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右美托咪定联合七氟醚麻醉对下肢骨折患者血流动力学、 应激反应的影响及心肌保护作用研究*

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摘要 目的:探讨右美托咪定联合七氟醚麻醉对下肢骨折患者应激反应、血流动力学的影响及心肌保护作用研究。**方法:**选取下肢骨折患者 116 例,分为对照组($n=58$)和观察组($n=58$),对照组给予右美托咪定联合丙泊酚麻醉,观察组给予右美托咪定联合七氟醚麻醉,对比两组血流动力学指标、应激反应指标、心肌指标、术后疼痛及不良反应。**结果:**观察组拔管时(T_2)~拔管 10 min 后(T_4)时间点心率(HR)、平均动脉压(MAP)低于对照组($P<0.05$)。两组不良反应发生率比较无差异($P>0.05$)。两组术后 1 d 皮质醇(Cor)、肾上腺素(E)均较术前升高,但观察组低于对照组($P<0.05$)。观察组术后 1 d 肌酸激酶(CK)、乳酸脱氢酶(LDH)、心肌肌钙蛋白(cTnI)低于对照组($P<0.05$)。观察组术后 6 h、术后 12 h、术后 24 h 视觉模拟评分法(VAS)评分均低于对照组($P<0.05$)。**结论:**右美托咪定联合七氟醚麻醉可稳定下肢骨折患者血流动力学,减轻机体应激反应及术后疼痛,同时还可发挥一定的心肌保护作用。

关键词:右美托咪定;七氟醚;下肢骨折;血流动力学;应激反应;心肌保护

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Study of Influences of Dexmedetomidine Combined with Sevoflurane Anesthesia on Hemodynamics, Stress Response and Its Myocardial Protective Effects in Patients with Lower Limb Fracture*

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ABSTRACT Objective: To investigate the study of influences of dexmedetomidine combined with sevoflurane anesthesia on stress response, hemodynamics and its myocardial protective effects in patients with lower limb fracture. **Methods:** 116 patients with lower limb fracture were selected. They were divided into control group ($n=58$) and observation group ($n=58$) according to the random stratified sampling method, the control group was given dexmedetomidine combined with propofol during anesthesia, the observation group was given dexmedetomidine combined with sevoflurane during anesthesia, hemodynamic indexes, stress response indexes, myocardial indexes, postoperative pain and adverse reactions were compared between the two groups. **Results:** The heart rate (HR), mean arterial pressure (MAP) of the observation group were lower than those of the control group on the time point of during extubating (T_2) ~ 10min after extubation (T_4) ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). The cortisol (Cor), epinephrine (E) of the two groups were higher than those of before operation 1d after operation, but the observation group was lower than that of the control group ($P<0.05$). The creatine kinase (CK), lactate dehydrogenase (LDH), cardiac troponin (cTnI) in the observation group were lower than those of the control group 1d after operation ($P<0.05$). The visual analogue scale (VAS) scores of the observation group were all lower than those of the control group 6 h after operation, 12 h after operation, 24 h after operation ($P<0.05$). **Conclusion:** Dexmedetomidine combined with sevoflurane anesthesia can stabilize the hemodynamics of patients with lower limb fracture, reduce the body stress response and postoperative pain, which can also play a certain role in myocardial protection at the same time.

Key words: Dexmedetomidine; Sevoflurane; Lower limb fracture; Hemodynamics; Stress response; Myocardial protection

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前言

下肢骨折是临床常见的骨折,目前,临床治疗骨折的主要手段为保守治疗和手术治疗,由于保守治疗复位效果差,故多数患者选择手术治疗^[1,2]。随着人口老龄化进程地加速,交通事故发生率地提高,下肢骨折的发病率呈逐年升高趋势^[3]。由于下肢骨折手术作为较大型的外科手术,手术创伤以及术后的疼痛刺激可引起患者交感神经兴奋和体内的内源性递质及活性物质的释放,引起血流波动及强烈的应激反应,甚至还会增加心肌缺血和梗死的发生率^[4,5]。故麻醉在围术期中起到了不可忽视的作用。右美托咪定、七氟醚均是临床常用的麻醉药物,右美托咪定具有抗交感、镇静、镇痛作用^[6],七氟醚具有很好的心肌保护作用^[7]。现临床有关右美托咪定联合七氟醚麻醉对下肢骨折患者的具体影响的相关报道尚不十分多见,所以本文对此进行了研究,现报道如下。

1 资料与方法

1.1 一般资料

选取 2018 年 2 月~2020 年 3 月期间来我院进行治疗的下肢骨折患者 116 例。纳入标准:(1)下肢骨折均经 X 线、CT 等影像学证实,均符合手术指征;(2)患者及其家属知情本研究并签署了同意书;(3)手术均由同一组医师完成;(4)美国麻醉医师协会(ASA)^[8]分级 I~II 级;(5)骨折发生 2 周之内即接受手术治疗。排除标准:(1)既往已有下肢手术史者;(2)伴有高血压、糖尿病等基础性疾病者;(3)伴有认知障碍及精神疾患者;(4)合并下肢其他疾病者;(5)存在急慢性感染者。根据随机分层抽样法分为对照组(n=58)和观察组(n=58),两组一般资料比较无差异($P>0.05$),临床资料均衡可比,见表 1。研究已通过医院伦理学委员会批准进行。

表 1 两组基线资料比较

Table 1 Comparison of baseline data between the two groups

Groups	Male / Female	Age (year)	ASA classification		Fracture side		Causes of fracture		
			Grade I	Grade II	Left	Right	Fall and hurt oneself	Traffic injury	Fall injury
Control group (n=58)	26/32	56.87± 5.29	31	27	30	28	19	25	14
Observation group (n=58)	28/30	57.13± 6.44	33	25	32	26	17	26	15
χ^2/t	0.139	0.216	0.139		0.139		0.178		
P	0.710	0.829	0.709		0.710		0.921		

1.2 方法

术前常规禁饮、禁食,肌注阿托品(国药准字 H21021924,东北制药集团沈阳第一制药有限公司,规格:盐酸吗啡 10 mg,硫酸阿托品 0.5 mg)0.5 mg,入室后开放静脉通路,给予面罩吸氧,常规监测心率(HR)、平均动脉压(MAP)等。两组均给予右美托咪定[国药准字 H20090248,江苏恒瑞医药股份有限公司,规格:2 mL:200 μ g (按右美托咪定计)]0.5 μ g/kg 持续泵注 10 min,依次静脉注射咪达唑仑(国药准字 H20153019,江苏九旭药业有限公司,规格:3 mL:15 mg)1.5 mg、舒芬太尼(国药准字 H20054171,宜昌人福药业有限责任公司,规格:按 $C_{22}H_{30}N_2O_2S$ 计 1 mL:50 μ g)0.25 μ g/kg、维库溴铵(国药准字 H20066941,扬子江药业集团有限公司,规格:4 mg)0.6 mg/kg 进行麻醉诱导,肌肉松弛后进行气管插管,潮气量为 8 mL/kg,并持续泵注右美托咪定 0.5 μ g/(kg·h),在此基础上,对照组给予丙泊酚(国药准字 H20133360,广东嘉博制药有限公司,规格:50 mL:500 mg)2~3 mg/(kg·h)持续泵注,观察组持续性吸入 1%~3%七氟醚(国药准字 H20173156,河北一品制药股份有限公司,规格:250 mL)。两组均于手术结束前 5 min 停用所有麻醉药物。

1.3 观察指标

(1)疼痛:记录两组术后 1 h、术后 6 h、术后 12 h、术后 24 h 的视觉模拟评分法(VAS)^[9]评分,其中 VAS 评分分数越高,痛感越强烈。(2)血流动力学:监测并记录两组麻醉诱导前(T0)、麻醉诱导后(T1)、拔管时(T2)、拔管 5 min 后(T3)、拔管 10 min 后(T4)的 HR、MAP。(3)应激反应指标、心肌指标:抽取患者术前、术后 1 d 的肘部静脉血 3 mL,室温下静置 0.5 h,经常规离

心处理(离心半径 13 cm,3200 r/min 离心 12 min)待测。采用放射法检测应激反应指标:皮质醇(Cor)、肾上腺素(E)。采用化学发光免疫法检测心肌指标:肌酸激酶(CK)、乳酸脱氢酶(LDH)、心肌肌钙蛋白(cTnI)。试剂盒均采购自美国贝克曼公司,严格遵守试剂盒说明书进行操作。(4)记录两组麻醉安全性。

1.4 统计学方法

应用 SPSS 23.0 统计学软件分析数据。血流动力学、应激反应指标等计量资料以均数± 标准差表示,采用 t 检验。计数资料以例数及率表示,采用 χ^2 检验。 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组血流动力学指标比较

两组 T0、T1 时间点 HR、MAP 比较无差异($P>0.05$),对照组 T1~T4 时间点 HR、MAP 升高后下降($P<0.05$),观察组 T0~T4 时间点 HR、MAP 组内比较无差异($P>0.05$),观察组 T2~T4 时间点 HR、MAP 低于对照组($P<0.05$),见表 2。

2.2 两组应激反应指标比较

两组术前 Cor、E 比较无差异($P>0.05$),两组术后 1dCor、E 均较术前升高($P<0.05$),观察组术后 1dCor、E 低于对照组($P<0.05$),见表 3。

2.3 两组心肌指标比较

两组术前 CK、LDH、cTnI 比较无差异($P>0.05$),对照组术后 1dCK、LDH、cTnI 均较术前升高($P<0.05$),观察组术前、术后 1dCK、LDH、cTnI 组内比较无差异($P>0.05$),观察组术后 1dCK、LDH、cTnI 低于对照组($P<0.05$),见表 4。

表 2 两组血流动力学指标比较($\bar{x} \pm s$)

Table 2 Comparison of hemodynamic indexes between the two groups($\bar{x} \pm s$)

Groups	Time	HR(beat/min)	MAP(mmHg)
Control group (n=58)	T0	79.22± 5.76 ^{cd}	86.98± 7.62 ^{cd}
	T1	80.14± 6.57 ^{cd}	88.73± 6.51 ^{cd}
	T2	96.99± 7.31	99.13± 5.38
	T3	91.84± 5.29 ^c	95.17± 6.25 ^c
	T4	84.85± 6.49 ^{cd}	91.79± 5.26 ^{cd}
Observation group (n=58)	T0	79.31± 5.48	87.13± 6.36
	T1	80.27± 6.42	87.38± 5.38
	T2	80.82± 5.37 ^c	88.95± 7.34 ^c
	T3	80.15± 6.27 ^c	88.23± 6.21 ^c
	T4	79.88± 5.66 ^c	87.74± 5.16 ^c

Note: Compared with T2, ^c $P<0.05$; compared with T3, ^d $P<0.05$; compared with control group, ^c $P<0.05$.

表 3 两组应激反应指标比较($\bar{x} \pm s$)

Table 3 Comparison of stress response indexes between the two groups($\bar{x} \pm s$)

Groups	Time	Cor(mol/ml)	E(ng/L)
Control group (n=58)	Before operation	82.81± 7.34	44.69± 4.31
	1 d after operation	149.13± 8.22 ^c	75.23± 5.26 ^c
Observation group(n=58)	Before operation	82.13± 6.44	45.16± 5.35
	1 d after operation	124.27± 5.35 ^{ce}	58.48± 4.42 ^{ce}

Note: Compared with before operation, ^c $P<0.05$; compared with the control group, ^c $P<0.05$.

表 4 两组心肌指标比较($\bar{x} \pm s$)

Table 4 Comparison of myocardial indexes between the two groups($\bar{x} \pm s$)

Groups	Time	CK(U/L)	LDH(U/L)	cTnI(μ g/L)
Control group (n = 58)	Before operation	149.21± 12.19	162.67± 21.36	0.08± 0.01
	1 d after operation	168.45± 17.26 ^c	191.32± 23.41 ^c	0.18± 0.03 ^c
Observation group (n = 58)	Before operation	149.78± 10.46	161.13± 20.39	0.08± 0.02
	1 d after operation	150.38± 16.33 ^c	162.91± 16.47 ^c	0.09± 0.01 ^c

Note: Compared with before operation, ^c $P<0.05$; compared with the control group, ^c $P<0.05$.

2.4 两组不同时间点疼痛比较

术后 6 h、术后 12 h、术后 24 hVAS 评分低于对照组($P<0.05$),

两组术后 1 h VAS 评分比较($P>0.05$),两组术后 6 h、术后 12 h、术后 24 h VAS 评分呈升高后降低趋势($P<0.05$),观察组

见表 5。

表 5 两组不同时间点疼痛比较($\bar{x} \pm s$, 分)

Table 5 Comparison of pain at different time points between the two groups($\bar{x} \pm s$, score)

Groups	1 h after operation	6 h after operation	12 h after operation	24 h after operation
Control group (n=58)	1.53± 0.28	2.78± 0.34 ^a	3.89± 0.35 ^{ab}	3.03± 0.47 ^{abc}
Observation group(n=58)	1.48± 0.26	2.14± 0.25 ^a	3.17± 0.29 ^{ab}	2.75± 0.34 ^{abc}
t	0.997	13.116	12.064	3.676
P	0.321	0.000	0.000	0.000

Note: Compared with 1 h after operation, ^a $P<0.05$; compared with 6 h after operation, ^b $P<0.05$; compared with 12 h after operation, ^c $P<0.05$.

2.5 两组不良反应发生率比较

对照组的不良反应发生率为 10.34%(6/58),包括心动过缓

2 例、低氧血症 2 例、低血压 1 例、恶心呕吐 1 例;观察组的不良反应发生率为 6.90%(4/58),包括心动过缓 1 例、低氧血症 1

例、低血压 1 例、恶心呕吐 1 例;两组不良反应发生率比较无差异($\chi^2=0.438$, $P=0.508$)。

3 讨论

随着外科技术的飞速发展,临床对下肢骨折的治愈率明显提高,但临床实施下肢骨折手术时,插拔管、切皮等操作以及术中造成的组织损伤均会对机体产生伤害性刺激,引起机体强烈的应激反应,同时可引起交感神经系统兴奋,导致患者血流动力学异常^[10-12]。此外,相较于年轻人而言,老年人健康状况不佳,身体机能退化,骨质持续地流失,且老年群体易合并高血压、骨质疏松等慢性疾病,致使老年患者的下肢骨折发生率相对更高^[13-15]。而此类群体在麻醉苏醒期易出现血压升高、心率增快、心肌耗氧量增加等情况,可加重或诱发心律失常、心肌缺血缺氧等意外^[16-17]。因此,如何维持下肢骨折术后患者血流动力学平稳,减轻机体应激反应,减少术后心血管事件发生率是麻醉医师亟需解决的问题。

本次研究结果显示,对照组患者围术期血流动力学有一定的波动,而观察组患者围术期血流动力学可维持平稳,此外,观察组的术后疼痛更轻。显示右美托咪定联合七氟醚麻醉对机体血流动力学影响较轻,且镇痛效果确切。右美托咪定是具有镇痛、镇静、利尿、抗焦虑等作用的一种高选择性和高亲和能力的 α_2 肾上腺素受体激动剂,其镇痛机制主要在于通过抑制疼痛信号传导、直接阻滞外周神经纤维以及减少有害性肽类的释放等,其中镇静、催眠作用主要体现为可降低细胞内环磷酸腺苷的浓度、减少去甲肾上腺素的释放,进而抑制交感神经和细胞兴奋^[18-20]。丙泊酚是目前临床上常见的麻醉药物,可通过提高 GABA 受体功能而发挥镇静、镇痛效果,但其若对海马突触传递长时间抑制可导致患者大脑氧代谢紊乱,引起机体应激^[21-23]。而七氟醚属于新型吸入型麻醉剂,具有麻醉诱导迅速平稳、血气分配系数低、对呼吸道刺激小等特点,可协调右美托咪定机体的应激反应产生一定的抑制或减弱作用^[24,25]。进一步观察两组应激反应指标发现,右美托咪定联合七氟醚麻醉造成的应激反应程度明显更轻。既往研究结果显示^[26],右美托咪定联合七氟醚麻醉有利于抑制机体应激反应,与本文结论基本一致。下肢骨折患者血循环不良或者完全中断,易导致骨折不愈合,加上手术创伤等因素均会对心肌造成一定程度的影响,若患者本身已经存在心肌损害,手术创伤可加重心肌的损害,严重的甚至引起心源性猝死和心肌梗死^[27]。本研究中对对照组患者存在一定程度的心肌损伤,而右美托咪定联合七氟醚麻醉者未见明显的心肌损伤。究其原因,七氟醚可通过降低冠状动脉阻力,增加心肌的灌注,减少心肌梗死面积。同时七氟醚可以通过抑制线粒体通透孔的开放,而降低患者的乳酸释放,以发挥心肌保护作用^[28]。近年来有研究表明在手术中运用七氟醚处理可以发挥对心肌的保护作用^[29]。同时有基础实验结果表明了七氟醚的心肌保护作用优于丙泊酚^[30]。良好的心肌保护措施,可有效稳定血流动力学,减少机体刺激,提高患者转机后心肌功能,促进患者术后恢复,提高治疗效果。另两组不良反应发生率比较无差异,可见右美托咪定联合七氟醚麻醉可使患者安全耐受,不见明显不良反应增加。

综上所述,右美托咪定联合七氟醚麻醉可稳定下肢骨折患

者血流动力学,减轻机体应激反应及术后疼痛,同时还可发挥一定的心肌保护作用,可作为下肢骨折手术适用的麻醉方案。

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