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·临床研究·

右美托咪定对老年胸腔镜肺癌根治术患者拔管时血流动力学及术后疼痛的影响*

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摘要 目的:探讨右美托咪定对老年胸腔镜肺癌根治术患者拔管时血流动力学以及术后疼痛的影响。**方法**:选取 67 例择期行胸腔镜肺癌根治术的老年患者,根据随机数字表法分为对照组(n=33 例)和研究组(n=34 例),均予咪达唑仑、顺苯磺酸阿曲库铵、舒芬太尼、丙泊酚麻醉诱导,对照组同时予 15 mL 生理盐水静脉注射,研究组同时予 0.5 μg/kg 右美托咪定静脉注射(15 min),术毕后均开启自控静脉镇痛(PCIA)泵。监测两组诱导前(T_0)、诱导后 5 min(T_1)、入 PACU 时(T_2)、拔管即刻(T_3)、拔管后 5 min(T_4)血流动力学指标,评估出 PACU 时(T_5)、术后 2 h(T_6)、术后 4 h(T_7)、术后 6 h(T_8)、术后 12 h(T_9)、术后 24 h(T_{10}) 疼痛视觉模拟量表(VAS)评分,检测 T_0、T_8、T_9、T_{10} 动脉血气评价肺功能,同时比较拔管时间、拔管质量评分、镇痛泵按压次数、24 h 舒芬太尼用量及围术期不良反应。**结果**:与 T_0 相比,对照组 T_3、T_4 时平均动脉压(MAP)、心率(HR)、中心静脉压(CVP)升高($P<0.05$),研究组 T_3 时 MAP、HR、CVP 升高($P<0.05$),与对照组相比,研究组 T_3、T_4 时 MAP、HR、CVP 较低 ($P<0.05$);与对照组相比,研究组 T_6、T_7、T_8、T_9、T_{10} 时 VAS 评分较低($P<0.01$);两组 T_8、T_9、T_{10} 时 Qs/Qt 升高($P<0.05$),OI、PaO_2/P_AO_2 降低($P<0.05$),与对照组相比,研究组 T_8、T_9、T_{10} 时 Qs/Qt 较低($P<0.05$),OI、PaO_2/P_AO_2 较高($P<0.05$);与对照组相比,研究组拔管质量评分未见差异($P>0.05$),镇痛泵按压次数较少($P<0.05$),24 h 舒芬太尼用量较少($P<0.01$)。**结论**:右美托咪定可明显稳定老年胸腔镜肺癌根治术拔管期血流动力学,并有较好的术后镇痛效果,一定程度上改善患者术后肺功能。

关键词:肺癌根治术;右美托咪定;血流动力学;术后疼痛

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A Study on the Effect of Dexmedetomidine on the Hemodynamics and Postoperative Pain in Elderly Patients Undergoing Thoracoscopic Radical Resection of Lung Cancer*

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ABSTRACT Objective: To investigate the effect of dexmedetomidine on the hemodynamics and postoperative pain in elderly patients undergoing thoracoscopic radical resection of lung cancer. **Methods:** 67 cases of elderly patients undergoing thoracoscopic radical resection of lung cancer were randomly divided into the control group (n=33 cases) and the study group (n=34 cases), both groups were given midazolam, CIS atracurium, sufentanil, propofol anesthesia, the control group was given saline intravenous 15 mL, and the study group was given 0.5 μg/kg dexmedetomidine intravenous injection (15 min), patient-controlled intravenous analgesia (PCIA) pump were given to both groups after open surgery. The hemodynamic index were detected at before induction (T_0), 5min after induction (T1), PACU (T_2), extubation (T_3), 5 min after extubation (T_4), pain visual analogue scale (VAS) score were compared at PACU (T_5), 2 h after operation (T_6), 4 h after operation (T_7), 6 h after operation (T_8), 12 h after operation (T_9), 24 h postoperative (T_{10}), arterial blood gas indexed were compared at T_0, T_8, T_9,T_{10}, and extubation time, extubation quality score, analgesic pump press times, 24 h sufentanil dosage and perioperative adverse reactions were compared. **Results:** Compared with T_0, the mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP) at T_3, T_4 in control group were increased ($P<0.05$), the MAP, HR and CVP at T3 in the study group were increased($P<0.05$), compared with the control group, the VAS scores at 2h after operation (T_6), 4h after operation (T_7), 6h after operation (T_8), 12 h after operation (T9), 24 h postoperative(T_{10}) in the study group were lower($P<0.05$), the Qs/Qt increased at T_8, T_9 and T_{10} in both groups ($P<0.05$), OI and PaO_2/P_AO_2 were decreased ($P<0.05$). Compared with the control group, the Qs/Qt were lower at T_8, T_9 and T_{10} in study group ($P<0.05$), the OI and PaO_2/P_AO_2 were higher ($P<0.05$). Compared with the control group, there was no significant difference in the quality of extubation in the study group ($P>0.05$), and the number of pain pump pressing and amount of 24 h sufentanil werelower

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(P<0.05). **Conclusion:** Dexmedetomidine can obviously stabilize the hemodynamics of elderly patients undergoing thoracoscopic radical resection of lung cancer during the extubation period, and have better postoperative analgesic effect.

Key words: Radical resection of lung cancer; Dexmedetomidine; Hemodynamics; Postoperative pain

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前言

近年来,伴随人口老龄化加剧,老年肺癌发病率居高不下,其病死率占恶性肿瘤第一位,手术是目前有效的治疗手段[1]。在胸腔镜手术后拔管期,由于疼痛、兴奋、躁动、尿道管等因素刺激,血流动力学波动较大,造成循环剧烈波动[2],甚至可诱发心血管意外。因此,维持拔管期血流动力学相对稳定及良好的术后镇痛对肺癌根治术的治疗效果和预后具有重要临床价值。

右美托咪定(dexmedetomidine,Dex)因有较强的镇静镇痛作用并可产生一定的抗交感神经效果[3]已被广泛用于术前及术后镇痛等。此外,Dex 还可抑制肺癌手术中炎症反应,减轻肺部损伤,并有一定的肺保护作用[4]。本研究对行胸腔镜肺癌根治术老年患者予右美托咪定辅助麻醉,探讨其对拔管期血流动力学与术后镇痛效果的影响,旨在为临床麻醉或 ICU 治疗提供参考。

1 资料与方法

1.1 临床资料

选取 2016 年 2 月至 2017 年 4 月本院择期行胸腔镜肺癌根治术老年患者 67 例,均签署知情同意书。纳入标准:年龄>60 岁,性别不限;美国麻醉医师协会(ASA)分级Ⅰ或Ⅱ级;术后均要求镇痛治疗。排除标准:术前患有严重心、脑血管疾病,和/或伴有免疫系统或内分泌系统疾病;术前服用免疫抑制剂,或行放射、化学治疗。脱落标准:术中快速冰冻切片病理学检查结果提示良性病变;术中出血量≥ 1000 mL;手术时间≥ 4 h。本研究未有脱落病例,根据随机数字表法分为对照组(n=33 例)和研究组(n=34 例),两组性别、年龄、体重、手术时间等临床资料经统计学处理无明显差异(P>0.05),有可比性,见表 1。

表 1 两组一般临床资料比较[($\bar{x}\pm s$),n(%)]

Table 1 Comparison of the baseline clinical information between two groups[($\bar{x}\pm s$),n(%)]

Groups	n	Sex (M/F)	Age (Y)	Height (m)	Weight(kg)	ASA Ⅰ/Ⅱ	Operation time (min)
Control group	33	17/16	69.17± 8.97	1.68± 0.22	60.47± 8.34	19/14	114.36± 16.24
Study group	34	16/18	70.02± 9.16	1.69± 0.24	60.23± 8.28	15/19	119.22± 16.78
P		0.715	0.706	0.860	0.906	0.271	0.233

1.2 干预方法

两组均无术前用药,入室后常规监测 BP、HR、SpO_2 和 ECG,予颈内静脉穿刺置入双腔深静脉导管补液并监测中心静脉压(CVP),同时左桡动脉穿刺监测有创血压。麻醉诱导:咪达唑仑 0.05 mg/kg、顺苯磺酸阿曲库铵 0.2 mg/kg 、舒芬太尼 0.3-0.5 μg/kg 及丙泊酚 1 mg/kg,成功诱导后行双腔气管导管插管,诱导药物使用完毕后对照组予 15 mL 生理盐水静脉注射,研究组 0.5 μg/kg 右美托咪定(江苏恒瑞医药股份有限公司,生产批号 13103032)静脉泵注(浓度 4 μg/mL 持续 15 min)。术中泵注丙泊酚 4～6 mg/(kg·h)、瑞芬太尼 8～10 μg/(kg·h),间断追加顺苯磺酸阿曲库铵维持麻醉,控制脑电双频指数(BIS)值在 40～60 内,$EtCO_2$ 30-40 mmHg。MAP 升高或降低大于 20% 予乌拉地尔或麻黄碱处理,心率大于 120 bpm 或小于 50 bpm 予艾斯洛尔或阿托品处理。缝合切口时予舒芬太尼 5 μg 并开启自控静脉镇痛(PCIA)泵,配方如下:2 μg/kg 舒芬太尼及胃复安 20 mg 用生理盐水配至 100 mL,背景输注速率 2 mL/h,PCI-A 剂量 2 mL,锁定时间 15 min。

1.3 观察指标

(1)血流动力学:在诱导前(T_0)、诱导后 5 min(T_1)、入 PACU 时(T_2)、拔管即刻(T_3)、拔管后 5 min(T_4)监测并记录平均动脉压(MAP)、心率(HR)、中心静脉压(CVP)。(2)疼痛:疼痛视觉模拟量表(VAS)评估疼痛,记录出 PACU 时(T_5)、术后 2 h(T_6)、术后 4 h(T_7)、术后 6 h(T_8)、术后 12 h(T_9)、术后 24h(T_{10})的 VAS 评分,维持 VAS≤ 3 分。(3)相关临床指标:拔管时间、拔管质量评分[5]、拔管后动脉血气(PO_2、PCO_2)、镇痛泵按压次数、24 h 舒芬太尼用量。(4)围术期不良反应:记录恶心呕吐、嗜睡、心动过缓、呼吸抑制等不良反应,并积极予对症处理。

1.4 统计学方法

使用 spss17.0 统计软件分析,计量资料以均数± 标准差($\bar{x}\pm s$)表示,组内比较予单因素方差分析,若有意义两两比较予 LSD 法,组间予独立样本 t 检验,计数资料以(%)表示,予 R× C 卡方检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组不同时点血流动力学指标的比较

T_0、T_1 时,两组 MAP、HR、CVP 比较差异无统计学意义(P>0.05);与对照组相比,研究组 T_2 时 MAP、HR、CVP 较低(P<0.05);与 T_0 时间相比,对照组 T_3、T_4 时 MAP、HR、CVP 升高(P<0.05),研究组 T_3 时 MAP、HR、CVP 升高(P<0.05),T_4 时 MAP、HR、CVP 无变化(P>0.05);与对照组相比,研究组 T_3、T_4

时 MAP、HR、CVP 较低(P＜0.05),见表 2。

表 2 两组不同时间点 MAP、HR、CVP 的比较($\bar{x}\pm s$)

Table 2 Comparison of the levels of MAP, HR, CVP at different time points between two groups($\bar{x}\pm s$)

Groups	n	Time points	MAP(mmHg)	HR(times/min)	CVP(cmH_2O)
Control group	33	T_0	78.07± 8.68	70.24± 10.34	4.62± 0.55
		T_1	83.54± 11.27	76.52± 10.83	4.74± 0.60
		T_2	73.25± 8.81	77.04± 10.88	9.24± 1.26
		T_3	94.46± 13.28[a]	96.03± 12.88[a]	10.37± 1.42[a]
		T_4	83.21± 10.26[a]	82.21± 12.12[a]	8.08± 1.01[a]
Study group	34	T_0	76.68± 8.79	74.41± 10.44	4.64± 0.574
		T_1	82.13± 10.68	74.23± 10.16	4.72± 0.61
		T_2	68.73± 7.25[ab]	69.38± 9.79[ab]	8.39± 1.04[ab]
		T_3	87.82± 11.24[ab]	80.49± 11.23[ab]	9.44± 1.12[ab]
		T_4	79.82± 9.81[b]	74.26± 10.33[b]	5.05± 0.67[b]

Note: compared with T_0, [a]P＜0.05; Compared with control group, [b]P＜0.05.

2.2 两组不同时点 VAS 评分的比较

T_6 时间,两组 VAS 评分比较差异无统计学意义(P＞0.05);与对照组相比,研究组 T_6、T_7、T_8、T_9、T_{10} 时 VAS 评分均显著降低(P＜0.01),见表 3。

表 3 两组不同时间点 VAS 评分的比较($\bar{x}\pm s$,分)

Table 3 Comparison of the VAS scores at different time points between two groups($\bar{x}\pm s$, scores)

Groups	n	Out of PACU(T_5)	Postoperative				
			2h(T_6)	4 h(T_7)	6 h(T_8)	12 h(T_9)	24 h(T_{10})
Control group	33	1.64± 0.22	1.36± 0.27	1.62± 0.24	1.97± 0.23	1.99± 0.22	1.90± 0.34
Study group	34	1.67± 0.23	0.87± 0.14[b]	1.21± 0.10[b]	1.59± 0.09[b]	1.88± 0.38[b]	1.89± 0.27[b]

Note: Compared with control group, [b]P＜0.05.

2.3 两组不同时点肺功能指标的比较

T_0 时,两组 Qs/Qt、OI、PaO_2/P_AO_2 比较差异无统计学意义(P＞0.05);与 T_0 时相比,两组 T_8、T_9、T_{10} 时 Qs/Qt 升高(P＜0.05),OI、PaO_2/P_AO_2 降低(P＜0.05);与同时间对照组相比,研究组 T8、T9、T10 时间 Qs/Qt 较低(P＜0.05),OI、PaO_2/P_AO_2 较高(P＜0.05),见表 4。

表 4 两组不同时间点肺功能指标的比较($\bar{x}\pm s$)

Table 4 Comparison of the index of lung of function at different time points between two groups($\bar{x}\pm s$)

Groups	n	time points	Qs/Qt	OI	PaO_2/P_AO_2
Control group	33	T_0	7.08± 0.94	487.84± 66.53	0.81± 0.11
		T_8	28.46± 4.02[a]	341.37± 47.55[a]	0.75± 0.09[a]
		T_9	33.84± 4.76[a]	288.36± 40.73[a]	0.64± 0.07[a]
		T_{10}	21.59± 3.03[a]	311.63± 44.43[a]	0.67± 0.08[a]
Study group	34	T_0	7.12± 1.01	485.29± 67.08	0.80± 0.10
		T_8	24.54± 3.44 [ab]	371.82± 52.14 [ab]	0.77± 0.09 [ab]
		T_9	27.82± 3.87 [ab]	323.34± 46.12 [ab]	0.68± 0.08 [ab]
		T_{10}	16.19± 2.28 [ab]	348.27± 48.69 [ab]	0.71± 0.09 [ab]

Note: compared with T_0, [a]P＜0.05. Compared with the control group, [b]P＜0.05.

2.4 两组相关临床指标的比较

与对照组相比,研究组拔管时间、拔管质量评分差异无统计学意义(P＞0.05),镇痛泵按压次数较少(P＜0.01),24h 舒芬太尼用量较少(P＜0.01),见表 5。

表 5 两组相关临床指标比较($\bar{x}\pm s$)

Table 5 Comparison of the clinical indicators between two goups($\bar{x}\pm s$)

Groups	n	Extubation time(min)	Extubation quality score	Analgesic pump pressing times (times)	24h amount of sufentanil (μg)
Control group	33	15.83± 2.18	1.77± 0.22	8.74± 1.44	74.62± 8.38
Study group	34	15.92± 2.22	1.84± 0.25	5.97± 0.97[b]	62.14± 7.36[b]

Note: Compared with the control group, [b]P＜0.05.

2.5 两组围术期不良反应发生情况的比较

两组均未出现呼吸抑制,对照组发生恶心 4 例,呕吐 2 例,不良反应的发生率为 18.18%; 研究组发生恶心 3 例, 呕吐 2 例,予雷莫司琼 0.3 mg 静推后症状缓解,不良反应的发生率为 14.71%,与对照组比较差异无统计学意义(P=0.701)。

3 讨论

老年患者交感神经系统活性伴随年龄增长而增强[6],加上重要脏器功能减退,故其手术耐受性差。此外,老年患者因年龄因素自身免疫功能较为低下, 而癌细胞激活体内免疫抑制因子,进一步抑制免疫功能,手术过程中创伤、应激反应、麻醉药物的使用等不可避免的影响老年患者围术期免疫状态[7]。为老年患者的手术创造良好条件,使其平稳、舒适地度过围术期显得尤为重要。在胸科手术中,需行双腔气管插管行单肺通气,但麻醉拔管期麻醉药物停止输注使声门、气道敏感性升高,从而在拔管时引起交感神经兴奋,大量释放儿茶酚胺,导致 BP 升高、HR 增快[8],干扰机体内环境稳定,导致血流动力学紊乱,甚至诱发心血管事件,危及患者生命。

Dex 是一种高选择性 α2 肾上腺素能受体激动剂, 属于咪唑类衍生物,无呼吸抑制[9]。Dex 能通过激动突触后膜 α2A 受体抑制交感神经活性,引起 BP、HR 下降[10]。另外,Dex 下调血浆皮质醇水平,抑制儿茶酚胺的释放,控制血管收缩,缓解术中应激反应,降低血压[11]。本研究结果显示两组 MAP、HR、CVP 在组间、时间点及组间·时间点交互作用比较差异均有统计学意义,其中研究组 MAP、HR、CVP 波动较小,拔管后的值更接近麻醉前,亦证实 Dex 具有稳定血流动力学作用。刘臻[12]等人报道全麻诱导前泵注 0.4～0.6 μg/kgDex 可通过抑制肾素 - 血管紧张素 - 醛固酮系统(RAAS)的分泌,使患者在气管插管、切皮及拔管期围术期应激反应下降,血流动力学更平稳。在心胸外科手术中,Dex 不仅有稳定血流动力学作用, 还能减少麻醉药物的使用量,并减轻围术期炎症反应与应激反应。

肺癌根治术将对肺部周围组织进行扩大根治手术治疗,对患者产生严重创伤,直接导致术后疼痛剧烈,影响术后恢复,甚至会引起一些不良反应,如肺不张、低氧血症等。良好的镇痛不但减轻患者痛苦,还明显减少术后并发症的发生,故越来越受到临床重视。目前,临床上多应用静脉 PCIA 镇痛泵,其具有安全、有效、舒适等优点,受到广泛欢迎[13]。本研究结果显示研究组 T_6、T_7、T_8、T_9、T_{10} 时刻 VAS 评分均显著低于对照组, 镇痛泵按压次数、24 h 舒芬太尼用量较少, 提示 Dex 有良好的术后镇痛效果。Dex 半衰期短,消除半衰期 2h,是目前唯一兼备镇痛、镇静作用的麻醉药物,用于辅助麻醉用药的效果理想[14]。Dex 镇痛机制有以下两点:(1)抑制 Aδ 和 C 纤维,从而抑制疼痛信号传导产生外周镇痛作用[15];(2)激动突触前膜 α2 受体,抑制 P 物质等伤害性肽类释放, 从而抑制脊髓背角伤害性刺激的传导, 终止疼痛信号传递产生中枢镇痛作用 [16]。也有文献表明 Dex 抑制 RAAS,使血儿茶酚胺浓度下降,产生镇静和抗交感神经效果,在一定程度上减轻应激反应,起到镇静、镇痛和维持血流动力学稳定作用[17]。

两组均有患者在 T_2 出现心动过缓, 对照组中出现的最慢心率 58 bpm,研究组最慢心率 55 bpm,且研究组较对照组出现心动过缓病例数的更多, 这可能与手术结束后麻醉相对较深,且研究组处于单次负荷剂量右美托米啶使用后,交感活性受到抑制,但并未出现心率小于 50 bpm 并需要使用阿托品的情况,这可能与 Dex 给药剂量偏小有关。

综上,右美托咪定可明显稳定老年胸腔镜肺癌根治术拔管期血流动力学,并有较好的术后镇痛效果,一定程度上改善患者术后肺功能。

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