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右美托咪定用于复合麻醉对腹部手术患者血流动力学及神经认知功能的影响*

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摘要 目的:研究右美托咪定用于复合麻醉对腹部手术患者血流动力学及神经认知功能的影响。**方法:**选择 2016 年 9 月至 2017 年 9 月在我院接受复合麻醉条件下腹部手术的患者 172 例,按照随机分配的原则将其分为试验组(n=90)及对照组(n=82)。观察和比较两组拔管前后平均动脉压、心率、血清肿瘤坏死因子 α (TNF- α)、白介素 6(IL-6)、钙粒蛋白 β (S100 β)水平的变化、拔管时间及躁动的发生情况。术后 24 小时,通过简易精神状态量表(MMSE)评分评估和比较两组的神经认知功能。**结果:**试验组拔管前、拔管时及拔管后 2 小时的平均动脉压、心率、血清 TNF- α 及 IL-6 水平均明显低于对照组 ($P<0.05$),拔管时间及躁动发生率分别为 (11.07 ± 2.82) min 及 5.55%,均显著低于对照组($P<0.05$)。术后 24 小时,试验组的血清 S100 β 蛋白水平为 $(1.32\pm 0.56)\mu\text{g/L}$,明显低于对照组,而 MMSE 评分为 (28.35 ± 2.14) 分,显著高于对照组($P<0.05$)。**结论:**右美托咪定应用于施行复合麻醉的腹部手术患者可以更有有效的稳定血流动力学,减轻炎症反应,减少躁动,保护患者神经认知功能。

关键词:腹部手术;复合麻醉;右美托咪定;血流动力学;神经认知功能

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Effects of Dexmedetomidine on Hemodynamics and Neurocognitive Function in Patients Undergoing Abdominal Surgery with Combined Anesthesia*

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ABSTRACT Objective: To investigate the effect of dexmedetomidine on the hemodynamics and neurocognitive function of patients undergoing abdominal surgery with combined anesthesia. **Methods:** 172 cases of patients undergoing abdominal surgery were selected in our hospital from September 2016 to September 2017, the patients were divided into the experimental group (n=90) and the control group (n=82) according to the principle of random distribution. The changes of arterial pressure, heart rate, serum tumor necrosis factor alpha (TNF- α), interleukin 6 (IL-6) and calcium granulin beta (S100 beta) before and after extubation and the occurrence of extubation time and agitation were compared between two groups. The neurocognitive function of the two groups was evaluated and compared by the Mini Mental State Scale (MMSE) score at 24 hours after operation. **Results:** The mean arterial pressure, heart rate, serum TNF- alpha and IL-6 water of experimental group before extubation, extubation and at 2 hours after extubation were significantly lower than those in the control group ($P<0.05$). The extubation time and the incidence of restlessness were (11.07 ± 2.82) min and 5.55%, respectively, which were significantly lower than those in the control group ($P<0.05$). At 24 hours after operation, the serum S100 beta protein level of the test group was $(1.32\pm 0.56)\mu\text{g/L}$, obviously lower than that of the control group, and the MMSE score was (28.35 ± 2.14) scores, which was significantly higher than that of the control group ($P<0.05$). **Conclusion:** Dexmedetomidine should be used in patients with abdominal surgery for complex anesthesia, which could more effectively stabilize the hemodynamics, relieve the inflammation, reduce the agitation and protect the neurocognitive function of the patients.

Key words: Abdominal surgery; Combined anesthesia; Dexmedetomidine; Hemodynamics; Neurocognitive function

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前言

消化道疾病如肝肿瘤、消化性溃疡、肠梗阻等均需要通过腹部手术进行治疗。手术麻醉是可有效缓解患者紧张焦虑的情绪并减轻手术所致的疼痛。目前,各种全麻药单独应用都不够

理想,为克服其不足,常采用联合用药或辅以其他药物,即复合麻醉。复合麻醉是指同时或先后应用两种以上麻醉药物或其他辅助药物以达到完善的手术中和术后镇痛及满意的腹部手术条件^[1,2]。但有研究报道^[3,4]部分患者会在麻醉后出现血流动力学的不稳定,甚至出现神经认知功能障碍,如何改善这一麻醉后

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缺陷是当前麻醉重要的研究问题之一。

吸入七氟烷联合静脉输注瑞芬太尼的静吸复合麻醉是最常见的麻醉维持。近些年有专家提出建议在常见的静吸复合麻醉条件下辅助应用右美托咪定,可以在提高镇痛镇静效果的同时,稳定血压心率,保护患者神经认知功能^[5,6]。因此,本研究选择2016年9月至2017年9月我院在复合麻醉条件下接受腹部手术的患者172例作为研究对象,观察了右美托咪定用于复合麻醉对腹部手术患者血流动力学及对神经认知功能的影响。结果报道如下:

1 资料与方法

1.1 临床资料

表1 两组患者一般临床资料的比较

Table 1 Comparison of the general clinical data between two groups of patients

	Experimental group(n=90)	Control group(n=82)	Statistical value	P value
Age($\bar{x} \pm s$, year)	52.73 $\pm$ 10.38	53.18 $\pm$ 10.90	0.2773	0.7819
Gender[n(%)]			0.1216	0.7273
male	47	45		
female	43	37		
Course of disease($\bar{x} \pm s$, year)	2.31 $\pm$ 1.03	2.03 $\pm$ 1.19	1.6537	0.1000
BMI($\bar{x} \pm s$, kg/m ²)	24.36 $\pm$ 2.36	24.10 $\pm$ 2.09	0.7619	0.4472

1.2 麻醉方法

入选患者均在腹部手术前12小时开始禁食、4小时禁水。进入手术室后,监测血压、血氧饱和度、心率、心电图等指标。由同一组麻醉医师进行手术过程中麻醉。全麻诱导采用静脉输注丙泊酚(生产厂家:北京费森尤斯卡比医药有限公司 生产批号:国药准字 H20153093)2 mg/kg、咪达唑仑(生产厂家:江苏恩华药业股份有限公司 生产批号:国药准字 H20143222)2 mg、顺式阿曲库铵 0.15 mg/kg、芬太尼 4 μ g/kg。腹部手术过程中采用静吸复合麻醉:瑞芬太尼(生产厂家:江苏恩华药业股份有限公司 生产批号:国药准字 H20143314)1.5 μ g/(kg $\cdot$ h)泵注,吸入七氟烷(生产厂家:鲁南贝特制药有限公司 生产批号:国药准字 H20080681)0.6至1最低肺泡有效浓度,间断给予顺式阿曲库铵 0.05 mg/kg。观察组在麻醉诱导前微泵输注右美托咪定(生产厂家:江苏恒瑞医药股份有限公司 生产批号:国药准字 H20110097)1 μ g/kg,对照组对应给予同剂量生理盐水对比研究。

1.3 观察指标

① 记录两组在整个麻醉期间的血流动力学变化,主要观察

本研究取得医院医学伦理委员会讨论同意。选择2016年9月至2017年9月在我院接受复合麻醉条件下腹部手术(肝癌根治术)的患者172例。纳入标准:① 年龄超过18岁;② 有腹部手术指证的疾病;③ 术前神经认知功能无障碍;④ 患者及其家属对本研究充分知情,并签字同意。排除标准:① 有颅脑损伤、脑卒中、脑肿瘤等病史;② 患精神障碍疾病;③ 曾经或正在使用可致精神类副反应的药物;④ 有严重的高血压、冠心病、糖尿病等基础疾病史;⑤ 曾接受过右美托咪定,患者不适应甚至出现过敏。按照随机分配的原则将入选患者分为试验组(n=90)及对照组(n=82)。两组患者一般资料如年龄、性别分布、病程及体重指数等方面比较差异均无明显统计学意义(P>0.05),具有可比性。见表1。

指标为血压及心率;⑥ 记录拔管时间及发生躁动的例数;⑦ 在拔管前、拔管时、拔管后2 h三个阶段,分别抽取患者的静脉血5 mL,采用ELISA检测血清炎症因子包括肿瘤坏死因子 α (TNF- α)、白介素6(IL-6)、钙粒蛋白 β (S100 β)水平,试剂盒由美国RD公司提供;⑧ 术后24h对入选患者进行简易精神状态量表(MMSE)评估神经认知功能,测试满分为30分,分数越低,代表神经认知功能受损越重。

1.4 统计学分析

选择spss18.0对本次研究数据进行统计分析。计量资料数据采用均数 $\pm$ 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为差异具有统计学意义。

2 结果

2.1 两组患者拔管前后血流动力学的比较

试验组拔管前、拔管时及拔管后2 h的平均动脉压及心率均明显低于对照组,差异具有统计学意义(P<0.05),见表2。

表2 两组患者拔管前后的血流动力学比较

Table 2 Comparison of the hemodynamics between two groups of patients before and after extubation

	Mean arterial pressure($\bar{x} \pm s$, mmHg)			Heart rate($\bar{x} \pm s$, BPM)		
	Before extubation	Extubation	At 2 hours after extubation	Before extubation	Extubation	At 2 hours after extubation
Experimental group(n=90)	103.25 $\pm$ 6.98	110.36 $\pm$ 7.25	102.36 $\pm$ 5.25	70.55 $\pm$ 5.25	74.36 $\pm$ 6.21	68.61 $\pm$ 4.92
Control group(n=82)	112.39 $\pm$ 5.93	118.69 $\pm$ 6.35	111.09 $\pm$ 5.93	81.02 $\pm$ 5.68	86.39 $\pm$ 4.68	83.17 $\pm$ 6.25
Pvalue	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

2.2 两组患者拔管时间及躁动发生情况的比较 及 5.55%, 均显著低于对照组, 差异具有统计学意义($P<0.05$), 试验组的拔管时间及躁动发生率分别为(11.07 ± 2.82)min 见表 3。

表 3 两组患者的拔管时间与躁动发生情况比较

Table 3 Comparison of the extubation time and incidence of restlessness between two groups of patients

	Time of extubation ($\bar{x}\pm s$, min)	Number of restless cases[n(%)]
Experimental group(n=90)	11.07± 2.82	5(5.55)
Control group(n=82)	18.81± 3.28	12(14.63)
P value	<0.0001	0.0463

2.3 两组患者血清炎症因子水平比较 水平均明显低于对照组, 差异具有统计学意义($P<0.05$), 见表 4。试验组拔管前、拔管时、拔管后 2 h 的血清 TNF- α 及 IL-6

表 4 两组患者拔管前后血清炎症因子水平的比较

Table 4 Comparison of the serum levels of inflammatory factors between two groups of patients before and after extubation

	TNF- α ($\pm s$, pg/ml)			IL-6($\bar{x}\pm s$, pg/ml)		
	Before extubation	Extubation	At 2 hours after extubation	Before extubation	Extubation	At 2 hours after extubation
Experimental group(n=90)	305.47± 30.69	332.98± 36.25	299.14± 32.08	31.25± 5.27	39.98± 4.93	33.11± 2.08
Control group(n=82)	338.36± 29.81	427.36± 41.37	351.04± 40.93	41.36± 5.18	49.01± 5.05	45.22± 3.99
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

2.4 两组患者术后 24 小时的神经功能情况比较 0.56)ug/L, 明显低于对照组, 而 MMSE 评分为(28.35 ± 2.14)分, 术后 24 小时, 试验组的血清 S100 β 蛋白水平为 ($1.32\pm$ 显著高于对照组, 差异具有统计学意义($P<0.05$), 见表 5。

表 5 两组患者术后 24 小时的神经功能比较

Table 5 Comparison of the nerve function between two groups of patients at 24h after operation

	S100 β ($\bar{x}\pm s$, μ g/L)	MMSE($\bar{x}\pm s$, scores)
Experimental group(n=90)	1.32± 0.56	28.35± 2.14
Control group(n=82)	3.17± 1.02	22.01± 3.98
P value	<0.0001	<0.0001

3 讨论

常见的静吸复合麻醉即瑞芬太尼联合七氟醚被广泛应用于各类腹部手术中。瑞芬太尼是阿片类镇痛药的一种, 代谢清除快、苏醒快、不依赖肝肾起效, 七氟醚是吸入性麻醉的一种, 时效短、麻醉深度易被调节^[7,8]。但有文献报道在静吸复合麻醉过程中出现痛觉过敏、出现躁动、心率血压升高等不良反应, 而迅速觉醒后立即感觉到的不适是造成术后躁动的重要原因, 易导致手术患者出现神经认知功能损伤、心肌缺血、脑出血等危险^[9,10]。如何在使用复合麻醉的腹部手术患者中, 稳定麻醉期间的血压心率, 减少应激反应, 提高神经认知功能保护, 是麻醉关注的重要焦点问题^[11,12]。

有临床研究显示在腹部手术的患者中, 复合麻醉时同时使用右美托咪定可以有效的解决以上问题^[13,14]。在 20 世纪 90 年代, Hoffman 等发现右美托咪定对重要器官如脑、心等有重要的器官保护作用^[15]。动物实验结果显示右美托咪定可以有效降低齿状回及海马的细胞凋亡, 有利于神经功能的保护^[16]。而在腹部手术过程中, 气腹的建立、手术的创伤均会引起体内炎症

因子的大量释放, 如 TNF- α 及 IL-6 等^[17]。这些炎症因子不仅会产生瀑布级联反应, 还能够促使血流动力学的不稳定性, 透过血脑屏障损害脑组织。故有专家学者提出降低麻醉期间产生的大量炎症因子是最重要的关键手段。最新的文献显示右美托咪定能够抑制机体炎症因子的释放, 减轻全身的炎症系列反应, 稳定血压心率, 降低神经认知功能的损伤, 其具体作用机制可能为下调了炎症因子的表达, 减轻了应激反应, 避免了血流动力学的波动^[18,20]。

本次研究结果显示应用右美托咪定的患者血清 TNF- α 及 IL-6 炎症因子水平显著低于对照组, 与 Khare A^[21]等研究较为一致。另外, 使用了右美托咪定的 90 例患者血压心率波动均较小, 这是因为右美托咪定具有抗交感的作用, 可以降低血浆中儿茶酚胺水平, 对于稳定血流动力学具有较好的保护作用。Hernández G^[22]等发现在缺血再灌注治疗过程中, 应用右美托咪定可以减少低氧饱和度的小静脉数量, 提高脑等组织的氧耗, 改善代谢状况, 维持脑氧的供需平衡, 有利于降低神经认知的损伤。使用右美托咪定可以使躁动发生率降低 1.64 倍, 而将 MMSE 评分提高至(28.35 ± 2.14)分。S100 β 蛋白是神经胶质细

胞的一种标志物,其含量水平可以反映神经胶质细胞的损伤程度及预后情况^[23,24]。Patil Y^[25]等研究发现右美托咪定能使 S100 β 蛋白稳定在较低水平,这与本次研究的结果一致,说明了右美托咪定确实能发挥神经功能保护作用。

本次研究仍存在以下两点不足:① 本次研究的观察时间范围较短,只观察了麻醉期间至拔管后 2h,需要进一步探讨患者后续的机体炎症反应、认知功能变化等;② 不同疾病是否会对患者接受手术产生炎症反应有不同的结果,需要在后续研究中扩大病例数,细化内容、分类讨论。

综上所述,右美托咪定应用于施行复合麻醉的腹部手术患者可以更有效的稳定血流动力学,减轻炎症反应,减少躁动,保护患者神经认知功能。

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