

doi: 10.13241/j.cnki.pmb.2019.06.024

甲状腺功能减退患者血清甲状腺激素、同型半胱氨酸 及血脂水平测定的临床意义*

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摘要 目的:探讨甲状腺功能减退患者血清同型半胱氨酸(Hcy)、甲状腺激素(TH)及血脂水平测定的临床意义。**方法:**选取 2016 年 2 月-2017 年 2 月期间我院收治的甲状腺功能减退患者 101 例为观察组,选取同期于我院体检的健康志愿者 80 例为对照组。检测所有研究对象甲状腺素(FT4)和三碘甲状腺原氨酸(FT3)、Hcy 及血脂[甘油三酯(TG)、总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)]变化水平。比较观察组治疗前后、对照组与观察组治疗前 FT3、FT4、Hcy 及血脂水平,采用 Pearson 相关性分析血清 Hcy 与 FT3、FT4、血脂水平的相关性。**结果:**观察组患者治疗后 FT3、FT4 均较治疗前升高,Hcy、TC、LDL-C 均较治疗前降低($P<0.05$),而观察组患者治疗前后 TG、HDL-C 比较差异无统计学意义($P>0.05$)。观察组治疗前 FT3、FT4、HDL-C 水平明显低于对照组,而 Hcy、TG、TC、LDL-C 则明显高于对照组($P<0.05$)。经 Pearson 相关性分析显示,甲状腺功能减退患者 Hcy 与 FT3、FT4 呈负相关($P<0.05$),与 TC、TG 呈正相关($P<0.05$),而与 LDL-C、HDL-C 无相关性($P>0.05$)。**结论:**甲状腺功能减退患者的 FT3、FT4、Hcy 及血脂水平表达异常,且 Hcy 与 FT3、FT4、血脂水平密切相关,临床上可通过监测甲状腺功能减退患者的上述指标,有助于评估患者的病情程度。

关键词:甲状腺功能减退;甲状腺激素;同型半胱氨酸;血脂;临床意义

中图分类号:R581.2 **文献标识码:**A **文章编号:**1673-6273(2019)06-1115-04

Clinical Significance of Serum Thyroid Hormones, Homocysteine and Blood Lipid Levels in Patients with Hypothyroidism*

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ABSTRACT Objective: To investigate the clinical significance of homocysteine(Hcy), serum thyroid hormone(TH) and blood lipid levels in patients with hypothyroidism. **Methods:** 101 cases of hypothyroidism who were admitted to our hospital from February 2016 to February 2017 were selected as the observation group, 80 healthy volunteers in our hospital during the same period were selected as control group. Thyroxine (FT4), three iodine thyroxine (FT3), Hcy and blood lipid levels [triglyceride (TG), total cholesterol(TC), high-density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C)] in the all subjects were detected. The levels of FT3, FT4, Hcy and blood lipid in the observation group before and after treatment, the control group and the observation group before treatment were compared. The correlation of serum Hcy, FT3, FT4 and blood lipid levels were analyzed by Pearson correlation analysis. **Results:** The FT3 and FT4 of the observation group were higher than those before treatment, while Hcy, TC and LDL-C were all lower than those before treatment ($P<0.05$). But there were no statistical differences between TG and HDL-C in patients with observation group before and after treatment ($P>0.05$). The levels of FT3, FT4 and HDL-C in the observation group were significantly lower than those in the control group before treatment, while the Hcy, TG, TC and LDL-C were significantly higher than those in the control group ($P<0.05$). Pearson correlation analysis showed that Hcy was negatively correlated with FT3 and FT4 in hypothyroidism patients($P<0.05$), and there was a positive correlation with TC and TG ($P<0.05$), but there were not correlation with LDL-C and HDL-C ($P>0.05$). **Conclusion:** The levels of FT3, FT4, Hcy and lipid in patients with hypothyroidism were abnormal, and Hcy is closely related to the level of FT3, FT4 and blood lipid. These indicators can be monitored clinically in patients with hypothyroidism, it helps to assess the extent of the patient's condition.

Key words: Hypothyroidism; Thyroid hormone; Homocysteine; Blood lipid; Clinical significance

Chinese Library Classification(CLC): R581.2 **Document code:** A

Article ID: 1673-6273(2019)06-1115-04

* 基金项目:新疆维吾尔自治区自然科学基金项目(201301DC437)

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(收稿日期:2018-08-07 接受日期:2018-08-30)

前言

甲状腺属于机体重要的内分泌器官,主要参与生长、代谢及其他系统的调控^[1]。相关研究表明^[2,3],当甲状腺激素分泌过多或缺乏时患者会出现心血管、神经以及消化系统等多种疾病并发症,严重影响患者健康,甚至出现死亡。当甲状腺激素合成或分泌不足时,或出现自身生理效应不足导致的机体代谢下降,则为甲状腺功能减退^[4,5]。由于该病早期临床症状不明显,漏诊、误诊情况频发,早期检测常需结合实验室指标进行。血清甲状腺激素(thyroid hormone, TH)包括甲状腺素(thyroxine, FT4)和三碘甲状腺原氨酸(three iodide thyroic acid, FT3),是评价甲状腺功能的常用指标^[6,7]。近年来研究证实^[8,9],同型半胱氨酸(homocysteine, Hcy)是冠心病的独立危险因素,而甲状腺功能减退会诱发心脑血管等疾病,由此推测 Hcy 可能在甲状腺功能减退发病机制中发挥重要作用。另有研究表明^[10],甲状腺功能减退患者常合并高脂血症。鉴于此,本次研究通过探讨甲状腺功能减退患者中血清 TH、Hcy 及血脂水平的表达情况,为临床治疗提供参考依据。

1 资料与方法

1.1 临床资料

选择于 2016 年 2 月-2017 年 2 月期间在我院接受治疗的 101 例甲状腺功能减退患者作为观察组。纳入标准:(1)所有患者均符合《实用内科学》中有关甲状腺功能减退的相关诊断标准^[11];(2)所有患者均未接受甲状腺激素等替代治疗;(3)均为首次确诊;(4)患者及其家属对本研究知情,同时签署同意书。排除标准:(1)全身恶性肿瘤并发症者;(2)合并心、肝、肺、肾等脏器功能障碍者;(3)合并垂体瘤、下丘脑病变者;(4)合并有其他严重内分泌疾病者;(5)伴高血脂、高血压、糖尿病等疾病者。甲状腺功能减退患者中男 43 例,女 58 例,年龄 21-58 岁,平均

(36.98±4.72)岁。选取同期于我院体检的健康志愿者 80 例为对照组,其中男 34 例,女 46 例,年龄 22-56 岁,平均(35.29±5.02)岁。两组研究对象的一般资料比较无统计学差异($P>0.05$)。此次研究经本院医学伦理学委员会批准同意。

1.2 方法

观察组患者入院后给予甲状腺片(上海长城药业有限公司,国药准字:H31022151)进行治疗,早餐前 0.5 h 或餐后 4 h 服用,初始剂量 25-50 $\mu\text{g/d}$,每 1-2 周增加一次剂量,增加剂量为 25 $\mu\text{g/d}$,直至甲状腺功能恢复正常。观察组患者治疗前后采集清晨空腹静脉血、对照组则在体检当日采集空腹静脉血 4 mL,均 4000 r/min 离心 10 min,分离血清,置于 -30℃ 冰箱中待测。采用罗氏 e602 全自动免疫分析仪电化学发光法测定 FT3、FT4 水平;采用罗氏 combas8000c502 全自动生化分析仪免疫散射比浊法检测 Hcy 水平,试剂盒来源于罗氏原装试剂;采用罗氏 combas8000c701 全自动生化分析仪测定甘油三酯(triglyceride, TG)、总胆固醇(total cholesterol, TC)、高密度脂蛋白胆固醇(high density lipoprotein cholesterol, HDL-C)及低密度脂蛋白胆固醇(low density lipoprotein cholesterol, LDL-C)水平。

1.3 统计学方法

采用 SPSS 21.0 统计学软件进行数据分析。计数资料以%表示,行 χ^2 检验,计量资料以均值±标准差表示,行 t 检验,采用 Pearson 相关性分析血清 Hcy 与 FT3、FT4、血脂水平的相关性,检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 观察组患者治疗前后 FT3、FT4、Hcy 及血脂水平比较

观察组患者治疗后 FT3、FT4 均较治疗前升高,Hcy、TC、LDL-C 均较治疗前降低($P<0.05$);而观察组患者治疗前后 TG、HDL-C 比较差异无统计学意义($P>0.05$);详见表 1。

表 1 观察组患者治疗前后 FT3、FT4、Hcy 及血脂水平比较($\bar{x}\pm s$)

Table 1 Comparison of FT3, FT4, Hcy and blood lipid levels before and after treatment in the observation group($\bar{x}\pm s$)

Time	FT3(pmol/L)	FT4(pmol/L)	Hcy($\mu\text{mol/L}$)	TC(mmol/L)	TG(mmol/L)	LDL-C(mmol/L)	HDL-C(mmol/L)
Before treatment	2.84±0.98	8.35±1.87	19.67±3.86	5.65±1.40	2.31±0.52	4.56±1.80	0.93±0.16
After treatment	4.51±1.17	16.89±2.28	11.19±4.32	4.23±1.05	2.13±0.76	3.23±1.55	0.98±0.24
t	16.874	29.106	14.711	8.155	1.964	5.627	1.324
P	0.000	0.000	0.000	0.000	0.051	0.000	0.187

2.2 对照组、观察组治疗前 FT3、FT4、Hcy 及血脂水平比较

观察组治疗前 FT3、FT4、HDL-C 水平明显低于对照组,而

Hcy、TC、TG、LDL-C 则明显高于对照组($P<0.05$);详见表 2。

表 2 对照组、观察组治疗前 FT3、FT4、Hcy 及血脂水平比较($\bar{x}\pm s$)

Table 2 Comparison of FT3, FT4, Hcy and blood lipid levels between the control group and the observation group before treatment($\bar{x}\pm s$)

Groups	FT3(pmol/L)	FT4(pmol/L)	Hcy($\mu\text{mol/L}$)	TC(mmol/L)	TG(mmol/L)	LDL-C(mmol/L)	HDL-C(mmol/L)
Control group(n=80)	4.84±0.76	17.35±1.75	11.67±3.56	4.15±1.32	1.32±0.74	2.44±0.84	1.31±0.43
Observation group(n=101)	2.84±0.98	8.35±1.87	19.67±3.86	5.65±1.40	2.31±0.52	4.56±1.80	0.93±0.16
t	15.731	21.088	13.531	7.421	10.555	9.725	8.198
P	0.000	0.000	0.000	0.000	0.000	0.000	0.000

2.3 Hcy 与 FT3、FT4、血脂水平的相关性分析

经 Pearson 相关性分析显示,甲状腺功能减退患者 Hcy 与 FT3、FT4 呈负相关($r=-0.396, -0.403, P=0.000, 0.000$), 与 TC、TG 呈正相关($r=0.437, 0.412, P=0.000, 0.000$), 而与 LDL-C、HDL-C 无相关性($r=0.098, 0.121, P=0.109, 0.158$)。

3 讨论

甲状腺功能减退是内分泌系统的常见疾病,该病发病隐匿,早期症状不典型,长期发病可引起心脑血管疾病、消化系统、神经系统等多系统疾病,给患者生命安全带来严重威胁^[12-14]。因此,早发现、早治疗在甲状腺功能减退的诊治中具有积极的临床意义。目前,临床针对甲状腺功能减退的诊断主要依靠患者的临床症状、体征以及血清甲状腺功能指标进行检测^[15,16]。甲状腺激素是甲状腺所分泌的激素,循环血浆中的甲状腺激素主要以 FT3、FT4 为主,其绝大部分与甲状腺结合球蛋白 TBG 结合从而丧失生物活性,在人体发挥主要作用的是其游离部分^[17-19],因此,准确测定人体中 FT3、FT4 的含量,可准确反映甲状腺功能。有研究表明^[20],当机体出现甲状腺功能减退症状时,FT3、FT4 水平明显降低,因此,上述二者可作为甲状腺激素水平评价指标。Hcy 属于甲硫氨酸的代谢产物,Catena C 等学者研究报道,Hcy 是心脑血管疾病发病的独立危险因素^[21]。而甲状腺功能减退是心脑血管疾病发病的主要诱因,推测 Hcy 参与着甲状腺功能减退的发生、发展。目前,临床有关 FT3、FT4、Hcy 以及血脂水平等指标在甲状腺功能减退患者的联合诊断报道较为少见,本研究就此展开探讨。

本次研究表明,甲状腺功能减退患者治疗后 FT3、FT4 均较治疗前升高,Hcy、TC、LDL-C 均较治疗前降低,而甲状腺功能减退患者治疗前后 TG、HDL-C 比较差异无统计学意义。提示甲状腺功能减退患者进行甲状腺激素对症治疗,Hcy 以及部分血脂水平均恢复,这可能是由于患者治疗后 FT3、FT4 水平上升,加快了 Hcy 的代谢速度,降低血清 Hcy 水平^[22]。而 TC、LDL-C 降低的原因可能是由于甲状腺激素可影响血脂从胆汁的排除速率,患者经治疗后 FT3、FT4 升高,TC、LDL-C 排出速度加快,从而降低其在血清的含量^[23,24]。而治疗前后 TG、HDL-C 无明显变化可能是由于甲状腺功能减退病理发展过程对上述两种指标影响较小。另外本研究还显示,观察组治疗前 FT3、FT4、HDL-C 水平明显低于对照组,而 Hcy、TC、TG、LDL-C 则明显高于对照组,提示甲状腺功能减退患者存在 FT3、FT4、Hcy 以及血脂指标的异常表达,甲状腺功能减退患者 FT3、FT4 水平均明显降低,而 Hcy 升高的主要原因可能为甲状腺功能减退时亚甲基四氢叶酸还原酶等代谢调节酶活力降低,Hcy 转化受阻,其水平升高^[25,26]。同时也可能由于甲状腺激素的不足导致机体代谢率降低,导致肾功能受损,致使 Hcy 清除率下降,患者血清 Hcy 水平升高^[27-29]。而甲状腺功能减退患者血脂指标水平均较健康志愿者低,表明甲状腺功能减退可影响机体血脂代谢水平^[30]。经 Pearson 相关性分析显示,甲状腺功能减退患者 Hcy 与 FT3、FT4 呈负相关,与 TC、TG 呈正相关,而与 LDL-C、HDL-C 无相关性。提示临床上可通过监测甲状腺功能减退患者的上述指标,更为准确的评估患者的病情。

综上所述,甲状腺功能减退患者的 Hcy 与 FT3、FT4、血脂

水平关系密切,临床上可通过监测甲状腺功能减退患者的上述指标,从而明确患者的病情程度,以降低患者并发心脑血管神经系统的风险。

参考文献(References)

- [1] Seong CY, Chai YJ, Lee SM, et al. Significance of distance between tumor and thyroid capsule as an indicator for central lymph node metastasis in clinically node negative papillary thyroid carcinoma patients[J]. PLoS One, 2018, 13(7): e0200166
- [2] Sun Y, Li Y, Liu Z, et al. Environmentally relevant concentrations of mercury exposure alter thyroid hormone levels and gene expression in the hypothalamic-pituitary-thyroid axis of zebrafish larvae [J]. Fish Physiol Biochem, 2018, 44(4): 1175-1183
- [3] 张晶虹,张立军,计嘉军,等.甲状腺全切除术与半切除术治疗甲状腺癌的临床效果分析[J].现代生物医学进展, 2017, 17(18): 3467-3469
- [4] Desai R, Goyal H, Kumar G, et al. Impact of Hypothyroidism on Outcomes of Percutaneous Coronary Intervention with Coronary Atherectomy for Calcified Coronary Lesions: A Propensity-matched Analysis[J]. Cureus, 2018, 10(5): e2600
- [5] Hirayama T, Saijo H, Kohji T, et al. Anti-epileptics alter hypothyroidism of patients with severe motor and intellectual disabilities[J]. No To Hattatsu, 2017, 49(1): 19-24
- [6] 程洋,戴丽,夏国光,等.慢性阻塞性肺疾病急性加重患者血清甲状腺激素水平变化及临床意义[J].中华结核和呼吸杂志, 2016, 39(12): 939-943
- [7] Pang C, Fan Y, Zhang H, et al. Case report:incidental parathyroid adenoma in a Chinese diabetic patient with hypercalcemia and normal parathyroid hormone levels[J]. Medicine (Baltimore), 2018, 97(28): e11333
- [8] El-Amrousy D, Hassan S, Hodeib H. Prognostic value of homocysteine and highly sensitive cardiac troponin T in children with acute heart failure[J]. J Saudi Heart Assoc, 2018, 30(3): 198-204
- [9] Varela Almanza KM, Puebla-Pérez AM, Delgado-Saucedo JI, et al. Increased homocysteine plasma levels in breast cancer patients of a Mexican population[J]. Exp Oncol, 2018, 40(2): 114-118
- [10] 王艳,裴妙荣.组分配伍四逆汤对甲状腺功能减退并发高脂血症及心血管系统损害的影响[J].中西医结合心脑血管病杂志, 2016, 14(19): 2236-2240
- [11] 陈灏珠.实用内科学[M].北京:人民卫生出版社, 2002, 1480-1482
- [12] Cataldo E, Columbano V, Nielsen L, et al. Phosphate binders as a cause of hypothyroidism in dialysis patients: practical indications from a review of the literature[J]. BMC Nephrol, 2018, 19(1): 155
- [13] 杨永红,王彩霞,贾英民,等.肾小球毛细血管内皮病合并甲状腺功能减低 1 例病例报道并文献复习[J].现代生物医学进展, 2015, 15(5): 870-872
- [14] Rastogi P, Dua A, Attri S, et al. Hypothyroidism-induced reversible dilated cardiomyopathy[J]. J Postgrad Med, 2018, 64(3): 177-179
- [15] Amouzegar A, Kazemian E, Abdi H, et al. Association Between Thyroid Function and Development of Different Obesity Phenotypes in Euthyroid Adults: A Nine-Year Follow-Up [J]. Thyroid, 2018, 28(4): 458-464
- [16] Martínez-Hernández R, Sampedro-Núñez M, Serrano-Somavilla A, et al. A MicroRNA Signature for Evaluation of Risk and Severity of Autoimmune Thyroid Diseases [J]. J Clin Endocrinol Metab, 2018,

- 103(3): 1139-1150
- [17] 刘一鸣,李丽,何伟波,等.甲亢及甲减患者血清瘦素水平与甲状腺激素相关性研究[J].新医学, 2015, (6): 387-390
- [18] Park E, Jung J, Araki O, et al. Concurrent TSHR mutations and DIO2 T92A polymorphism result in abnormal thyroid hormone metabolism [J]. Sci Rep, 2018, 8(1): 10090
- [19] 李美. 正常甲状腺功能病态综合征 FT3、FT4 和 TSH 与老年性疾病相关性研究[J].标记免疫分析与临床, 2017, 24(12): 1362-1365
- [20] 孙敬茹,韩梅,王露,等.左甲状腺素钠联合补硒治疗甲状腺功能减退的临床疗效及对甲状腺功能的影响[J].疑难病杂志, 2017, 16(1): 52-55, 63
- [21] Catena C, Colussi G, Nait F, et al. Elevated Homocysteine Levels Are Associated With the Metabolic Syndrome and Cardiovascular Events in Hypertensive Patients[J]. Am J Hypertens, 2015, 28(7): 943-950
- [22] Barjaktarovic M, Steegers EAP, Jaddoe VWV, et al. The Association of Thyroid Function With Maternal and Neonatal Homocysteine Concentrations[J]. J Clin Endocrinol Metab, 2017, 102(12): 4548-4556
- [23] Chen C, Xia F, Chen Y, et al. Association Between Thyroid-Stimulating Hormone and Renal Function: a Mendelian Randomization Study[J]. Kidney Blood Press Res, 2018, 43(4): 1121-1130
- [24] 刘璟,向鹏月,罗心凯,等.甲状腺癌术后停用甲状腺激素替代治疗血脂水平及对甲状腺功能的影响 [J]. 实用癌症杂志, 2018, 33(2): 230-232
- [25] Kweon SS, Shin MH, Kim HN, et al. Polymorphisms of methylenetetrahydrofolate reductase and glutathione S-transferase are not associated with the risk of papillary thyroid cancer in Korean population[J]. Mol Biol Rep, 2014, 41(6): 3793-3799
- [26] Grasberger H, Noureldin M, Kao TD, et al. Increased risk for inflammatory bowel disease in congenital hypothyroidism supports the existence of a shared susceptibility factor [J]. Sci Rep, 2018, 8(1): 10158
- [27] Han B, Cheng T, Ye L, et al. Comparison between acute kidney injury(AKI)and non-AKI patients secondary to severe hypothyroidism [J]. Clin Case Rep, 2018, 6(6): 1066-1069
- [28] Rosario PWS, Calsolari MR. Impact of subclinical hypothyroidism with TSH $\leq$ 10 mIU/L on glomerular filtration rate in adult women without known kidney disease[J]. Endocrine, 2018, 59(3): 694-697
- [29] Bajaj S, Purwar N, Gupta A, et al. Prevalence of hypothyroidism in nondiabetic chronic kidney disease and effect of thyroxine replacement on estimated glomerular filtration rate [J]. Indian J Nephrol, 2017, 27(2): 104-107
- [30] Olenych LV, Pylypiv LI, Bek NS, et al. Correlations between lipid metabolism indices in patients with hypertension and hypothyroidism [J]. Wiad Lek, 2018, 71(2pt1): 281-284

(上接第 1086 页)

- [22] 高志冬,王有利,韩龙,等.吻合器经肛门直肠切除术与吻合器痔上黏膜环形切除术治疗Ⅳ度痔的对比研究 [J]. 中华普通外科杂志, 2015, 30(9): 719-722
- [23] Sammarco G, Ferrari F, Carpino A, et al. PPH vs Milligan-Morgan: early and late complications in the treatment of haemorrhoidal disease with circumferential prolapse[J]. Ann Ital Chir, 2014, 85(5): 464-469
- [24] González-Macedo EA, Cosme-Reyes C, Belmonte-Montes C. Modification to stapled mucosectomy technique with PPH. Experience of a surgical group[J]. Cir Cir, 2015, 83(2): 124-128
- [25] Tsang YP, Fok KL, Cheung YS, et al. Comparison of transanal haemorrhoidal dearterialisation and stapled haemorrhoidopexy in management of haemorrhoidal disease: a retrospective study and literature review[J]. Tech Coloproctol, 2014, 18(11): 1017-1022
- [26] 张华峰.吻合器痔上黏膜环形切除术治疗 66 例老年重度痔[J].中国现代普通外科进展, 2016, 19(1): 59-61
- [27] Ruiz-Tovar J, Duran M, Alias D, et al. Reduction of postoperative pain and improvement of patients' comfort after Milligan-Morgan hemorrhoidectomy using topical application of vitamin E ointment[J]. Int J Colorectal Dis, 2016, 31(7): 1371-1372
- [28] Bhatti MI, Sajid MS, Baig MK. Milligan-Morgan (Open) Versus Ferguson Haemorrhoidectomy (Closed): A Systematic Review and Meta-Analysis of Published Randomized, Controlled Trials[J]. World J Surg, 2016, 40(6): 1509-1519
- [29] 王庆华,钟志风,杜金林,等.PPH 联合外痔切除术治疗混合痔的临床疗效观察[J].浙江医学, 2014, 53(18): 1565-1567
- [30] 彭勃,白月奎.吻合器痔上黏膜环形切除术与传统痔切除术临床疗效对比分析 [J]. 中华临床医师杂志 (电子版), 2016, 10(11): 1524-1527