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甲状腺根治术后不同剂量 ^{131}I 清甲治疗对分化型甲状腺癌患者唾液流率、骨代谢和生活质量的影响 *

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摘要 目的：探讨甲状腺根治术后不同剂量^{131}I 清甲治疗对分化型甲状腺癌患者唾液流率、骨代谢和生活质量的影响。**方法：**选取 2018 年 1 月 ~2020 年 1 月期间我院诊治的分化型甲状腺癌患者 141 例，根据随机数字表法分为低剂量组 [治疗剂量为 1.1～3.7GBq(30～100 mci)]、中剂量组[治疗剂量为 3.7～5.5GBq(100～150 mci)]、高剂量组[治疗剂量为 5.5～7.4GBq(150 ～ 200 mci)]，各 47 例。对比三组患者唾液流率、骨代谢、生活质量、腮腺和颌下腺的摄取参数(UR)和排泌参数(ER)。**结果：**高剂量组、中剂量组腮腺、颌下腺的左侧 UR、右侧 UR、左侧 ER、右侧 ER 均低于低剂量组，且高剂量组低于中剂量组(P<0.05)。三组治疗后静态唾液流率(UWSFR)、动态唾液流率(SWSFR)均较治疗前下降(P<0.05)，高剂量组、中剂量组治疗后 UWSFR、SWSFR 低于低剂量组，且高剂量组低于中剂量组(P<0.05)。低剂量组、中剂量组的优良率高于高剂量组，且中剂量组高于低剂量组(P<0.05)。三组治疗前后、组间总Ⅰ型胶原氨基端前肽 (PINP)、β- 胶原降解产物(β-CTX)、骨密度(BMD)对比，差异均无统计学意义(P>0.05)。**结论：**不同剂量^{131}I 清甲治疗对分化型甲状腺癌患者的骨代谢无明显影响，但不同剂量 ^{131}I 清甲治疗均会影响患者唾液腺功能及生活质量，其中高剂量^{131}I 清甲对患者的影响最为显著。

关键词：甲状腺根治术；不同剂量；^{131}I 清甲治疗；分化型甲状腺癌；唾液流率；骨代谢；生活质量
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Effects of Different Doses of ^{131}I Nail Removal Therapy on Salivary Flow Rate, Bone Metabolism and Quality of Life in Patients with Differentiated Thyroid Cancer after Radical Thyroidectomy*

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ABSTRACT Objective: To investigate the effect of different doses of ^{131}I nail removal therapy on salivary flow rate, bone metabolism and quality of life in patients with differentiated thyroid cancer after radical thyroidectomy. **Methods:** 141 patients with differentiated thyroid cancer from January 2018 to January 2020 in our hospital were selected, and were randomly divided into low-dose group [therapeutic dose was 1.1~3.7 GBq(30 ~ 100 MCI)], medium dose group [therapeutic dose was 3.7～5.5 GBq(100～150 mci)] and high-dose group [therapeutic dose was 5.5~7.4GBq(150～200mci)], 47 cases in each group. Salivary flow rate, bone metabolism, quality of life, uptake fraction (UR) and excretion fraction (ER) of parotid and submandibular glands were compared among the three groups. **Results:** The left UR, right UR, left ER and right ER of parotid gland and submandibular gland in high-dose group and middle dose group were lower than those in low-dose group, and those in high-dose group were lower than those in medium dose group (P<0.05). After treatment, the static salivary flow rate (UWSFR) and dynamic salivary flow rate (SWSFR) of the two groups decreased compared with those before treatment (P<0.05). After treatment, the UWSFR and SWSFR of the high-dose group and the medium dose group were lower than those of the low-dose group, and the high-dose group was lower than the medium dose group (P<0.05). The excellent and good rate of low-dose group and medium dose group were higher than that of high-dose group, and that of medium dose group was higher than that of low-dose group (P<0.05). Between three groups before and after treatment, the total collagen type Ⅰ amino terminal propeptide (PINP), β-collagen degradation products (β-CTX), bone mineral density (BMD) in contrast, there were no statistically significant differences (P>0.05). **Conclusion:** Different doses of ^{131}I nail removal therapy has no significant effect on bone metabolism in patients with differentiated thyroid cancer, but different doses of ^{131}I nail removal therapy all have an effect on salivary gland function and quality of life in pa-

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tients, among which high-dose of ^{131}I nail removal therapy has the most significant effect

Key words: Radical thyroidectomy; Different doses; ^{131}I nail removal therapy; Differentiated thyroid cancer; Salivary flow rate; Bone metabolism; Quality of life

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前言

甲状腺癌是指起源于甲状腺滤泡上皮的恶性肿瘤,其中约有 90%为分化型甲状腺癌[1]。随着环境污染的加重,人们生活方式的改变,该病的发病率呈逐年递增趋势,且趋于年轻化[2,3]。多数分化型甲状腺癌患者预后良好,可长期生存,手术是治疗该病最主要的方法,甲状腺根治术可有效切除病灶,阻止疾病进展[4-6]。但近来临床实践证实[7],甲状腺根治术可诱发甲状腺转移灶摄取放射性碘,手术预后降低。^{131}I 清甲治疗可将残留的甲状腺癌细胞和转移灶有效清除,发挥延长生存期、降低复发率的作用[8,9]。现临床有关 ^{131}I 清甲治疗甲状腺根治术后分化型甲状腺癌患者的具体剂量仍存在一定的争议。鉴于此,本研究通过探讨不同剂量 ^{131}I 清甲治疗对甲状腺根治术后分化型甲状腺癌患者唾液流率、骨代谢和生活质量的影响,以期为其临床治疗提供数据参考。

1 资料与方法

1.1 一般资料

选取 2018 年 1 月 ~2020 年 1 月期间我院诊治的分化型甲状腺癌患者 141 例,纳入标准:(1)均经病理检查确诊;(2)均符合甲状腺根治术手术指征,且均成功完成手术者;(3)患者知情本研究并签署了同意书;(4) 手术均由同一组医师完成;(5)对 ^{131}I 清甲治疗耐受者。排除标准:(1)合并有其他影响唾液腺疾病如结缔组织病的患者;(2)既往有头颈部放射治疗史的患者;(3)出现严重器官功能衰竭的患者;(4)伴有严重器质性功能障碍的患者;(5)中途退出治疗者。 根据随机数字表法将其分为低剂量组 47 例、中剂量组 47 例、高剂量组 47 例。其中低剂量组男 17 例,女 30 例,平均年龄(38.64± 4.65)岁;临床分期:Ⅱ期 26 例,Ⅲ期 21 例;甲状腺根治术方式:全切 25 例,部分切除 22 例。中剂量组男 19 例,女 28 例,平均年龄(38.92± 5.13)岁;临床分期:Ⅱ期 28 例,Ⅲ期 19 例;甲状腺根治术方式:全切 26 例, 部分切除 21 例。高剂量组男 18 例, 女 29 例, 平均年龄(38.81± 4.93)岁;临床分期:Ⅱ期 29 例,Ⅲ期 18 例;甲状腺根治术方式:全切 24 例,部分切除 23 例。三组患者一般资料对比未见统计学差异(P>0.05)。

1.2 方法

所有患者常规行甲状腺癌根治术,术后给予 ^{131}I 清甲治疗,低剂量组治疗剂量为 1.1～3.7 GBq(30～100 mci),中剂量组治疗剂量为 3.7～5.5GBq (100～150 mci), 高剂量组治疗剂量为 5.5～7.4GBq (150 ～ 200 mci),^{131}I 清甲治疗前忌食富含碘的食物及相关药物,^{131}I 清甲治疗后均给予维生素 C 咀嚼片,嘱患者多饮水。

1.3 观察指标

(1) 使用美国 phillips BrightView XCT 双探头路单光子发射计算机体层摄影术计算患者腮腺和颌下腺治疗后的摄取参数(UR)和排泌参数(ER)。(2)记录三组治疗前后的静态唾液流率(UWSFR)、动态唾液流率(SWSFR)。其中 UWSFR:要求患者检查前 8h 不刷牙漱口,空腹,坐位、头稍前倾,采集患者唾液,嘱被检者勿咽下、吸吮唾液,使唾液沿下唇逐渐滴入量筒内,持续 10 min。SWSFR:UWSFR 测量完后将 0.1 mol/L 的枸橼酸滴于舌背前部 6 min,随后采集方法同 UWSFR。(3)抽取三组患者治疗前后静脉血 2 mL,采用 Roche Cobas8000 型全自动电化学发光免疫分析仪检测总Ⅰ型胶原氨基端前肽 (PINP)和 β- 胶原降解产物(β-CTX)。采用美国 GE DPX-NT 第 4 代笔尖式线束双能 X 线全身骨密度仪检测三组患者治疗前后的骨密度(BMD)。(4)采用欧洲癌症治疗研究组颁布的肿瘤生存质量调查表(QLQ)[10]评价患者生活质量,QLQ 包括认知功能、角色功能、身体功能、总体健康状况、社会功能,分数越高生活质量越好, 本次研究采用百分制,＜60 分为差。60～79 分为中,80～99 分为良,100 分为优。优良率 = 优率 + 良率。

1.4 统计学方法

数据采用 SPSS25.0 软件进行分析。计量资料用 ($\bar{x}\pm s$)表示,多组数据比较采用单因素方差分析 +LSD-t 检验。计数资料用率表示,采用 x^2 检验。α=0.05 为检验水准。

2 结果

2.1 三组腮腺和颌下腺治疗前后的 UR、ER 比较

高剂量组、中剂量组腮腺、颌下腺的左侧 UR、右侧 UR、左侧 ER、右侧 ER 均低于低剂量组, 且高剂量组低于中剂量组(P<0.05),见表 1。

2.2 三组唾液流率比较

三组治疗前 UWSFR、SWSFR 对比, 差异无统计学意义(P>0.05),三组治疗后 UWSFR、SWSFR 均较治疗前下降(P<0.05),高剂量组、中剂量组治疗后 UWSFR、SWSFR 低于低剂量组,且高剂量组低于中剂量组(P<0.05),见表 2。

2.3 三组生活质量比较

低剂量组、中剂量组的优良率高于高剂量组,且中剂量组高于低剂量组(P<0.05),见表 3。

2.4 三组骨代谢指标比较

三组治疗前后、组间 PINP、β-CTX、BMD 对比,差异均无统计学意义(P>0.05),见表 4。

3 讨论

^{131}I 是碘元素的放射性同位素,在临床医学上,^{131}I 可以用于甲状腺功能的检查以及甲状腺疾病的治疗[11,12]。^{131}I 清甲辅助治疗的主要作用机制在于利用分化型甲状腺癌细胞或者其转移的病变组织具有极强的摄碘能力特性,进入人体后浓聚于甲状腺组织内,依赖靶向作用 ^{131}I 衰变过程中发射出的 β 射线,杀死

周边组织中的癌细胞及正常细胞，最终抑制其移及复发[13-15]。但在 ^{131}I 清甲治疗时，^{131}I 还可被正常的唾液腺组织所摄取，唾液腺能够通过钠 / 碘同向转运因子从血液中自主获取 ^{131}I，其碘浓度可以高达血浆碘浓度的 30 ～40 倍，^{131}I 衰变过程中发射出的 β 射线可直接损伤唾液腺腺泡和导管，故而不少患者在 ^{131}I 治疗后的几天内可出现颈部肿胀、疼痛、喉部疼痛及吞咽困难等症状，可对患者的生活质量造成严重影响[16-18]。此外，唾液腺的损伤程度还与 ^{131}I 治疗剂量和对放射线灵敏度息息相关[19,20]。目前在临床上对于 ^{131}I 治疗剂量无统一标准，临床疗效各异。

表 1 三组腮腺和颌下腺治疗前后的 UR、ER 比较（$\bar{x}\pm s$，%）

Table 1 Comparison of UR and ER between parotid gland and submandibular gland before and after treatment among the three groups（$\bar{x}\pm s$，%）

Groups	Parotid gland				Submandibular gland			
	Left UR	Right UR	Left ER	Right ER	Left UR	Right UR	Left ER	Right ER
Low-dose group（n=47）	0.32± 0.06	0.34± 0.07	85.39± 5.26	86.08± 6.29	0.21± 0.04	0.19± 0.03	92.20± 6.35	85.33± 6.27
Medium dose group（n=47）	0.24± 0.07[a]	0.26± 0.05[a]	67.29± 6.37[a]	69.12± 5.28[a]	0.15± 0.05[a]	0.13± 0.04[a]	81.68± 7.29[a]	73.75± 6.34[a]
High-dose group（n=47）	0.13± 0.04[ab]	0.14± 0.06[ab]	43.41± 5.49[ab]	45.79± 4.32[ab]	0.09± 0.03[ab]	0.08± 0.02[ab]	69.46± 6.55[ab]	64.07± 5.25[ab]
F	15.628	31.468	23.518	18.721	23.416	20.528	19.684	26.841
P	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000

Note: compared with the low-dose group, [a]*P*<0.05; compared with the medium dose group, [b]*P*<0.05.

表 2 三组唾液流率比较（$\bar{x}\pm s$，mL/min）

Table 2 Comparison of salivary flow rates among the three groups（$\bar{x}\pm s$, mL/min）

Groups	UWSFR		SWSFR	
	Before treatment	After treatment	Before treatment	After treatment
Low-dose group（n=47）	0.31± 0.08	0.24± 0.03*	2.29± 0.06	1.89± 0.08*
Medium dose group（n=47）	0.32± 0.09	0.17± 0.05*[a]	2.31± 0.08	1.68± 0.09*[a]
High-dose group（n=47）	0.30± 0.11	0.11± 0.04*[ab]	2.33± 0.09	1.35± 0.07*[ab]
F	0.864	16.841	0.531	20.512
P	0.524	0.000	0.406	0.000

Note: compared with before treatment, **P*<0.05; compared with the low-dose group, [a]*P*<0.05; compared with the medium dose group, [b]*P*<0.05.

表 3 三组生活质量比较 例（%）

Table 3 Comparison of quality of life among the three groups [n(%)]

Groups	Excellent	Good	Middle	Bad	Excellent and good rate
Low-dose group（n=47）	9（19.15）	19（40.43）	11（23.40）	8（17.02）	28（59.57）
Medium dose group（n=47）	12（25.53）	25（53.19）	7（14.89）	3（6.38）	37（78.72）[a]
High-dose group（n=47）	7（14.89）	13（27.66）	15（31.91）	12（25.53）	20（42.55）[ab]
F					12.863
P					0.016

Note: compared with the low-dose group, [a]*P*<0.05; compared with the medium dose group, [b]*P*<0.05.

表 4 三组骨代谢指标比较（$\bar{x}\pm s$）

Table 4 Comparison of bone metabolism indexes among the three groups（$\bar{x}\pm s$）

Groups	PINP（ng/mL）		β-CTX（ng/mL）		BMD（g/cm^2）	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Low-dose group（n=47）	42.77± 3.75	42.83± 3.97	0.38± 0.07	0.39± 0.06	0.87± 0.07	0.89± 0.06
Medium dose group（n=47）	42.49± 4.64	42.95± 4.83	0.37± 0.04	0.40± 0.08	0.85± 0.06	0.88± 0.08
High-dose group（n=47）	42.97± 5.56	43.24± 4.34	0.40± 0.06	0.39± 0.09	0.84± 0.08	0.87± 0.08
F	1.624	0.938	0.834	0.624	0.728	0.925
P	0.196	0.461	0.357	0.639	0.506	0.431

唾液腺主要由腮腺、舌下腺、颌下腺和小唾液腺组成，其中，65%唾液由颌下腺分泌，约 30%的唾液由腮腺分泌，其他唾液腺分泌 5%[21,22]。而唾液的分泌包括静态和动态两种形式，其中动态分泌可反映唾液腺的贮备和应激功能，静态分泌可反映唾液腺基础状况下的分泌情况[23,24]。唾液流率则可有效反映唾液腺分泌功能，唾液腺分泌功能减弱，唾液流率明显偏低[25]。^{131}I 治疗过程中对唾液腺的损伤最直接的表现为口干症，口干症可导致患者唾液分泌量减少。本研究结果显示，^{131}I 治疗过程中可对唾液腺功能产生不同程度地影响，其中以低剂量影响最小，中剂量、高剂量紧随其后。当 ^{131}I 在唾液中浓度超过血液浓度 ≥ 30 倍即可引起唾液腺导管上皮细胞功能下降，导致细胞凋亡，损伤唾液腺的排泌、摄取功能[26]。同时，研究结果还显示，中剂量的患者其生活质量相对优于低剂量和高剂量患者，可能是因为 ^{131}I 的剂量越大，其抗癌能力越强，可有效阻止疾病进展，提高患者生活能力，但过高的 ^{131}I 剂量又伴随着更大的唾液腺组织损伤，故而高剂量患者的生活质量反而下降[27,28]。由于分化型甲状腺癌患者多发于中老年女性群体，而中老年女性群体中骨质疏松和骨折的发病率也居高不下。β-CTX 能够反映破骨细胞骨吸收的程度，与骨破坏相关；PINP 能反映骨基质Ⅰ型胶原地合成转化，受外界影响较小[29]。既往有研究结果表明[30]，绝经后女性甲状腺癌患者 ^{131}I 治疗后引起甲状腺激素抑制进而引起骨密度下降。本研究中两组治疗前后、组间 PINP、β-CTX、BMD 对比，差异均无统计学意义，与上述研究结果存在一定的差异。分析原因可能是本研究病例未局限在绝经后女性患者，有关 ^{131}I 治疗对骨代谢的影响仍有待进一步研究。

综上所述，不同剂量 ^{131}I 清甲治疗对分化型甲状腺癌患者的骨代谢无明显影响，但 ^{131}I 清甲治疗均会影响患者唾液流率及生活质量，其中剂量越大，唾液流率降低的程度就越大，唾液腺损伤程度亦越大。临床可视患者具体情况选择低剂量或中剂量治疗。

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