

doi: 10.13241/j.cnki.pmb.2018.20.030

碘 131 与他巴唑治疗甲状腺功能亢进症的临床疗效比较

李玉娟¹ 祁 岗¹ 李海燕² 李梦婕¹ 吴葆华³

(1 青海省人民医院核医学科 青海 西宁 810000; 2 青海省人民医院肿瘤内科 青海 西宁 810000;

3 青海省人民医院消化内科 青海 西宁 810000)

摘要 目的:观察和比较碘 131 与他巴唑治疗甲状腺功能亢进症的临床疗效及安全性。**方法:**选取 2012 年 1 月至 2016 年 1 月于我院确诊并治疗的甲状腺功能亢进患者 282 例,根据随机数字表法分为碘 131 治疗组和药物治疗组,碘 131 治疗组采用 ¹³¹I 进行治疗,药物治疗组采用他巴唑口服治疗。比较两组患者的临床疗效,治疗前后血清 TSH(thyroid stimulating hormone,促甲状腺激素)、FT(free triiodothyronine,游离三碘甲状腺原氨酸)、FT4(free thyroxine concentration assay,血清游离甲状腺素)水平及 TRAb(TRAb thyrotropin receptor antibodies,促甲状腺激素受体抗体)阳性率的变化及治疗期间不良反应的发生情况(心功能、肝功能、肾功能、甲状腺功能下降、白细胞减少),并对患者进行 6 个月的随访,记录和比较患者甲亢复发情况。**结果:**治疗后,碘 131 治疗组的总有效率为 92.9%,显著高于药物治疗组(64.5%, $P<0.05$);两组患者血清 TSH 水平较治疗前显著升高,而血清 FT3、FT4 水平及 TRAb 阳性率均较治疗前显著降低($P<0.05$),且碘 131 治疗组血清 TSH 水平明显高于碘 131 治疗组,而血清 FT3、FT4 水平及 TRAb 阳性率明显低于碘 131 治疗组($P<0.05$);碘 131 治疗组复发率及总不良反应发生率均明显低于药物治疗组($P<0.05$)。**结论:**碘 131 对甲状腺功能亢进症的疗效优于他巴唑口服治疗,可明显增加血清 TSH 水平,降低血清 FT3、FT4 水平及 TRAb 阳性率,且患者复发率及不良反应发生率均较低。

关键词:碘 131;他巴唑;甲状腺功能亢进症;疗效;不良反应

中图分类号:R581.1 **文献标识码:**A **文章编号:**1673-6273(2018)20-3933-04

Comparison of the Clinical Efficacy of Iodine 131 and Methimazole in the Treatment of Hyperthyroidism

LI Yu-juan¹, QI Gang¹, LI Hai-yan², LI Meng-jie¹, WU Bao-hua³

(1 Nuclear Medicine Department, Qinghai Provincial People's Hospital, Xining, Qinghai, 810000, China;

2 Medical Oncology Department, Qinghai Provincial People's Hospital, Xining, Qinghai, 810000, China;

3 Gastroenterology Department, Qinghai Provincial People's Hospital, Xining, Qinghai, 810000, China)

ABSTRACT Objective: To observe and compare the clinical efficacy and safety of iodine 131 in the treatment of hyperthyroidism.

Methods: 282 cases of patients with hyperthyroidism diagnosed and treated in our hospital from January 2012 to January 2016 were randomly divided into the iodine 131 treatment group and the drug treatment group according to the random number table method. Iodine 131 treatment group was treated with ¹³¹I, the drug treatment group was given oral administration of methimazole. The clinical efficacy, serum TSH, FT and FT4 levels, TRAb positive rate and incidence of adverse effects (cardiac function, liver function, renal function, decreased thyroid function, leukopenia) of patients in two groups during treatment were observed and compared, and patients were followed up for 6 months to record the recurrence. **Results:** After treatment, the total effective rate of iodine 131 treatment group was 92.9%, which was significantly higher than that of drug treatment group (64.5%, $P<0.05$); the levels of serum TSH were significant higher than before treatment, while the FT3, FT4 and TRAb positive rate were significantly decreased ($P<0.05$), the recurrence rate and incidence of adverse events in iodine 131 treatment group was significantly lower than that of drug treatment group ($P<0.05$). **Conclusions:** Iodine 131 had better clinical efficacy in the treatment of hyperthyroidism than oral tapazol therapy, it could significantly increase the serum TSH level, reduce the serum FT3, FT4 levels and TRAb positive rate, lower the recurrence rate and the incidence of adverse reactions.

Key words: Iodine 131; Methimazole; Hyperthyroidism; Efficacy; Adverse reactions

Chinese Library Classification(CLC): R581.1 **Document code:** A

Article ID: 1673-6273(2018)20-3933-04

前言

作者简介:李玉娟(1979-),女,本科,主治医师,研究方向:核素治疗, E-mail: liyujuan_1979@papedhos.top

(收稿日期:2018-02-24 接受日期:2018-03-19)

甲状腺由侧叶和甲状腺峡部构成,主要功能为分泌降钙素及分泌甲状腺素,具有加速新陈代谢及维持机体正常生长发育的作用。甲状腺功能亢进症又称为甲亢,为一种内分泌系统疾病,由多种因素综合导致甲状腺分泌甲状腺激素过量,以机体代谢功能亢进、交感神经过度兴奋为主要表现的临床综合征,

包括炎性甲亢、弥漫性毒性甲状腺肿、药物致甲亢、人绒毛膜促性腺激素相关性甲亢、垂体促甲状腺激素瘤甲亢等^[1-3],临床表现为甲状腺肿大、心悸、乏力、多食消瘦、眼突、视力下降等症状^[3,4]。甲亢的发病率约为1%,多发于中青年女性,女性发病率高于男性^[5]。根据病因甲亢可分为原发性甲亢、继发性甲亢和高功能腺瘤,其中原发性甲亢最常见^[6],治疗时应根据患者病情选择合适的治疗方法。

目前,甲亢的治疗方法主要包括手术治疗、放射性同位素治疗、药物治疗等^[7-10]。手术全切或者次切甲状腺对甲亢疗效较好,但是在老年患者中应用较少;临床多以他巴唑治疗甲亢,他巴唑主要由甲硫咪唑制成,但是训在部分患者疗效高、部分患者疗效差的情况^[11],放射性同位素治疗多采用碘¹³¹治疗,给药方式简单、治疗费用低且疗效显著,近年来已成为治疗甲亢的首选药物^[12,13]。本研究主要观察和比较了碘¹³¹与他巴唑治疗甲状腺功能亢进症的临床效果和安全性,具体如下。

1 资料与方法

1.1 一般资料

选取2012年1月至2016年1月于我院确诊并治疗的甲状腺功能亢进患者282例,根据随机数字表法分为碘¹³¹治疗组和药物治疗组。其中,碘¹³¹治疗组141例,男性65例,女性76例,年龄为32~75岁,平均为 47.9 ± 14.5 岁,病程1~5年,甲亢程度轻度53例、中度64例、重度24例;药物治疗组141例,男性62例,女性79例,年龄34~76岁,平均 49.2 ± 16.1 岁,病程1~5年,甲亢程度轻度51例、中度63例、重度27例。两组患者的一般资料比较差异无统计学意义($P > 0.05$),具有可比性。本研究经我院伦理委员会批准通过,所有患者均知情同意。

纳入标准:①符合《中国甲状腺疾病诊治指南》^[14]中诊断标准;②病情明确,能匹配治疗者;③无其他严重合并症者。排除标准:①妊娠及哺乳期妇女;②合并甲状腺危象者;③合并其他重大疾病者;④需要手术治疗者。

1.2 治疗方法

碘¹³¹治疗组:碘¹³¹治疗组采用¹³¹I进行治疗,治疗前为患者详细介绍该治疗方法,包括方法、目的、意义及可能出现的

不良反应等,并进行心电图、肝功能、肾功能、促甲状腺激素TSH、血清游离三碘甲状腺原氨酸FT3、血清游离甲状腺素FT4及TSH受体抗体TRAb检查。治疗前4周开始禁服含碘药物及食物,根据甲状腺大小、患者年龄、病情等确定给药剂量,¹³¹I治疗剂量为109~534 MBq,均为一次性口服给药。有关公式如下:

$$\text{甲状腺肿大} = \text{左右平均叶高} \times \text{平面甲状腺面积} \times 0.31$$

$$^{131}\text{I用量} = \frac{\text{甲状腺计划}^{131}\text{I每克量} \times \text{甲状腺质量}}{\text{最高摄取量}}$$

药物治疗组:药物治疗组采用他巴唑口服治疗,用量为6~29 mg/d,1~2个月进行早期治疗期,3~4个月减少患者用药剂量,5~12个月为维持期,在不同用药时期,根据患者病情为剂量进行调整。

1.3 评价指标

疗效标准:痊愈为患者甲亢症状小时、甲状腺大小恢复正常,维持时间超过6个月;显效为患者部分甲亢症状好转,甲状腺大小有所减小但为恢复正常水平;无效为患者甲亢症状为缓解或加重。总有效率=(痊愈例数+有效例数)/总例数 $\times 100\%$ 。两组患者均在治疗6个月后,空腹抽取静脉血,采用酶联免疫吸附法按试剂盒说明书方法检测TSH、FT₃及FT₄,试剂盒购自武汉华美生物工程有限公司,采用化学发光测定仪按说明书方法检测TRAb, $>30 \text{ IU/mL}$ 为阳性,试剂盒新产业生物医学工程有限公司。观察记录治疗期间患者的不良反应情况,并对患者进行6个月的随访,记录治疗有效患者再次出现甲亢的情况,比较复发率,复发率=复发例数/总例数 $\times 100\%$ 。

1.4 统计学处理

所有数据采用SPSS17.0进行分析,计量资料以 $(\bar{x} \pm s)$ 表示,组间比较采用t检验,计数资料以%表示,组间比较采用卡方检验,以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

如表1所示,碘¹³¹治疗组的总有效率为92.9%,显著高于药物治疗组(64.5%, $P < 0.05$)。

表1 两组甲亢患者临床疗效的比较[例(%)]

Table 1 The comparison of clinical efficacy of patients with hyperthyroidism between two groups

Groups	Cases	Heal	Effective	Invalid	Total efficiency
¹³¹ I treatment group	141	108	23	10	92.9
Drug treatment group	141	52	39	50	64.5
<i>P</i>			0.000		0.000

2.2 两组患者治疗前后血清TSH、FT₃、FT₄水平及TRAb阳性率的比较

如表2所示,两组患者血清TSH水平较治疗前显著升高,而血清FT₃、FT₄水平及TRAb阳性率均较治疗前显著降低($P < 0.05$),且碘¹³¹治疗组血清TSH水平明显高于碘¹³¹治疗组,而血清FT₃、FT₄水平及TRAb阳性率明显低于碘¹³¹治疗组($P < 0.05$)。

2.3 两组复发率及不良反应发生情况的比较

如表3所示,碘¹³¹治疗组复发率明显低于药物治疗组($P < 0.05$),碘¹³¹治疗组患者有1例出现甲状腺功能下降,总不良反应发生率明显低于药物治疗组($P < 0.05$)。

3 讨论

甲状腺功能亢进症由甲状腺激素异常增多导致,可引起机体相关系统兴奋度异常增加和机体代谢亢进^[15,16]。甲亢的治疗疗程较长,使得部分患者依从性不高,影响了甲状腺功能的恢

表 2 两组患者治疗前后血清 TSH、FT3、FT4 水平及 TRAb 阳性率的比较

Table 2 The comparison of serum TSH, FT3, FT4 levels and TRAb positive rate of patients between two groups before and after treatment

Groups		Cases	TSH(mU/L)	FT3(pmol/L)	FT4(pmol/L)	TRAb positive rate(%)
¹³¹ I treatment group	Before treatment	141	2.6± 0.3	13.4± 1.9	30.7± 5.2	116(82.3)
	After treatment	141	4.5± 0.7 ^{ab}	7.6± 1.0 ^{ab}	15.9± 1.7 ^{ab}	2(1.4) ^{ab}
Drug treatment group	Before treatment	141	2.6± 0.4	14.1± 1.8	31.9± 6.0	117(83.0)
	After treatment	141	3.0± 0.5 ^{ab}	5.9± 0.8 ^{ab}	19.9± 2.1 ^{ab}	25(17.7) ^b

Note: a. Compared with the control group, $P < 0.05$; b. Compared with before treatment, $P < 0.05$.

表 3 两组患者复发率及不良反应比较[例(%)]

Table 3 The comparison of recurrence rate and incidence of adverse reactions of patients between two groups[n(%)]

Groups	Cases	Recurrence rate	Adverse reactions					Total incidence of adverse reactions
			Cardiac Function	Liver function	Renal function	Decreased thyroid function	Leukopenia	
¹³¹ I treatment group	141	3(2.13)	0	0	0	1	0	1(0.07)
Drug treatment group	141	27(19.15)	1	9	1	0	8	19(13.48)

复,合理而有效的治疗手段是控制疾病发展、降低并发症,进而促进患者康复的关键^[17-19]。甲亢的药物治疗多采用他巴唑^[20],可以通过抑制甲状腺过氧化酶的活性,切断络氨酸碘化途径,使甲状腺激素的合成减少,进而发挥对甲亢的治疗作用^[21]。目前,对甲亢的放射同位素治疗多采用碘 131^[22,23]。本研究对两组的临床疗效进行比较,结果显示碘 131 治疗组的总有效率为 92.9%,显著高于药物治疗组的 64.5%。碘元素为机体合成甲状腺激素的主要成分,甲状腺对含碘化合物亲和性较高,碘 131 被机体摄入后可富集于甲状腺中,由于碘 131 的不稳定性,其在体内会发生衰变,衰变中释放出的 α 射线可破坏甲状腺细胞,使甲状腺功能降低,甲状腺激素分泌量减少,同时对周围组织损伤较小,其远期疗效要好于近期疗效^[24]。

甲状腺功能亢进症为一种自生免疫性疾病,发病机理尚未明确,一般认为与促甲状腺素受体抗体 TRAb 直接相关。TRAb 中的甲状腺刺激抗体 TSAb 与 TSH 受体结合,模拟 TSH 作用,引起甲状腺腺泡细胞膜上的 TSH 受体过度兴奋,使甲状腺细胞增生甲状腺体积增大,甲状腺激素合成及分泌增多,FT3、FT4 水平升高^[25,26]。本研究结果显示两组患者治疗后血清 TSH、FT3、FT4 水平及 TRAb 阳性率均显著改善,其中 TSH 水平明显升高,其他指标明显降低,且碘 131 治疗组各指标改善情况显著优于药物治疗组。

他巴唑主要成分为甲巯咪唑,可引起粒细胞减少、肝损伤、皮疹等不良反应,所引起的粒细胞减少有剂量依赖性,所引起的肝损伤与剂量无关^[27,28]。碘 131 能被甲状腺组织高度选择性吸收,通过发射高能射线抑制甲状腺功能发挥治疗目的^[29]。本研究结果显示碘 131 治疗组复发率及总不良反应发生率明显低于药物治疗组。应用碘 131 治疗后,一般只有较轻的肠胃不适、颈部肿胀、疼痛,手术患者有唾液腺受损、膀胱炎、脱发及骨髓抑制等严重的不良反应,及时治疗应对均可恢复^[30]。

综上所述,碘 131 对甲状腺功能亢进症的疗效优于他巴唑口服治疗,可明显增加血清 TSH 水平,降低血清 FT3、FT4 水平及 TRAb 阳性率,且患者复发率及不良反应发生率均较低。

参考文献(References)

- [1] Chen Y, Liang L, Fang Y, et al. Iodine 131 joint radio frequency ablation treatment for child with hyperthyroidism goiter: one case report[J]. Zhejiang da xue xue bao, 2017, 46(1): 89
- [2] Cramon P, Winther K H, Watt T, et al. Quality of life impairments persist six months after treatment of Graves' hyperthyroidism and toxic nodular goiter: A prospective cohort study [J]. Thyroid Official Journal of the American Thyroid Association, 2016, 26(8): 35-41
- [3] Evans R W, Timm J S. New Daily Persistent Headache Caused by a Multinodular Goiter and Headaches Associated With Thyroid Disease [J]. Headache the Journal of Head & Face Pain, 2017, 57(2): 285
- [4] Serim B D, Korkmaz U, Can U, et al. Intrathoracic toxic thyroid nodule causing hyperthyroidism with a multinodular normal functional cervical thyroid gland [J]. Indian Journal of Nuclear Medicine Ijnm the Official Journal of the Society of Nuclear Medicine India, 2016, 31(3): 229
- [5] Kornelius E, Chiou C Y, Yang Y S, et al. Iodinated Contrast Media-Induced Thyroid Dysfunction in Euthyroid Nodular Goiter Patients[J]. Thyroid, 2016, 26(8): 45
- [6] Giesecke P, Rosenqvist M, Frykman V, et al. Increased Cardiovascular Mortality and Morbidity in Patients Treated for Toxic Nodular Goiter Compared to Graves' Disease and Nontoxic Goiter [J]. Thyroid Official Journal of the American Thyroid Association, 2017, 27(7): 31
- [7] Bukvic B, Zivaljevic V, Sipetic S, et al. Improved quality of life in hyperthyroidism patients after surgery [J]. Journal of Surgical Research, 2015, 193(2): 724-730
- [8] Walter M A, Christ Crain M, Eckard B, et al. Radioiodine therapy in hyperthyroidism: inverse correlation of pretherapeutic iodine uptake level and post therapeutic outcome [J]. European Journal of Clinical Investigation, 2015, 34(5): 365-370
- [9] Piantanida E, Lai A, Sassi L, et al. Outcome Prediction of Treatment of Graves' Hyperthyroidism with Antithyroid Drugs [J]. Horm Metab Res, 2015, 47(10): 767-772
- [10] Sundawa K A H, Stepanus M. The Influence of Antithyroid Drug Discontinuation to the Therapeutic Efficacy of ¹³¹I in Hyperthyroidism

- [J]. World Journal of Nuclear Medicine, 2016, 15(2): 81-84
- [11] Riva M A, Ferretti C, Pagni F. Duran Madonna (c. 1435-1438) by Rogier van der Weyden: a case of congenital goiter [J]. Internal & Emergency Medicine, 2016, 11(8): 1-2
- [12] Olson AC, Haugen BR, Walter J, et al. SPECT/CT and I131 therapy of brain metastases from follicular variant papillary thyroid carcinoma (FVPTC)[J]. J Clin Endocrinol Metab, 2014, 99(10): 3511-3512
- [13] Hussein O, Karen D, Zidan J. Cisplatin based chemotherapy in patients with advanced differentiated thyroid carcinoma refractory to I131 treatment[J]. Indian J Med Paediatr Oncol, 2013, 34(4): 234-237
- [14] Vos X G, Ender E, Zwinderman A H, et al. Predicting the Risk of Recurrence Before the Start of Antithyroid Drug Therapy in Patients With Graves' Hyperthyroidism [J]. J Clin Endocrinol Metab, 2016, 101(4): 1381-1389
- [15] Cunha F M, Rodrigues E, Oliveira J, et al. Graves' disease in a mediastinal mass presenting after total thyroidectomy for nontoxic multinodular goiter: a case report[J]. Journal of Medical Case Reports, 2016, 10(1): 70
- [16] Szatkowska M, Zimny D, Barg E. Down syndrome and hyperthyroidism - two case reports [J]. Pediatric Endocrinology Diabetes & Metabolism, 2016, 21(2): 93
- [17] Cao L, Ding W, Du J, et al. Effects of curcumin on antioxidative activities and cytokine production in Jian carp (Cyprinus carpio var. Jian) with CCl₄-induced liver damage [J]. Fish & Shellfish Immunology, 2015, 43(1): 150-157
- [18] Gauthé M, Sarfati J, Bourcigaux N, et al. Pituitary Adenoma Recurrence Suspected on Central Hyperthyroidism Despite Empty Sella and Confirmed by 68Ga-DOTA-TOC PET/CT [J]. Clinical Nuclear Medicine, 2017, 42(6): 454
- [19] Burhan I, Khan A K, Adam A K. Significance of TPO and Some Biochemical Parameters in Goiter Patients[J]. International Journal of Pharmaceutical Sciences Review & Research, 2016, 40(2 46): 251-254
- [20] Kruljac I, Solter D, Vrkljan A M, et al. Remission of Graves' disease is not related to early restoration of euthyroidism with high-dose methimazole therapy[J]. Endocrine Research, 2015, 40(1): 1-4
- [21] Amato E, Campenni A, Leotta S, et al. Treatment of hyperthyroidism with radioiodine targeted activity: A comparison between two dosimetric methods[J]. Physica medica : PM: an international journal devoted to the applications of physics to medicine and biology: official journal of the Italian Association of Biomedical Physics (AIFB), 2016, 32(6): 847
- [22] Kuanrakcharoen P. Radioiodine (1-131) Dose for the Treatment of Hyperthyroidism in Rajavithi Hospital [J]. Journal of the Medical Association of Thailand, 2016, 99 Suppl 2(3): S123
- [23] Darwish S M, Ghadban W K, Zirie M A, et al. Success rate of radioiodine treatment of hyperthyroidism in Qatari patients [J]. Qatar Medical Journal, 2016, 18(1): 42-46
- [24] Zuhur S S, Baykiz D, Kara S P, et al. Relationship Among Pulmonary Hypertension, Autoimmunity, Thyroid Hormones and Dyspnea in Patients With Hyperthyroidism [J]. American Journal of the Medical Sciences, 2017, 353(4): 374
- [25] Donangelo I, Suh S Y. Subclinical Hyperthyroidism: When to Consider Treatment[J]. American Family Physician, 2017, 95(11):710
- [26] Shyamasunder A H, Abraham P. Measuring TSH receptor antibody [TRAb] to influence treatment choices in Graves' disease[J]. Clinical Endocrinology, 2017, 86(5): 652-657
- [27] Köhler I, Ballhausen B D, Stockhaus C, et al. Prevalence of and risk factors for feline hyperthyroidism among a clinic population in Southern Germany [J]. Tierärztliche Praxis Ausgabe K Kleintiere/heimtiere, 2016, 44(3): 89-92
- [28] Sharma S D, Kumar G, Guner K, et al. Hyperthyroidism in patients with thyroid cancer[J]. Ear Nose Throat J, 2016, 95(6): 236-239
- [29] Kadia B M, Dimala C A, Bechem N N, et al. Concurrent hyperthyroidism and papillary thyroid cancer: a fortuitous and ambiguous case report from a resource-poor setting[J]. BMC Research Notes, 2016, 9(1): 369
- [30] V. G. Likhvantseva, E. A. Rudenko, S. G. Kapkova, et al. Explore the Possibility of Early Clinical Diagnosis of Endocrine Ophthalmopathy Based on Eye Symptoms of Hyperthyroidism [J]. Ophthalmology in Russia, 2016, 13(4): 252-259

(上接第 3948 页)

- [19] Prabhakar H, Singh GP, Anand V, et al. Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy [J]. Cochrane Database Syst Rev, 2014, 16(7): CD010026
- [20] Mangat HS, Chiu YL, Gerber LM, et al. Hypertonic saline reduces cumulative and daily intracranial pressure burdens after severe traumatic brain injury[J]. J Neurosurg, 2015, 122(1): 202-210
- [21] Burgess S, Abu-Laban RB, Slavik RS, et al. A Systematic Review of Randomized Controlled Trials Comparing Hypertonic Sodium Solutions and Mannitol for Traumatic Brain Injury: Implications for Emergency Department Management[J]. Ann Pharmacother, 2016, 50(4): 291-300
- [22] Sokhal N, Rath GP, Chaturvedi A, et al. Comparison of 20% mannitol and 3% hypertonic saline on intracranial pressure and systemic hemodynamics[J]. J Clin Neurosci, 2017, 42: 148-154
- [23] Dostalova V, Astapenko D, Dostalova V Jr, et al. The Effect of Fluid Loading and Hypertonic Saline Solution on Cortical Cerebral Microcirculation and Glycocalyx Integrity [J]. J Neurosurg Anesthesiol, 2018 Jul 13.[Epub ahead of print]
- [24] Gu J, Huang H, Huang Y, et al. Hypertonic saline or mannitol for treating elevated intracranial pressure in traumatic brain injury: a meta-analysis of randomized controlled trials [J]. Neurosurg Rev, 2018, Jun 15[Epub ahead of print]
- [25] Correia CJ, Armstrong R Jr, Carvalho PO, et al. Hypertonic Saline Solution Reduces Microcirculatory Dysfunction and Inflammation in a Rat Model of Brain Death[J]. Shock, 2018, 23[Epub ahead of print]