

doi: 10.13241/j.cnki.pmb.2020.24.034

瑞芬太尼复合异丙酚靶控输注对脊柱结核手术患者麻醉效果、血流动力学及应激反应的影响*

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摘要 目的:探讨瑞芬太尼复合异丙酚靶控输注对脊柱结核手术患者麻醉效果、血流动力学及应激反应的影响。**方法:**选取 2018 年 3 月 15 日~2019 年 12 月 24 日期间我院收治的 100 例行脊柱结核手术患者,根据随机数字表法将患者分为对照组($n=50$)和研究组($n=50$),对照组患者给予瑞芬太尼+异丙酚静吸复合麻醉,研究组给予瑞芬太尼+异丙酚靶控输注,比较两组患者麻醉效果、血流动力学、应激反应及不良反应情况。**结果:**研究组术后 2 h 视觉模拟评分(VAS)低于对照组($P<0.05$),睁眼时间、睫毛反射时间、术后自主呼吸恢复时间、指令动作恢复时间、拔管时间均短于对照组($P<0.05$)。研究组术毕时、拔管时、拔管后 5 min 平均动脉压(MAP)、心率(HR)高于对照组($P<0.05$)。研究组术后 1 d、术后 3 d 血管紧张素 II (Ang II)、去甲肾上腺素(NE)、醛固酮(ALD)低于对照组($P<0.05$)。两组不良反应发生率比较无统计学差异($P>0.05$)。**结论:**脊柱结核手术患者采用瑞芬太尼复合异丙酚靶控输注,麻醉效果确切,可有效减轻血流波动及应激反应,且安全性较好。

关键词:血流动力学;靶控输注;瑞芬太尼;脊柱结核;应激反应;异丙酚

中图分类号:R529.2;R614 **文献标识码:**A **文章编号:**1673-6273(2020)24-4752-04

Effects of Target Controlled Infusion of Remifentanyl Combined with Propofol on Anesthesia, Hemodynamics and Stress Response in Patients Undergoing Spinal Tuberculosis Surgery*

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ABSTRACT Objective: To investigate the effect of target controlled infusion of remifentanyl combined with propofol on anesthesia, hemodynamics and stress response in patients undergoing spinal tuberculosis surgery. **Methods:** From March 15, 2018 to December 24, 2019, 100 patients with spinal tuberculosis who were admitted to our hospital were selected, they were divided into control group ($n=50$) and study group ($n=50$), patients in control group were given remifentanyl and propofol combined anesthesia, patients in study group was given remifentanyl and propofol target controlled infusion, and the anesthesia effect, blood flow mechanics, stress response and adverse reactions of the two groups were compared. **Results:** The visual pain simulation score (VAS) of the study group was lower than that of the control group 2 h after operation ($P<0.05$), and the eye opening time, eyelash reflex time, recovery time of spontaneous respiration after operation, command action recovery time and extubation time were shorter than those of the control group ($P<0.05$). The mean arterial pressure (MAP) and heart rate (HR) of the study group at the end of operation, extubation time, 5 min after extubation were higher than those of the control group ($P<0.05$). The angiotensin II (Ang II), norepinephrine (NE), aldosterone (ALD) of the study group at 1 d after operation, 3 d after operation were lower than those of the control group ($P<0.05$). There was no statistic difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Target controlled infusion of remifentanyl combined with propofol has a definite anesthetic effect, and can effectively reduce blood flow fluctuation and stress response, with good safety.

Key words: Hemodynamics; Target controlled infusion; Remifentanyl; Spinal tuberculosis; Stress response; Propofol

Chinese Library Classification(CLC): R529.2; R614 **Document code:** A

Article ID: 1673-6273(2020)24-4752-04

前言

结核病发病率在全球范围内不断上升,据相关资料显示^[1],

亚洲每年约有 180 万人死于结核病。骨关节是除肺部之外结核的另一好发部位,而脊柱结核发病率则占骨关节结核发病率之首。近年来随着抗结核药物的进步,脊柱结核的发病率已有所

* 基金项目:陕西省卫生计生委科研基金项目(2016D1246)

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(收稿日期:2020-04-23 接受日期:2020-05-18)

减少,但有关脊柱结核的治疗仍不容懈怠^[23]。脊柱结核早期可给予抗结核等保守治疗,但临床预后通常较差,随着病情进展,往往需进行手术以阻止疾病进展^[45]。脊柱结核手术的麻醉方式一般采取全麻,但是若术中麻醉不当,易导致患者较大的血流波动及较强的应激反应,不利于手术的顺利进行^[67]。异丙酚属于短效静脉全麻药物,可快速起效,且无显著蓄积,可发挥良好的镇静效果,但其镇痛效果相对较差^[8]。瑞芬太尼是人工合成的一种短效阿片类药物,镇静、镇痛等麻醉效果突出,但其半衰期短,作用时间不持久^[9]。既往研究^[10]认为,瑞芬太尼复合异丙酚可获得较好的麻醉效果。靶控输注、静吸复合麻醉均是临床常用的麻醉方式,但关于何种麻醉方式较具优势尚存在一定争议。鉴于此,本研究通过探讨异丙酚复合瑞芬太尼靶控输注对脊柱结核手术患者麻醉效果、血流动力学及应激反应的影响,以期临床脊柱结核手术麻醉方式选择提供参考。

1 资料和方法

1.1 一般资料

选取 2018 年 3 月 15 日~2019 年 12 月 24 日期间我院收治的 100 例行脊柱结核手术患者,纳入标准:(1)脊柱活动受限,经 CT 显示患有脊柱结核者;(2)对本次研究知情且签署同意书者;(3)美国麻醉医师协会(American Society of Anesthesiologists, ASA) 分级 I~II 级者;(4)手术操作由同一组医师完成。排除标准:(1)合并其他结核疾病者;(2)对本次研究用药存在禁忌症者;(3)伴有精神障碍,无法正常沟通交流者;(4)合并心肝肾等重要脏器功能不全者;(5)妊娠或哺乳期妇女。根据随机数字表法将患者分为对照组(n=50)和研究组(n=50),其中对照组男 31 例,女 19 例,年龄 27~79 岁,平均(46.82±4.51)岁;ASA 分级 I 级 32 例,II 级 18 例;疾病类型:胸椎结核 21 例,腰椎结核 18 例,胸腰椎多段结核 11 例。研究组男 33 例,女 17 例,年龄 28~77 岁,平均(46.74±4.33)岁;ASA 分级 I 级 37 例,II 级 13 例;疾病类型:胸椎结核 18 例,腰椎结核 19 例,胸腰椎多段结核 13 例。两组一般资料比较无统计学差异($P>0.05$),具有可比性。

1.2 方法

患者入院后行常规检查,择期行脊柱结核手术。入室前均禁饮禁食 6h,并未接受术前用药。入室后常规监测平均动脉压(Mean arterial pressure, MAP)、心率(Heart rate, HR)等,建立静脉通道。麻醉诱导前 0.5 h,予以咪达唑仑(宜昌人福药业有限责任公司,国药准字 H20067040,规格:2 mL:2 mg)0.05 mg/kg 肌肉注射。研究组采用 TCL-I 型靶控输液泵,予以瑞芬太尼(宜昌人福药业有限责任公司,国药准字 H20030197,规格:按

$C_{20}H_{28}N_2O_5$ 计 1mg)联合异丙酚(广东嘉博制药有限公司,国药准字 H20133360,规格:50 mL:500 mg)静脉靶控麻醉,瑞芬太尼初始血浆靶浓度为 2 ng/mL,2 min 后给予异丙酚,异丙酚初始血浆靶浓度为 2 μ g/mL,随后逐渐提高为 4~6 μ g/mL,瑞芬太尼靶浓度为 4~5 ng/mL,当患者完全麻醉时,予以罗库溴铵注射液(峨眉山通惠制药有限公司,国药准字 H20183305,规格:5 mL:50 mg)0.5~0.6 mg/kg 静脉注射,并予以 2% 利多卡因(江苏朗欧药业有限公司,国药准字 H20055377,规格:以利多卡因计 10 mL:0.173 g)2~5 mL 气管内表面麻醉,利多卡因乳膏(同方药业集团有限公司,国药准字 H20063466,规格:每 g 含丙胺卡因 25 mg 与利多卡因 25 mg)外涂,2 min 后予以单腔气管插管。对照组患者则予以异丙酚 2~2.4 mg/kg,瑞芬太尼 2~3 μ g/kg 静脉注射,待患者入睡后,气管插管;若麻醉诱导过程中,患者心率<55 次/min,予以 0.5 mg 阿托品(东北制药集团沈阳第一制药有限公司,国药准字 H21021924,规格:盐酸吗啡 10 mg,硫酸阿托品 0.5 mg)静脉注射;患者出现收缩压<80 mmHg,予以盐酸甲氧明(远大医药(中国)有限公司,国药准字 H42021934,规格:1 mL:10 mg)5~10 mg 静脉注射。

1.3 观察指标

(1)记录术后 2 h 记录视觉模拟评分(Visual Analogue Scale, VAS)^[11]、指令动作恢复时间、睁眼时间、术后自主呼吸恢复时间、睫毛反射时间、拔管时间。其中 VAS 评分 0~10 分,分数越高,痛感越强烈。(2)记录两组手术期间不良反应发生情况。(3)记录两组患者术前、术毕时、拔管时、拔管后 5 min 的 HR、MAP。(4)分别于术前、术后 1 d、术后 3 d 抽取患者的晨时空腹肘静脉血 4 mL,常规离离心处理(3500 r/min 离心 12 min,离心半径 8 cm)分离上清液保存待测。采用放射免疫法检测患者血管紧张素 II (Angiotensin II, Ang II)、去甲肾上腺素(Norepinephrine, NE)、醛固酮(Aldosterone, ALD)水平,严格遵守试剂盒(深圳晶美生物科技有限公司)说明书进行操作。

1.4 统计学方法

采用 SPSS25.0 进行数据分析,以比或率表示计数资料,行 χ^2 检验,计量资料以($\bar{x} \pm s$)的形式表示,行 t 检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组围术期指标比较

研究术后 2 h VAS 低于对照组,睁眼时间、术后自主呼吸恢复时间、指令动作恢复时间、睫毛反射时间、拔管时间均短于对照组($P<0.05$);详见表 1。

表 1 两组围术期指标比较($\bar{x} \pm s$)

Table 1 Comparison of perioperative indicators between the two groups($\bar{x} \pm s$)

Groups	2 h after operation VAS(score)	Recovery time of spontaneous respiration after operation(min)	Eye opening time (min)	Eyelash reflex time(min)	Command action recovery time(min)	Extubation time (min)
Control group(n=50)	4.19±0.24	7.41±0.69	6.93±0.55	5.31±0.38	11.79±0.95	18.67±1.95
Study group(n=50)	3.02±0.27	6.04±0.58	4.69±0.63	3.93±0.34	8.92±0.82	15.14±1.79
t	22.902	10.747	18.940	19.137	16.171	9.430
P	0.000	0.000	0.000	0.000	0.000	0.000

2.2 两组血流动力学指标比较

两组患者术前 HR、MAP 比较无差异 ($P>0.05$); 两组患者术毕时 ~ 拔管后 5 min HR、MAP 均呈升高趋势 ($P<0.05$); 研究

组术毕时、拔管时、拔管后 5 min HR、MAP 高于对照组 ($P<0.05$); 详见表 2。

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 point	HR (beats/min)	MAP (mmHg)
Control group (n=50)	Before operation	79.23 ± 6.25	94.53 ± 6.87
	End of operation	63.71 ± 7.36 ^a	78.93 ± 6.95 ^a
	Extubation time	68.16 ± 6.21 ^{ab}	83.49 ± 6.24 ^{ab}
	5 min after extubation	72.13 ± 7.45 ^{abc}	88.38 ± 7.04 ^{abc}
Study group (n=50)	Before operation	78.99 ± 7.13	94.05 ± 8.91
	End of operation	68.85 ± 7.94 ^{ad}	84.62 ± 6.95 ^{ad}
	Extubation time	73.09 ± 6.38 ^{abd}	88.31 ± 7.69 ^{abd}
	5 min after extubation	77.08 ± 7.87 ^{abcd}	93.27 ± 8.71 ^{abcd}

Notes: compared with before operation, ^a $P<0.05$; compared with end of operation, ^b $P<0.05$; compared with extubation time, ^c $P<0.05$; compared with control group, ^d $P<0.05$.

2.3 两组应激反应指标比较

两组术前 Ang II、NE、ALD 比较无差异 ($P>0.05$); 两组术后 3 d Ang II、NE、ALD 低于术前 1 d 但高于术前 ($P<0.05$); 研

究组术后 1 d、术后 3 d Ang II、NE、ALD 低于对照组 ($P<0.05$); 详见表 3。

表 3 两组应激反应指标比较 ($\bar{x} \pm s$)

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

Groups	Time point	Ang II (μg/L)	NE (mg/L)	ALD (ng/L)
Control group (n=50)	Before operation	34.48 ± 2.32	316.35 ± 18.04	216.98 ± 19.13
	1 d after operation	68.30 ± 4.95 ^a	397.09 ± 21.52 ^a	282.85 ± 26.12 ^a
	3 d after operation	53.18 ± 3.65 ^{ab}	362.91 ± 23.86 ^{ab}	264.93 ± 17.09 ^{ab}
Study group (n=50)	Before operation	34.11 ± 3.42	317.11 ± 19.62	215.56 ± 20.72
	1 d after operation	59.75 ± 4.55 ^{ad}	374.92 ± 18.26 ^{ad}	258.21 ± 22.25 ^{ad}
	3 d after operation	47.34 ± 3.04 ^{abd}	341.31 ± 25.79 ^{abd}	237.63 ± 23.12 ^{abd}

Notes: compared with before operation, ^a $P<0.05$; compared with 1 d after operation, ^b $P<0.05$. compared with control group, ^d $P<0.05$.

2.4 两组不良反应发生情况比较

对照组手术期间发生体动反应 2 例、呼吸抑制 1 例、躁动 1 例、低血压 1 例, 不良反应发生率为 10.00% (5/50), 研究组手术期间出现寒战 1 例、心动过缓 1 例, 不良反应发生率为 4.00% (2/50), 经比较两组不良反应发生率无差异 ($\chi^2=1.382$, $P=0.240$)。

3 讨论

脊柱结核是临床最常见的骨结核类型, 占全身骨关节结核的 50%~70%^[12]。因脊柱结核患者多伴有后凸成角畸形, 且有些患者的病变累及多个节段, 故导致患者在病变时期脊柱稳定性差, 容易造成病灶处形成瘻, 若未能及时进行有效的治疗, 将会严重影响患者生活质量^[13-15]。由于脊柱结核手术操作复杂, 当患者心肺储备功能较弱时, 患者的血流动力学在手术时可能会受到明显的影响, 造成明显的应激反应^[16-18]。以往研究证实^[19], 有效的麻醉药物及恰当的麻醉方式可帮助患者维持血流稳定, 控制术中应激反应, 保证手术的有效性及安全性。异丙酚为临床常用的一种短效麻醉药, 5~10 min 即可起效^[20]。瑞芬太尼可抑制神经 - 内分泌系统应激反应, 维持血流动力学稳定^[21]。异丙酚、瑞芬太尼二者具有协同效应, 代谢快, 可获得充分的镇痛、

镇静效果。传统的静吸复合麻醉一直存在可控性不佳这一不足, 麻醉过浅易导致患者血流波动过大, 而麻醉过量又可引起药物积累, 产生呼吸抑制, 增加术后并发症发生风险^[22]。靶控输注是近年来新兴的静脉麻醉方法, 主要是指通过计算机控制给药速度^[23]。但有关此麻醉方式应用于脊柱结核手术的效果尚需进一步的实验以证实。

本次研究结果显示, 研究组的麻醉效果优于对照组, 分析其原因, 瑞芬太尼进入患者体内后, 可在较短时间内使患者的血 - 脑平衡, 起效迅速, 同时具有在人体内可被快速清除以及对肝肾功能负担轻等优点^[24]。异丙酚可增加氯离子通道, 从而使细胞处于超极化状态, 发挥神经系统抑制作用^[25]。两种药物联合使用, 发挥协同效应, 提高麻醉效果。另靶控输注主要是应用电脑来控制输注速率, 可灵活地调节药物浓度, 给药准确迅速, 使患者有较高的意识清醒度, 减少药物残留, 促进患者术后恢复^[26]。HR、MAP 均为反映血流动力学稳定程度的重要指标, 本研究中两组患者术中均存在血流波动, 但研究组患者血流波动明显更轻。靶控输注以药代 - 药动力学为理论基础, 可更加客观合理的将麻醉与药物代谢有机结合, 维持血浆浓度恒定, 监测患者镇静、镇痛状态, 更好的维持血流动力学稳定^[27]。手术操作、气管插管等操作均可导致机体强烈的应激反应, 肾

素-血管紧张素是一个应激激素反应系统,Ang II、NE、ALD 均是重要的应激激素,当机体受到外来刺激时,其水平迅速上升。本研究中研究组上述应激反应指标水平上升幅度小于对照组,表明瑞芬太尼复合异丙酚靶控输注可有效减轻机体应激反应。这可能是因为瑞芬太尼具有易被非特异酯酶代谢的酯键,表现出超短效镇痛的麻醉效果,而异丙酚具有保护微循环,抑制炎症反应的作用,可避免器官损伤,联合靶控输注可更好的维持血流动力学稳定,保持机体正常循环代谢,进一步减轻机体应激反应^[28-30]。对比两组安全性可知,两组不良反应发生率比较无差异,可见瑞芬太尼复合异丙酚靶控输注安全性较好,不会增加不良反应发生率。

综上所述,脊柱结核手术患者采用瑞芬太尼复合异丙酚靶控输注,麻醉效果确切,可有效减轻血流波动及应激反应,且不增加不良反应发生率。

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