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不同剂量盐酸羟考酮复合右美托咪定对开腹手术患者镇痛效应及血流动力学的影响

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摘要 目的:探讨不同剂量盐酸羟考酮复合右美托咪定对开腹手术患者镇痛效应及血流动力学的影响。**方法:**选择从2015年3月到2017年3月期间在我院接受开腹手术治疗的患者100例进行研究。根据随机数字表法对患者进行分组,A组(应用1.0 mg/kg的盐酸羟考酮及2.5 μg/kg的右美托咪定麻醉)、B组(应用0.75 mg/kg的盐酸羟考酮及2.5 μg/kg的右美托咪定麻醉)、C组(应用0.5 mg/kg的盐酸羟考酮及2.5 μg/kg的右美托咪定麻醉)和D组(应用1.0 mg/kg的盐酸羟考酮麻醉),每组各25例。对比各组镇痛效应满意度以及麻醉诱导前(T0)、插管即刻(T1)、插管后5 min(T2)时的血流动力学指标,并统计各组不良反应情况。**结果:**A、B、C三组的镇痛效应满意度均分别明显高于D组,差异均有统计学意义(均P<0.05),A、B、C三组的镇痛效应满意度对比差异无统计学意义(P>0.05)。A、B组T1时的收缩压(SBP)、舒张压(DBP)、平均动脉压(MAP)及心率(HR)水平均分别高于C、D组,差异有统计学意义(P<0.05);T0和T2时,各组的SBP、DBP、MAP及HR水平相比差异均无统计学意义(均P>0.05)。各组T1时SBP、DBP、MAP及HR水平与T0时相比明显上升,而T2时又明显下降,差异均有统计学意义(P<0.05)。B组不良反应总发生率为12.00%,明显低于A组的36.00%、C组的44.00%及D组的40.00%,差异均有统计学意义(均P<0.05)。**结论:**不同剂量的盐酸羟考酮与右美托咪定复合麻醉对开腹手术患者的镇痛效应较好,并对患者的血流动力学水平均造成一定影响,但随着时间的延长而逐渐减弱,2.5 μg/kg的右美托咪定以及0.75 mg/kg的盐酸羟考酮复合麻醉的安全性较高,值得在临床上推广应用。

关键词:不同剂量;盐酸羟考酮;右美托咪定;开腹手术;镇痛效应;血流动力学

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Influence of Analgesic Effect and Hemodynamics of Different Doses of Oxycodone Hydrochloride Combine Dexmedetomidine in Patients with Abdominal Surgery

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ABSTRACT Objective: To investigate the influence of analgesic effect and hemodynamics of different doses of oxycodone hydrochloride combine dexmedetomidine in patients with abdominal surgery. **Methods:** 100 patients who underwent abdominal surgery in our hospital from March 2015 to March 2017 were selected in the study. According to the random number table method, the patients were divided into group A (application of 1.0 mg/kg oxycodone and 2.5 μg/kg dexmedetomidine), group B (application of 0.75 mg/kg oxycodone and 2.5 μg/kg dexmedetomidine), group C (application of 0.5 mg/kg oxycodone and 2.5 μg/kg dexmedetomidine), and group D (application of 1.0 mg/kg oxycodone), each group contained 25 cases. The satisfaction degree of analgesia effect in each group and hemodynamics indexes before anesthesia induction (T0), immediate intubation (T1), and 5min after intubation (T2) were compared, and the adverse reactions of each group were statistically analyzed. **Results:** The satisfaction degree of analgesia effect in group A, B and C were significantly higher than those in group D, and the differences were statistically significant (all P<0.05), there was no significant difference in the satisfaction degree of analgesia effect between the three groups of A, B and C (P>0.05). The systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR) levels in group A and B at T1 were higher than those in group C and D respectively, the differences were statistically significant (P<0.05). There was no statistically significant difference between SBP, DBP, MAP and HR at T0 and T2 in each groups (P>0.05). The levels of SBP, DBP, MAP and HR at T1 increased significantly compared with those at T0, but decreased significantly at T2, the differences were statistically significant (P<0.05). The total incidence of adverse reactions in group B was 12.00%, which was significantly lower than 36.00% in group A, 44.00% in group C and 40.00% in group D, and the differences were statistically significant (all P<0.05). **Conclusion:** Different doses of oxycodone hydrochloride combine dexmedetomidine have better anesthesia on the analgesic effect of abdominal surgery patients, it has some influence on the hemodynamic level of the patients, but as time goes on, it gradually decreases. The treatment with 2.5 μg/kg dexmedetomidine and 0.75

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mg/kg oxycodone hydrochloride compound anesthesia of the higher safety, which is worthy of clinical application.

Key words: Different doses; Oxycodone hydrochloride; Dexmedetomidine; Abdominal surgery; Analgesic effect; Hemodynamics

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前言

由于手术对患者造成创伤较大,手术时间较长,以及手术会对患者腹腔内各脏器造成一定干扰等,开腹手术患者通常在术后会出现疼痛等并发症。临床研究发现,术后疼痛会导致患者出现呼吸加快以及肺功能下降等情况,严重者甚至会引发肺部并发症[1]。因此,临床对于存在术后疼痛情况的患者需给予有效的镇痛治疗处理,否则可能会影响其术后恢复。当前,临床对于术后镇痛通常选择阿片类药物和非阿片类药物复合使用,但研究发现,以往常用的阿片类药物如激动μ 受体,虽然镇痛疗效较好,但是对患者肠胃功能的影响较大[2]。因此制定镇痛效果理想并且不良反应少的用药模式成为当前研究的重点。有报道提出,盐酸羟考酮复合右美托咪定适用于术后镇痛治疗,但盐酸羟考酮的用药剂量问题仍需深入研究[3,4]。本文通过研究分析不同剂量盐酸羟考酮复合右美托咪定对开腹手术患者镇痛效应及血流动力学的影响,旨在为临床麻醉用药方案的选择提供相应的数据支持,现报道如下。

1 资料与方法

1.1 一般资料

选择从 2015 年 3 月到 2017 年 3 月期间在我院接受开腹手术治疗的患者 100 例进行研究。入选标准:(1) 有手术指征者;(2)年龄>45 岁者;(3)美国麻醉医师协会(ASA)分级为Ⅰ~Ⅱ级者[5];(4)对此次研究知情同意且已签署了同意书者。排除标准:(1)有肝肾功能的严重异常者;(2)存在窦性心动过缓或是房室传导阻滞者;(3)有精神类疾病者;(4)术前服用过抗抑郁类药物者;(5)对本研究使用药物过敏者。根据随机数字表法对患者进行分组, 分成 A 组、B 组、C 组和 D 组, 每组各 25 例。各组的性别、年龄以及其他临床资料相比,差异均无统计学意义(P>0.05),见表 1。我院的伦理委员会已经评审并通过了本次研究。

表 1 各组一般资料比较

Table 1 Comparison of general information between each group

Groups	n	Age(years)	Male/Female	Weight(kg)	Height(cm)	ASA classification (Ⅰ/Ⅱ)	Anesthesia time (min)
Group A	25	52.06± 3.24	15/10	67.94± 3.26	169.54± 2.36	16/9	235.68± 32.44
Group B	25	51.87± 2.78	16/9	68.01± 2.12	171.03± 2.97	15/10	231.94± 33.58
Group C	25	52.11± 3.19	15/10	67.96± 2.94	169.88± 3.62	14/11	234.50± 29.60
Group D	25	52.32± 4.05	14/11	68.21± 1.33	170.63± 3.15	15/10	232.66± 31.02
F/x^2	-	2.068	1.394	1.942	2.114	1.402	1.977
P	-	0.137	0.263	0.146	0.108	0.258	0.132

1.2 研究方法

各组患者在进入手术室后均为其开放静脉通道,并监测患者收缩压(SBP)、舒张压(DBP)、平均动脉压(MAP)、心率(HR)等指标。而后实施麻醉诱导,为患者静注 0.4 μg/kg 的舒芬太尼及 2 mg/kg 的异丙酚, 待其意识消失之后再静注 0.15 mg/kg 的顺阿曲库铵,在气管插管之后实施机械通气,通气参数:(1)潮气量为 6~8 mL;(2)呼吸比为 1:1.5;(3)通气频率为 12~15 次 /min;(4)呼气末二氧化碳($PETCO_2$)维持在 35~45 mmHg。再进行麻醉维持,为患者靶控输注药物异丙酚(确保血浆靶浓度为 2.0~3.5 μg/mL)及瑞芬太尼(确保血浆靶浓度为 3~6 ng/mL),使脑电双频指数(BIS)值维持于 40~60。在手术完成前的 20 min 静注 5 mg 的托烷司琼,并在完成前 15 min 再静注 0.1 mg/kg 的盐酸羟考酮。而后连接好 ZZB 型镇痛泵(购自南通的爱普医疗器械公司)对各组患者实施不同用药方案的镇痛。其中 A 组予以 1.0 mg/kg 的盐酸羟考酮 (购自 NAPP PHARMACEUTICALS LIMITED,国药准字:J20130142)及 2.5 μg/kg 的右美托咪定(购自江苏恒瑞医药股份有限公司,国药准字:H20130093);B 组予以 0.75 mg/kg 的盐酸羟考酮及 2.5 μg/kg 的右美托咪定;C 组予以 0.5 mg/kg 的盐酸羟考酮及 2.5 μg/kg 的右美托咪定;D 组予以 1.0 mg/kg 的盐酸羟考酮。各组均使用生理盐水将药物稀释到 100 mL, 设置输注速率为 2 mL/h,且患者自控镇痛(PCA)剂量为 0.5 mL,而锁定时间为 15 min。通过静注 0.05 mg/kg 的盐酸羟考酮实施补救镇痛,并维持视觉模拟评分(VAS)值≤ 4 分。

1.3 观察指标

对比各组临床资料、镇痛效应满意度以及麻醉诱导前(T0)、插管即刻(T1)、插管后 5 min(T2)时的血流动力学指标(SBP、DBP、MAP、HR),同时统计各组不良反应情况。镇痛效应应用语言评价量表(VDS)对患者进行评价,分值为 0~10 分。根据评分进行镇痛满意度评估,得分值为 0~2 分记为非常满意,3~4 分记为满意,5~6 分记为一般,7~10 分记为不满意。满意度 = (非常满意例数 + 满意例数 + 一般例数)/ 总例数× 100%。

1.4 统计学方法

数据的处理应用 SPSS21.0 统计软件,计数资料用(n,%)表示,其比较选用 x^2 检验。计量资料用($\bar{x}\pm s$)表示,其比较实施

t 检验。多组间的计量资料比较用方差分析，计算 F 值。等级资料的比较选用秩和检验，计算 Z 值，P<0.05 为差异有统计学意义。

2 结果

2.1 各组镇痛效应的对比

各组镇痛效应满意度整体对比差异有统计学意义（P＜0.05）。A、B、C 三组的镇痛效应满意度均分别明显高于 D 组，差异均有统计学意义（均 P＜0.05），A、B、C 三组的镇痛效应满意度对比，差异无统计学意义（P＞0.05），见表 2。

表 2 各组镇痛效应的对比（n，%）

Table 2 Comparison of analgesic effects in each group（n, %）

Groups	n	Very satisfied	Satisfied	Commonly satisfied	Dissatisfied	Satisfaction degree
Group A	25	17	6	1	1	24(96.00)*
Group B	25	21	3	1	0	25(100.00)*
Group C	25	9	9	4	3	22(88.00)*
Group D	25	4	8	4	9	16(64.00)
Z/x^2	-		5.612			4.028
P	-		0.001			0.023

Note: compared with group D, *P＜0.05.

2.2 各组血流动力学指标的对比

在 T1 时，各组血流动力学指标整体对比差异有统计学意义（P<0.05），T0、T2 时各组血流动力学指标整体对比差异无统计学意义（P>0.05）。T1 时，各组 SBP、DBP、MAP 及 HR 水平均较 T0 时明显上升，且 A、B 组的 SBP、DBP、MAP 及 HR 水平均分别高于 C、D 组，差异有统计学意义（P＜0.05），但 A 组与 B 组之间、C 组与 D 组之间比较差异无统计学意义（P>0.05）；而 T2 时，各组 SBP、DBP、MAP 及 HR 水平较 T1 时下降，但各组间两两比较差异无统计学意义（P>0.05）。见表 3。

表 3 各组血流动力学指标的对比（$\bar{x}\pm s$）

Table 3 Comparison of hemodynamic indexes in each group（$\bar{x}\pm s$）

Groups	n	SBP（mmHg）			DBP（mmHg）			MAP（mmHg）			HR（times/min）		
		T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
Group A	25	119.94± 9.68	133.68± 10.57*[ab]	126.34± 12.39[△]	68.76± 6.21	73.16± 3.51*[ab]	70.23± 5.12[△]	85.96± 9.33	92.37± 5.68*[ab]	88.49± 5.83[△]	78.34± 1.86	83.99± 11.27*[ab]	80.34± 6.96[△]
Group B	25	118.64± 10.53	131.24± 8.56*[ab]	125.57± 10.63[△]	67.29± 5.39	72.21± 3.16*[ab]	69.54± 3.03[△]	85.56± 8.39	91.64± 6.52*[ab]	85.29± 7.66[△]	78.89± 8.14	82.44± 6.78*[ab]	79.59± 5.32[△]
Group C	25	118.24± 11.33	126.48± 11.29*	124.57± 15.30[△]	66.38± 8.17	70.13± 4.06*	66.58± 5.24[△]	84.28± 10.17	89.54± 4.62*	84.58± 6.12[△]	76.83± 7.55	81.06± 10.25*	77.36± 3.28[△]
Group D	25	120.64± 11.33	123.68± 10.57*	122.95± 11.41[△]	65.56± 5.84	69.72± 3.10*	64.83± 4.29[△]	87.28± 8.33	88.49± 4.06*	83.57± 5.29[△]	77.14± 10.68	79.29± 7.52*	76.44± 3.07[△]
F		1.024	5.874	2.329	1.031	3.926	2.793	2.287	6.108	2.325	1.149	8.524	2.534
P		0.187	0.001	0.067	0.173	0.012	0.082	0.123	0.000	0.071	0.163	0.000	0.060

Note: compared with T0, *P＜0.05; compared with T1, [△] P＜0.05; compared with group C, [a]P＜0.05; compared with group D, [b]P＜0.05.

2.3 各组不良反应的对比

各组不良反应的总发生率相比差异有统计学意义（P＜0.05）。B 组不良反应的总发生率为 12.00%，明显低于 A 组的 36.00%、C 组的 44.00%及 D 组的 40.00%，差异均有统计学意义（均 P＜0.05），A、C、D 组间总发生率比较差异无统计学意义（P>0.05），见表 4。

表 4 各组不良反应的对比（n，%）

Table 4 Comparison of adverse reactions in each group（n, %）

Groups	n	Nausea and vomiting	Sleepiness	Bradycardia	Skin Itch	Total incidence
Group A	25	4(16.00)	1(4.00)	2(8.00)	2(8.00)	9(36.00)*
Group B	25	1(4.00)	1(4.00)	1(4.00)	0(0)	3(12.00)
Group C	25	5(20.00)	0(0)	5(20.00)	1(4.00)	11(44.00)*
Group D	25	4(16.00)	2(8.00)	3(12.00)	1(4.00)	10(40.00)*
x^2	-					6.271
P	-					0.000

Note: compared with group B, *P＜0.05.

3 讨论

术后疼痛是临床十分常见的症状,通常是指机体受到一定伤害性刺激之后所表现出的复杂性生理和心理反应。有报道指出,有效的术后镇痛措施以及高舒适度的镇静措施能够帮助降低术后并发症发生率,并且利于患者早日康复[6,7]。伴随镇痛技术的不断提高以及镇痛类药物种类的大量更新,如何选择理想镇痛药物并制定出高效的术后镇痛用药方案是提高镇痛效果的关键。临床研究发现,盐酸羟考酮属于中枢神经类型的止痛药,其具有较高的生物利用度,整体镇痛效果理想,但是该药使用后患者呕吐情况较明显[8,9]。而右美托咪定是 α2 肾上腺素类型受体激动剂,既能够镇痛,还有助于降低患者术后呕吐的发生率。本研究通过探讨不同剂量的盐酸羟考酮与右美托咪定复合应用的临床效果,进而总结出镇痛以及镇静效果均非常满意的合适剂量方案,以降低开腹手术患者术后疼痛所造成的不良影响。

本文经研究发现,A、B、C 三组的镇痛效应满意度均分别明显高于 D 组(均 P<0.05),A、B、C 三组的镇痛效应对比,差异无统计学意义(P>0.05),但 B 组的满意度最高,为 100%。这提示了 B 组的镇痛效果满意度相对较好,分析原因,主要可能与 B 组在右美托咪定的用药基础上应用剂量较合适的盐酸羟考酮有关。疼痛对神经元轴产生作用,导致儿茶酚胺过量释放,并促进糖皮质激素大量分泌,增大肠黏膜发生溃烂以及出血的风险。同时,疼痛会造成呼吸加快,患者无法用力咳嗽,进而影响分泌物正常排出,较大程度地提升了术后并发症的危险。盐酸羟考酮属于阿片类中枢神经型止痛药物,其能够对 μ 以及κ 受体产生激动作用[10,11]。临床研究结果显示,较高剂量的盐酸羟考酮生物利用度较高,并且镇痛效果理想,可快速发挥药理作用,并且药效持久[12,13]。右美托咪定为新研制的高选择性质 α2 肾上腺素类受体激动剂,其通常被临床用作全麻辅助性药物。研究发现该药不仅能够起到镇静作用,同时还可以发挥镇痛效果,其有助于交感神经自身张力下降以及血流动力学恢复稳定等[14]。其次,该药对脑电活动不会造成干扰,可达到接近自然睡眠的理想镇静效果。同时,本文发现,组间比较,A、B 组 T1 时的 SBP、DBP、MAP 及 HR 水平均分别高于 C、D 组(P<0.05),但 A、B 组 T0～T2 时的 SBP、DBP、MAP 及 HR 水平相比,差异均无统计学意义(均 P>0.05)。组内比较,各组 T1 时 SBP、DBP、MAP 及 HR 水平与 T0 时相比明显上升,而 T2 时又明显下降,差异均有统计学意义(P<0.05),这提示了各种麻醉方式均会对患者机体的血流动力学水平造成一定影响,但随着时间的延长,此种影响逐渐减弱。分析原因,可能与各组麻醉用药在机体中的正常代谢等因素有关。患者在插管时,由于受到应激作用,其机体的血流动力学有关指标均表现出不同程度的上升,但伴随麻醉药物的作用,发挥了较为明显的镇静镇痛效果,因此血流动力学又逐渐趋于稳定。此外,本文还发现,B 组不良反应的总发生率为 12.00%,明显低于 A 组的 36.00%、C 组的 44.00%及 D 组的 40.00%(均 P<0.05),这提示了 B 组麻醉用药方案的安全性最高。原因主要可能是因为 B 组应用的 2.5μg/kg 的右美托咪定以及 0.75mg/kg 的盐酸羟考酮最大程度地符合了手术时机体的镇静及镇痛需求,此种用药方案既未因过高剂量的盐酸羟考酮产生更高的不良反应,又未因过低剂量而导致麻醉效果不足[15,16]。申军梅等人[17,18]报道指出,盐酸羟考酮所产生的不良反应较小,十分适用于术后疼痛治疗。但是该药容易造成恶心呕吐等不良反应,因此,不适于单独用药。将盐酸羟考酮与右美托咪定联合应用,能够较好地帮助临床控制麻醉药物以及阿片类药物的总使用量,同时在临床镇痛治疗当中,有利于交感神经的抑制,进而起到预防寒颤的效果,并且可使得患者术后呕吐发生率显著降低。这在 Wang X 等人[19,20]的报道结果中也有类似的结论可以进行佐证。

综上所述,对于开腹手术患者的镇痛效应而言,不同剂量的盐酸羟考酮与右美托咪定复合麻醉对患者的血流动力学水平均造成一定影响,但以 2.5 μg/kg 的右美托咪定以及 0.75 mg/kg 的盐酸羟考酮复合麻醉的安全性较高,临床可考虑选择此种药物配比方式进行麻醉,值得推广。

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