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右美托咪定在腹腔镜全子宫切除术中的应用效果 *

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摘要 目的：探讨右美托咪定在腹腔镜全子宫切除术中的应用效果及对抗凝血酶 (AT) Ⅲ、D-二聚体 (D-D)、纤维蛋白降解产物(FDP)、皮质醇(Cor)的影响。**方法：**选择 2015 年 5 月至 2016 年 10 月我院接诊的 90 例行腹腔镜全子宫切除术的患者，通过随机数表法分为观察组(n=45)和对照组(n=45)。两组均采用静脉吸入复合全麻，观察组在入室后给予 1 μg/kg 的右美托咪定(10 min 内完成输注)，之后以 0.5 μg/(kg·h)的速度持续泵注，持续输注 60 min；对照组以同样的方式输注生理盐水。比较两组在 T0(麻醉前)、T1(麻醉后 10 min)、T2(拔管后)、T3(术后 24 h)各时点血流动力学、纤溶功能及应激反应的变化。**结果：**对照组在 T1、T2 时平均动脉压(MAP)、心率(HR)较 T0 时点显著升高(P＜0.05)，T3 时回落至正常水平；观察组各时点 MAP、HR 均无明显变化(P＞0.05)；两组 T1、T2 时点 ATⅢ均显著降低，D-D、FDP 显著升高(P＜0.05)，观察组 T3 时点 ATⅢ、D-D、FDP 均恢复到正常水平，与 T0 时比较无显著差异(P＞0.05)，但对照组各指标和 T0 时比较仍具有显著差异(P＜0.05)，观察组在各时点 ATⅢ均高于对照组，D-D、FDP 均低于对照组(P＜0.05)；与 T0 比较，两组 T1、T2、T3 时点 Cor 均显著升高(P＜0.05)；但观察组在 T1、T2、T3 时点 Cor 均比对照组低(P＜0.05)。**结论：**右美托咪定用于腹腔镜全子宫切除术有助于维持患者血流动力学稳定，改善应激反应及纤溶功能，麻醉效果优异。

关键词：腹腔镜；全子宫切除术；右美托咪定；纤溶功能；应激反应

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Efficacy of Dexmedetomidine in Treatment of Laparoscopic Panhysterectomy *

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ABSTRACT Objective: To study the efficacy of dexmedetomidine in the treatment of laparoscopic panhysterectomy and its effects on the serum antithrombin(AT)Ⅲ, D-dimer(D-D), Fibrin degradation product (FDP) and cortisol(Cor) levels. **Methods:** 90 patients of laparoscopic panhysterectomy who were treated from May 2015 to October 2016 in our hospital were selected. According to the random number table, those patients were divided into the observation group (n=45) and the control group (n=45). The observation group was given 1 μg/kg dexmedetomidine after entering the operation room (complete infusion within 10 min), then 0.5 μg/(kg·h)of the speed of continuous pump, continuous infusion for 60 minutes, the control group received saline in the same way. The changes of hemodynamics, fibrinolytic function and stress response were compared between the two groups at T0 (before anesthesia), T1(after anesthesia10min), T2 (after extubation), T3 (postoperative 24h). **Results:** At T1 and T2, the mean arterial pressure (MAP) and heart rate (HR) in the control group were significantly higher than those of T0(P＜0.05), and T3 down to normal level; there was no significant change in MAP and HR at each time point in the observation group (P＞0.05); At T1 and T2 point, the ATⅢ in two groups significantly reduced, D-D and FDP significantly increased (P＜0.05). At T3 point, the ATⅢ, D-D and FDP in the observation group restored to normal level, and there was no significant difference compared with T0 (P＞0.05), but there were significant differences in the control group compared with T0 point (P＜0.05); The AT III in the observation group were higher than that of the control group at each time point, and the D-D and FDP were lower than those of the control group (P＜0.05); Compared with T0 point, two groups Cor at T1, T2 and T3 point significantly increased (P＜0.05); Cor in the observation group were lower than that of the control group at T1, T2 and T3 point (P＜0.05). **Conclusion:** Laparoscopic hysterectomy combined with dexmedetomidine contributed to maintain the hemodynamic stability, improve the stress response and fibrinolytic function, the anesthesia effect was good, it's worthy of application and promotion.

Key words: Laparoscope; Panhysterectomy; Dexmedetomidine; Fibrinolytic function; Stress response

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前言

随着内镜技术的不断进步和发展,腹腔镜子宫切除术已广泛应用于临床,其具有创伤小、术后恢复快、住院时间短等优点[1]。但较多研究显示手术及麻醉过程仍会对患者造成较强的疼痛刺激、牵拉反射等,极易诱发全身性应激反应,致使凝血因子水平升高,增强血小板活性,令机体处于高凝状态;同时围术期所产生的应激及持续的高凝状态会增加机体纤溶系统的亢进,致使凝血功能障碍,增加血栓、出血等并发症的发生率,不仅给患者带来痛苦,也会影响术后恢复[2,3]。右美托咪定是一种新型α2 肾上腺素能受体激动剂,具有高选择性,可发挥较强的镇痛、抗焦虑效果[4],但其对纤溶功能、应激反应等的影响尚不明确。本研究在腹腔镜全子宫切除术中给予右美托咪定的使用,并探讨其对患者纤溶功能、应激反应的影响,结果报道如下。

1 资料与方法

1.1 一般资料

选择我院接诊的 90 例行腹腔镜全子宫切除术的患者,研究已获得伦理委员会批准。纳入标准[5]:① 经过临床诊断、B 超等确诊为子宫肌瘤;② 美国麻醉医师协会(ASA)分级为Ⅰ、Ⅱ级;③ 近期未服用过激素类药物;④ 对此次研究知情同意。排除标准[6]:① 伴有神经系统、内分泌、凝血功能等疾病;② 肝、肾功能不全;③ 严重心血管疾病。通过随机数表法分为 2 组。观察组 45 例,年龄 42~59 岁,平均(50.16± 2.14)岁;ASAⅠ级 24 例,Ⅱ级 21 例。对照组 45 例,年龄 41~58 岁,平均(50.12± 2.17)岁;ASAⅠ级 22 例,Ⅱ级 23 例。两组患者的一般资料比较差异均无统计学意义(P>0.05),具有可比性。

1.2 麻醉方法

两组均采用静脉吸入复合全麻,入室后常规对心率、血压、血氧饱和度等进行监测。

麻醉诱导:0.05 mg/kg 咪达唑仑(规格 2 mL: 2 mg,厂家:宜昌人福药业有限责任公司,国药准字 H20067040)、3 μg/kg 芬太尼(规格 2 mL: 0.1 mg,厂家:宜昌人福药业有限责任公司,国药准字 H42022076)、0.2 mg/kg 顺式阿曲库铵(规格 5 mg,厂家:浙江仙琚制药股份有限公司,国药准字 H20090202)、2 mg/kg 丙泊酚(规格 50 mL: 0.5 g,厂家:AstraZeneca 产品批号 MT923)的静脉注射。气管插管后,使用麻醉剂控制呼吸。术中给予 4~6 mg/(kg·h)丙泊酚,0.1~0.2 μg/(kg·min)瑞芬太尼(规格 1 mg,厂家:宜昌人福药业有限责任公司,国药准字 H20030197)的持续泵注,并吸入 2~3%的七氟烷。手术均由同一级别医师所完成。

观察组在入室后给予 1 μg/kg 的右美托咪定(规格 2 mL: 200 μg,厂家:江苏恒瑞医药股份有限公司,国药准字 H20090248),在 10 min 内输注完毕,之后以 0.5 μg/(kg·h)的速度持续泵注,保持 60 min;对照组以同样的方式输注生理盐水。

1.3 观察指标

在 T0(麻醉前)、T1(麻醉后 10 min)、T2(拔管后)、T3(术后 24 h)各时点记录以下结果:① 血流动力学:平均动脉压(MAP)、心率(HR);② 纤溶功能:抽取 3 mL 空腹静脉血,以酶联免疫吸附法对抗凝血酶(AT)Ⅲ、D- 二聚体(D-D)、纤维蛋白降解产物(FDP)进行检测;③ 应激反应:皮质醇(Cor)的检测采用放免法,试剂盒购于北京东亚放免研究所。

1.4 统计学分析

采用 spss18.0 软件包处理,组内比较以重复测量数据方差分析,组间比较以两两样本 t 检验,计数资料采用 x^2 检验,以 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组各时点血流动力学指标变化的比较

在 T0 时,两组 MAP、HR 比较差异均无统计学意义 (P>0.05);对照组在 T1、T2 时 MAP、HR 均较 T0 时显著升高(P<0.05),T3 时回落至正常水平;观察组各时点 MAP、HR 均无明显变化(P>0.05),见表 1。

表 1 两组各时点血流动力学指标变化的比较($\bar{x}\pm s$)

Table 1 Comparison of the changes of hemodynamics index between two groups at different time points($\bar{x}\pm s$)

Indexes	Groups	T0	T1	T2	T3
MAP(mmHg)	Observation group	85.48± 11.54	86.12± 11.36#	86.43± 11.29#	85.12± 11.62
	Control group	85.53± 11.50	95.69± 12.42*	97.56± 12.17*	85.94± 12.12
HR(time/min)	Observation group	68.19± 5.97	68.72± 5.63#	69.04± 5.18#	67.98± 6.05
	Control group	68.21± 5.95	79.45± 6.28*	84.56± 7.25*	68.14± 5.97

Note: Compared with T0, *P<0.05; compared with the control group, #P<0.05.

2.2 两组各时点 ATⅢ、D-D、FDP 的变化比较

在 T0 时点,两组 ATⅢ、D-D、FDP 水平比较差异无显著用于(P>0.05);两组 ATⅢ在 T1、T2 时点均显著降低,D-D、FDP 均显著升高(P<0.05);在 T3 时点,观察组 ATⅢ、D-D、FDP 均恢复到正常水平,与 T0 时比较无显著差异(P>0.05),但对照组各指标和 T0 时比较仍具有显著差异(P<0.05);观察组在各时点 ATⅢ均高于对照组,D-D、FDP 均低于对照组 (P<0.05),见表 2。

2.3 两组各时点 Cor 水平的变化比较

两组 T0 时点 Cor 比较差异无统计学意义(P>0.05);与 T0 比较,两组 T1、T2、T3 时点 Cor 均显著升高(P<0.05);但观察组在 T1、T2、T3 时点 Cor 均比对照组低(P<0.05),见表 3。

3 讨论

右美托咪定主要通过激动中枢突触后 α2 受体,使神经张力降低,并促使迷走神经活性增加[7]。国内外均研究显示右美托咪定可有效抑制交感神经过度兴奋,并减少交感神经末梢释放去甲肾上腺素,有利于保持围术期血流动力学的稳定[8,9]。在本

表 2 两组各时点 ATⅢ、D-D、FDP 的变化比较($\bar{x}\pm s$)

Table 2 Comparison of the changes of ATⅢ, D-D and FPD between two groups at different time points($\bar{x}\pm s$)

Indexes	Groups	T0	T1	T2	T3
ATⅢ(%)	Observation group	105.67± 9.14	92.45± 7.65*#	79.46± 6.89*#	102.72± 9.46#
	Control group	105.78± 9.05	81.23± 7.18*	62.15± 6.73*	84.59± 8.15*
D-D(μg/L)	Observation group	1.18± 0.22	2.36± 0.35*#	13.74± 3.14*#	1.29± 0.21#
	Control group	1.30± 0.21	4.89± 0.74*	29.87± 4.57*	3.49± 0.34*
FDP(μg/ml)	Observation group	4.04± 1.17	5.83± 1.46*#	21.49± 3.72*#	4.12± 1.15#
	Control group	4.01± 1.20	7.92± 1.54*	38.75± 5.84*	8.04± 1.53*

Note: Compared with T0, *P＜0.05; compared with the control group, #P＜0.05.

表 3 两组各时点 Cor 的变化比较($\bar{x}\pm s$, ng/mL)

Table 3 Comparison of the changes of Cor level between two groups at different time points($\bar{x}\pm s$, ng/mL)

Index	Groups	T0	T1	T2	T3
Cor	Observation group	106.12± 14.58	111.34± 14.93*#	128.45± 15.82*#	156.45± 16.84*#
	Control group	106.31± 14.29	120.58± 15.62*	176.85± 17.94*	214.73± 20.17*

Note: Compared with T0, *P＜0.05; compared with the control group, #P＜0.05.

研究中，应用生理盐水的患者在围术期 MAP、HR 水平波动较大，在术后 24 小时才恢复至正常水平，而应用右美托咪定的患者在各时点均未发生明显变化，证实右美托咪定具有保持血流动力学稳定的优点。和 Reade MC 等[10]的研究具有相似性。

在子宫内，有较多组织纤溶酶原激活物存在，在实施腹腔镜子宫切除术时，会造成受损组织中的组织纤溶酶原激活物在血中释放，促使纤溶酶原激活；并且在手术过程中，可能会造成广泛性的组织缺氧、缺血损伤，释放组织因子，且可能会对血细胞造成破坏，继而释放一系列的促凝活性物质，令患者处于高凝状态，激活纤溶功能，造成原发性纤溶亢进[11,12]。D-D、FDP 在纤溶亢进过程中是两种标志性产物，其表达的增加可反应纤溶亢进严重程度；而患者若长期处于高凝状态，则会消耗较多的 ATⅢ，致使其活性不足，并由于手术对内皮的损伤，降低 ATⅢ的合成，且随着凝血因子的高度活化以及凝血酶的大量生成，ATⅢ也随之被大量消耗[13,14]。本研究显示，两组患者在 T1、T3 时均有不同程度的纤溶亢进，ATⅢ水平降低，而 D-D、FDP 升高，但应用右美托咪定的患者在 T3 时点 ATⅢ、D-D、FDP 均已恢复至正常水平，但应用生理盐水的患者各指标和 T0 时比较仍有明显差异，提示右美托咪定可明显降低纤溶亢进程度。分析是由于右美托咪定具有阻滞交感神经的效果，促使血液流动，避免血液处于高凝状态，进而改善纤溶功能[15,16]。El-Hamid AMA 等[17]研究中也指出，右美托咪定可令术中不利的交感有害刺激明显降低。

较多研究证实麻醉和手术均会给患者造成较强烈的应激反应，若反应过度则可损害机体，对术后恢复造成影响，并增加围术期并发症[18,19]。Cor 由肾上腺皮质束状带所分泌，是反映机体应激反应程度的敏感指标。研究表明无论是机体内部还是来自外源性的不良刺激，均可引发 Cor 的分泌，且和刺激严重程度、持续时间呈正相关，Cor 的升高不仅是人体对刺激的正常反应，也可作为衡量应激水平的客观指标[20,21]。已有较多研究证实，在气管插管即刻，机体便会遭受到应激反应，Cor 水平升高[22,23]。本研究结果也显示拔管后，患者 Cor 水平均呈持续升高趋势，并在拔管后 24 小时达到高峰。Wang X 等[24]研究也显示 Cor 的高峰期多数出现在术后 1 d，一般在术后 3 d 才会逐渐回落到正常水平。但应用右美托咪定的患者在各时点 Cor 水平虽有所升高，但结果仍明显比应用生理盐水的患者要低，通过分析可能和右美托咪定可抑制促肾上腺皮质激素有关，从而令 Cor 的分泌降低，缓解机体应激反应[25]。国外 González-Gil A 等[26]的动物试验显示，右美托咪定有助于降低家兔手术过程中肾上腺激素的分泌。

综上所述，在腹腔镜全子宫切除术中应用右美托咪定有助于保持血流动力学稳定，改善应激反应及纤溶功能，麻醉效果优异。

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