly. In a recent systematic review by Akintola et al [23], by reviewing 15 studies comprising 19,944 subjects that of whom 1,199 had subclinical hypothyroidism, subclinical hypothyroidism was shown not to be significantly associated with accelerated cognitive decline in older adults. Thus, it seems that subclinical hypothyroidism cannot predispose older patients to cognitive disorders, while overt hypothyroidism can potentially alert cognitive deficit. In this regard, some mechanisms have been explained on this association. It has been even in the elderly shown that because thyroid hormones play a crucial role in the development and function of the central nervous system, there was a "resetting" of the hypothalamus-pituitary thyroid axis, characterized by a decrease in pituitary sensitivity to changes in thyroid hormones, with lower response in the production of TSH respect to younger subjects in which TSH increases in the face of even slight reductions in thyroid hormones levels [24]. It has been also shown by SPECT imaging devices that cerebral hypo-perfusion following hypothyroidism can affect areas controlling attention, motor speed, memory and visual-spatial processes [25]. In fact, global cerebral perfusion in hypothyroidism can be related to increased vascular resistance in these areas [26].

In the present study and among various baseline variables, only lower educational level was associated with lower cognitive function. This association can be explained by two points. First, it seems that those with higher educational level have higher knowledge and alertness toward their disease and thus performed to treat their deficit by approaching proper anti-hypothyroid treatments. Also, it seems that those with high memory working have higher brain perfusion state and thus memorial deficits may occurred less in these patients than those with lower alertness.

Conclusion

In summary, patients with clinical hypothyroidism more suffer from cognition deficit especially as memory loss compared to euthyroid individuals. This association is more evident in those with lower educational level probably because of lower knowledge toward disease and also lower brain perfusion state especially in brain areas responsible for memory regulation.

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