Effects of thyroid hormone replacement therapy on thyroid hormone levels and electrocardiogram changes in geriatric patients with hypothyroidism

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Abstract: This paper aims to analyze the effects of thyroid hormone replacement therapy on thyroid hormone levels and electrocardiogram changes in elderly patients with hypothyroidism. 48 elderly patients with hypothyroidism admitted to our hospital from January 2014 to December 2014 were selected as subjects. All the patients were treated with thyroid hormone replacement therapy. The changes of thyroid hormone levels and ECG parameters were compared before and after treatment. After treatment, serum thyroid stimulating hormone (TSH) was significantly lower than that before treatment, and the free triiodothyronine (FT3) and free thyroxine (FT4) were significantly higher than those before treatment (t=15.587, 17.396, 19.593, P<0.05); R-R interval, QT interval, QTc interval were significantly lower than before treatment, and the Heart rate (HR), standard deviation of all normal R-R intervals (SDNN), standard deviation of 5 min average R-R intervals (SDANN) within 24h, high frequency power (HF) were significantly higher than before treatment (t=2.171, 2.354, 4.264, 3.100, 10.754, 11.467, 16.776, P<0.05). Thyroid hormone replacement therapy is helpful to improve the level of thyroid hormone and ventricular repolarization in patients with hypothyroidism, and to regulate the function of cardiac autonomic nervous system.

Keywords: Hypothyroidism, thyroid hormone replacement therapy, heart rate variability, cardiac electrical activity.

INTRODUCTION

Thyroid hormone is one of the most important hormone to maintain the body's normal physiological function, which can not only avoid excessive increase in lipid levels through the degradation of human lipid, but ensure the normal function of the heart tube system by increasing cardiac contractility and reducing vascular resistance (Huang *et al* 2014; Zhang H *et al*, 2012). Hypothyroidism is a metabolic disease characterized by elevated thyroid stimulating hormone levels and normal thyroid function, which early symptoms are not obvious, prone to misdiagnosis and missed diagnosis and delayed treatment (Fan *et al*, 2016). Due to the long-term lack of thyroid hormones, patients with hypothyroidism prone to lipid deposition in the vascular endothelium, resulting in thickening of the arterial wall, the formation of atherosclerotic plaques, and thus the occurrence of cardiovascular diseases (Voronych *et al*, 2010). Related studies showed that thyroid hormone levels in patients with hypothyroidism were significantly lower, while the thyroid stimulating hormone expressed abnormally (Jin *et al*, 2013). hyroid hormone replacement therapy is an internationally recognized standard treatment for patients with hypothyroidism (Bagattini *et al*, 2014; Tian *et al*, 2015). Many scholars at home and abroad have analyzed the level of thyroid hormone and cardiac function, but there has not yet analyzed from the heart rate variability (HRV). In the study, we randomly selected 48 cases of elderly patients with hypothyroidism in our hospital for treatment and they were given thyroid hormone replacement therapy. Then, the effects of thyroid hormone replacement therapy on thyroid hormone levels and the ECG changes in patients with hypothyroidism were analyzed by the method of "before and after controlled study". In order to provide some support for the promotion of clinical treatment of thyroid hormone replacement therapy.

MATERIALS AND METHODS

Research objects

48 geriatric patients with hypothyroidism admitted to endocrinology department from January 2014 to December 2014 were selected as subjects, with 22 male and 26 female, aged between 61-82 years old, averaged aged between (67.85±3.24) years old, disease course 0.2-6 years, and average disease course (1.78±0.24) years. Inclusion criteria: (1) All patients are in line with the diagnostic criteria in *Guidelines for diagnosis and treatment of thyroid diseases - hypothyroidism* of Endocrine Society of Chinese Medical Association, and age >60 years old (Writing Group of "Guidelines for diagnosis and treatment of thyroid diseases in China" of Endocrinology branch of Chinese Medical Association, 2007); (2) patients with limb weakness, abnormal body, loss of appetite, memory loss, cardiac damage and so on; (3) All patients were treated with thyroid hormone replacement therapy after hospitalization; (4) The study had been approved by the Ethics Committee of

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Zhengzhou Hospital of Traditional Chinese Medicine, China and all patients or family members have signed informed consent. Exclusion criteria: (1) patients with severe heart, liver and kidney disease; (2) patients with neurological and psychiatric disorders.

Therapeutic method

All patients were treated with Levothyroxine Sodium Tablets (China Associated Pharmaceutical, Shenzhen) orally, 50-150μg/d, TID. According to the severity of the disease, the dose was decreased every 2 weeks until thyroid hormone levels returned to normal, maintenance treatment for 3 months.

Observation index

Thyroid hormone level

4 ml fasting venous blood of patients were collected before and after treatment, respectively to centrifuge 10 min at 3000r/min (centrifugal radius of 3cm) to take serum. The content of free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH) were measured by Elecsys 2010, an German electrochemical luminescence immunoassay analyzer. Detection methods: Chemiluminescence immunoassay. All the reagents were purchased from the Beijing Jingmei Biological Engineering Co., Ltd. Reference range: FT3: 2.8-7.1pmol/L; FT4: 12-22pmol/L; TSH: 0.27-4.2mU/L.

ECG variation

Before and after treatment, the heart rate (HR), R-R interval, QT interval, heart rate variability and other indexes were measured by Heart One 12 combined with dynamic electrocardiogram of Aerome Medical Sysyen Company. Heart rate variability parameters included time domain parameters and frequency domain parameters, and the time domain parameters included standard deviation of all normal R-R intervals (SDNN), standard deviation of 5 min average R-R intervals (SDANN) within 24h; while the frequency domain parameters included low frequency power (LF), high frequency power (HF), etc.

STATISTICAL ANALYSIS

SPSS software was used for statistical analysis. Thyroid hormone levels and other measurement data were expressed with ($\bar{x}\pm s$), and *t* test was used. $P < 0.05$ meant that the difference was statistically significant.

RESULTS

Thyroid hormone levels

After treatment, the serum thyroid stimulating hormone (TSH) was significantly lower than that before treatment, and the free triiodothyronine (FT3) and free thyroxine (FT4) were significantly higher than those before treatment ($P<0.05$). As shown in table 1.

Electrocardiogram correlation logarithm

The R-R interval, QT interval, QTc interval after treatment were significantly lower than before treatment, and the Heart rate (HR), standard deviation of all normal R-R intervals (SDNN), standard deviation of 5min average R-R intervals (SDANN) within 24h, high frequency power (HF) were significantly higher than before treatment ($P<0.05$). There was no statistically significant difference between low frequency before and after treatment ($P>0.05$). As shown in table 2.

DISCUSSION

Hypothyroidism is a common systemic metabolic disease, mostly caused by the lack of thyroid hormone synthesis, secretion or biological effects (Oner *et al*, 2011). The prevalence rate is about 0.8%-1.0%, with more female than male, and the old is the main population, accounting for 95% of the primary hypothyroidism (Hu *et al*, 2014). The main clinical manifestations were decreased metabolic rate and decreased sympathetic excitability (Zhang Z *et al*, 2015). The early symptoms are not obvious, which often delay the treatment time. Thyroid hormone replacement therapy is mainly adopted in clinic to control the serum thyroid hormone levels in the normal range, and most of them can get better treatment effect (Sangun *et al*, 2015).

In this study, the thyroid hormone levels of 48 elderly patients with hypothyroidism were all significantly improved. Domestic and foreign scholars also have similar reports (Li *et al*, 2015; Hirata *et al*, 2015), suggesting that thyroid hormone replacement therapy is helpful to improve the level of thyroid hormones in patients.

Although there are a lot of literatures about thyroid replacement therapy at home and abroad, there are few reports about the study of QT interval and heart rate variability (HRV). Most of the patients with hypothyroidism were involved in the cardiovascular system, manifested as sinus bradycardia, QT interval, QTc interval prolongation. In the study of Niu Yonghong et al (Niu *et al*, 2011), 43 elderly patients with sub clinical hypothyroidism were compared with 45 healthy controls, and the results showed that sub clinical thyroid dysfunction will affect ventricular repolarization, suggesting early clinical intervention. In our study, after adopting the thyroid hormone replacement therapy, the HR of 48 patients with hypothyroidism were significantly prolonged, and R-R interval, QT interval, QTc interval shortened significantly, suggesting that thyroid hormone replacement therapy can improve ventricular repolarization in patients with hypothyroidism.

Heart rate variability (HRV) is not only an index of autonomic nervous function, but also a common method

Table 1: Analysis on the changes of thyroid hormone levels before and after treatment in 48 cases ($\bar{x}$±s).

Time	Cases	FT3 (pmol/L)	FT4 (pmol/L)	TSH (mol/L)
Before treatment	48	2.65±0.58	10.32±1.24	8.65±1.32
After treatment	48	4.73±0.72	16.25±2.01	4.21±0.85
t		15.587	17.396	19.593
P		0.000	0.000	0.000

Table 2: Comparison of ECG variability before and after treatment in 48 patients

Time	Cases	HR(time/min)	R-R interval (ms)	QT(ms)	QTc(ms)
Before treatment	48	67.58±7.12	860.02±72.15	386.45±42.12	398.12±46.21
After treatment	48	72.48±8.32	828.45±70.32	367.12±38.25	360.42±40.22
t		3.100	2.171	2.354	4.264
P		0.021	0.026	0.024	0.018
Time	Cases	SDNN(ms)	SDANN(ms)	LF(ms2)	HF(ms2)
Before treatment	48	135.02±15.24	125.32±14.21	1028.12±57.23	244.12±36.14
After treatment	48	174.11±20.05	162.45±17.36	1040.21±62.35	410.25±58.32
t		10.754	11.467	0.990	16.776
P		0.000	0.000	0.102	0.000

for noninvasive electrophysiological physiological examination, which is widely used in predicting cardiovascular events (Guo *et al*, 2010). SDNN, SDANN and other time domain indexes of sympathetic nervous tension in hypothyroidism were decreased significantly, and LF, HF and other frequency domain indexes reflecting sympathetic nerve and vagus nerve were also significantly lower than that after treatment, which indicated that the autonomic nervous function was impaired and the sympathetic nerve and vagus nerve dysfunction in patients with hypothyroidism (Echeverria *et al*, 2012). Thyroid hormone replacement therapy can improve the abnormal ECG in patients with hypothyroidism, regulate cardiac autonomic nerve function, thereby improving the heart rate variability of thyroid function.

CONCLUSION

The results of this study indicate that thyroid hormone replacement therapy is helpful to improve the level of thyroid hormones and ventricular repolarization in patients with thyroid hormone, and to regulate the function of cardiac autonomic nervous system. The limitations of this study is that the number of samples is small and there is no comparative study of different methods, meanwhile lacking of clinical efficacy, adverse reactions and other indicators. Therefore, it is necessary to expand the sample in the future.

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