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术中持续输注右美托咪定对腹腔镜子宫肌瘤切除术患者术后睡眠质量的影响

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[摘　要]　**目的：**探讨术中持续输注右美托咪定对腹腔镜子宫肌瘤切除术患者术后睡眠质量的影响。**方法：**选取2019年6月至2021年5月在秦皇岛市工人医院行腹腔镜子宫肌瘤切除术患者150例为研究对象，随机分为对照组(n=75)与观察组(n=75)。观察组于麻醉诱导开始予以右美托咪定0.5 μg/(kg·h)持续泵注，对照组则予以生理盐水0.125 mL/(kg·h)泵注，直至术毕。2组术后均予以自控静脉镇痛(patient controlled intravenous analgesia，PCIA)。于术前和术后1 d、2 d行多导睡眠监测仪监测和匹兹堡睡眠指数量表(Pittsburgh Sleep Quality Index，PSQI)评分以评价2组患者睡眠质量；于术后6 h、24 h和48 h行数字镇静评分(numerical sedation scale，NSS)评价2组术后镇静效果；记录2组术后舒芬太尼用量和补救镇痛率。**结果：**术后1 d和2 d，观察组睡眠效率指数(sleep efficiency index，SEI)显著高于对照组(P<0.05)，觉醒指数(arousal index，AI)和PSQI评分显著低于对照组(P<0.05)；且观察组术后当晚睡眠障碍发生率为18.67%，显著低于对照组的34.67%，差异有统计学意义(P<0.05)。相比对照组，观察组术后6 h和24 h的NSS评分显著增高(P<0.05)。相比对照组，观察组术后舒芬太尼用量减少，补救镇痛率降低，差异有统计学意义(P<0.05)。**结论：**术中持续输注右美托咪定能够改善腹腔镜子宫肌瘤切除术患者术后睡眠质量，对于睡眠障碍的发生有预防作用。

[关键词]　右美托咪定；术中持续泵注；腹腔镜；子宫肌瘤切除术；术后睡眠障碍

Effect of intraoperative continuous infusion of dexmedetomidine on postoperative sleep quality in patients underwent laparoscopic hysteromyomectomy

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Abstract　**Objective:** To investigate the effect of intraoperative continuous infusion of dexmedetomidine on postoperative

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sleep quality in patients undergoing laparoscopic hysteromyomectomy. **Methods:** A total of 150 patients undergoing laparoscopic hysteromyomectomy in Qinhuangdao Workers' Hospital from June 2019 to May 2021 were selected and randomly divided into control group (n=75) and observation group (n=75). The observation group was continuously pumped with dexmedetomidine 0.5 μg/(kg·h) after anesthesia induction, while the control group was pumped with normal saline 0.125 mL/(kg·h) until the end of operation. Both groups received patient controlled intravenous analgesia (PCIA) after operation. The sleep quality of the 2 groups was evaluated by polysomnography and Pittsburgh Sleep Quality Index (PSQI) score before operation and 1 d and 2 d after operation. Numerical sedation scale (NSS) was used to evaluate the sedative effect at 6 h, 24 h and 48 h after operation. The postoperative sufentanil dosage and remedial analgesia rate were recorded in the 2 groups. **Results:** At 1 d and 2 d after operation, the sleep efficiency index (SEI) in the observation group was significantly higher than that in the control group (P<0.05), and the arousal index (AI) and PSQI score were significantly lower than those in the control group (P<0.05). The incidence of sleep disorder in the observation group was 18.67%, which was significantly lower than 34.67% in the control group, and the difference was statistically significant (P<0.05). Compared with the control group, the NSS scores at 6 h and 24 h after operation in the observation group were significantly increased (P<0.05). Compared with the control group, the amount of sufentanil and the rate of remedial analgesia in the observation group were decreased, and the difference was statistically significant (P<0.05). **Conclusion:** Continuous intraoperative infusion of dexmedetomidine can improve the postoperative sleep quality of patients undergoing laparoscopic hysteromyomectomy and prevent the occurrence of sleep disorders.

Keywords dexmedetomidine; intraoperative continuous pumping; laparoscope; hysteromyomectomy; postoperative sleep disorder

睡眠障碍在大手术患者术后较为普遍，常表现为睡眠剥夺及睡眠节律紊乱[1]。术后疼痛、手术创伤所致的机体生理功能改变等因素引起的不良感受，是导致患者术后睡眠障碍的主要原因[2]。术后睡眠障碍的发生不仅会加重术后疼痛，延迟康复，还可能导致神经内分泌、心血管系统等并发症，进而使得围手术期死亡风险提高[3]。因此，采取有效措施改善患者术后睡眠质量尤为重要。目前，临床对于术后睡眠的干预策略包括应用镇痛药物和苯二氮卓类安眠药物等，但这些手段改善术后睡眠质量的效果仍欠满意[4-5]。右美托咪定是一种高选择性的α2肾上腺素能受体激动剂，可发挥镇静、镇痛、抗焦虑等多重作用[6-7]。最新研究[8]表明术后予以右美托咪定输注能够通过增加N2期睡眠，减少N1期睡眠从而改善重症患者睡眠结构，进而使得术后睡眠质量得以改善。还有研究[9]显示术中应用右美托咪定能够增加乳腺癌全麻手术患者术后当晚的睡眠时间。目前，关于术中应用右美托咪定能否改善大手术患者术后睡眠质量的仍有待明确。本研究拟评价术中持续输注右美托咪定对腹腔镜子宫肌瘤切除术患者睡眠质量的影响。

1 对象与方法

1.1 研究对象

参照文献[9]进行样本量估算，样本量计算结果为：当2组病例数目相等时，每组例数应不少于70例；样本量计算公式为：$n_1=n_2=2[(t_{\alpha/2}+t_{\beta})s/\delta]^2$。本试验设计为每组病例数各75例，共纳入150例样本。选取2019年6月至2021年5月在秦皇岛市工人医院行腹腔镜子宫肌瘤切除术患者150例为研究对象。纳入标准：1)择期行腹腔镜子宫肌瘤切除术；2)美国麻醉医师协会(American Society of Anesthesiologists，ASA)分级为I或II级；3)年龄40~65岁；4)体重指数(body mass index，BMI)范围为18~24 kg/m^2。排除标准：1)术前存在睡眠障碍；2)术前伴有精神疾病；3)术前1周有使用安眠药；4)伴严重器质性疾病；5)严重呼吸循环系统疾病；6)孕妇及哺乳期妇女；7)有右美托咪定使用禁忌证；8)术后需入住重症监护室。采用随机数字表法随机分为对照组(n=75)与观察组(n=75)。本研究经秦皇岛市工人医院伦理审批通过，患者均签署知情同意书。

1.2 麻醉方法

入室后，行心电图、血压、心率、脉搏血氧饱和度等常规监测，建立外周静脉通路。观察组于麻醉诱导开始予以右美托咪定0.5 μg/(kg·h)持续泵注，对照组则予以生理盐水0.125 mL/(kg·h)泵注，直至术毕。麻醉诱导：予以咪达唑仑(江苏恩华药业股份有限公司)0.05 mg/kg，舒芬太尼(宜昌人福药业有限责任公司)0.4 μg/kg，丙泊酚(西安力邦制药有限公司)2 mg/kg，罗库溴铵(浙江仙琚制药股份有限公司)0.8 mg/kg静脉注射，行气管插管后，行机械通气，参数设置：潮气量为6~8 mL/kg，呼吸频率为10~14次/min，I:E=1:2，氧流量为2 L/min，吸入氧浓度为50%，呼气末二氧化碳分压(end-tidal pressure of carbon dioxide，$P_{ET}CO_2$)维持35~45 mmHg(1 mmHg=0.133 kPa)。麻醉维持：予以瑞芬太尼(江苏恩华药业股份有限公司)0.1~0.3 μg/(kg·min)，丙泊酚4~8 mg/(kg·min)，并予以罗库溴铵0.05 mg/kg间断推注，维持平均动脉压、心率波动程度小于基础值的20%。

患者术毕送至麻醉恢复室，2组均连接自控静脉镇痛(patient controlled intravenous analgesia，PCIA)泵，药液配方：舒芬太尼2.0 μg/kg+酮咯酸氨丁三醇3 mg/kg，并加生理盐水稀释到100 mL，无背景剂量，患者自控镇痛(patient controlled analgesia，PCA)单次剂量设定为4 mL，锁定时间设定为15 min，将视觉模拟评分法(Visual Analogue Scale，VAS)评分维持在<4分，必要时可予以哌替啶50 mg肌肉注射进行补救镇痛处理。

1.3 观察指标

于术前1 d晚和术后1 d、2 d晚采用Alice 5多导睡眠监测仪对患者睡眠状态进行监测，记录觉醒指数(arousal index，AI)、睡眠效率指数(sleep efficiency index，SEI)以及快动眼睡眠时间(rapid eye movement，REM)在总睡眠时间中所占的百分比；并行匹兹堡睡眠指数量表(Pittsburgh Sleep Quality Index，PSQI)评分[10]，以评价患者睡眠质量，PSQI评分越高说明睡眠质量越差，≥5分则判定为存在睡眠障碍。于术后6 h、24 h和48 h行数字镇静评分(Numerical Sedation Scale，NSS)：1分(烦躁)、2分(安静)、3分(嗜睡，能够听从指令)、4分(睡眠状态，能够唤醒)、5分(对呼吸反应迟钝)、6分(深睡眠，不能唤醒)。记录2组术后镇痛情况，包括舒芬太尼用量、补救镇痛率等。

1.4 统计学处理

采用SPSS24.0进行数据处理。计量资料(满足正态分布)均采取均数±标准差($\bar{x}\pm s$)进行表示，组间对比用独立样本t检验，不同时间点PSQI评分、NSS评分的比较用重复测量方差分析；计数资料采取例或率进行表示，组间对比用χ^2检验。P<0.05为差异有统计学意义。

2 结果

2.1 一般资料及手术一般情况

2组一般资料和手术一般情况对比差异无统计学意义(P>0.05，表1)。

2.2 术后睡眠质量

术前，2组睡眠监测指标(SEI、AI、REM)和PSQI评分对比差异无统计学意义(P>0.05)。术后1 d和2 d，2组SEI和REM相比术前降低(均P<0.05)，AI和PSQI评分相比术前均增高(P<0.05)；而观察组SEI显著高于对照组，AI和PSQI评分显著低于对照组(P<0.05，表2、3)。另外，观察组术后当晚睡眠障碍发生率为18.67%(14/75)，对照组术后当晚睡眠障碍发生率为34.67%(26/75)，差异有统计学意义(χ^2=4.909，P=0.027<0.05)。

表1 2组一般资料及手术一般情况比较(n=75)

Table 1 Comparison of general information and general operation conditions between the 2 groups (n=75)

组别	年龄/岁	BMI/(kg·m^{-2})	ASA 分级(I/II)/例	手术时间/min	麻醉时间/min	术中失血量/mL	术中瑞芬太尼用量/mg	麻醉唤醒时间/min
观察组	48.51 ± 7.54	21.74 ± 3.21	30/45	131.54 ± 28.43	156.32 ± 18.54	225.47 ± 43.68	1.56 ± 0.49	4.31 ± 0.92
对照组	49.17 ± 6.89	22.19 ± 3.17	34/41	127.41 ± 26.17	153.41 ± 19.65	221.69 ± 40.56	1.53 ± 0.46	4.06 ± 0.85
t/χ^2	0.560	0.864	0.436	0.926	0.933	0.549	0.387	1.729
P	0.577	0.389	0.509	0.356	0.352	0.584	0.700	0.087

表2 2组睡眠监测指标比较(n=75)

Table 2 Comparison of sleep monitoring indexes between the 2 groups (n=75)

组别	时间点	SEI	AI	REM/%
观察组	术前1 d晚	80.64 ± 10.31	4.49 ± 1.31	22.15 ± 5.78
	术后1 d晚	62.36 ± 11.57[ab]	7.78 ± 1.46[ab]	13.38 ± 3.12[a]
	术后2 d晚	68.97 ± 10.36[ab]	6.74 ± 1.56[ab]	15.25 ± 3.58[a]
对照组	术前1 d晚	80.36 ± 11.29	4.56 ± 1.24	21.89 ± 5.06
	术后1 d晚	51.64 ± 8.76[a]	9.38 ± 1.51[a]	12.69 ± 3.25[a]
	术后2 d晚	59.65 ± 9.89[a]	8.67 ± 1.74[a]	14.89 ± 4.12[a]

与术前相比，[a]P<0.05；与对照组同时间点相比，[b]P<0.05。

Compared with preoperative, [a]P<0.05; Compared with the control group at the same time point, [b]P<0.05.

表3 2组不同时间点PSQI评分比较(n=75)

Table 3 Comparison of PSQI scores between the 2 groups at different time points (n=75)

组别	PSQI评分		
	术前	术后1 d	术后2 d
观察组	3.25 ± 0.67	7.12 ± 2.21[a]	5.12 ± 1.29[a]
对照组	3.29 ± 0.71	7.98 ± 2.34[a]	6.87 ± 1.47[a]
t	0.355	2.314	7.749
P	0.723	0.022	<0.001

与术前相比，[a]P<0.05。

Compared with preoperative, [a]P<0.05.

2.3 术后不同时间点 NSS 评分

相比对照组，观察组术后6 h和24 h的NSS评分显著增高(均P<0.001，表4)。

2.4 术后镇痛情况

相比对照组，观察组术后舒芬太尼用量减少(P<0.001)，补救镇痛率降低(P=0.026，表5)。

表4 2组术后不同时间点NSS评分比较(n=75)

Table 4 Comparison of NSS scores between the 2 groups at different time points after operation (n=75)

组别	NSS评分		
	术后6 h	术后24 h	术后48 h
观察组	4.12 ± 0.71	4.39 ± 0.69	3.62 ± 0.68
对照组	3.43 ± 0.58	3.51 ± 0.72	3.57 ± 0.79
t	6.518	7.642	0.415
P	<0.001	<0.001	0.678

表5 2组术后镇痛情况比较(n=75)

Table 5 Comparison of postoperative analgesia between the 2 groups (n=75)

组别	舒芬太尼用量/μg	补救镇痛/[例(%)]
观察组	146.58 ± 15.14	7 (9.33)
对照组	155.43 ± 16.78	17 (22.67)
t/χ^2	3.391	4.960
P	0.001	0.026

3 讨论

术后睡眠质量与术后恢复紧密关联，良好的睡眠状况有助于促进术后恢复，减少患者住院时间和经济负担。故探寻改善术后睡眠质量的有效方法尤为重要。近年研究[11]表明静脉予以右美托咪定能够改善重症患者睡眠质量。但右美托咪定的使用存在心动过缓、低血压等一些风险[12]，特别是对术后缺乏监护的患者有着更高的使用风险。因此，该药在术后患者中的使用尚未成为常规。而术中在麻醉医师监护下持续对患者予以右美托咪定泵注，能够保证患者安全，若能够改善患者术后睡眠质量，将有利于患者术后恢复。

PSQI量表广泛应用于精神障碍和睡眠障碍患者睡眠质量的评价，对于一般人群也适用。PSQI操作简便，并且评价结果与客观睡眠质量较为接近[10]。多导睡眠监测仪是目前临床广泛认可的睡眠监测手段，能够客观、科学、定量评估睡眠状态[13]。本研究显示：观察组术后1 d和2 d的睡眠监测指标(SEI、AI)及PSQI评分显著优于对照组，并且观察组术后当晚睡眠障碍发生率为18.67%，也显著低于对照组的34.67%，这说明术中持续输注右美托咪定有助于改善腹腔镜子宫肌瘤切除术患者术后睡眠质量，减少术后睡眠障碍的发生。张伟等[14]研究表明：PCIA中使用右美托咪定是患者术后睡眠障碍的保护因素。程森等[15]研究报道：右美托咪定能够有效改善子宫切除术患者术后12 h和48 h的睡眠质量指数。这些都支持本研究结果。

右美托咪定是一种新型的α2受体激动剂，能够通过激活蓝斑上α2受体而对睡眠发挥促进作用[16]。Oto等[17]研究发现：右美托咪定可使昼夜睡眠周期得以保留，并可提高睡眠效率而有效改善患者睡眠结构。并且张小伟等[18]报道，术后应用右美托咪定能够通过减少N1期睡眠和增加N2期睡眠而改善睡眠结构，进而改善患者术后睡眠质量。以上研究表明：右美托咪定术后应用可改善术后睡眠结构进而对患者术后睡眠质量有益。另外，相关报道[19]表明：右美托咪定半衰期较长，其作用效果与用药剂量和用药时间具有正相关关系。本研究术中持续输注右美托咪定，术后遗留的右美托咪定仍能够发挥其效应，进而改善术后睡眠质量。

术中持续输注右美托咪定改善子宫肌瘤切除术患者术后睡眠质量的机制还可能在于：1)右美托咪定具有镇静作用[20]。尽管镇静与睡眠是不同的2种状态，但镇痛药的使用能够诱导患者的睡眠更加接近生理状况。在本研究中，术中持续输注右美托咪定能够增强患者术后镇静效果(观察组术后6 h和24 h的NSS评分显著增高)，从而有效改善患者术后睡眠质量。2)疼痛和阿片类药物可抑制深睡眠，进而对睡眠有着不利影响[21]。本研究中，术中持续输注右美托咪定能够增强术后镇痛效果，减少患者术后舒芬太尼用量，从而可减少阿片类药物对睡眠的不良影响。本研究存在一些局限性：1)作为单中心研究，样本量有限，其结论仍需多中心、大样本量研究加以验证；2)仅仅纳入了子宫肌瘤切除术患者，右美托咪定改善术后睡眠质量的作用在其他手术患者中是否依然有效，有待进一步验证。

综上，术中持续输注右美托咪定能够有效改善腹腔镜子宫肌瘤切除术患者术后睡眠质量，降低睡眠障碍发生率。

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