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纳米碳标记技术用于甲状腺全切除术的效果及对患者血清 PTH、 Ca^{2+} 水平的影响 *

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摘要 目的: 探讨纳米碳标记技术用于甲状腺全切除术的效果及对患者血清甲状旁腺素 (parathyroid hormone, PTH)、钙离子 (calcium ion, Ca^{2+}) 水平的影响。**方法:** 回顾性分析 2017 年 1 月至 2018 年 12 月于本院接受甲状腺全切除术治疗的 120 例患者的临床资料,根据术中处理方式不同将其分为观察组和对照组,每组 60 例。两组患者均实施甲状腺全切除术+中央区淋巴结清扫手术,观察组术中使用的纳米碳混悬注射液,对照组不使用。比较两组的手术情况、治疗前后血清 PTH、 Ca^{2+} 水平的变化及术后并发症的发生情况。**结果:** 两组术中出血量、术后引流流量、甲状旁腺误切率比较差异无统计学意义 ($P>0.05$),观察组手术时间、住院时间比对照组明显缩短 ($P<0.05$); 两组手术后 1d、3d、7d 时血清 PTH、 Ca^{2+} 均明显低于治疗前,且观察组手术后 1d、3d、7d 时血清 PTH、 Ca^{2+} 均明显高于对照组 ($P<0.05$)。观察组甲状旁腺、喉返神经功能暂时性损伤及低钙血症的发生率均明显低于对照组 ($P<0.05$),两组甲状旁腺、低钙血症、喉返神经功能永久性损伤比较差异无统计学意义 ($P>0.05$)。**结论:** 纳米碳标记技术在甲状腺全切除术中效果显著,可有效降低甲状旁腺误切率,降低甲状旁腺、喉返神经功能暂时性损伤、低钙血症的发生率。

关键词: 纳米碳标记技术; 甲状腺全切除术; 甲状旁腺; 钙离子; 分化型甲状腺癌

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Efficacy of Nano-carbon Labeling Technique in the Total Thyroidectomy and Its Effect on the serum PTH and Ca^{2+} Levels*

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ABSTRACT Objective: To study the efficacy of nano-carbon labeling technique in the treatment of total thyroidectomy and its effect on the serum parathyroid hormone (PTH) and calcium ion (Ca^{2+}) levels. **Methods:** A retrospective analysis of 120 cases of total thyroidectomy in our hospital from January 2017 to December 2018 were divided into the observation group and the control group according to different intraoperative treatment methods, with 60 cases in each group. They were treated with total thyroidectomy and central lymph node dissection were performed, the observation group was treated with nano-carbon suspension injection. The operation conditions, changes of serum PTH, Ca^{2+} before and after treatment and incidence of complications were compared between the two groups. **Results:** There was no significant difference in the intraoperative bleeding volume, postoperative drainage volume and parathyroidectomy rate between the two groups ($P>0.05$); the operation time and hospitalization time in the observation group were significantly shorter than those in the control group ($P<0.05$); at postoperative 1, 3 and 7 days, the serum PTH and Ca^{2+} in the two groups were significantly lower than those before treatment, and the serum PTH and Ca^{2+} in the observation group were significantly higher than those of the control group at postoperative 1, 3 and 7 days ($P<0.05$); the incidence of parathyroid, recurrent laryngeal nerve function temporary injury and hypocalcemia in the observation group were significantly lower than those in the control group ($P<0.05$); there was no significant difference in the incidence of parathyroid injury, hypocalcemia and recurrent laryngeal nerve injury between the two groups ($P>0.05$). **Conclusion:** Nano-carbon labeling technique is well for total thyroidectomy, which can effectively reduce the misresection rate of thyroid gland, and reduce the incidence of parathyroid, recurrent laryngeal nerve function temporary injury and hypocalcemia.

Key words: Nano-carbon labeling technology; Total thyroidectomy; Parathyroid gland; Calcium ion; Differentiated thyroid cancer

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前言

甲状腺癌是临床上最为常见的甲状腺恶性肿瘤,在全身恶

性肿瘤中发病率约在 1%,女性发病率高于男性。根据组织学类型不同,甲状腺癌可分为分化型、未分化型甲状腺癌^[1,2]。临床治疗分化型甲状腺癌患者的治疗中,建议采取甲状腺全切除术或近

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全切术,并积极清除病灶和周围淋巴结转移^[3,4]。但由于甲状旁腺特殊的解剖结构位置,术后极易发生甲状旁腺功能衰退、低钙血症、喉返神经损伤等并发症,降低生活质量^[5,6]。

纳米碳标记技术是一种性能优秀的淋巴示踪剂,具有染色速度快、黑染绿高、清晰示踪、不容易外渗等优点,可将转移的淋巴结准确定位,近年来在胃癌、直肠癌等恶性肿瘤根治术中得到普及应用,并取得较好成效^[7,8]。本研究主要探讨了纳米碳标记技术在甲状腺全切术中的应用效果,并观察其对术后血清甲状旁腺素(parathyroid hormone, PTH)、钙离子(calcium ion, Ca^{2+})水平的影响,现报道如下。

1 资料与方法

1.1 一般资料

表 1 两组一般资料的比较($\bar{x} \pm s, n(\%)$)

Table 1 Comparison of the general information between two groups($\bar{x} \pm s, n(\%)$)

Item	Observation group(n=60)	Control group(n=60)
Sex(M/F)	19/41	16/44
Age(years)	48.96 $\pm$ 8.41	49.34 $\pm$ 8.10
BMI(kg/m ²)	22.21 $\pm$ 1.86	22.07 $\pm$ 2.03
Course of disease(years)	5.86 $\pm$ 1.92	5.79 $\pm$ 1.99
Maximum tumor diameter(cm)	1.78 $\pm$ 0.39	1.83 $\pm$ 0.31
Number of tumors	Single	45(75.00)
	Multiple	15(25.00)
Pathological types	Papillary thyroid cancer	44(73.33)
	Follicular thyroid cancer	16(26.67)

1.2 治疗方法

两组患者均实施甲状腺全切术+中央区淋巴结清扫手术,手术方式如下:①采取气管插管全身麻醉,头部后仰、颈过伸体位,于胸骨上切迹的上方,沿着皮纹方向作 Kocher 切口,并将皮肤逐层切开;②钝性分离真假被膜,显露双侧腺叶并游离,完成中央区淋巴结清扫,将舌骨下缘和胸骨上窝作为上下便捷,将气管内侧和颈动脉鞘作为内外接线,全面清扫器官周围、甲状腺旁、喉返神经节等周围淋巴结;③术后常规放置平压引流管,并预防性给予甲状腺片、钙剂等补充,持续用药 1~3d,若术后 1d 发生口周麻木、四肢麻木等低钙症状的患者则增加静脉补钙剂量。

观察组在游离腺叶后,选择甲状腺中上、中下的 1/3 处的两个位置,使用皮试针抽取 0.2 mL 纳米碳混悬注射液(规格 1 mL:50 mg,厂家:重庆莱美药业股份有限公司,国药准字 H20041829),分别由斜向刺入上述两个位置的甲状腺体,并各自注射 0.1 mL 纳米碳混悬注射液,注射时需放置药物外溢或注射进甲状腺腺内血管,待甲状腺和淋巴结染黑后再继续实施手术。对照组正常进行手术治疗,不给予纳米碳混悬注射液使用。

1.3 观察指标

1.3.1 手术情况 包括手术时间、术中出血量、术后引流量、住

院时间及甲状旁腺误切率。

1.3.2 血清 PTH、 Ca^{2+} 于术前、术后 1d、3d、7d 时,分别两组采集 3 mL 静脉血,使用 3500 r/min 的速度离心 15 min,收集上层清液,使用罗氏公司生产全自动电化学发光免疫法分析仪 E170 型检测血清 PTH,并使用美国贝克曼库尔特公司生产的全自动生化分析仪 UniCel DxC 800 Synchron 型检测血清 Ca^{2+} 。

1.3.3 并发症 对所有患者随访 6 个月,记录术后甲状旁腺损伤、低钙血症、喉返神经功能损伤发生率,甲状旁腺损伤判定标准:血清 PTH 低于 15~65 mg/mL;低钙血症判定标准:血清 Ca^{2+} 低于 2.1~2.9 mmol/L,并发生口周麻木、四肢麻木等症状,部分合并手足抽搐;喉返神经功能损伤判定标准:出现声音嘶哑症状,通过喉镜检查显示声带活动功能遭受到限制;其中暂时性损伤为经对症治疗 1~6 个月内恢复正常,永久性损伤为经过对症治疗 6 个月后仍未得到回复,需给予持续性治疗。

1.4 统计学分析

以 spss18.0 软件包处理实验数据,计量资料用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,组间比较采用 t 检验,计数资料组间比较采用 χ^2 检验,以 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组手术情况的比较

两组术中出血量、术后引流量、甲状旁腺误切率比较差异较对照组显著缩短($P<0.05$),见表2。
均无统计学意义($P>0.05$),观察组手术时间、住院时间明显

表2 两组手术情况的比较($\bar{x}\pm s, n(\%)$)Table 2 Comparison of the surgical condition between two groups($\bar{x}\pm s, n(\%)$)

Groups	Operation time(min)	Intraoperative bleeding volume(mL)	Postoperative drainage (mL)	Hospitalization time(d)	Misresection rate of thyroid gland[n(%)]
Observation group (n=60)	115.74 $\pm$ 17.94*	25.44 $\pm$ 4.05	29.75 $\pm$ 3.04	5.47 $\pm$ 1.32 *	1(1.67)
Control group (n=60)	146.08 $\pm$ 21.32	25.70 $\pm$ 3.92	30.06 $\pm$ 2.89	6.06 $\pm$ 1.64	5(8.33)

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

2.2 两组手术前后血清 PTH、Ca²⁺ 比较

两组手术前血清 PTH、Ca²⁺ 比较差异无统计学意义 ($P>0.05$)。两组手术后 1d、3d、7d 时,血清 PTH、Ca²⁺ 水平均明显低

于治疗前($P<0.05$),观察组手术后 1d、3d、7d 时血清 PTH、Ca²⁺ 均明显高于对照组($P<0.05$),见表3。

表3 两组手术前后血清 PTH、Ca²⁺ 水平的比较($\bar{x}\pm s$)Table 3 Comparison of the PTH and Ca²⁺ before and after treatment between two groups($\bar{x}\pm s$)

Groups	Time	PTH(mg/ml)	Ca ²⁺ (mmol/L)
Observation group(n=60)	Preoperative	52.48 $\pm$ 6.11	2.52 $\pm$ 0.19
	Postoperative 1d	30.03 $\pm$ 4.54*	2.34 $\pm$ 0.16*
	Postoperative 3d	25.60 $\pm$ 3.42*	2.29 $\pm$ 0.18*
	Postoperative 7d	35.04 $\pm$ 4.19*	2.32 $\pm$ 0.19*
Control group(n=60)	Preoperative	52.73 $\pm$ 5.73	2.50 $\pm$ 0.20
	Postoperative 1d	22.73 $\pm$ 3.71**	2.25 $\pm$ 0.18**
	Postoperative 3d	17.19 $\pm$ 3.02**	2.18 $\pm$ 0.17**
	Postoperative 7d	21.92 $\pm$ 3.19**	2.20 $\pm$ 0.18**

Vs the preoperative, * $P<0.05$; vs the control group, ** $P<0.05$.

2.3 两组甲状旁腺损伤、低钙血症、喉返神经功能损伤发生情况的比较

观察组甲状旁腺、低钙血症、喉返神经功能暂时性损伤均

明显低于对照组($P<0.05$),两组甲状旁腺、低钙血症、喉返神经功能永久性损伤的发生情况比较差异无统计学意义($P>0.05$),见表4。

表4 两组甲状旁腺损伤、低钙血症、喉返神经功能损伤发生率的比较[n(%)]

Table 4 Comparison of the incidence of parathyroid injury, hypocalcemia and recurrent laryngeal nerve injury between two groups[n(%)]

Groups	Parathyroid injury		Hypocalcemia		Recurrent laryngeal nerve function injury	
	Temporary	Permanent	Temporary	Permanent	Temporary	Permanent
Observation group (n=60)	1(1.67)*	0(0.00)	1(1.67)*	0(0.00)	2(3.33)*	0(0.00)
Control group (n=60)	8(13.33)	1(1.67)	7(11.67)	0(0.00)	9(15.00)	1(1.67)

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

3 讨论

甲状腺癌是临床上常见的恶性肿瘤,甲状腺全切除术是目前治疗分化型甲状腺癌的首选治疗方案,和次切除相比,在减少肿瘤局部复发率、远期转移率方面效果更佳显著,可更好的延长远期生存时间^[11,12]。但由于甲状旁腺解剖位置相对不孤独,尤

其是下甲状旁腺的解剖范围变化较大,在手术过程中容易造成损伤甚至误切,导致术后甲状旁腺损伤、低钙血症、喉返神经功能损伤等发生率的增加,不仅对术后生活质量产生影响,还易增加医患纠纷^[13,14]。

淋巴示踪剂主要是通过术中给予示踪剂,对目的淋巴结进行染色^[15,16]。目前,临床上常用的包括蓝染色剂和碳示踪剂,其

中蓝染色剂中安全性最高的蓝染色剂,但该方式也有持续时间短的缺点^[17,18]。纳米碳混悬液属于第三代示踪剂,平均直径为150 nm,注射后可直接进入处于血管内皮细胞间隙与毛细淋巴管内皮细胞间隙中,不会进入血管,具有高效的淋巴系统趋向性,可迅速进入淋巴管,并在巨噬细胞吞噬异物的作用下发挥作用,凝聚于淋巴结并进行黑染,为中央区淋巴结清扫提供准确的处理位置^[19,20]。目前已有较多报道显示和既往的淋巴示踪剂相比,纳米碳具有更快的染色速度和更高的黑染率,在乳腺癌、胃癌等较多恶性肿瘤中均体现出明显优势^[21,22]。并有研究证实,蓝染色剂相比,纳米碳持续的时间更长,淋巴示踪更加清晰,且不容易外渗,效果更好^[23,24]。此外,在经过纳米碳注射后,随着肿瘤和淋巴结的清扫,纳米碳的颗粒也会被随之清除,不会对患者预后产生不良影响,安全性好^[25,26]。

本研究结果显示使用纳米碳标记技术在手术时间更短,分析是由于在纳米碳标记技术的作用下,可更好的帮助医师找到甲状旁腺,辨别其和周围组织的关系,利于手术操作^[27,28]。此外,本研究中使用纳米碳标记技术的患者甲状旁腺误切率更低,术后血清PTH、Ca²⁺的下降程度更低,且通过随访显示,甲状旁腺损伤、低钙血症、喉返神经功能损伤暂时性损伤的发生率也更低;纳米碳示踪剂的平均直径约为150 nm,毛细血管内皮细胞的间隙约为30~50 nm,基底膜发育完整,纳米碳示踪剂注射液后很难进入毛细血管,而毛细淋巴管的内皮细胞间隙可达100~500 nm,基底膜发育不完整,可帮助纳米碳示踪剂的顺利通过^[29,30]。因此在甲状腺全切术中给予纳米碳示踪剂注射液后,不会通过血-甲状旁腺屏障,可在直视下可表现为甲状腺染色,但甲状旁腺不会被染色,产生视觉差异,可更准确的了解甲状旁腺的位置,降低甲状旁腺误切率,同时也可减少术中喉返神经所产生的不必要损伤,对术后甲状旁腺损伤、低钙血症、喉返神经功能损伤发生率也具有积极的预防作用。

综上所述,纳米碳标记技术在甲状腺全切术中效果显著,可有效降低甲状旁腺误切率,减轻甲状旁腺、喉返神经功能暂时性损伤、低钙血症的发生率。

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