

¹³¹碘对Graves病合并甲状腺结节的疗效

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【摘要】目的:观察Graves病(GH)合并甲状腺结节患者¹³¹碘(¹³¹I)治疗后甲状腺结节的大小变化,以了解¹³¹I在治疗GH的同时对合并的甲状腺结节的疗效。**方法:**回顾性分析GH合并甲状腺结节患者行个体化¹³¹I治疗的106例病例资料,共发现193个结节,根据结节大小分为3组,A组:结节直径≤5 mm,B组:5 mm<结节≤10 mm,C组:结节>10 mm。分析3组病例行¹³¹I治疗前后结节大小的变化,了解¹³¹I治疗后不同结节大小的治疗效果,并采用多重线性回归方法分析与治疗效果相关的因素。**结果:**A组结节共59个,¹³¹I治疗甲亢痊愈后结节消失83.33%、结节变小7.41%、结节不变或增大9.26%,总有效率90.74%;B组结节共108个,¹³¹I治疗甲亢痊愈后结节消失61.82%、结节变小21.82%、结节不变或增大16.36%,总有效率为83.64%;C组结节共26个,¹³¹I治疗甲亢痊愈后结节消失31.58%、结节变小31.58%、结节不变或增大36.84%,总有效率为63.16%。3组结节治疗前后变化差异有统计学意义($P<0.05$)。甲状腺结节大小、年龄与治疗效果有相关性,而甲状腺质量、个体化服¹³¹I剂量、性别、总三碘甲状腺原氨酸、总甲状腺素、促甲状腺素、2 h吸碘率、24 h吸碘率等因素与治疗效果均无相关性。**结论:**¹³¹I治疗GH合并甲状腺良性小结节效果明显,尤以小于10 mm的小结节效果显著。

【关键词】Graves病;¹³¹碘;内放射治疗;甲状腺结节

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Therapeutic effect of ¹³¹iodine on Graves hyperthyroidism with thyroid nodules

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Abstract: Objective To observe the changes in the size of thyroid nodules after ¹³¹iodine (¹³¹I) therapy in patients with Graves hyperthyroidism (GH) and thyroid nodules for exploring the efficacy of ¹³¹I for thyroid nodules while treating GH. **Methods** A retrospective analysis was conducted on 106 patients with GH and thyroid nodules receiving individualized ¹³¹I therapy. A total of 193 nodules were identified and categorized into 3 groups according to their size (group A: nodule diameter ≤ 5 mm, group B: 5 mm < nodule diameter ≤ 10 mm, group C: nodule diameter > 10 mm). The changes in nodule size before and after ¹³¹I therapy were analyzed in the 3 groups to analyze the therapeutic effects of ¹³¹I on nodules of different sizes. Multiple linear regression analysis was used to identify factors related to therapeutic effects. **Results** In group A, there were 59 thyroid nodules, of which 83.33% disappeared after ¹³¹I therapy, 7.41% decreased in size, and 9.26% remained unchanged or enlarged, with an overall response rate of 90.74%. In group B, there were 108 thyroid nodules, with 61.82% disappearing after ¹³¹I therapy, 21.82% decreasing in size, and 16.36% remaining unchanged or enlarged, and the overall response rate was 83.64%. There were 26 nodules in group C, with 31.58% disappearing after ¹³¹I therapy, 31.58% decreasing in size, and 36.84% remaining unchanged or enlarged, and the overall response rate was 63.16%. The nodule size in the 3 groups changed differently ($P<0.05$). Nodule size and age were found to be correlated with therapeutic effect, while thyroid weight, individualized dose of ¹³¹I, gender, TT3, TT4, TSH, 2-h iodine uptake rate, and 24-h iodine uptake rate had no correlation with therapeutic effect. **Conclusion** ¹³¹I therapy is effective for GH and benign small nodules in the thyroid, especially for nodules smaller than 10 mm.

Keywords: Graves disease; ¹³¹iodine; inner radiation therapy; thyroid nodule

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前言

Graves病(GH)合并甲状腺多发结节较常见。甲状腺结节在甲状腺显像时分为:热结节、温结节和冷结节^[1],前两者良性结节多见,少部分冷结节为恶性病变。GH合并“热结节或温结节”其良性可能性大且可以摄取¹³¹I碘(¹³¹I),患者¹³¹I治疗GH同时对摄取¹³¹I的甲状腺结节亦有治疗作用^[2]。GH合并良性的“冷结节”患者其甲状腺结节不摄取¹³¹I,¹³¹I治疗是否对其有治疗效果,本研究纳入了这部分良性患者,旨在探讨¹³¹I对Graves甲亢合并甲状腺结节的疗效。

1 资料与方法

1.1 一般资料

回顾性分析2008年~2016年确诊为GH合并甲状腺结节门诊病历106例,共计甲状腺结节193个。年龄13~76岁,其中男30例,平均年龄(35.33±9.78)岁,女76例,平均年龄(39.89±13.55)岁。

1.2 纳入、排除标准和诊断标准

1.2.1 纳入标准 (1)GH合并甲状腺结节,GH已痊愈;(2)甲状腺超声检查提示无低回声或可疑恶低回声、微小钙化、边界模糊/微性分叶、纵横比>1的表现,TI-RADS分类≤3,同时该部位甲状腺显像示:甲状腺结节处血流灌注无异常及静态相结节摄取与周围组织相近(温结节)或不摄取(“冷结节”表现)。

1.2.2 排除标准 甲状腺结节质地硬、边界不清、活动性差、增长速度较快、超声甲状腺TI-RADS分类≥4,颈部可疑恶性转移灶等情况;甲状腺结节在甲状腺显像中表现为“热结节”。

1.2.3 GH的诊断标准^[3] 有高代谢征候群、突眼、甲状腺肿大等临床表现,总三碘甲状腺原氨酸(TT3)增高、总甲状腺素(TT4)增高、促甲状腺素(TSH)下降、¹³¹I摄取率增高且高峰前移、甲状腺超声示甲状腺血流分布“火海征”^[4];甲状腺动静态显像示甲状腺血流灌注增加及甲状腺摄碘率增高。

1.3 方法

¹³¹I治疗前后106例患者均进行甲状腺激素、甲状腺超声、甲状腺动静态显像及甲状腺吸¹³¹I率检查,以评价甲状腺功能、有无合并结节、结节大小及初步判定良恶性。患者治疗前停用ATD药物及无碘饮食2周以上。治疗前所有检查均在服药前1周内进行。¹³¹I治疗剂量:μCi=计划量(MBq或μCi/g)×甲状腺质量(g)/甲状腺24h摄碘率。空腹1次口服¹³¹I,根据甲状腺的大小、质地及结节情况适当增加或减少¹³¹I剂量。服药后随访6~12个月。根据甲状腺功能、肿大程度及临床表现对未痊愈患者进行重复治疗。根据甲状腺结

节大小将患者分为3组,A组:结节直径≤5 mm,B组:5 mm<结节≤10 mm,C组:结节>10 mm。治疗后甲状腺超声在临床评价甲亢痊愈后1周内完成。

GH¹³¹I疗效的判断标准^[5]。(1)缓解或临床痊愈:随访半年以上,GH症状和体征完全消失,血清TT4恢复正常;出现甲减症状和体征,血清TT4低于正常,TSH高于正常。(2)部分缓解:GH症状减轻,体征部分消失,血清TT4降低,但未恢复正常。(3)无效:症状和体征均无改善或反而加重,血清TT4无明显变化。

结节的疗效判定:治疗后甲状腺超声提示原结节消失,甲状腺显像放射性分布均匀,视为结节消除;甲状腺超声提示原结节较治疗前缩小,该部位甲状腺显像示“冷、温结节”,视为结节缩小;甲状腺超声提示原结节无变化或增大,该部位甲状腺显像示“冷、温结节”,视为无效。

1.4 显像设备和药物

SIEMENS ECAM双探头SPECT,矩阵128×128,低能平行孔准直器,能峰140 keV,^{99m}TcO₄和¹³¹I(碘化钠)来自广东希埃医药有限公司,放化纯度>95%。高频超声检查:仪器采用PHILIP iu22、GE VolusonE8及LOGIO F8高档彩色多普勒超声仪,探头频率8~12 MHz。

1.5 统计学处理

采用SPSS 19.0软件进行统计学分析,应用多样本等级资料秩和检验进行统计学处理,治疗效果影响因素采用多重线性回归分析, $P<0.05$ 为差异有统计学意义。

2 结果

106例GH合并甲状腺结节患者临床特征及分组情况见表1。106例患者共检出193个甲状腺结节,单发16.03%(17/106),多发83.96%(89/106)。A组结节共59个,¹³¹I治疗甲亢痊愈后结节消失83.33%、结节变小7.41%、结节不变或增大9.26%,总有效率90.74%;B组结节共108个,¹³¹I治疗甲亢痊愈后结节消失61.82%、结节变小21.82%、结节不变或增大16.36%,总有效率为83.64%;C组结节共26个,¹³¹I治疗甲亢痊愈后结节消失31.58%、变小31.58%、不变或增大36.84%,总有效率为63.16%。3组结节治疗前后变化有统计学差异($Z=73.014$, $P<0.001$)。各影响因素对甲状腺结节¹³¹I治疗效果相关性见表2。

3 讨论

近年来分化性甲状腺癌发病率有所增加,文献报道为2%~17%^[6]。据报道GH患者中可触及的甲状腺结节的恶性肿瘤率低至2.3%~45.8%,可见以良性

表1 106例GH合并甲状腺结节患者临床特征
Table 1 Clinical characteristics of 106 patients with Graves
hyperthyroidism and thyroid nodules

变量	A组	B组	C组
性别(男/女)	11/48	38/70	3/23
年龄/岁	36.33±9.66	38.57±12.22	42.65±16.01
结节/个	59	108	26
TT3/nmol·L ⁻¹	10.82±7.33	9.71±6.41	7.61±6.55
TT4/nmol·L ⁻¹	231.12±231.13	218.94±115.54	201.09±132.95
TSH/μIU·mL ⁻¹	0.017±0.026	0.021±0.042	0.271±0.810
2 h吸碘率/%	61.48±22.35	61.48±22.79	62.18±22.65
24 h吸碘率/%	89.42±14.62	88.34±12.31	88.60±14.10
甲状腺质量/g	41.59±11.35	46.42±19.13	44.63±15.60
¹³¹ I剂量/mCi	3.89±1.69	4.26±1.68	4.31±1.37

结节多见^[7-12]。良性结节如有明确的手术指征者及恶性结节合并GH应考虑手术治疗,如果患者不愿意手术治疗或不适合手术治疗可选择¹³¹I治疗或抗甲状腺药物(ATD)。ATD对GH有效率不高,对结节无治疗作用。国内有报道¹³¹I治疗GH伴结节性甲状腺肿是较好的治疗方法^[13]。¹³¹I治疗GH是国际公认的有效方法,GH初次及2次治疗总有效率为95%^[14]。本研究中GH合并结节患者GH症状经1次或2次重复治疗后消失及各项检查指标正常,疗效与服¹³¹I后的时间存在线性趋势,随着观测时间的延长,部分缓解率逐渐降低,完全缓解率逐渐上升,与文献报道无合并甲状腺结节患者疗效相近^[15-16]。

¹³¹I治疗对GH合并的甲状腺结节的疗效与结节的大小相关,结节大小不同3组间疗效不同。本研究

表2 甲状腺结节¹³¹I治疗疗效影响因素的多重线性回归分析
Table 2 Multiple linear regression analysis for identifying factors affecting the efficacy of ¹³¹I therapy for thyroid nodules

因变量	自变量	非标准化系数		t值	P值	B的95%可变区间	
		B	标准误			下限	上限
疗效	(常量)	3.128	1.060	2.952	0.004	1.037	5.219
	甲状腺质量	0.001	0.020	0.056	0.955	-0.038	0.040
	¹³¹ I剂量	-0.033	0.214	-0.152	0.879	-0.455	0.389
	年龄	-0.011	0.004	-2.526	0.012	-0.019	-0.002
	性别	-0.032	0.119	-0.269	0.788	-0.268	0.203
	是否多发	0.012	0.138	0.900	0.369	-0.148	0.396
	TT3	-0.019	0.009	-2.033	0.074	-0.037	-0.001
	TT4	-0.001	0.001	-1.568	0.119	-0.002	0.000
	TSH	-0.329	0.181	-1.814	0.072	-0.687	0.030
	2 h吸碘率	0.002	0.003	0.777	0.439	-0.004	0.009
	24 h吸碘率	0.003	0.005	0.610	0.543	-0.007	0.013

中3组结节疗效不同的主要原因考虑为所选病例中部分结节为“冷结节”,其本身对¹³¹I不摄取,依赖结节周围的甲状腺组织摄取¹³¹I,对结节产生的电离辐射效应来达到治疗作用,而¹³¹I发射的β射线的最大射程约为3.63 mm,平均0.48 mm,当结节较大时,周围甲状腺组织照射结节中心的距离增加,β射线射程有限,故较大结节可能与瘤体内血供不佳、对¹³¹I不摄取及β射线射程较短、辐射生物学作用弱有关,导致¹³¹I治疗效果不佳。

¹³¹I治疗影响甲状腺结节的疗效相关因素与甲亢治疗影响因素相近,如年龄,年龄大者结节的治疗效果不佳,可能与不同年龄对射线的敏感性不同相关^[17]。本研究将甲状腺质量与结节的疗效进行评

价,结果表明不同分组甲状腺质量对结节治疗效果差异无统计学意义,这主要可能是GH合并结节患者每克甲状腺所给予的¹³¹I剂量相对稳定,故单位质量甲状腺组织对结节所产生的辐射剂量相近有关。另外,性别、TT3、TT4、TSH、2 h吸碘率、24 h吸碘率及结节单发与多发均与甲状腺结节的¹³¹I治疗效果无相关性。

总之,GH合并甲状腺结节患者,在治疗甲亢的同时,也会对其合并甲状腺结节具有治疗效果,尤其以小于10 mm的结节治疗效果最好,患者在治愈GH同时结节也缩小甚至消失,避免了手术治疗。同时本研究也发现A组及B组治疗前后大小变化不明显的结节,在治疗后复查B超,显示部分结节的回声发

生改变,向好的方向发展。对于甲状腺合并多发大小不等结节,其中个别大于10 mm,在排除恶性病变的情况下仍可选择¹³¹I治疗,因为¹³¹I对小结节有治疗作用,如需手术治疗时可针对大结节进行处理,可以降低结节的复发率,并且¹³¹I不会增加良性结节恶变的几率;但对于GH合并结节较大(大于25 mm),尤其可疑恶性病变及胸骨后的结节情况,手术治疗仍是首选。

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