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不同剂量右美托咪定对妇科腹腔镜手术患者应激反应、血流动力学和术后认知功能的影响*

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摘要 目的:探讨不同剂量右美托咪定对妇科腹腔镜手术患者血流动力学、术后认知功能以及应激反应的影响。**方法:**选取2016年3月~2018年5月在我院行妇科腹腔镜手术的150例患者,按照随机数字表法分为甲、乙、丙三组,各50例,甲组在麻醉诱导后以 $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 的速率输注右美托咪定,乙组在麻醉诱导后以 $0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 的速率输注右美托咪定,丙组给予患者注射等量生理盐水,对比不同时间点三组患者血流动力学变化情况、应激指标、麻醉恢复时间、气腹时间、拔管时间、麻醉恢复室(PACU)停留时间、改良镇静-躁动评分(RASS)、不良反应发生率,统计患者术后认知功能障碍(POCD)发生情况。**结果:**T0(麻醉诱导前10 min)时,三组HR、MAP对比差异无统计学意义($P>0.05$);T1(气管插管后1 min)、T2(气腹后5 min)时,甲组、乙组HR、MAP均低于丙组,甲组HR、MAP低于乙组($P<0.05$);T3(术毕)时,甲组、乙组HR均低于丙组($P<0.05$),甲、乙、丙三组MAP对比,差异无统计学意义($P>0.05$)。甲、乙两组术后1 h、6 h、12 h时RASS评分均低于丙组($P<0.05$),甲组术后1 h、6 h、12 h时RASS评分低于乙组($P<0.05$);T1、T2、T3时,甲组、乙组去甲肾上腺素(NA)、促肾上腺皮质激素(ACTH)水平均低于丙组,甲组NA、ACTH水平均低于乙组($P<0.05$)。甲、乙组拔管时间、PACU停留时间均短于丙组,甲组短于乙组($P<0.05$)。甲组、乙组、丙组术后POCD发生率为2.00%(1/50)、10.00%(5/50)、24.00%(12/50),甲组POCD发生率低于丙组($P<0.05$)。三组麻醉恢复时间、气腹时间、不良反应发生率相比较,差异无统计学意义($P>0.05$)。**结论:**妇科腹腔镜术患者围术期应用右美托咪定有利于维持血流动力学稳定,减轻应激反应,降低术后认知功能障碍发生率,其中 $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 右美托咪定作用更明显。

关键词:右美托咪定;腹腔镜手术;认知功能;血流动力学;应激反应

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Effects of Different Doses of Dexmedetomidine on Stress Response, Hemodynamics and Postoperative Cognitive Function in Patients Undergoing Gynecological Laparoscopic Surgery*

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ABSTRACT Objective: To investigate the effects of dexmedetomidine on postoperative cognitive function, hemodynamics and stress response in patients undergoing laparoscopic gynecological surgery. **Methods:** 150 cases of gynecological laparoscopic surgery in our hospital from March 2016 to May 2018 were selected as the study object, they were divided into three groups according to random number table method. Dexmedetomidine was infused at a rate of $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ in group A, dexmedetomidine was infused at a rate of $0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ in group B after anesthesia induction, while patients in the group C was given the same amount of normal saline. The hemodynamic changes, stress indicator, anaesthesia recovery time, pneumoperitoneum time, extubation time, residence time of PACU, improved sedation - agitation score (RASS) were compared among the three groups at different time points. The occurrence of postoperative cognitive dysfunction (POCD) in the patients were recorded. **Results:** At T0(10 minutes before anesthesia induction), there were no significant differences in HR and MAP in the three groups ($P>0.05$). At T1 (1 min after tracheal intubation) and T2 (5min after pneumoperitoneum), HR and MAP in group A and group B were lower than those in group C, while HR and MAP in group A were lower than those in group B ($P<0.05$). At T3(end of surgery), HR in group A and group B were lower than that in group C ($P<0.05$). There were no significant differences in group A, group B and group C ($P>0.05$). The RASS score of group A and group B at 1 h, 6 h and 12 h after surgery were lower than that of group C ($P<0.05$), while that of group A at 1h, 6h and 12h after surgery was lower than that of group B ($P<0.05$). At T1, T2 and T3, the levels of Norepinephrine(NA) and Adrenocorticotropic hormone(ACTH) in group A and group B were lower than those in group C, while those in group A were lower than those in group B ($P<0.05$). The incidence of postoperative POCD in group A, group B, group C were 2.00% (1/50), 10.00% (5/50), 24.00% (12/50) respectively, the incidence of POCD in group A was

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lower than that in group C ($P<0.05$). There was no significant difference in the recovery time of anesthesia and pneumoperitoneum in the three groups ($P>0.05$). **Conclusion:** The perioperative application of dexmedetomidine in gynecological laparoscopic surgery is conducive to maintaining hemodynamic stability, reducing stress response and reducing the incidence of postoperative cognitive dysfunction, of which the effect of $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ dexmedetomidine is more obvious.

Key words: Dexmedetomidine; Laparoscopy surgery; Cognitive function; Hemodynamics; Stress response

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前言

现阶段,腹腔镜因具有微创特点,已被广泛应用于妇科手术中^[1,2]。相较于传统手术,腹腔镜手术具有微创、痛苦小、术后恢复快、并发症发生率低等诸多优点^[3,4],尽管腹腔镜手术优势众多,但同时也会对呼吸循环系统产生一定影响,引发机体应激反应,影响术中血流动力学稳定性,故为了减轻机体应激反应,需科学选择麻醉药物^[5,6]。盐酸右美托咪定属于 α_2 肾上腺素能受体激动剂,能对交感神经兴奋进行抑制,具有理想的镇静效果^[7],但临床关于右美托咪定在妇科腹腔镜手术中的使用剂量尚未见定论,且对妇科腹腔镜手术患者的认知功能、血流动力学以及应激反应的影响尚未明确。鉴于此,本研究探讨了不同剂量右美托咪定应用于妇科腹腔镜术对患者血流动力学、应激反应及术后认知功能的影响,旨在为妇科腹腔镜术中右美托咪定的使用剂量提供一定参考,现报道如下。

1 资料与方法

1.1 一般资料

将2016年3月~2018年5月在我院行妇科腹腔镜手术的150例患者作为研究对象,纳入标准: \oplus 患者知情同意; \ominus 美国麻醉医师协会(American society of anesthesiologists, ASA)分级为I-II级^[8]; \oplus 无凝血功能障碍; \ominus 研究获得我院医学伦理委员会批准。排除标准: \oplus 既往有开腹手术史; \ominus 存在代谢性疾病; \oplus 存在严重心、肝、肾等器质性疾病; \ominus 存在精神障碍。按照随机数字表法将患者分为甲、乙、丙三组,其中甲组患者共50例,年龄23~48岁,平均年龄(34.92 ± 1.05)岁,体重42~62 kg,平均(52.16 ± 3.28)kg;多囊卵巢综合征、子宫肌瘤、异位妊娠患者分别有18例、17例、15例;ASA分级I、II级患者分别有26例、24例。乙组患者共50例,年龄21~47岁,平均年龄(35.09 ± 1.02)岁,体重43~61 kg,平均(52.13 ± 3.25)kg;多囊卵巢综合征、子宫肌瘤、异位妊娠患者分别有19例、15例、16例;ASA分级I、II级患者分别有28例、22例。丙组患者共50例,年龄23~47岁,平均年龄(35.13 ± 1.09)岁,体重42~61 kg,平均(52.09 ± 3.23)kg;多囊卵巢综合征、子宫肌瘤、异位妊娠患者分别有16例、18例、16例;ASA分级I、II级患者分别有27例、23例。对比三组患者年龄、体重、疾病类型及ASA分级,差异无统计学意义($P>0.05$),具有可比性。

1.2 方法

三组患者入术后均快速开放静脉通道,同时输注乳酸钠林格注射液(四川科伦药业股份有限公司批准文号:国药准字H20055488 规格:500 mL*12瓶),行全麻诱导时,采用枸橼酸芬太尼(人福医药股份有限公司,批准文号:H42022076 规格:

0.1 mg×10支) $3 \mu\text{g}/\text{kg}$,注射用苯磺顺阿曲库胺(浙江仙琚制药股份有限公司 批准文号:国药准字 H200090202 规格:5 mg×10支) $0.15 \mu\text{g}/\text{kg}$,丙泊酚乳状注射液(西安力邦制药有限公司 批准文号:国药准字 H19990282 规格:0.2 g×5支) $1.5 \mu\text{g}/\text{kg}$,咪达唑仑注射液(江苏恩华药业股份有限公司 批准文号:国药准字 H10980025 规格:10 mg×5支) $0.06 \mu\text{g}/\text{kg}$,诱导完成后行气管插管操作,连接呼吸机,进行人工通气,通气频率设置为12~15次/min,潮气量设置为8~10 mL/kg,氧流量设置为3 L/min,呼吸比设置为1:2,二氧化碳分压设置为35~45 mmHg,对患者血氧饱和度、心率(Heart Rate, HR)以及血压进行常规监测;行麻醉维持时,输注瑞芬太尼(人福医药股份有限公司,批准文号:H20030197 规格:1 mg×5瓶) $0.3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$,丙泊酚3~5 mg·kg⁻¹·h⁻¹,同时间断性静注苯磺顺阿曲库胺0.04~0.05 mg/kg;行麻醉诱导前10 min,三组患者均给予负荷量 $1.0 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 盐酸右美托咪定(扬子江药业集团有限公司 批准文号:国药准字 H20183219 规格:0.2 mg×4支),甲组在麻醉诱导后给予患者输注 $0.8 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 右美托咪定,乙组输注 $0.4 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ 右美托咪定,一直到手术结束前30 min,丙组输注等量生理盐水。

1.3 观察指标

(1) 血流动力学:对比三组患者T0(麻醉诱导前10 min)、T1(气管插管后1 min)、T2(气腹后5 min)、T3(术毕)时的平均动脉压(Mean arterial pressure, MAP)、HR。(2) 改良镇静-躁动评分(Richmond agitation sedation scale, RASS) 术后1 h、术后6 h以及术后12 h对三组患者进行RASS评分^[9]。(3) 应激反应指标:分别在T0、T1、T2、T3时抽取三组患者静脉血,检测血浆去甲肾上腺素(Norepinephrine, NA)、促肾上腺皮质激素(Adrenocorticotropic hormone, ACTH)水平。(4) 术后认知功能障碍(Postoperative cognitive dysfunction, POCD)发生情况:术后1 d采用简易精神状态量表(Mini-Mental State Examination, MMSE)对三组患者认知功能状况进行评价,27~30分表示认知正常,<27分表示存在认知功能障碍^[10]。(5) 对比三组麻醉恢复时间、气腹时间、拔管时间、PACU停留时间以及不良反应发生情况。

1.4 统计学分析

选择SPSS 24.0分析数据,计数资料以%表示,行 χ^2 检验。计量资料以($\bar{x} \pm s$)表示,两两间比较行t检验,多组间比较行单因素方差分析,多时点观测资料行重复测量方差分析。检验标准 $\alpha=0.05$ 。

2 结果

2.1 各组不同时间点血流动力学指标对比

T1、T2时甲组、乙组HR、MAP均低于丙组,甲组HR、

MAP 低于乙组($P<0.05$)。T3 时,三组 HR 整体比较差异有统计学意义($P<0.05$),甲组、乙组 HR 均低于丙组($P<0.05$);三

组 MAP 对比差异无统计学意义($P>0.05$),见表 1。

表 1 不同时间点血流动力学指标对比($\bar{x}\pm s$)
Table 1 Comparison of hemodynamic indexes at different time points($\bar{x}\pm s$)

Indexes	Groups	T0	T1	T2	T3
HR(times/min)	group A(n=50)	84.15±5.25	84.56±8.63*&	83.56±9.45*&	78.96±6.15*
	group B(n=50)	86.23±8.52	88.56±8.56*	87.65±8.15*	78.25±8.12*
	group C(n=50)	85.56±5.52	91.46±9.28	99.26±5.52	87.52±8.25
MAP(mmHg)	group A(n=50)	75.85±7.52	77.45±8.45&	79.35±7.15*&	78.46±6.12
	group B(n=50)	74.46±8.52	82.58±7.25*	83.56±9.45*	79.52±6.52
	group C(n=50)	74.59±8.52	89.45±9.52	94.78±9.15	80.56±7.15

Note: compared with group B, * $P<0.05$; compared with group C, * $P<0.05$.

2.2 三组 RASS 评分对比

甲、乙两组术后 1 h、6 h、12 h 时 RASS 评分均低于丙组

($P<0.05$);甲组术后 1 h、6 h、12 h 时 RASS 评分低于乙组($P<0.05$),见表 2。

表 2 三组 RASS 评分对比($\bar{x}\pm s$,分)
Table 2 Comparison of RASS scores in three group($\bar{x}\pm s$,scores)

Groups	1h after surgery	6h after surgery	12h after surgery
group A(n=50)	-0.68±0.15*&	0.01±0.01*&	0.31±0.02*&
group B(n=50)	-0.56±0.21*	0.29±0.12*	0.45±0.12*
group C(n=50)	0.58±0.12	0.39±0.25	0.59±0.15

Note: compared with group B, * $P<0.05$; compared with group C, * $P<0.05$.

2.3 三组应激反应对比

T1、T2、T3 时,甲组、乙组 NA、ACTH 均低于丙组,甲组

NA、ACTH 均低于乙组($P<0.05$),见表 3。

表 3 三组应激反应对比($\bar{x}\pm s$,pg/mL)
Table 3 Comparison of stress response among three groups($\bar{x}\pm s$,pg/mL)

Indexes	Groups	T0	T1	T2	T3
NA	group A(n=50)	227.89±15.52	302.15±5.63*&	311.25±3.15*&	285.12±1.25*&
	group B(n=50)	227.91±15.02	318.96±5.05*	325.63±2.58*	290.15±2.85*
	group C(n=50)	228.02±15.49	344.52±6.15	369.98±6.38	313.25±2.85
ACTH	group A(n=50)	12.32±2.15	23.45±1.05*&	25.15±2.05*&	36.18±2.56*&
	group B(n=50)	12.35±2.12	32.56±1.03*	35.96±3.58*	45.15±6.35*
	group C(n=50)	12.38±2.29	45.85±3.26	57.89±4.56	61.48±6.52

Note: compared with group B, * $P<0.05$; compared with group C, * $P<0.05$.

2.4 三组麻醉恢复时间、气腹时间、拔管时间、PACU 停留时间的比较

对比三组麻醉恢复时间、气腹时间,差异无统计学意义($P>0.05$);甲、乙组拔管时间、PACU 停留时间均短于丙组,甲组短于乙组($P<0.05$),见表 4。

2.5 各组不良反应和 POCD 发生情况对比

甲组术后 POCD 发生率为 2.00%(1/50),低于丙组的 24.00%(12/50)($\chi^2=10.698, P=0.001$)。乙组术后 POCD 发生率为 10.00%(5/50),与甲组、丙组的 POCD 发生率相比差异无统计学意义($\chi^2=2.837, 3.473, P=0.092, 0.062$)。三组患者均未出现

呼吸抑制、心律失常等情况,仅出现恶心呕吐的不良反应,甲、乙、丙三组恶心呕吐发生率分别为 10.00%(5/50)、8.00%(4/50)、6.00%(3/50),组间两两比较差异无统计学意义($\chi^2=0.122, 0.543, 0.154, P=0.727, 0.461, 0.685$)。

3 讨论

随着内镜技术发展水平提高,腹腔镜已被广泛应用于各类妇科疾病治疗中^[1],虽然妇科腹腔镜手术具有微创、术后恢复快的优点,但术中 CO₂ 气腹会造成机械性刺激与高碳酸血症,进而引发一系列生理病理变化,导致下丘脑-垂体-肾上腺轴

表 4 三组麻醉恢复时间、气腹时间、拔管时间、PACU 停留时间的比较($\bar{x} \pm s$, min)Table 4 Comparison of anesthesia recovery time, pneumoperitoneum time, extubation time and PACU stay time among the three groups ($\bar{x} \pm s$, min)

Groups	Anesthesia recovery time	Pneumoperitoneum time	Extubation time	Residence time of PACU
group A(n=50)	7.75±2.56	46.58±8.52	21.52±2.58* ^{&}	25.63±2.52* ^{&}
group B(n=50)	6.98±2.12	45.46±8.35	28.96±3.28*	27.15±1.22*
group C(n=50)	7.59±2.16	46.85±7.15	35.69±4.28	33.58±2.39
F	1.576	0.421	210.893	197.142
P	0.210	0.657	0.000	0.000

Note: compared with group B, *P<0.05; compared with group C, *P<0.05.

异常激活,促使机体出现应激反应^[12-14]。为预防此类应激反应,临床通常采用联合用药、气管插管的方式。理想的麻醉药物不仅能使患者意识消失,同时还会对围术期各种伤害性刺激引发的应激反应进行抑制,最大程度上减小对血流动力学产生的影响,确保手术顺利进行^[15,16]。

右美托咪定主要通过血管运动中枢、脑干蓝斑区α2受体发挥抗交感作用,可激活神经节突触前膜上肾上腺素能受体,并通过负反馈机制对节前神经细胞肾上腺素的释放进行抑制,防止交感神经过度兴奋^[17-19],与此同时,右美托咪定还可通过激活α2肾上腺素能受体促使交感神经节细胞膜超极化,抑制交感神经去甲上腺素的释放,降低交感神经活性,进而达到抗交感作用^[20,21]。右美托咪定还具有理想的镇痛、镇静作用,可和麻醉药物协同作用,达到加深麻醉的效果,对CO₂气腹建立后引发的应激反应进行抑制,维持血流动力学稳定^[22]。研究显示,右美托咪定对血流动力学的影响受给药剂量的影响^[23]。本研究中,不同时间点甲组HR、MAP波动最小,乙组次之,丙组最大;甲、乙组拔管时间、PACU停留时间均短于丙组,甲组短于乙组,提示妇科腹腔镜术围术期应用右美托咪定利于维持血流动力学稳定,且0.8 μg·kg⁻¹·h⁻¹右美托咪定作用更加明显,这可能是因为高浓度右美托咪定可通过对儿茶酚胺激素释放、交感神经兴奋进行抑制,进而维持血流动力学稳定^[24]。

氧化应激是机体在创伤过程中内环境发生变化的另一种特征,炎症反应、疼痛以及手术创伤均属于应激源,能激活氧化应激反应。NA、ACTH均为临床两种常见的氧化应激反应指标,NA主要由脑内去甲肾上腺素能神经元、交感节后神经元分泌、合成,正常人体内NA水平较低,在炎症反应、疼痛以及手术创伤等情况下,其水平明显提高^[25]。ACTH为肾上腺皮质活性的主要调节者,通过对其水平进行测定,可有效反映下丘脑-垂体-肾上腺皮质的功能状态,手术、创伤等情况下,其水平会明显升高^[26]。本研究中,T1、T2、T3时,甲组、乙组NA、ACTH均低于丙组,甲组NA、ACTH均低于乙组;甲组术后1h、6h、12h时RASS评分低于乙组,甲组T1、T2、T3时NA、ACTH均低于乙组,提示0.8 μg·kg⁻¹·h⁻¹右美托咪定减轻妇科腹腔镜手术后应激反应的作用更为明显。POCD是术后常见的并发症,主要表现为社交能力变化、人格改变、精神错乱、记忆力下降等^[27],这是因为建立CO₂气腹会对肺部机械性压迫,导致气道中气体流通不畅,同时大量CO₂快速弥漫进入血液中,引起机体供氧不足,进而引起认知功能损害^[28-30]。本研究中,甲组术后POCD发生率为2.00%(1/50),低于丙组的24.00%,提示0.8 μg·kg⁻¹·h⁻¹右美托咪定可降低术后POCD发生率,除此之外,本研究结果还显示,三组麻醉恢复时间、气腹时间、不良反应回比无差异,提示不同剂量的右美托咪定应用于妇科腹腔镜手术中不会对术后麻醉恢复、不良反应发生情况产生实质影响。

综上所述,在相同气腹条件下,妇科腹腔镜术中应用0.8 μg·kg⁻¹·h⁻¹右美托咪定维持血流动力学稳定,减轻应激反应,可降低术后POCD发生率。

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