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右美托咪定联合地佐辛在臂丛神经阻滞麻醉中的应用及对血清 VEGF、IL-6、IL-10 的影响 *

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摘要 目的：右美托咪定联合地佐辛在臂丛神经阻滞麻醉中的应用及对血清 VEGF（内皮细胞生长因子）、IL-6（白介素 -6）、IL-10（白介素 -10）的影响。**方法：**选择我院 2016 年 10 月至 2017 年 12 月 94 例上肢骨折内固定术患者作为本次研究对象，随机分为对照组和联合组，各 47 例。对照组于臂丛阻滞实施前 10 分钟持续泵注右美托咪定，联合组在此基础上辅助静脉推注地佐辛。随之在超声引导下行肌间沟臂丛神经阻滞对比分析两组患者臂丛神经麻醉前（T0），药物注射分钟后（T1），手术切皮（T2）、手术操作 5 分钟（T3）、手术操作 30 分钟（T4）和手术结束（T5）各时间点血流动力学、Ramsay 镇静评分、VEGF、IL-6 和 IL-10 水平。**结果：**联合组 T1~T5 时间 MAP（血压）、HR（心率）均低于对照组（P<0.05）；两组 SpO_2（血氧饱和度）在各时间点比较差异无统计学意义（P>0.05）；联合组 T1~T5 时间点的 Ramsay 镇静评分明显优于观察组（P<0.05）；两组 T1~T5 时间点 VEGF 均上升，且联合组各时间点明显高于对照组（P<0.05）；术后 24 小时显示，联合组 IL-6、IL-10 水平显著低于对照组（P<0.05）；联合组麻醉起效时间明显短于对照组（P<0.05），镇痛持续时间、感觉神经和运动神经阻滞的持续时间明显比对照组长（P<0.05）。**结论：**在行上肢手术过程中，联合使用右美托咪定和地佐辛行臂丛神经阻滞麻醉镇痛效果明显，同时可有效刺激 VEGF 分泌，降低 IL-6、IL-10 炎症因子水平，加速患者术后恢复。

关键词：右美托咪定；地佐辛；臂丛神经阻滞；内皮细胞生长因子；炎症因子

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Effect of Dexmedetomidine and Dezocine on Anesthesia in Brachial Plexus Block and Its Effect on Serum VEGF, IL-6 and IL-10*

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ABSTRACT Objective: The application of dexmedetomidine combined with dezocine in the brachial plexus block anesthesia and its effect on the expression of serum VEGF, IL-6, IL-10 influence. **Methods:** 90 cases of upper extremity fracture fixation in our hospital from March 2015 to August 2017 were selected as the study subjects and randomly divided into control group and combination group, 45 cases in each group. The control group in the brachial plexus block before the implementation of 10 minutes of continuous infusion of dexmedetomidine combined group based on assisted intravenous injection of dezocine. The intermusculus brachial plexus block was followed by ultrasound guidance. Comparative analysis of two groups of patients before brachial plexus anesthesia (T0), drug injection after minute (T1), [what started? For specific time points, surgical skin incision (T2), operative operation 5 minutes (T3), operation 30 minutes (T4) and end of operation (T5) at different time points, including hemodynamics, Ramsay sedation score, VEGF, IL-6 and IL-10 levels. **Results:** The combined group T1~T5 time MAP (blood pressure), HR (heart rate) were lower than the control group (P<0.05); two SpO_2 (oxygen saturation) there is no significant difference between each time points (P>0.05); group T1~T5 time Ramsay sedation score of observation group was significantly higher than that in group two(P<0.05); T1~T5 VEGF time increased, and the combination group at each time point was significantly higher than that of the control group (P<0.05); 24 hours after operation, the level of IL-10 and IL-6 in combined group was significantly lower than the control group (P<0.05); combined anesthesia onset time was significantly shorter than the control group (P<0.05), The duration of analgesia, the duration of sensory nerve and motor nerve block were significantly longer than those of the control group(P<0.05). **Conclusion:** During the operation of upper limbs, the combination of dexmedetomidine and dezocine in brachial plexus block anesthesia has obvious analgesic effect and at the same time can effectiely stimulate the secretion of VEGF and decrease the levels of IL-6 and IL-10, Accelerate the recovery of patients after surgery.

Key words: Dexmedetomidine; Dezocine; Brachial plexus nerve block; Endothelial cell growth factor; Inflammatory factors

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前言

臂丛神经阻滞麻醉因操作便捷,良好的镇痛麻醉效果以及较小的生理创伤常被应用于临床骨折手术治疗中,尤其多见于上肢骨折,但因骨折疼痛、患者情绪的影响往往易产生阻滞不全的现象,因此术中配合镇静、镇痛类药物已成为趋势[1]。目前临床主要采用芬太尼、咪达唑仑类药物,但阻滞过程中极易镇静过度,出现呼吸抑制。地佐辛和右美托咪定作为新型镇痛镇静类药物,在保证麻醉效果的同时对呼吸系统几乎无抑制作用,还可维持血流动力学稳定,已得到广泛应用[2,3]。另一方面炎症反应是骨折创伤和手术的必经过程,炎性细胞因子增加将产生过度应激反应,因此炎症和抗炎细胞因子活动状态的平衡对预后至关重要,有研究表明内皮细胞因子与骨折后预后有着密切联系[4]。本次研究将对右美托咪定联合地佐辛在臂丛神经阻滞中的作用进行对比分析,探讨其对炎症因子和内皮细胞因子的释放影响。现报道如下:

1 资料与方法

1.1 一般资料

选择拟在我院接受上肢骨折手术的患者 94 例,按照随机数字法分为 2 组,各 47 例,对照组男 21 例,女 26 例,年龄 21~58 岁,平均年龄(37.8± 9.6)岁,体重 48~69 公斤,平均体重(57.1± 6.2)公斤,手掌骨折 16 例,指骨骨折 17 例,尺挠骨骨折 14 例;联合组男 25 例,女 22 例,年龄 20~62 岁,平均年龄(36.7± 10.2)岁,体重 45~69 公斤,平均体重(57.4± 5.8)公斤,手掌骨折 12 例,指骨骨折 24 例,尺挠骨骨折 11 例。一般资料具有可比性(P>0.05)。

纳入标准[5]:① 所有患者择期行上肢手术;② 心肺、肝肾功能正常;③ 无臂丛神经阻滞禁忌证,均满足手术适应症;④ 未服用任何止痛类药物;⑤ ASA Ⅰ~Ⅱ级。

排除标准:① 对本次研究所采用的药物过敏者;② 妊娠及哺乳期妇女;③ 伴有心血管、呼吸系统类等严重器质性疾病;④ 伴有神经源性疾病患者;⑤ 神经功能不全者。

1.2 麻醉方法

患者术前 8 小时禁食、4 小时禁水,入室后常规进行血压、心电图等监测。术前准备完毕后,患者仰卧,取患肢侧方位手臂作为臂丛神经阻滞位,并开放外周静脉通路,超声引导下按肌间沟阻滞两点法行臂丛神经阻滞[4],采用局麻药物为 0.375%罗哌卡因 30 毫升(肌间沟 10 毫升,腋路 20 毫升)。对照组于臂丛阻滞实施前 10 分钟以 1 μg/kg 作为首次剂量持续泵注右美托咪定,后按照 0.5 μg/kg/h 进行泵注。联合组在此基础上注射地佐辛 0.1 mg/kg;阻滞操作完毕后 30 分钟进行手术,两组药物持续使用至手术结束前 20 分钟。本次研究中发现另有 5 例患者出现阻滞效果不全(对照组 2 例,联合组 3 例),为保证手术治疗效果改为喉罩全麻,未纳入本次研究统计中。

1.3 观察指标

① 监测患者臂丛神经麻醉前(T0),药物注射分钟后(T1),手术切皮(T2)、手术操作 5 分钟(T3)、手术操作 30 分钟(T4)和手术结束(T5)各时间点关于血压、血氧饱和度、心率和 Ramsay 镇静评分情况。② 空腹静脉采血,对血清进行离心分离后使用双抗夹心酶联免疫吸附法 (ELISA) 监测内皮细胞生长因子、白介素 -6、白介素 -10 变化情况。③ 观察记录治疗前后麻醉起效、镇痛持续、感觉及运动神经阻滞的时间。④ 记录两组患者治疗中药物不良反应的发生情况。

1.4 统计学分析

用 SPSS19.0 统计软件对研究相关数据进行统计分析,不同时间点比较,采用重复测量方差分析;计量资料采用均数± 标准差($\bar{x}$± s)表示,进行独立样本 t 检验比较;计数资料采用率或百分比表示,x^2 检验,用 P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组臂丛神经阻滞血流动力学改变

联合组 MAP 于 T1~T5 时间点明显下降,且患者各时间明显低于对照组(P<0.05);联合组 HR 于 T1 时间点上升后持续下降,T2~T5 明显低于 T0,且低于对照组(P<0.05);两组血氧饱和度在各时间点比较差异无统计学意义(P>0.05),见表 1。

表 1 两组臂丛神经阻滞血流动力学改变比较($\bar{x}$± s)

Table 1 Comparison of hemodynamic of brachial plexus block in two groups($\bar{x}$± s)

Index	Group	n	Time					
			T0	T1	T2	T3	T4	T5
MAP	Control	45	105.71± 10.34	107.91± 13.21	112.91± 16.31	107.49± 13.13	106.37± 11.82	104.71± 13.71
	Combination	44	105.43± 12.71	104.31± 13.64	101.22± 12.68▲	98.42± 10.37▲*	98.41± 14.21▲*	98.22± 12.63▲*
HR	Control	45	69.52± 8.91	74.12± 8.72	74.94± 10.42	75.22± 7.91	75.24± 8.42	74.68± 9.22
	Combination	44	68.41± 9.42	70.31± 8.62▲	69.31± 11.72▲	69.21± 7.92▲	68.31± 12.65▲	68.29± 7.33▲
SpO_2	Control	45	98.51± 0.91	98.31± 0.71	98.41± 0.74	98.31± 0.92	97.72± 1.12	97.81± 0.54
	Combination	44	98.31± 0.45	97.83± 0.65#	98.02± 0.58#	97.43± 1.78#	97.25± 0.63#	98.33± 0.42#

Note: compared with T0, *P<0.05; compared with Control, #P>0.05; compared with Control, ▲P<0.05.

2.2 两组 Ramsay 镇静评分比较

对照组在 T1 时间点明显上升,而后下降,T3~T5 持续上升(P<0.05),联合组 Ramsay 镇静评分 T1~T5 均高于 T0,联合组 T1~T5 时间点 Ramsay 镇静评分明显优于联合组 (P<0.05),见表 2。

表 2 两组 Ramsay 镇静评分比较($\bar{x}\pm$ s)

Table 2 Two groups Ramsay sedation score comparison($\bar{x}\pm$ s)

Group	n	Time					
		T0	T1	T2	T3	T4	T5
Control	45	1.53± 0.54	1.68± 0.65	1.47± 0.65	1.78± 0.62*	1.82± 0.56*	2.14± 0.51*
Combination	44	1.56± 0.53	1.81± 0.42*	2.84± 0.84*	2.62± 0.62*	2.77± 1.23*	2.95± 0.75*

Note: compared with T0, *P<0.05; compared with Control, #P<0.05

2.3 两组不同时间点 VEGF 水平比较($\bar{x}\pm$ s)

两组 T0 时间点的 VEGF 处于最低水平,经治疗,T1~T5 时间点的 VEGF 均得到上升（P<0.05），且联合组水平明显较高（P<0.05),见表 3。

表 3 两组不同时间点 VEGF 水平比较($\bar{x}\pm$ s)

Table 3 Compared two groups at different time points VEGF levels($\bar{x}\pm$ s)

Group	n	Time					
		T0	T1	T2	T3	T4	T5
Control	45	159.31± 35.43	170.59± 36.52*	176.31± 41.71*	205.22± 35.71*	234.87± 34.22*	265.31± 35.17*
Combination	44	160.51± 32.74	182.59± 38.56*#	194.41± 32.66*#	233.12± 41.22*#	288.31± 37.53*#	317.86± 38.72*#

Note: compared with T0, *P<0.05; compared with Control, #P<0.05.

2.4 两组 IL-6、IL-10 水平比较($\bar{x}\pm$ s)

治疗后 24 小时显示,两组 IL-6 水平均显著上升,联合组低于对照组(P<0.05);两组 IL-10 水平明显上升,联合组高于对照组(P<0.05)。

表 4 两组 IL-6、IL-10 水平比较($\bar{x}\pm$ s)

Table 4 Compare the levels of IL-6, L-10 in two groups($\bar{x}\pm$ s)

Group	n	IL-6(U/L)		IL-10(U/L)	
		Before	After	Before	After
Control	45	73.24± 7.19	127.69± 10.46#	1.04± 0.35	1.21.± 0.37#
Combination	44	72.87± 8.36	97.75± 7.46*#	1.13± 0.38	1.37± 0.29*#

Note: compared with control group, *P<0.05; Compared with before treatment, #P<0.05.

2.5 两组麻醉起效、镇痛持续、感觉和运动神经阻滞持续时间对比

与对照组比较,联合组麻醉起效明显较短(P<0.05),镇痛持续时间、感觉及运动神经阻滞持续时间明显延长（P<0.05），见表 5。

表 5 两组麻醉起效、镇痛持续、感觉和运动神经阻滞持续时间比较($\bar{x}\pm$ s, min)

Table 5 Two groups of anesthesia onset, analgesic persistence, sensory and motor nerve block duration contrast($\bar{x}\pm$ s, min)

Group	n	Sensory nerve block duration	Motor nerve block duration	Duration of analgesia	Anesthesia onset time
Control	45	358.21± 36.72	401.16± 40.19	362.84± 14.79	21.45± 4.73
Combination	44	438.58± 45.72*	494.82± 41.23*	457.23 ± 21.42*	9.84± 1.55*

Note: compared with control group, *P<0.05.

2.6 两组不良药物反应情况比较

联合组止窦性心动过缓、血带不适、低血压和呼吸抑制不良反应总发生率 13.13%低于对照组 17.78%(P>0.05),见表 5。

表 6 两组不良药物反应情况比较(n%)

Table 6 Compared The adverse drug reactions in two groups (n%)

Group	n	Tourniquet discomfort	Respiratory depression	Sinus bradycardia	Hypotension	Total
Control	45	5(11.11)	0(0.00)	2(4.44)	1(2.22)	8(17.78)
Combination	44	3(6.67)*	1(2.22)*	1(2.22)*	1(2.22)*	6(13.13)*

Note: compared with control group, *P>0.05.

3 讨论

臂丛神经阻滞作为一种安全高效的局部麻醉方式,将药物注射入局部神经干,使患处感觉和运动功能受到阻滞,可有效缓解术中的疼痛和肌肉紧张,被广泛用于上肢骨折手术[6]。但因机体解剖特点等诸多原因极易造成阻滞不全,同时单一臂丛神经阻滞无法完全缓解因手术带来的消极情绪,还将导致血压增高、心率过快以及炎症等反应,影响手术操作和术后骨折愈合,鉴于此已有研究证明应在臂丛神经组织麻醉过程中辅以镇静、镇痛类药物[7]。

右美托咪定作为新型选择性α2 肾上腺素受体激动剂,能产生适度的镇静和镇痛作用,并能明显控制患者血糖和肾上腺素等激素水平,可有效缓解手术围期中的不良反应,其区别于咪达唑仑和芬太尼均等常用麻醉药物的过度镇静,避免对呼吸和循环系统造成消极作用[8-10]。造成该结果主要是由于右美托咪定可分别对外周交感神经末梢的突触前 α2 肾上腺素受体和去甲肾上腺素的释放及神经纤维动作电位起到兴奋和抑制作用[11],同时还激活蓝斑核上的 α2 肾上腺素能受体,有效保留机体唤醒系统功能,使患者麻醉状态与自然睡眠状态相似,从而避免对呼吸系统的过度抑制[12,13]。在上肢骨折手术过程中常伴随难以忍受的疼痛,因而臂丛神经阻滞需配合强效镇痛药物。研究表明阿片类药物与局部药物的联合应用在降低麻醉药物用量的同时增强阻滞和镇痛效果,地佐辛作为一种新型阿片受体混合激动 - 拮抗镇痛药,其能与甲肾上腺素转运体(NET)和血清素转运体(5- 羟色胺转运体)两个作用靶点间相互作用,研究证明地佐辛作为一种部分 μ 受体激活剂,其兼具 K 受体拮抗剂,可有效较低耐药性,地佐辛可以减轻阿片类药物的副作用,适当的配合使用可能不减低镇痛作用,反而可增强镇痛效应目前已作为术中术后辅助镇痛的有效药物广泛应用[14,15]。本次研究中,联合组 T1~T 各 5 时间点 MAP(血压)、HR(心率)和 Ramsay 镇静评分改善较好($P<0.05$),两组 SpO_2 在各随访时间点无较大差异($P>0.05$),这一结果提示联合用药在加强臂丛神经阻滞效果的同时稳定了生命体征,兼具强有力的镇静功效。

骨折损伤后其恢复期包括:血肿机化、骨痂形成和骨痂塑型[16,17],研究证明血管新生和局部供血功能的恢复对骨折患处供氧和再生具有重要作用,血管内皮生长因子广泛分布于各脏器和骨骼中,可有效促进血管内皮细胞增殖,促进血管新生,同时还有利于骨细胞生产,可作为骨折愈合的重要参考指标[18,19]。本次研究显示治疗后,两组 T1~T5 时间点的 VEGF 均得到上升,联合组 VEGF 指标上升幅度更大($P<0.05$),这一结果提示联合用药可有效增加血液中 VEGF 浓度,促进骨折愈合。另一方面身体在外科手术过程中遭受较大刺激,引发细胞因子大量释放,改变患者全身炎症状态,不利于预后效果[20],因此本次研究将 IL-6(促炎)和 IL-10(抗炎)纳入炎症反应观察指标,研究显示治疗 24 小时以后 IL-6 和 IL-10 显著下降,且明显低于对照组($P<0.05$),这一现象提示受右美托咪定的抗炎作用的影响,另一方面臂丛神经阻滞麻醉可快速有效定点穿刺,使麻药迅速且均匀起效,在一定程度上控制麻醉药用量,避免药物过量使用而破坏患者自我恢复功能[21]。

鉴于以上情况,针对上肢骨折手术,采用臂丛神经阻滞麻醉配合右美托咪定与地佐辛,具有较好的镇静和镇痛效果,有利于改善患者炎症因子和 VEGF 水平,加速骨折愈合,同时药物不良反应少。但本次样本容量较小,且未对药物进行不同剂量研究,其药物效能和影响因素有待进一步研究。

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