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序贯式多模式镇痛在甲状腺癌功能性颈部淋巴结清扫术加速康复中的应用

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[摘要] **目的:** 探讨序贯式多模式镇痛对甲状腺癌功能性颈部淋巴结清扫术患者的镇痛效果、费用、恢复指标及并发症的影响。**方法:** 选取甲状腺癌颈部淋巴结清扫术患者88例, 采用随机数表将88例患者分为序贯式多模式镇痛组(D组)和传统单一模式镇痛组(T组), 每组各44例。D组镇痛方案为: 麻醉诱导时给予盐酸帕瑞昔布钠40 mg超前镇痛; 插管前在气管导管前端1/3处涂抹1%达克罗宁胶浆2 mL; 手术前在B超引导下双侧颈浅丛阻滞, 手术缝合切口前, 由外科医生直视下在患侧胸锁乳突肌中点后缘的外侧下方, 埋入22G静脉留置套管针于颈浅丛神经点处, 对侧在缝合切口后, B超引导下埋入套管针, 并追加一次局麻药, 术后6 h通过埋入颈浅丛的留置套管再追加一次局麻药并拔除套管针; 术后12 h开始口服氨酚羟考酮片。T组镇痛方案为: 无超前镇痛, 直接缝合切口, 术后使用静脉自控镇痛PCIA(地佐辛40 mg+舒芬太尼50 μg+托烷司琼4 mg)。分别于术后1、6、12、24 h采用静息与运动疼痛视觉模拟评分法(visual analogue scale, VAS)评价两组患者的镇痛效果; 测定两组患者术前、术后24 h的血清IL-6浓度; 记录术中瑞芬太尼总量、首次下床时间、首次进食流质时间、住院天数、镇痛费用、自评舒适度(Bruggermann Comfort Scale, BCS)及不良反应发生率等评价指标。**结果:** D组患者术后1、6、12、24 h的静息疼痛VAS评分与T组同时间点比较, 差异无统计学意义($P>0.05$), 但颈部活动疼痛VAS评分各时间点均显著低于传统单一模式镇痛组($P<0.05$); 术中瑞芬太尼用量、镇痛费用均显著少于T组(P 值均 <0.05); 术后首次下床时间、首次进食流质时间、自评舒适度均显著优于T组(P 值均 <0.05); 两组患者术后24 h的IL-6浓度均明显高于术前, 但D组的升高幅度低于T组; D组住院天数、术后不良反应发生率有低于T组的趋势, 但差异无统计学意义($P>0.05$)。**结论:** 对于甲状腺癌功能性颈部淋巴结清扫术患者, 相比传统单一的镇痛模式, ERAS理念下的序贯式多模式镇痛可明显提高患者的满意度, 降低患者术后动态疼痛评分和术后的镇痛费用, 促进了患者的早期康复。

[关键词] 序贯式多模式镇痛; 甲状腺癌; 功能性颈部淋巴结清扫术; 术后加速康复

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Application of sequential multimodal analgesia in the accelerated rehabilitation of functional neck lymphadenectomy for thyroid cancer

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Abstract **Objective:** To explore the effect of sequential multimodal analgesia on the analgesic effect, cost, recovery index and complications of functional neck lymphadenectomy for thyroid cancer. **Methods:** A total of 88 patients who underwent functional neck lymphadenectomy for thyroid cancer were included. Random number table was used to divide them into sequential multimodal analgesia group (D group) and traditional single-modal analgesia group (T group), with 44 patients in each group. In group D, 40 mg of parecoxib hydrochloride was given for preemptive analgesia during anesthesia induction; before intubation, 2 mL of 1% Dyclonine glue to 1/3 of the front end of the tracheal tube was applied; before operation, bilateral superficial cervical plexus block was conducted under the guidance of B-ultrasound. Before suturing the incision, the surgeon placed a 22G intravenous indwelling trocar at the nerve point of the superficial cervical plexus under direct vision below the posterior edge of the midpoint of the sternocleidomastoid muscle on the affected side. After the incision was sutured on the opposite side, a trocar was inserted under the guidance of ultrasound, and a local anesthetic was added. 6 hours after the operation, another local anesthetic was added through the indwelling cannula embedded in the superficial cervical plexus and the trocar was removed. Oral administration of paracetamol and oxycodone tablets was started 12 hours after the operation. In group T, there was no preemptive analgesia, the incision was sutured directly, and PCIA was used for intravenous analgesia (dazocine 40 mg + sufentanil 50 µg + tropisetron 4 mg) after surgery. At 1, 6, 12 and 24 hours after operation, visual analog scale VAS was used to evaluate the analgesic effect of the two groups; the serum IL-6 concentration before and 24 hours after operation was measured; the total amount of remifentanil during operation, the first time to get out of bed, the first time to eat fluid, the length of hospitalization, the cost of analgesia and the self-rated Bruggmann Comfort Scales (BCS) and incidence of adverse reactions were recorded. **Results:** There was no significant difference in the VAS scores of resting pain at 1, 6, 12, and 24 h after operation in group D and those in group T at the same time point ($P>0.05$), but the VAS scores for neck pain at the same time point were significantly lower than that in the traditional single mode analgesia group ($P<0.05$); Intraoperative remifentanil dosage and analgesia costs were significantly lower than those in the group T (all P values <0.05); the time to get out of bed for the first time after surgery, the time of first eating liquid, and self-evaluation comfort were significantly better than those in the group T (P value all <0.05); The levels of IL-6 at 24 hours after surgery in the two groups were significantly higher than those before surgery, but the increase in group D was lower than that in group T; the length of hospitalization in group D and the incidence of postoperative adverse reactions tended to be lower than those in group T, but the difference was not statistically significant ($P>0.05$). **Conclusion:** Compared with the traditional single analgesic mode, the sequential multi-mode analgesia based on ERAS concept can significantly improve the satisfaction of patients, reduce the dynamic pain score and the cost of postoperative analgesia, and promote the early recovery of patients.

Keywords sequential multimodal analgesia; thyroid cancer; functional neck lymphadenectomy; postoperative accelerated rehabilitation

加速康复外科(enhanced recovery after surgery, ERAS)是指通过围手术期优化处理措施,减少手术创伤和应激损害,实现外科术后充分镇痛、早期活动以及保护和加快器官功能恢复,从而促进患者快速康复、缩短住院时间以及节省医疗费用等^[1]。在实现ERAS过程中,完善、有效的镇痛是极其重要的环节,优化的多模式镇痛可以促进患者的快速康复。甲状腺癌功能性颈部淋巴结清扫术较普通甲状腺手术切口大、范围广、耗时长,产生的应激反应强、创伤大,目前临床上术后镇痛主要采用静脉自控镇痛(patient-controlled intravenous analgesia, PCIA),以阿片类镇痛药配伍为主,但阿片类镇痛药的呼吸抑制、恶心呕吐、皮肤瘙痒等不良反应可能会影响患者的快速康复且术后镇痛费用较高;临床上也有采用术前行单次颈浅丛阻滞予以镇痛,但受限于阻滞时间,做不到全程镇痛,不能达到满意的应用效果。本研究旨在将ERAS理念运用于此类患者,在痛觉信号传入前,使用超前镇痛以减少外周前列腺素合成,抑制中枢痛觉敏化;用套管针埋置于颈浅丛神经点附近合并术后口服镇痛药的方式来优化多模式镇痛方案,达到良好的镇痛效果、满意的舒适度,并降低术后并发症发生率以促进患者术后的快速康复。

1 对象与方法

1.1 对象

本研究经江苏省江原医院医学伦理委员会批准,所有患者签署知情同意书。纳入标准:2019年3至12月在江苏省原子医学研究所附属江原医院择期行甲状腺癌功能性颈部淋巴结清扫术的患者88例,性别不限,年龄18~65岁,BMI 19~24 kg/m²,ASA分级I~II级。采用随机、单盲的研究方法,将患者分为序贯式多模式镇痛组(D组, n=44)和传统单一模式镇痛组(T组, n=44)。

排除标准:1)二次行甲状腺手术的患者;2)严重的心肺及神经系统疾病者;3)药物滥用及酗酒史者;4)有阿片类药物、局部麻醉药物过敏史者;5)有精神疾病或其他原因不易配合者。

1.2 镇痛方法

患者入室前无麻醉前用药。入室后监测ECG、SpO₂及无创血压,开放上肢静脉通道,麻醉诱导前常规输注乳酸钠林格液6 mL/kg,局麻下行桡动脉穿刺置管监测有创动脉血压(invasive

blood pressure, IBP)。麻醉诱导:T组静脉注射咪达唑仑0.03 mg/kg,芬太尼5 μg/kg,丙泊酚1.5 mg/kg及罗库溴铵0.6 mg/kg,诱导后行气管插管,给予间歇正压通气(intermittent positive pressure ventilation, IPPV),潮气量6~8 mL/kg,通气频率10~12 min⁻¹,吸呼比为1:2,FiO₂70%,维持呼气末二氧化碳分压35~45 mmHg左右。D组诱导时静脉加用盐酸帕瑞昔布钠40 mg行超前镇痛;插管前在气管导管前端1/3处涂抹1%达克罗宁胶浆2 mL,其余诱导过程同T组;手术前行超声引导下双侧颈浅丛阻滞,注入0.375%罗哌卡因各7 mL。麻醉维持:靶控输注丙泊酚、瑞芬太尼、间断输注罗库溴铵,依据Narcotrend值,调整泵注速度,预设NTS在D1~E0,即NTI在27~56水平。D组因颈淋巴结清扫术后,组织解剖改变,且外科医生在缝合伤口前要在颈丛附近放置引流管、止血材料等,可能会影响B超埋入套管针的准确性和有效性,在缝合患侧切口前由外科医生直视下在颈淋巴结清扫侧的胸锁乳突肌中点后缘的外侧下方,远离皮肤切口位置,埋入22G静脉穿刺套管针于颈浅丛神经点处(图1),拔除针芯,接头处连接肝素帽,并用3M无菌薄膜贴固定,对侧在缝合切口后在B超引导下埋入套管针于颈浅丛处,并追加0.375%罗哌卡因各7 mL,留观15 min;术后6 h通过埋入颈浅丛的留置套管再追加1次0.375%罗哌卡因7 mL并拔除套管针,留观15 min;术后第12 h开始口服氨酚羟考酮片,1次/12 h,每次50 mg。T组则直接缝合伤口,术后使用PCIA镇痛(地佐辛40 mg、托烷司琼6 mg、右美托咪定100 μg)。

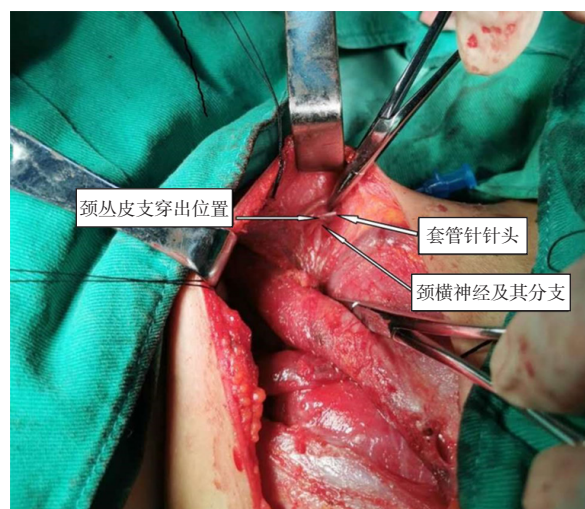


图1 静脉穿刺套管针置入位置

Figure 1 Implant location of intravenous trocar

1.3 观察与记录指标

1) 各组患者的年龄、身高、体重、手术时间等一般情况; 2) 术后1 h(T1)、6 h(T2)、12 h(T3)、24 h(T4)的静息时VAS评分、咳嗽时VAS评分; 3) 麻醉诱导前(T0)、术后24 h(T4)抽取患者动脉血3 mL, 离心后血浆放入-70 °C冰箱保存待测, 用ELISA法测定血清IL-6浓度; 4) 术中瑞芬太尼用量、首次下床时间、首次进食流质时间、住院天数、镇痛费用、自评舒适度(Bruggrmann Comfort Scale, BCS); 5) 两组患者的不良反应如苏醒期躁动、恶心呕吐、皮肤瘙痒、呼吸抑制等。

VAS评分: 无痛为0分, 轻度疼痛为1~3分, 中度疼痛为4~6分, 重度疼痛为7~9分, 剧烈疼痛为10分^[2]。自评舒适度(BCS): 分为5级, 0级为持续疼痛; 1级为安静时无痛; 2级为平卧或安静时无痛, 深呼吸或咳嗽时轻微疼痛; 3级为深呼吸也无痛; 4级为咳嗽时也无痛。

1.4 统计学处理

应用SPSS13.0统计软件进行统计分析。计量资料用均数±标准差($\bar{x} \pm s$)表示, 计量资料的比较采用独立样本 t 检验或秩和检验, 计数资料的比较采用 χ^2 检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 一般资料

两组间患者的性别构成、年龄、BMI、手术时间的差异均无统计学意义($P > 0.05$, 表1)。

2.2 VAS 评分

与T组比较, 患者静息疼痛VAS评分差异无统计学意义($P > 0.05$), 颈部活动时疼痛VAS评分D组明显降低($P < 0.05$, 表2)。

与T组比较, D组患者瑞芬太尼使用量减少($P < 0.05$), 首次下床时间更短, 饮食恢复时间更早, 镇痛费用明显减少, 24 h BCS评分更高($P < 0.05$), 住院天数比较差异无统计学意义($P > 0.05$, 表3)。

2.3 血清 IL-6 浓度

患者术后24 h的IL-6浓度明显升高($P < 0.05$), 但与T组比较D组的浓度较低($P < 0.05$, 表4)。

2.4 不良反应

两组不良反应发生率比较差异无统计学意义($P > 0.05$, 表5)。

表1 两组患者一般情况的比较($n=44$)

Table 1 Comparison of general data between the 2 groups ($n=44$)

组别	男/女	年龄/岁	BMI/(kg·m ⁻²)	手术时间/h
D组	9/35	38.9 ± 5.6	22.1 ± 2.8	4.5 ± 0.75
T组	7/37	40.2 ± 4.9	21.6 ± 3.0	4.3 ± 0.9

表2 两组患者不同时间点静息与颈部活动时VAS评分($n=44$, $\bar{x} \pm s$)

Table 2 VAS score of 2 groups when patients were at rest and moving neck at different time ($n=44$, $\bar{x} \pm s$)

组别	T1	T2	T3	T4
静息时VAS评分				
D组	1.4 ± 0.2	1.5 ± 0.2	1.5 ± 0.3	1.8 ± 0.3
T组	1.5 ± 0.3	1.5 ± 0.2	1.6 ± 0.2	2.0 ± 0.4
颈部活动时VAS评分				
D组	2.2 ± 0.2 ^a	2.5 ± 0.2 ^a	2.3 ± 0.2 ^a	2.2 ± 0.3 ^a
T组	3.6 ± 0.4	3.8 ± 0.3	4.2 ± 0.3	4.3 ± 0.4

与T组比较, ^a $P < 0.05$ 。

Compared with group T, ^a $P < 0.05$.

表3 两组患者VAS疼痛评分、下床时间、饮食恢复时间、镇痛费用、BCS评分($n=44$)Table 3 VAS pain score, the time of getting out of bed, the time of diet recovery, cost of analgesia, BCS score of 2 groups ($n=44$)

组别	瑞芬太尼总量/mg	下床时间/h	首次进食流质时间/h	镇痛费用/元	BCS评分	住院天数
D组	1.33 ± 0.12	7.62 ± 3.86 ^a	7.73 ± 1.62 ^a	385 ± 0 ^b	3 ± 0.3 ^a	10.53 ± 0.62
T组	1.93 ± 0.23	18.04 ± 4.47	11.94 ± 1.71	1041 ± 0	1.5 ± 0.2	14.82 ± 1.71

与T组比较, ^a $P<0.05$, ^b $P<0.01$ 。

Compared to group T, ^a $P<0.05$, ^b $P<0.01$.

表4 两组患者各时间点血清IL-6浓度($n=44$)Table 4 Serum levels of IL-6 of 2 groups at different time points ($n=44$)

组别	T0/(ng·L ⁻¹)	T4/(ng·L ⁻¹)
D组	3.41 ± 1.08	11.58 ± 2.65 ^d
T组	3.36 ± 1.14	14.97 ± 3.54 ^{cd}

注: 组内比较: 与T0时刻比较, ^d $P<0.05$ 。组间比较: 与T组比较, ^c $P<0.05$ 。

Compared within group: compared with that at T0, ^d $P<0.05$ 。

Compared between groups: compared with group T, ^c $P<0.05$ 。

表5 两组患者术后不良反应的比较($n=44$)Table 5 Comparison of postoperative adverse reaction of 2 groups ($n=44$)

组别	苏醒期躁动/例	恶心呕吐/例	呼吸抑制/例	皮肤瘙痒/局麻药中毒/例
D组	1	2	0	0/0
T组	4	7	1	3/0

与T组比较: 均 $P>0.05$ 。

Compared with group T, all $P>0.05$ 。

3 讨论

甲状腺癌是头颈部最常见的恶性肿瘤, 约占全身恶性肿瘤的1%。近年来, 我国甲状腺癌的发病率呈明显的上升趋势^[3]。虽然甲状腺癌伴功能性颈部淋巴结清扫术属于中等疼痛手术, 但是甲状腺手术区域神经血管分布丰富、手术切口较大且位于颈部, 术后的切口痛、咽痛、各种留置管道、继发性炎症反应刺激均可导致患者术后应激、睡眠不良, 甚至有可能演变成慢性疼痛, 严重影响其术后康复^[4]。完善的镇痛不仅可消除患者紧张、焦虑的情绪, 减轻围术期的应激水平, 还

会降低术后心、脑血管等意外事件的发生率, 促进患者术后早期下床活动, 加快胃肠功能恢复。

基于ERAS理念, 我们在甲状腺癌功能性颈部淋巴结清扫术的患者围术期镇痛的临床研究中, 采用了序贯式多模式镇痛方案, 包括帕瑞昔布纳超前镇痛, 气管导管涂抹达克罗宁胶浆, 双侧颈浅丛间断阻滞, 合并术后口服氨酚羟考酮片, 并与传统的以阿片类镇痛药物为主的单一模式镇痛方案进行比较。

超前镇痛是在痛觉信号传入前采取镇痛措施以阻止外界伤害性刺激传入, 降低疼痛阈值、抑制疼痛感受的镇痛方式^[5-6]。帕瑞昔布纳属于非甾体抗炎药, 通过高度选择性抑制COX-2的表达, 减少外周前列腺素合成, 抑制中枢痛觉敏化, 发挥外周和中枢双重镇痛抗炎作用。序贯式多模式镇痛组在诱导时注射帕瑞昔布纳是为了让其有充足的时间被前列腺素合成细胞(如巨噬细胞、中性粒细胞等)摄取, 在手术出现创伤前即阻断前列腺素的合成, 从而起到超前镇痛作用^[7]。有研究表明, 单剂量的帕瑞昔布纳可以有效地预防瑞芬太尼麻醉后诱发的痛觉过敏, 减少停药后再次要求镇痛的人数, 且不增加患者术后头痛、恶心呕吐的发生率^[8]。《成人手术后疼痛处理专家共识》指出, NSAIDs的镇痛作用具有封顶效应, 不应超剂量使用^[9], 鉴于其反复追加后的并发症, 术后应衔接其他镇痛方式实施全程联合镇痛。故本研究选用全麻复合双侧颈浅丛阻滞, 并于手术结束前在颈浅丛埋套管针, 实施术后神经阻滞联合镇痛, 神经阻滞局麻药选用低浓度(0.375%)的罗哌卡因, 具有明显的运动、感觉神经阻滞分离现象, 对喉返神经、膈神经等运动神经运动功能影响较小, 术后追加时安全系数高, 同时罗哌卡因具有收缩血管和局部抗炎作用, 故镇痛效果佳、维持时间长。甲状腺癌功能性颈部淋巴结清扫术的手术时间约为4 h, 0.375%罗哌卡因维持镇痛时间约为6~8 h, 我们分别于麻醉诱导后、手术结束时、手术结

束后6 h各追加1次0.375%罗哌卡因7 mL, 并观察15 min内有无并发症发生。有文献[10]显示甲状腺手术后疼痛特别是术后12 h内疼痛最明显, 随后逐渐减轻, 再加上长时间阻滞对神经会有损伤, 术后12 h开始改用口服氨酚羟考酮片衔接颈丛阻滞减退后的镇痛。氨酚羟考酮片是由盐酸羟考酮和对乙酰氨基组成的复方片剂, 可发挥中枢神经和周围神经止痛的双重作用, 关键是口服方便, 维持时间长^[11]。同时序贯式多模式镇痛组还于插管前在气管导管前端1/3处涂抹1%达克罗宁胶浆2 mL, 能在声门和气管内黏膜处发挥局部麻醉和润滑作用, 减少了声门和气管内黏膜的机械损伤以及黏膜内壁感受器所受刺激, 阻碍传导神经电活动, 降低交感神经兴奋性, 减轻围术期咽喉部的不良应激^[12]。

本研究结果显示: 序贯式多模式镇痛组患者术后1、6、12、24 h的静息疼痛VAS评分与传统单一模式镇痛组同时间点比较, 差异无统计学意义($P>0.05$); 但颈部活动疼痛VAS评分各同时间点均显著低于传统单一模式镇痛组, 提示序贯式多模式镇痛的镇痛效果优于以阿片类为主的传统单一模式镇痛; 序贯式多模式镇痛组术中瑞芬太尼用量、镇痛费用均显著少于传统单一模式镇痛组; 术后下床时间、饮食恢复时间、患者自评舒适度均显著优于传统单一模式镇痛组, 表明序贯式多模式镇痛显著加速了甲状腺癌功能性颈部淋巴结清扫患者的术后恢复; D组住院天数、术后不良反应发生率有低于T组的趋势, 但差异无统计学意义, 可能与标本量不足有关。手术切口的疼痛与炎症反应的激活存在密切关系, 持续的切口疼痛会激活炎症反应并增加多种炎症细胞因子的分泌, 过度分泌的炎症细胞因子能够降低周围组织的痛觉阈值并促进疼痛的发生^[13-14]。IL-6是一种重要的急性反应期炎症因子, 在机体应激反应和炎性疼痛中起重要作用。本研究结果显示, 两组患者术后24 h的IL-6浓度均明显高于术前, 但序贯式多模式镇痛组的升高幅度低于单一模式镇痛组, 提示虽然手术刺激本身是导致细胞因子浓度水平变化的主要因素, 但是序贯式多模式镇痛有效地减轻了围术期应激反应的发生; 同时超前镇痛药帕瑞昔布纳具有全身抗炎作用, 局部麻醉药物罗哌卡因也有轻度的收缩血管作用, 在局部产生抗炎效应。

本研究也有一定的局限性, 首先纳入的病例数不多, 可能存在统计学偏倚; 其次术后追加局麻药需谨防相关并发症, 留观15 min; 最后序贯

式多模式镇痛中的操作步骤、药物选择能否更合理, 需要进一步研究阐明。

综上所述, 相比传统单一的镇痛模式, ERAS理念下的序贯式多模式镇痛可明显提高患者的满意度, 降低患者术后动态疼痛评分和不良反应发生率, 且大大降低了术后的镇痛费用, 促进患者的早期康复。序贯式多模式镇痛在甲状腺癌功能性颈部淋巴结清扫术中安全、有效, 符合ERAS理念, 推荐在临床中选用。

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