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舒芬太尼复合地佐辛麻醉对腹腔镜胃癌切除患者血清炎性因子和早期认知功能的影响 *

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摘要 目的：研究舒芬太尼复合地佐辛对腹腔镜胃癌切除患者术后炎性因子、早期认知功能的影响。**方法：**选取 2015 年 4 月至 2016 年 3 月本院收治的 84 例胃癌患者，根据入院顺序分为观察组和对照组，每组 42 例。对照组采取单纯舒芬太尼术后镇痛，观察组使用舒芬太尼符合地佐辛术后镇痛。比较两组患者术前、术后的视觉模拟评分(VAS)、炎性因子水平和认知功能评分变化。**结果：**两组患者术后 6、12、24、48 小时 VAS 均较术前呈下降趋势，观察组在术后 6、12、24、48 h VAS 均显著低于对照组(P＜0.05)。术后 7 天，观察组患者血清 IL-6、TNF-α 水平显著低于对照组，IL-10 水平显著高于对照组，差异均有统计学意义(P<0.05)。观察组患者的认知功能评分(80.43± 1.32)显著高于对照组(66.54± 1.56)(P<0.05)。观察组和对照组的不良反应发生率比较无统计学差异[14.29%(6/42)比 19.05%(8/42)](P>0.05)。**结论：**腹腔镜胃癌切除患者应用舒芬太尼复合地佐辛术后镇痛可有效缓解患者术后疼痛感，调节术后炎性因子水平，改善早期认知功能障碍，且安全性较高。

关键词：舒芬太尼；地佐辛；腹腔镜胃癌切除术；炎性因子；认知功能

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Influence of Sufentanil Combined with Dezocine on the Inflammatory Factors Levels and Early Cognitive Function of Patients Underwent Laparoscopic Gastric Cancer Resection*

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ABSTRACT Objective: To investigate the effect of sufentanil combined with docetaxel on inflammatory factors and early cognitive function in patients undergoing laparoscopic resection of gastric cancer. **Methods:** 84 patients with gastric cancer admitted to our hospital from April 2015 to March 2016 were divided into the observation group and the control group. Patients in the control group were treated with sufentanil and patients in the observation group were treated with sufentanil combined with docetaxel. The visual analogue scale (VAS), changes of inflammatory factors before and after operation, and the postoperative cognitive function scores were compared between the two groups. **Results:** The VAS of both groups was decreased at 6, 12, 24 and 48 h after operation, and the VAS of observation group was lower than that of the control group at 6 , 12, 24 and 48 h after operation (P<0.05). At 7 days after operation, the levels of IL-6 and TNF-α in the observation group were significantly lower than those of the control group, the level of IL-10 was significantly higher than that of the control group (P<0.05). The cognitive function score of observation group (80.43± 1.32) was significantly higher than that of the control group (66.54± 1.56) (P<0.05). There was no statistically significant difference in the incidence of adverse reactions between two groups [14.29% (6/42) vs 19.05% (8/42)] (P>0.05). **Conclusion:** Laparoscopic resection of gastric cancer patients with sufentanil combined with dezocine after analgesia could relieve the postoperative pain, adjust the level of inflammatory factors after surgery, improve the early cognitive dysfunction, and have fewer adverse reactions.

Key words: Sufentanil; Dezocine; Laparoscopic Gastric Cancer Resection; Inflammatory factor; Cognitive function

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前言

肿瘤患者机体免疫功能多处于抑制状态，而手术和麻醉而导致的应激反应会进一步抑制患者的免疫功能，增加肿瘤细胞转移概率，进而影响肿瘤患者的预后[1]。在围术期应用于镇痛较为常见的药物主要是舒芬太尼，对应激反应具有有效的抑制作

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用,但舒芬太尼本身具备免疫抑制效果[2]。在阿片类药物中,地佐辛既拮抗μ 受体,又存在激动 k 受体的作用。在术后镇痛中,关于联合使用两种药物会对腹腔镜胃癌根治术患者围术期的免疫功能带来何种影响目前尚不明确[3]。为进一步明确舒芬太尼复合地佐辛的有效性,本研究将舒芬太尼复合地佐辛用于腹腔镜胃癌切除患者中,并对患者术前后炎性因子水平和认知功能的变化进行分析,现报道如下。

1 资料与方法

1.1 临床资料

从 2015 年 4 月至 2016 年 3 月收集 84 例拟在本院进行腹腔镜胃癌切除术的胃癌患者,纳入标准:① 临床诊断均和《胃癌治疗指南》[4]中的标准相符,疾病的持续时间在 3 个月以上,伴有一般上消化道症状,胃息肉或慢性胃炎患者,近期内胃病史有所加重,大便潜血阳性者,溃疡病史表现为规律性变化;② 肿瘤直径 >5 cm;③ 经 X 线或脱落学细胞检测以及显微镜检查被诊断为胃癌。排除标准:① 心、肾等脏器功能严重衰竭或障碍,高血压 3 级;② 伴有凝血功能障碍,对本次研究中所需药物存在过敏史;③ 近三个月内有过免疫抑制剂治疗史;④ 癫痫、皮质醇增多等神经系统疾病者。研究签署患者知情同意书,获得本院伦理委员会批准。按照患者入院顺序分为观察组和对照组,各 42 例。两组患者临床资料无显著差异(P>0.05),见表 1。

表 1 两组患者临床资料比较

Table 1 Comparison of the general information between two groups

Groups	n	Sex		Age(year)	Disease course (month)	Weight(kg)	ASA classification	
		Male	Female				Stage I	Stage II
Observation group	42	25(59.52)	17(40.48)	56.43± 0.75	5.87± 0.34	59.34± 1.43	27(64.29)	15(35.71)
Control group	42	28(66.67)	14(33.33)	56.42± 0.79	5.92± 0.38	60.11± 1.41	24(57.14)	18(42.86)

1.2 治疗方法

患者静脉注射 0.06 mg/kg 的咪达唑仑、0.2~0.3 mg/kg 的顺式阿曲库铵, 靶控输注丙泊酚,4 μg/mL 的血浆靶浓度,0.4 μg/kg 的舒芬太尼进行麻醉诱导。靶控输注丙泊酚,2.5~4 μg/mL 的血浆靶控浓度,持续输注 0.4~0.6 μg/(kg·h)的舒芬太尼直到手术完毕, 吸入七氟醚并使呼气末浓度维持在 1.5%~2.0%之间进行麻醉维持。手术完成后送至麻醉恢复室,其中对照组用 100 mL 的生理盐水和 2.5 μg/kg 的舒芬太尼相互稀释;观察组则使用 100 mL的生理盐水与 1.5 μg/kg 的舒芬太尼复合 0.2 mg/kg 的地佐辛进行稀释。在镇痛泵中均需加入 2 mg 的托烷司琼,2 mL/h 的背景剂量,单次给药量为 0.5 mL/ 次,时间为 15 min, 若患者在术后依然伴有疼痛感则需追加 100 mg 的加曲马多。

1.3 观察指标

1.3.1 VAS 疼痛评分 观察患者术后 6、12、24、48 小时的疼痛情况,使用视觉模拟评分(visual analogue scale,VAS)[5]对患者术后不同时间点疼痛情况进行评价,其中 10 分表现剧烈疼痛,0 分则为无痛,分数和患者的疼痛程度呈正比。

1.3.2 血清炎症因子水平检测 比较两组患者手术前 1 天及术后 7 天炎性因子水平,分别在术前 1 天及术后 7 天抽取 2 组患者 5 mL 的空腹静脉血,采取放射免疫法检测血清白介素 -6(IL-6)、白介素 -10(IL-10)水平,试剂盒由美国 Gen-zyme 公司提供;使用免疫吸附夹心法检测肿瘤坏死因子 -α(TNF-α)水平,试剂盒由北京邦定公司提供。

1.3.3 认知功能评价 手术前 1 天及术后 7 天对患者进行神经功能检测,主要包括下列 7 个项目,韦氏成人记忆量表中的累加评价注意力;视觉记忆试验视觉再生;试验数字广度区分患者逆向以及顺向;联想学习评价语言记忆;联想检验评价注意力转移;数字符号评价精神运动速度;顶板检测非利手以及分利手。功能恶化:术后评分≥ 术前指标评分,2 个或以上功能恶化指标则为认知功能障碍。总分为 100 分,低于 70 分则存在认知功能障碍。

1.4 统计学处理

实验数据通过 SPSS11.5 处理,计量资料用($\bar{x}$± s)表示,采取 t 检验,计数资料用[n(%)]表示,采取 x^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组术后不同时点 VAS 评分比较

术前, 两组患者的 VAS 评分比较无显著性差异(P>0.05)。两组患者术后 6、12、24、48 小时 VAS 评分均较术前显著下降,且观察组显著低于对照, 两组比较差异存在统计学意义 (P< 0.05),见表 2。

表 2 两组患者术后不同时间点 VAS 评分比较($\bar{x}$± s)

Table 2 Comparison of the VAS score between two groups at different time points($\bar{x}$± s)

Groups	Case	Before operation	6 h postoperation	12 h postoperation	24 h postoperation	48 h postoperation
Observation group	42	5.43± 0.23	4.31± 0.42*#	4.02± 0.37*#	3.51± 0.32*#	2.73± 0.26*#
Control group	42	5.47± 0.25	6.31± 0.76#	5.77± 0.65#	4.86± 0.42#	3.49± 0.31#

Note: Compared with those before operation in the same group, #P<0.05; Compared with the control group at the same time point,*P<0.05.

2.2 两组术后炎性因子水平比较

术前 1 天, 两组患者血清 IL-6、IL-10、TNF-α 水平比较差异无统计学意义(P>0.05),术后 7 天,两组患者血清 IL-6、TNF-α 水平较术前 1 天均显著降低(P<0.05),观察组显著低于对照组(P<0.05),血清 IL-10 水平有所升高,观察组显著高于对照组(P<0.05),见表 3。

表 3 两组患者术前后血清 IL-6、IL-10、TNF-α 水平比较($\bar{x}\pm s$)

Table 3 Comparison of the serum IL-6, IL-10, TNF-α levels between two groups before and after operation($\bar{x}\pm s$)

Groups	Case	IL-6(mmol/L)		IL-10(mmol/L)		TNF-α(mmol/L)	
		Before operation	After operation	Before operation	After operation	Before operation	After operation
Observation group	42	97.87± 6.66*#	68.32± 5.43*#	35.23± 4.21*#	49.43± 5.02*#	12.43± 1.02*#	7.43± 0.43*#
Control group	42	97.91± 6.71*	83.32± 5.31*	35.28± 4.18*	41.54± 3.21*	12.42± 1.08*	9.56± 0.29*

Note: Compared with before operation in the same group,*P<0.05; Compared with control group after operation, #P<0.05.

2.3 两组认知功能评分比较

术后,观察组患者的认知功能评分(80.43± 1.32)显著高于对照组(66.54± 1.56) (P<0.05)。

2.4 两组患者不良反应发生情况比较

观察组有 1 例患者伴有头晕症状,2 例患者为嗜睡,3 例患者出现恶心呕吐不良反应; 对照组中 2 例患者出现头晕,3 例患者发生嗜睡,3 例患者伴有恶心呕吐症状。观察组和对照组的不良反应发生率比较无统计学差异[14.29%(6/42)比 19.05%(8/42)](P>0.05)。

3 讨论

腹腔镜胃癌切除术是治疗胃癌较为有效的手段,然而大部分患者在术后伴有不同程度上的疼痛感和认知功能障碍[6-8]。舒芬太尼在阿片类镇痛药中的效果较为明显,属于特异性的 μ 阿片受体激动剂,在围术期镇痛中已得到广泛运用,从根本上而言舒芬太尼本来就有免疫抑制功效[9-10]。地佐辛在 k 受体中可发挥激动效应,脊髓镇痛效果较为显著,可有效拮抗 μ 受体,很难成瘾,已在临床中得到广泛应用[11,12]。本研究通过对腹腔镜胃癌切除术患者予以舒芬太尼复合地佐辛进行镇痛后,缓解了患者术后疼痛感, 其 VAS 评分降低的程度优于单纯舒芬太尼治疗者。

术后认知功能障碍主要是指患者在术前无精神障碍,但在围术期因受到各种因素的影响,术后出现抽象思维、注意力、感知、语言功能、记忆及学习等方面障碍,属于机体发生的波动性、可逆的急性精神紊乱综合征[13,14]。感染、术后低氧血症、创伤等多种因素均可能引发术后认知功能障碍,属于手术麻醉后较为常见的并发症[15]。相关研究提出认知功能障碍的发病率呈现出上升趋势,表明在治疗中采取腹腔镜胃癌切除术方式,会进一步影响病情,其预后较差[16]。本研究结果表明,腹腔镜胃癌切除术后患者经舒芬太尼复合地佐辛治疗后,患者术后认知功能评分明显提高,提示腹腔镜胃癌切除术患者应用舒芬太尼复合地佐辛麻醉,能有效改善认知功能障碍情况,预后良好。本研究还发现患者经舒芬太尼复合地佐辛进行术后镇痛,和单纯的舒芬太尼相比并没有增加患者的头晕、嗜睡、恶心呕吐不良反应率,可能和地佐辛部分拮抗 μ 阿片受体相关。

术后疼痛感常常会给机体带来刺激性影响, 血清 TNF-α 水平升高;IL-6 具有促炎作用,IL-10 作为细胞素的合成抑制因子,可调控炎症反应,包括细胞活性以及多项性功效,对机体免疫应答功能能发挥改变性作用[17,18]。相关研究表明机体一旦受到外界微生物侵袭或创伤后, 血清炎症因子水平会出现异常,主要表现为 IL-10 水平降低,IL-6、TNF-α 水平升高, 当机体愈合后,IL-10、L-6、TNF-α 水平均恢复至正常[19]。并且发现相对于使用单纯的舒芬太尼 IL-10 水平明显升高,IL-6、TNF-α 水平降低。原因主要是免疫系统在肿瘤的发展中起着关键性作用,在肿瘤患者中,大部分患者基本上有着异常的免疫功能,主要为免疫促进因子表达水平低下或免疫抑制因子水平升高,其中术后疼痛又会对免疫抑制造成影响,而在术后对患者予以良好的镇痛,可有效减轻患者的免疫抑制,激发免疫功能,有利于患者创伤的恢复[20],进而缓解患者免疫抑制。

总之,腹腔镜胃癌切除患者应用舒芬太尼复合地佐辛术后镇痛,能缓解患者术后疼痛感,有效调节患者术后炎性因子,有利于早期认知功能障碍改善,且安全性高。

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