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左甲状腺素联合碘 131 对甲状腺功能亢进症患者甲状腺体积、TR-Ab 和 TPOAb 水平的影响 *

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摘要 目的:研究左甲状腺素联合碘 131 对甲状腺功能亢进症患者甲状腺体积、促甲状腺激素受体抗体 (Thyrotropin receptor antibody, TR-Ab) 和甲状腺过氧化物酶抗体 (Thyroid peroxidase antibody, TPOAb) 水平的影响。**方法:**选择 2013 年 1 月-2019 年 1 月我院收治的 68 例甲状腺功能亢进症患者, 随机分为两组。对照组使用小剂量 (111~148 MBq) 的碘 131, 观察组在碘 131 的基础上, 联合服用左甲状腺素, 每次 12.5 μ g, 每日 1 次, 均治疗 3 个月后观察疗效及甲状腺体积、TR-Ab 和 TPOAb 水平变化。**结果:**观察组治疗 3 个月后的有效率明显高于对照组 ($P<0.05$); 治疗前, 两组的甲状腺体积、TR-Ab 和 TPOAb 水平无明显差异 ($P>0.05$), 治疗后, 两组的上述指标均明显降低 ($P<0.05$), 且观察组明显低于对照组 ($P<0.05$); 治疗前, 两组的血清游离三碘甲状腺原氨酸 (Free triiodothyronine, FT3)、促甲状腺素 (Thyroxine, TSH) 和游离四碘甲状腺素 (Free tetraiodothyroxine, FT4) 水平无明显差异 ($P>0.05$), 治疗后, 两组的血清 FT3 和 FT4 水平明显降低 ($P<0.05$), 血清 TSH 水平明显升高 ($P<0.05$), 观察组更加明显 ($P<0.05$); 治疗前, 两组的血清甲状腺球蛋白 (Thyroglobulin, Tg) 和半胱氨酸蛋白酶抑制剂 C (Cysteine protease inhibitor C, Cys C) 水平无明显差异 ($P>0.05$), 治疗后, 两组的血清 Tg 和 Cys C 水平明显降低 ($P<0.05$), 观察组明显低于对照组 ($P<0.05$)。**结论:**左甲状腺素联合碘 131 对甲状腺功能亢进症有确切的疗效, 能有效阻碍甲状腺自身抗体产生, 改善甲状腺功能, 降低血清 Tg 和 Cys C 水平。

关键词:左甲状腺素; 碘 131; 甲状腺功能亢进症; 甲状腺体积; 促甲状腺激素受体抗体; 甲状腺过氧化物酶抗体

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Effects of Levothyroxine Combined with Iodine 131 on Thyroid Volume, TR-Ab and TPOAb Levels in Patients with Hyperthyroidism*

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ABSTRACT Objective: To study the effect of levothyroxine combined with iodine 131 on thyroid volume, thyrotropin receptor antibody and thyroid peroxidase antibody levels in patients with hyperthyroidism. **Methods:** Sixty-eight patients with hyperthyroidism who were admitted to our hospital from January 2013 to January 2019 were randomly divided into two groups. The control group used a small dose (111-148 MBq) of iodine 131, and the observation group based on iodine 131 in combination with levothyroxine, 12.5 μ g each time, once a day, both observed the efficacy and thyroid after 3 months of treatment Volume, TR-Ab, and TPOAb levels changed. **Results:** The effective rate of the observation group after 3 months of treatment was significantly higher than that of the control group ($P<0.05$). Before treatment, there was no significant difference in thyroid volume, TR-Ab and TPOAb levels between the two groups ($P>0.05$). After treatment, the thyroid volume, TR-Ab and TPOAb levels of the two groups decreased significantly ($P<0.05$), while the thyroid volume, TR-Ab and TPOAb levels of the observation group were significantly lower than those of the control group ($P<0.05$). Before treatment, there was no significant difference in serum FT3, TSH and FT4 levels between the two groups ($P>0.05$). After treatment, the serum FT3 and FT4 levels of the two groups decreased significantly ($P<0.05$), and the serum TSH levels increased significantly ($P<0.05$), especially in the observation group ($P<0.05$). Before treatment, there was no significant difference in serum Tg and Cys C levels between the two groups ($P>0.05$). After treatment, the serum Tg and Cys C levels of the two groups decreased significantly ($P<0.05$), while the serum Tg and Cys C levels of the observation group were significantly lower than those of the control group ($P<0.05$). **Conclusion:** Levothyroxine combined with iodine 131 has definite curative effect on hyperthyroidism. It can effectively block the production of thyroid autoantibodies, improve thyroid function and reduce serum Tg and Cys C levels.

Key words: Levothyroxine; Iodine 131; Hyperthyroidism; Thyroid volume; Thyrotropin receptor antibody; Thyroperoxidase antibody

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前言

甲状腺功能亢进症指的是机体中的甲状腺素合成出现异常的增多,使得机体交感神经兴奋和代谢亢进的一种内分泌疾病^[12]。甲状腺功能亢进症主要表现为食欲亢进,怕热多汗,消瘦乏力,兴奋性增高,易激动,心率增快,活动后加剧,心悸,甲状腺肿大,并且会伴有视力减退、非浸润性突眼或者浸润性突眼等比较严重的眼疾等,甚至发生甲状腺危象^[3-6]。虽然临床关于该病的研究在不断的深入,但目前其病机尚未完全明确,多数研究认为,毒性弥漫性甲状腺肿是引起该病发生的主要原因,而作息不规律、长期炎症反应以及精神压力过大等因素也会使甲状腺功能亢进症的发病风险明显升高^[7-9]。治疗甲状腺功能亢进患者的原则是快速地纠正代谢紊乱以及缓解甲状腺亢进。碘 131 治疗甲状腺功能亢进具有费用低廉、起效快和不良反应小等优点^[10]。左甲状腺素是由人工合成的一种甲状腺激素类似物。为进一步探究有效治疗甲状腺亢进的方法,本研究创新性地将左甲状腺素与碘 131 联用,分析其对甲状腺功能亢进症的疗效。

1 资料与方法

1.1 一般资料

选择 2013 年 1 月 -2019 年 1 月我院收治的 68 例甲状腺功能亢进症患者,纳入标准:均符合相关的诊断标准;入组前,没有接受过相关外科手术或者药物治疗;均知情同意。排除标准:(1)服用过影响钙、磷代谢的药物或者免疫制剂;(2)其他疾病造成甲状腺功能亢进的者;(3)合并恶性肿瘤、心脑血管疾病的者;(4)精神障碍者;(5)合并其他甲状腺疾病的者;(6)对左甲状腺素以及碘 131 过敏的患者。无脱落病例。用抽签法随机分为两组。观察组 34 例,男 16 例,女 18 例;年龄 54~78 岁,平均(61.13±5.38)岁;病程 1~10 个月,平均(6.23±1.04)个月;

体质量 42~67 kg,平均(59.34±12.99)kg;甲状腺肿大程度:I 度肿大 14 例,II 度肿大 12 例,III 度肿大 8 例。对照组 34 例,男 17 例,女 17 例;年龄 57~79 岁,平均(63.27±4.65)岁;病程 1~10 个月,平均(6.18±1.14)个月;体质量 41~67 kg,平均(59.72±13.41)kg;甲状腺肿大程度:I 度肿大 15 例,II 度肿大 13 例,III 度肿大 6 例。两组的基线资料具有可比性。

1.2 治疗方法

对照组:使用小剂量(111~148 MBq)的碘 131,对于病程较短、年龄较小、甲状腺较小和吸碘率较高的患者给予 111 MBq,对于病程较长、年龄较大、甲状腺较大和吸碘率较低的患者给予 148 MBq。观察组:在碘 131 的基础上,联合服用左甲状腺素,每次 12.5 μg,每日 1 次。均治疗 3 个月。

1.3 观察指标

疗效标准:(1)显效:患者的体质量有所增加,脉率基本恢复平稳,甲状腺功能恢复正常;(2)有效:患者的手颤以及甲状腺肿大等症状有所改善,脉率减慢,甲状腺功能恢复正常;(3)无效:患者的体质量、脉率、甲状腺功能无好转。

在治疗前后,用彩色多普勒超声检测仪检测甲状腺的长、厚度和宽,再计算甲状腺的体积;并采集 10 mL 肘静脉血,用免疫化学发光法检测 TR-Ab、TSH、FT3、Cys C、FT4、TPOAb 和 Tg 水平,试剂盒均购自江苏凯基生物公司。

1.4 统计学分析

采用 SPSS 20.0,计量资料用($\bar{x} \pm s$)示,采用 t 检验,计数资料用%表示,行 χ^2 检验, $P < 0.05$ 差异有统计学意义。

2 结果

2.1 疗效比较

观察组治疗 3 个月后的总有效率明显高于对照组($P < 0.05$),见表 1。

表 1 疗效比较[例(%)]

Table 1 Comparison of the clinical effect [n(%)]

Groups	n	Effective	Valid	Invalid	The total effect rate
Control group	34	14(41.18)	8(23.53)	12(35.29)	22(64.71)
Observation group	34	18(52.94)	13(38.24)	3(8.82)	31(91.18)*

Note: Compared with the control group, * $P < 0.05$.

2.2 甲状腺体积、TR-Ab 和 TPOAb 水平比较

治疗前,两组的甲状腺体积、TR-Ab 和 TPOAb 水平无明显

差异($P > 0.05$),治疗后,两组的上述指标明显降低($P < 0.05$),且观察组明显低于对照组($P < 0.05$),见表 2。

表 2 甲状腺体积、TR-Ab 和 TPOAb 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the thyroid volume, TR-Ab and TPOAb levels($\bar{x} \pm s$)

Groups	n		Thyroid volume (cm ³)	TR-Ab (U/L)	TPOAb (KU/L)
Control group	34	Before treatment	19.76±7.53	26.13±10.34	197.34±42.65
		After treatment	10.35±5.24 [#]	20.34±7.58 [#]	167.32±38.45 [#]
Observation group	34	Before treatment	19.34±6.29	25.78±10.23	196.28±44.76
		After treatment	7.03±2.27 ^{**}	16.39±4.32 ^{**}	142.67±31.74 ^{**}

Note: Compared with the control group, * $P < 0.05$; compared with before treatment, [#] $P < 0.05$.

2.3 血清 FT3、TSH 和 FT4 水平比较

治疗前, 两组的血清 FT3、TSH 和 FT4 水平无明显差异 ($P>0.05$), 治疗后, 两组的血清 FT3 和 FT4 水平明显降低 ($P<0.05$),

血清 TSH 水平明显升高 ($P<0.05$), 观察组更加明显 ($P<0.05$), 见表 3。

表 3 血清 FT3、TSH 和 FT4 水平比较 ($\bar{x} \pm s$)
Table 3 Comparison of serum FT3, TSH and FT4 levels ($\bar{x} \pm s$)

Groups	n		FT3 (pg/mL)	TSH (pmol/L)	FT4 (pg/mL)
Control group	34	Before treatment	15.73 $\pm$ 3.62	0.21 $\pm$ 0.14	69.34 $\pm$ 17.25
		After treatment	7.31 $\pm$ 2.29 [#]	2.19 $\pm$ 0.36 [#]	18.32 $\pm$ 4.27 [#]
Observation group	34	Before treatment	15.48 $\pm$ 3.49	0.22 $\pm$ 0.13	68.23 $\pm$ 16.41
		After treatment	4.65 $\pm$ 1.34 ^{**}	3.37 $\pm$ 0.42 ^{**}	11.63 $\pm$ 2.19 ^{**}

2.4 血清 Tg 和 Cys C 水平比较

治疗前, 两组的血清 Tg 和 Cys C 水平无明显差异 ($P>0.05$),

治疗后, 两组的上述指标均明显降低 ($P<0.05$), 且观察组的明显低于对照组 ($P<0.05$), 见表 4。

表 4 血清 Tg 和 Cys C 水平比较 ($\bar{x} \pm s$)
Table 4 Comparison of serum Tg and Cys C levels ($\bar{x} \pm s$)

Groups	n		Tg (μ g/L)	Cys C (mg/L)
Control group	34	Before treatment	135.48 $\pm$ 29.76	1.49 $\pm$ 0.32
		After treatment	79.25 $\pm$ 13.64 [#]	1.14 $\pm$ 0.23 [#]
Observation group	34	Before treatment	134.29 $\pm$ 27.41	1.50 $\pm$ 0.37
		After treatment	43.78 $\pm$ 10.13 ^{**}	0.83 $\pm$ 0.16 ^{**}

3 讨论

甲状腺功能亢进症主要是由于机体的甲状腺合成且分泌过多的甲状腺激素而导致, 会对患者的多个脏腑器官造成影响, 使得机体发生代谢亢进^[11,12]。甲状腺功能亢进症是一种全身性的病症, 常见的症状有多食、心悸、消瘦和多便等, 病情严重时还会发生脉搏不规则和脉搏加快、呕吐、发热等, 能导致多种器官受累, 肝脏的功能受到损伤时, 会进一步造成病情恶化, 导致肝大、肝功能衰竭、肝硬化和肝功能异常等比较严重的后果^[13-15]。目前针对此类患者主要可采取药物治疗、放射碘治疗和手术治疗^[16]。手术治疗会对患者造成较大的创伤, 主要适用于甲状腺明显肿大, 严重压迫气管, 疑似甲状腺恶性肿瘤或者引发呼吸困难的患者; 而放射碘治疗及药物治疗是当前具有较高使用率的疗法^[17]。

左甲状腺素是一种常用的辅助治疗甲状腺功能亢进症的药物, 该药的药效比较确切, 其作用功效与甲状腺片具有较多的相似之处, 但是与甲状腺片相比, 其具有更高的生物活性度, 而且起效更加平稳^[18-20]。碘 131 是临床上治疗甲状腺功能亢进症有效的方法, 但是容易发生甲减的不良发应, 因此, 本研究创新性的将左甲状腺素与碘 131 联用, 希望为甲状腺功能亢进症的临床治疗提供新的思路。

本研究结果显示, 观察组治疗 3 个月后的总有效率明显高于对照组, 说明左甲状腺素与碘 131 联合应用, 显著地提高了治疗效率, 提示左甲状腺素提供了患者正常代谢所需的激素, 患者口服之后, 可明显促进机体的新陈代谢, 明显增强交感-肾上腺系统的感受性作用^[21-23]。同时也能改善患者继发性的甲状腺功能减退症状, 抑制甲状腺继发性的增生, 缩小甲状腺的

体积, 还能改善患者机体反馈和甲状腺素过度下降导致的不良反应症状^[24-26]。从而提高患者的治疗效率。本研究治疗后, 观察组的甲状腺体积、TR-Ab 和 TPOAb 水平明显低于对照组; 观察组的血清 FT3 和 FT4 水平明显低于对照组, 血清 TSH 水平明显高于对照组, 这与 Jia YQ^[27]等人的研究相似, 表明在碘 131 的基础上, 联用左甲状腺素能有效抑制患者的 TSH 的生成, 有效改善甲状腺的功能, 明显抑制甲状腺自身抗体的产生, 降低血清 FT3 和 FT4 水平, 进而有效缩小甲状腺的体积。

绝大多数的 Tg 由甲状腺细胞合成, 是评估甲状腺功能亢进症疗效的重要检测指标, 其水平若发生降低, 则表示患者的甲状腺功能出现减退^[28,29]。TSH、甲状腺刺激性免疫球蛋白以及甲状腺体内碘缺乏等因素均能刺激 Tg 的产生。Cys C 主要由机体所有有核细胞产生, 且不受胆红素、炎性反应、三酰甘油和溶血的影响^[29,30]。本研究结果显示观察组的血清 Tg 和 Cys C 水平低于对照组。表明左甲状腺素联合碘 131 能更有效的改善甲状腺功能亢进症患者的血清 Tg 和 Cys C 水平。分析其原因可能为, 甲状腺功能亢进症患者机体内过量的甲状腺激素会直接对骨骼产生作用, 而左甲状腺素可以诱导包括特殊酶系的新生蛋白质的合成, 调节三大物质 (蛋白质、脂肪以及碳水化合物) 的代谢, 而且有效调节水、维生素以及盐的代谢, 从而改善了血清 Tg 和 Cys C 水平。本研究也存在一定的不足, 作为创新探究阶段, 没有进行远期追踪观察患者的不良反应, 因此还需要继续进行后续的观察研究, 在此基础上扩大样本量进行深入研究, 为临床治疗的新方法提供基础依据。

综上所述, 左甲状腺素联合碘 131 对甲状腺功能亢进症有确切的疗效, 能有效阻碍甲状腺自身抗体产生, 改善甲状腺功能, 降低血清 Tg 和 Cys C 水平。

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