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盐酸右美托咪定联合瑞芬太尼在骨科手术中的镇静效果及对患者血流动力学和呼吸功能的影响

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摘要 目的: 探讨盐酸右美托咪定联合瑞芬太尼在骨科手术中的镇静效果及对患者血流动力学和呼吸功能的影响。**方法:** 选择2016年3月至2017年5月在我院186例行骨科手术的患者,根据数表法随机分为对照组(93例)和观察组(93例),对照组采用丙泊酚联合瑞芬太尼进行麻醉,观察组采用盐酸右美托咪定联合瑞芬太尼进行麻醉,比较两组用药前(T_1)、联合用药后10 min (T_2)、联合用药后20 min(T_3)、联合用药后30 min(T_4)和患者清醒后(T_5)等时间点的镇静效果以及血流动力学和呼吸功能指标变化,并比较两组不良反应发生率。**结果:** T_3 、 T_4 时间点两组警觉/镇静(OAA/S)评分低于组内其他时间点,且观察组OAA/S评分低于对照组($P<0.05$)。两组 T_1 、 T_5 时间点呼吸频率(RR)、血氧饱和度(SpO_2)比较差异无统计学意义($P>0.05$);在 T_2 、 T_3 、 T_4 时间点观察组RR、 SpO_2 高于对照组($P<0.05$); T_3 、 T_4 时间点两组的RR水平均低于组内其他时间点($P<0.05$)。两组各时间点平均动脉压(MAP)、心率(HR)水平比较差异均无统计学意义($P>0.05$)。观察组呼吸抑制、呼吸道梗塞和恶心呕吐的发生率低于对照组($P<0.05$)。**结论:** 盐酸右美托咪定联合瑞芬太尼在骨科手术中镇静效果良好,对患者血流动力学的影响较小,呼吸抑制程度轻,安全性好。

关键词: 骨科手术;盐酸右美托咪定;瑞芬太尼;镇静效果;血流动力学;呼吸功能

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Sedative Effect of Hydrochloride Dexmedetomidine Combine with Remifentanil in Orthopedics Surgery and Its Influence on Hemodynamics and Respiratory Function

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ABSTRACT Objective: To explore the sedative effect of hydrochloride dexmedetomidine combined with remifentanil in the orthopedics surgery and its influence on hemodynamics and respiratory function. **Methods:** A total of 186 patients, who underwent orthopedics surgery in Tangshan People's Hospital from March 2016 to May 2017, were selected and randomly divided into observation group (93 cases) and control group (93 cases). The control group received propofol combined with remifentanil for anesthesia; the observation group received hydrochloride dexmedetomidine combined with remifentanil for anesthesia. The sedative effect between the two groups before treatment (T_1), 10 min after combined use of drugs (T_2), 20min after combined use of drugs (T_3), 30 min after combined use of drugs (T_4) and after the patients were conscious(T_5) and hemodynamics and respiratory function were compared, and the incidence of adverse reactions was compared between the two groups. **Results:** The Alertness / sedation (OAA/S) scores of the two groups at T_3 and T_4 time points were lower than those at other time points in the two group, and the OAA/S score of the observation group was lower than that of the control group ($P<0.05$). There were no significant differences in respiratory rate (RR) and oxygen saturation (SpO_2) between the two groups at T_1 and T_5 time points ($P>0.05$). At the time of T_2 , T_3 and T_4 , the RR and SpO_2 of the observation group were higher than those of the control group ($P<0.05$). The RR levels of the two groups at T_3 and T_4 time points were lower than those of the other time points ($P<0.05$). There were no significant differences in mean arterial pressure (MAP) and heart rate (HR) between the two groups at each time point ($P>0.05$). The incidence of respiratory depression, respiratory tract infarction and nausea and vomiting in the observation group was lower than that in the control group ($P<0.05$). **Conclusion:** Hydrochloride dexmedetomidine combined with remifentanil has a good sedative effect in the orthopedics surgery, with less influence on hemodynamics, mild respiratory depression and good safety.

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前言

随着现代麻醉技术的发展，区域阻滞麻醉技术已趋向成熟，并被广泛应用于骨科手术中^[1]。在区域阻滞下行骨科手术的患者，手术过程中其意识处于清醒的状态，这可能使患者产生焦虑、恐惧、紧张等负向心理应激反应，因而必须给予一定的镇静、镇痛药物治疗，以提高患者的舒适度，增强麻醉效果^[2,3]。盐酸右美托咪定是一种α2-肾上腺素受体激动剂，具有较强的镇静效果，同时具备稳定患者血流动力学的作用^[4,5]。瑞芬太尼是芬太尼类μ型阿片受体激动剂，镇痛作用较好，且起效快，维持时间短，但单独用药效果不佳^[6-8]。近年来已有研究表明^[9-11]，盐酸右美托咪定联合瑞芬太尼的镇痛镇静效果优于单独用药，但二药联合应用的系统研究报告较少，本文特采用随机试验进行研究，试图从镇静效果、患者血流动力学和呼吸功能三个方面探讨二药联合应用的优势，以期为临床提供参考经验。

1 资料和方法

1.1 一般资料

选择2016年3月至2017年5月在我院进行骨科手术的患者186例为研究对象。纳入标准：(1)符合骨科手术的条件，均为四肢骨折手术，患者及其家属均签署知情同意书；(2)根据美国麻醉医师协会(American society of anesthesiologists, ASA)的分级标准^[12]，所有患者均为I级或II级；(3)拟采用区域阻滞麻醉方式进行手术，完成本研究的所有调查项目者；(4)无相关药物过敏史者。排除标准：(1)伴心脑血管疾病者；(2)伴震颤麻痹、癫痫、认知功能障碍等精神科疾病者；(3)伴肝功能障碍及慢性心率者；(4)长期服用催眠药物者。采用随机数字表法分为观察组(93例)和对照组(93例)。观察组男56例，女37例；年龄20~73岁，平均(37.18±6.84)岁；ASA分级：I级41例，II级52例；体重44~72kg，平均(59.76±9.62)kg。对照组男54例，女39例；年龄21~72岁，平均(36.73±7.22)岁；ASA分级：I级40例，II级53例；体重45~74kg，平均(60.13±10.26)kg。两组患者一般资料比较无差异(P>0.05)。本研究经医院伦理委员会审核批准。

1.2 麻醉方法

两组患者入室后均常规准备，于下颌后静脉开放上肢静脉通路，均匀区域阻滞麻醉，由专业人员测量麻醉平面达到的预

期范围后进一步用药。观察组：在开始手术前10 min静脉注射盐酸右美托咪定和瑞芬太尼，盐酸右美托咪定注射液(江苏恩华药业股份有限公司，国药准字H20110085，规格2mL:0.2mg以右美托咪定计)1 μg/kg，注射用盐酸瑞芬太尼(江苏恩华药业股份有限公司，国药准字H20143315，规格2mg以瑞芬太尼计)0.8 μg/kg，术中以盐酸右美托咪定0.3 μg/kg·h和瑞芬太尼0.1 μg/kg·min维持。对照组：在手术开始前5 min静脉注射丙泊酚乳状注射液(西安力邦制药有限公司，国药准字H20010368，规格10mL:100mg)2 mg/kg，瑞芬太尼用法用量同观察组，术中以丙泊酚4 μg/kg·h和瑞芬太尼0.1 μg/kg·min维持。

1.3 观察指标

于用药前(T₁)、联合用药后10 min(T₂)、联合用药后20 min(T₃)、联合用药后30 min(T₄)和患者清醒后(T₅)比较两组患者的镇静效果、血流动力学和呼吸功能指标变化。镇静效果：根据警觉/镇静(The observer's assessment of alertness/sedation, OAA/S)评分标准进行评分^[13]，5分：患者对正常语调呼唤迅速反应；4分：对正常语调呼唤反应冷淡；3分：仅对大声呼唤或反复呼唤有反应；2分：仅对轻度摇推肩膀或头部有反应；1分：对轻度推摇无反应。0分：对挤压斜方肌无反应。采用MHM6000A型多功能心电监护仪(购于广州康迈医疗器械有限公司)动态监测两组呼吸频率(Respiratory rate, RR)、平均动脉压(Mean arterial pressure, MAP)、心率(Heart Rate, HR)、血氧饱和度(Oxygen saturation, SpO₂)。记录两组药物相关不良反应发生情况。

1.4 统计学方法

研究数据均采用SPSS21.0统计学软件进行统计分析，OAA/S评分、RR、MAP、HR、SpO₂等计量资料经正态性检验均符合正态分布，采用均数±标准差(±s)描述，实施t检验，计数资料用率(%)描述，实施χ²检验；以P<0.05为差异有统计学意义。

2 结果

2.1 两组各时间点OAA/S评分比较

T₁、T₂、T₅时间点两组OAA/S评分比较无差异(P>0.05)；T₃、T₄时间点观察组OAA/S评分低于对照组(P<0.05)；T₃、T₄时间点两组OAA/S评分低于组内其他时间点，差异有统计学意义(P<0.05)。详见表1。

表1 两组OAA/S评分比较(±s)

Table 1 Comparison of OAA/S scores between the two groups(±s)

Groups	n	T ₁	T ₂	T ₃	T ₄	T ₅
Observation group	93	5.00±0.00	4.12±0.13	3.07±0.21*	2.56±0.11*	4.92±0.21
Control group	93	5.00±0.00	4.23±0.14	3.67±0.18*	3.02±0.08*	4.89±0.16
t	-	0.000	0.165	2.743	2.663	0.083
P	-	1.000	0.903	0.027	0.028	0.962

Note: compared with other time points in the group, *P<0.05.

2.2 两组各时间点 RR 比较

T_1, T_5 时间点两组 RR 水平比较差异无统计学意义 ($P > 0.05$); 观察组 T_2, T_3, T_4 时间点 RR 水平高于对照组 ($P < 0.05$);

两组 T_3 及 T_4 时间点 RR 水平低于组内其他时间点, 差异有统计学意义 ($P < 0.05$)。详见表 2。

表 2 两组各时间点 RR 水平比较 ($\bar{x} \pm s$, 次 /min)

Table 2 Comparison of RR levels between two groups ($\bar{x} \pm s$, number of times/min)

Groups	n	T_1	T_2	T_3	T_4	T_5
Observation group	93	17.63± 2.78	16.57± 2.34	15.17± 1.79*	15.28± 2.03*	16.57± 1.43
Control group	93	17.45± 2.26	14.18± 2.26	11.52± 2.05*	12.62± 2.36*	15.92± 1.64
t	-	0.114	4.682	5.428	4.973	1.034
P	-	0.785	0.000	0.000	0.000	0.097

Note: compared with other time points in the group, * $P < 0.05$.

2.3 两组各时间点血流动力学指标比较

T_1, T_2, T_3, T_4, T_5 等时间点两组 MAP、HR 水平比较差异均无统计学意义 ($P > 0.05$); T_1, T_5 时间点两组 SpO_2 水平比较差异无统计学意义 ($P > 0.05$); 观察组 T_2, T_3, T_4 时间点 SpO_2 水平

高于对照组, 差异有统计学意义 ($P < 0.05$); 对照组 T_2, T_3, T_4 时间点 SpO_2 水平与组内其他时间点比较差异有统计学意义 ($P < 0.05$)。详见表 3。

表 3 两组各时间点 MAP、HR、 SpO_2 水平比较 ($\bar{x} \pm s$)

Table 3 Comparison of MAP, HR, SpO_2 levels at different time points between two groups ($\bar{x} \pm s$)

Index	Groups	n	T_1	T_2	T_3	T_4	T_5
MAP(mmHg)	Observation group	93	81.57± 9.64	80.26± 9.18	81.13± 9.94	82.08± 9.35	82.01± 9.62
	Control group	93	82.23± 9.78	81.72± 9.61	81.09± 9.67	80.79± 9.07	28.12± 9.47
HR(次 /min)	Observation group	93	76.08± 7.52	76.13± 7.61	75.62± 7.31	75.01± 7.08	75.80± 7.05
	Control group	93	75.82± 7.36	75.57± 7.80	74.98± 7.16	75.70± 7.44	76.17± 6.92
SpO_2 (%)	Observation group	93	99.41± 9.83	98.72± 9.44*	97.86± 9.03*	98.09± 9.17*	99.08± 9.64
	Control group	93	99.64± 9.48	95.73± 8.05*	92.15± 7.63*	94.07± 7.98*	98.25± 9.56

Note: compared with other time points in the group, * $P < 0.05$; compared with control group, * $P < 0.05$.

2.4 两组药物相关不良反应发生率比较

观察组呼吸抑制、呼吸道梗塞和恶心呕吐的发生率低于对照组, 差异有统计学意义 ($P < 0.05$); 两组低血压、躁动、肌紧张

等不良反应发生率比较差异无统计学意义 ($P > 0.05$)。详见表 4。所有发生不良反应的患者经对症处理或未处理好转, 均不影响手术的开展。

表 4 两组药物相关不良反应发生率比较 [n(%)]

Table 4 Comparison of incidence of drug-related adverse reactions between two groups[n(%)]

Groups	n	Respiratory depression	Hypotension	Dysphoria	Respiratory tract infarction	Muscle tension	Nausea and vomiting
Observation group	93	5(5.38)	2(2.15)	3(3.23)	4(4.30)	1(1.08)	6(6.45)
Control group	93	13(13.98)	3(3.23)	5(5.38)	14(15.05)	2(2.15)	17(18.28)
t	-	4.136	0.206	0.576	4.872	0.339	5.126
P	-	0.041	0.836	0.712	0.035	0.801	0.028

3 讨论

与其他麻醉方式相比, 区域阻滞麻醉费用较低, 加上其技术的成熟, 目前在骨科手术中的应用已较为普遍^[14]。区域阻滞麻醉最大的特点就是不能完全阻断内脏神经传导, 患者在处于意识清醒的状态下进行手术, 以致患者难免会产生害怕等各种负向心理应激, 影响手术的正常进行^[15,16]。因而在区域阻滞麻醉下进行手术的患者, 有效缓解患者的心理应激成为手术成功的关键环节之一, 同时也是国内外学者共同关注的热点问题。既

往研究发现^[17,18], 在区域阻滞下进行骨科手术的患者, 为了达到镇静催眠的效果, 往往给予镇静催眠药物干预, 如丙泊酚、氟哌利多等, 但以上两种药物由于镇静作用时间较长, 术后可能导致患者清醒不完善, 进而诱发多种不良反应, 且对患者血流动力学的稳定影响较大, 呼吸抑制作用强, 间接影响了手术效果。瑞芬太尼是一种新型的阿片类受体激动剂, 由于其脑平衡时间较短、分布容积较小、清除率快, 起效快, 是临幊上常用的麻醉药物, 但其单药效果欠佳^[19-21]。盐酸右美托咪定是分子量为 236.7 的 α_2 -肾上腺素受体激动剂, 是一种新型的辅助麻醉药

物,其可通过刺激脑中蓝斑 α_2 -肾上腺素受体起催眠、镇静的作用,且对患者中枢神经系统的影响较小,另外具有较好的稳定血流动力学的作用,能有效保护患者的心肌^[22,23]。

本研究显示,两组 OAA/S 评分 T₁、T₂、T₃ 时间点比较差异不明显,观察组 T₃、T₄ 时间点 OAA/S 评分低于对照组,两组 T₃、T₄ 时间点 OAA/S 评分低于组内其他时间点,说明盐酸右美托咪定联合瑞芬太尼在骨科手术中的镇静效果优于丙泊酚联合瑞芬太尼。两组 T₁、T₅ 时间点的 RR 比较差异不明显,对照组在 T₂、T₃、T₄ 时间点 RR 水平低于观察组,两组 T₃、T₄ 时间点 RR 水平明显低于组内其他时间点,说明在区域阻滞麻醉下进行骨科手术的患者,相比丙泊酚联合瑞芬太尼而言,盐酸右美托咪定联合瑞芬太尼对患者呼吸抑制作用更轻。两组 T₁、T₂、T₃、T₄、T₅ 等时间点 MAP、HR 水平比较及组内不同时间点比较差异均不明显,两组 T₁、T₅ 时间点 SpO₂ 水平比较差异不明显,T₂、T₃、T₄ 时间点观察组 SpO₂ 水平高于对照组,说明在区域阻滞麻醉下进行骨科手术的患者,采用盐酸右美托咪定联合瑞芬太尼对患者血流动力学稳定性的影响更小。观察组呼吸抑制、呼吸道梗塞和恶心呕吐的发生率低于对照组,但两组患者低血压、躁动、肌紧张等不良反应发生率比较差异不明显,这说明区域阻滞麻醉下进行手术的骨科患者,相比丙泊酚联合瑞芬太尼而言,盐酸右美托咪定联合瑞芬太尼的安全性更好。以上结果表明,盐酸右美托咪定联合瑞芬太尼具有良好的辅助镇静效果,安全性好,与相关研究^[24,25]基本吻合。盐酸右美托咪定联合瑞芬太尼的镇静效果佳、对呼吸抑制作用轻、对血流动力学稳定性影响小,其原因可能是:第一,盐酸右美托咪定通过刺激突触前膜 α_2 受体,可抑制去甲肾上腺素的释放和降低神经元兴奋,终止了疼痛信号的传递^[26,27]。第二,盐酸右美托咪定与髓内 α_2 受体结合后产生镇静效果,缓解患者产生的焦虑、恐惧等负向应激反应,且对呼吸抑制的程度轻^[28]。第三,已有研究表明^[29,30],盐酸右美托咪定联合瑞芬太尼可使患者达到近事遗忘的效果,近事遗忘可有效抵制患者术中出现的心理恐惧和应激反应。

综上所述,区域阻滞麻醉下进行骨科手术的患者给予盐酸右美托咪定联合瑞芬太尼的辅助镇静效果理想,对患者血流动力学的影响小,呼吸抑制作用轻,且呼吸抑制、呼吸道梗塞及恶心呕吐等相关不良反应发生率低,值得临床推广应用。

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