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地佐辛联合小剂量右美托咪定辅助全身麻醉对功能性鼻内镜鼻窦手术患者氧化应激水平和炎症因子的影响*

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摘要 目的:观察地佐辛联合小剂量右美托咪定辅助全身麻醉对功能性鼻内镜鼻窦手术患者氧化应激水平和炎症因子的影响。**方法:**选取2013年6月到2018年6月期间于我院接受功能性鼻内镜鼻窦手术的患者130例,根据信封抽签法将患者分为对照组($n=65$,单纯全身麻醉)和实验组($n=65$,地佐辛联合小剂量右美托咪定辅助全身麻醉),对比两组血流动力学、氧化应激和炎症因子水平,记录两组苏醒期躁动情况及呛咳发生率。**结果:**两组插管前(T1)~拔管后5 min(T4)心率(HR)、平均动脉压(MAP)呈升高后降低趋势,血氧饱和度(SpO_2)呈降低后升高趋势($P<0.05$),且实验组HR、MAP低于对照组, SpO_2 高于对照组($P<0.05$)。两组术后1d、术后3d超氧化物歧化酶(SOD)较术前升高,且实验组高于对照组($P<0.05$);丙二醛(MDA)较术前降低,且实验组低于对照组($P<0.05$)。两组术后1d、术后3d白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、C反应蛋白(CRP)呈降低趋势,且实验组低于对照组($P<0.05$)。两组拔管时~拔管后10 min Riker镇静躁动评分(SAS)评分呈降低趋势,且实验组低于对照组($P<0.05$)。实验组的呛咳发生率较对照组低($P<0.05$)。**结论:**地佐辛联合小剂量右美托咪定辅助全身麻醉用于功能性鼻内镜鼻窦手术患者,减少苏醒期躁动,预防呛咳发生,使血流动力学维持平稳,减轻机体氧化应激反应和炎症应激反应。

关键词:地佐辛;小剂量;右美托咪定;全身麻醉;功能性鼻内镜鼻窦手术;氧化应激;炎症因子

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Effects of Dezocine Combined with Low-dose Dexmedetomidine on Oxidative Stress Levels and Inflammatory Factors in Patients Undergoing Functional Endoscopic Sinus Surgery*

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ABSTRACT Objective: To observe the effect of dezocine combined with low-dose dexmedetomidine on oxidative stress levels and inflammatory factors in patients undergoing functional endoscopic sinus surgery. **Methods:** From June 2013 to June 2018, 130 patients who received functional endoscopic sinus surgery in our hospital were selected, and patients were divided into control group ($n=65$, given general anesthesia only) and experimental group ($n=65$, given dezocine combined with low-dose dexmedetomidine assisted general anesthesia) according to the envelope lottery method. Hemodynamics, oxidative stress and inflammatory factors levels were compared in the two groups, restlessness during awakening and incidence rate of cough in two groups were recorded. **Results:** The heart rate (HR) and mean arterial pressure (MAP) of the two groups before intubation (T1) ~ 5 min after extubation (T4) increased and then decreased, while the blood oxygen saturation (SpO_2) decreased and then increased ($P<0.05$). HR and MAP of the experimental group were lower than those of the control group, and SpO_2 was higher than that of the control group ($P<0.05$). Superoxide dismutase (SOD) of the two groups at 1d after operation and 3d after operation was increased than that before operation, and the experimental group was higher than the control group ($P<0.05$). The malondialdehyde (MDA) was decreased than that before operation, and the experimental group was lower than the control group ($P<0.05$). The interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α) and C-reactive protein (CRP) of the two groups at 1d after operation and 3d after operation showed a decrease trend, and the experimental group was lower than the control group ($P<0.05$). The Riker agitation score (SAS) scores of the two groups at extubation~10min after extubation showed a decreased trend, and the experimental group was lower than the control group ($P<0.05$). The incidence rate of cough of experimental group was lower than control group ($P<0.05$). **Conclusion:** Dezocine combined with low-dose dexmedetomidine assisted general anesthesia in patients undergoing functional endoscopic sinus surgery, reduce restlessness during recovery period, can effectively prevent cough, maintain stable hemodynamics, and reduce body oxidative stress and inflammatory stress.

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Key words: Dezocine; Low-dose; Dexmedetomidine; General anesthesia; Functional endoscopic sinus surgery; Oxidative stress; Inflammatory factors

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前言

功能性鼻内镜鼻窦手术是应用内镜操作的一种鼻部精细手术,因其手术创伤小、治愈率高、操作简单及并发症少而广泛应用于慢性鼻窦炎、鼻炎等鼻部病变的治疗中^[1,2]。患者术前的恐惧、术中的刺激性手术操作、术后鼻腔内填塞的膨胀海绵导致鼻腔不通畅、术后疼痛、气管导管等因素均可引起机体强烈的应激反应,导致呛咳、苏醒期躁动发生率较高^[3,4]。其中苏醒期躁动极易导致患者出现误吸、缺氧、出血或再次手术等,严重者甚至影响患者生命安全。因此选择合理安全的麻醉方案对于功能性鼻内镜鼻窦手术的顺利进行及围术期保障有积极的意义。现临床功能性鼻内镜鼻窦手术中常用的麻醉方案为全身麻醉,但存在窒息、呼吸抑制、易发生苏醒期躁动的缺陷^[5]。地佐辛是苯吗啡烷类衍生物,镇痛作用强,不良反应少^[6]。右美托咪定镇静、镇痛效果确切,可以减少阿片类药物和局麻药的使用量^[7]。本研究通过探讨地佐辛联合小剂量右美托咪定辅助全身麻醉对功能性鼻内镜鼻窦手术患者氧化应激水平和炎症因子的影响,以为临床该术式麻醉方案的选择提供参考。

1 资料与方法

1.1 临床资料

选取2013年6月到2018年6月期间于我院接受功能性鼻内镜鼻窦手术的患者130例,我院伦理学委员会已批准本研究,患者均签署同意书。纳入标准:(1)均符合手术指征,择期行功能性鼻内镜鼻窦手术且成功完成者;(2)手术均由同一组医师完成;(3)肝肾功能良好;(4)对本次研究麻醉方案耐受者;(5)美国麻醉医师协会(ASA)分级I~II级。排除标准:(1)伴有药物不能控制的高血压者;(2)合并凝血功能障碍者;(3)既往有长期服用阿片类及慢性镇痛药物史者;(4)合并精神病史或长期应用精神类药物者;(5)既往有脑梗死、脑外伤病史者;(6)合并传染性、免疫性疾病者。根据信封抽签法将患者分为对照组和实验组,各65例。其中对照组男38例,女27例,年龄26~58岁,平均 (41.67 ± 6.28) 岁;ASA分级I级34例,II级31例;体质量指数 $20 \sim 27 \text{ kg/m}^2$,平均 $(24.16 \pm 0.72) \text{ kg/m}^2$;疾病类型:鼻-鼻窦炎25例,鼻息肉17例,鼻中隔偏曲23例。实验组男40例,女25例,体质量指数 $20 \sim 26 \text{ kg/m}^2$,平均 $(23.97 \pm 0.81) \text{ kg/m}^2$;年龄28~59岁,平均 (41.15 ± 5.94) 岁;ASA分级I级36例,II级29例;疾病类型:鼻中隔偏曲24例,鼻-鼻窦炎23例,鼻息肉18例。两组患者一般资料对比未见统计学差异($P > 0.05$),具有可比性。

1.2 方法

术前两组患者禁饮6h、禁食8h,术前常规肌注阿托品(国药准字H44025273,广东南国药业有限公司,规格:2 mL:硫酸阿托品0.5 mg,盐酸异丙嗪25 mg)0.5 mg、苯巴比妥钠(重庆药友制药有限责任公司,国药准字H50021537,规格:2 mL:0.2 g)

0.1 g。入室后开放静脉通路,常规监测心率(HR)、血氧饱和度(SpO_2)、平均动脉压(MAP)等。对照组患者均依次静脉注射芬太尼[江苏恩华药业股份有限公司,国药准字H20113508,规格:2 mL:0.1 mg(以芬太尼计)]0.2 mg、丙泊酚(广东嘉博制药有限公司,国药准字H20133360,50 mL:500 mg)2 mg/kg、琥珀酸胆碱100 mg,诱导成功后气管插管,术中以瑞芬太尼[江苏恩华药业股份有限公司,国药准字H20143315,规格:2 mg(以瑞芬太尼计)]2~6 ng/mL、丙泊酚2~8 $\mu\text{g/mL}$ 进行麻醉维持。实验组患者则于诱导前15 min给予右美托咪定[宜昌人福药业有限责任公司,国药准字H20183390,规格:2 mL:200 μg (按右美托咪定计)]0.5 $\mu\text{g/kg}$ (将右美托咪定溶于10 mL生理盐水中,以60 mL/h的速率泵注),泵注结束前的5 min中静脉注射地佐辛(南京优科制药有限公司,国药准字H20193318,规格:1 mL:5 mg)5 mg,随后给予麻醉诱导,诱导方案同对照组。实验中在对照组术中维持的基础上再予以0.2 $\mu\text{g/kg} \cdot \text{h}$ 右美托咪定维持,直至手术结束前的30 min停止。手术结束后待患者自主呼吸恢复良好,吞咽反射恢复,拔出气管导管,送入苏醒室观察。

1.3 观察指标

(1)血流动力学:记录两组麻醉诱导前(T_0)、插管前(T_1)、插管后即刻(T_2)、拔管后1 min(T_3)、拔管后5 min(T_4)的HR、MAP以及 SpO_2 。(2)氧化应激、炎症因子指标:采集患者术前、术后1d、术后3d的肘静脉血4 mL,室温下静置0.5h,经2900 r/min离心12 min,半径14 cm,分离血清置于冰箱中待测。采用酶联免疫吸附试验检测丙二醛(MDA)、超氧化物歧化酶(SOD)水平,采用电化学发光法检测白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)、C反应蛋白(CRP),严格参考试剂盒(深圳晶美生物科技有限公司)说明书进行操作。(3)呛咳发生率:记录两组患者呛咳发生情况。(4)苏醒期躁动情况:记录两组患者拔管时、 T_4 、拔管后10 min的Riker镇静躁动评分(SAS)^[8],SAS共1~7分,其中1分:无法唤醒。2分:非常安静,对外界刺激有反应。3分:嗜睡,言语刺激或轻微摇动可唤醒。4分:安静,容易唤醒。5分:躁动,经言语劝阻可安静。6分:需要保护性束缚,并经言语反复劝阻。7分:危险躁动,在床上反复挣扎。

1.4 统计学方法

采用SPSS23.0进行数据分析。计数资料以率表示,行卡方检验。计量资料均为正态资料,以 $(\bar{x} \pm s)$ 表示,行t检验。 $\alpha = 0.05$ 为检验标准。

2 结果

2.1 血流动力学指标比较

T_0 时间点两组HR、MAP、 SpO_2 比较无差异($P > 0.05$),两组 $T_1 \sim T_4$ 时间点HR、MAP呈升高后降低趋势, SpO_2 呈降低后升高趋势($P < 0.05$),且实验组HR、MAP低于对照组, SpO_2 高于对照组($P < 0.05$),详见表1。

2.2 两组氧化应激指标比较

两组术前 SOD、MDA 比较差异无统计学意义 ($P>0.05$), 两组术后 1d、术后 3d MDA 较术前降低, 且实验组低 ($P<0.05$), 两组术后 1d、术后 3d SOD 较术前升高, 且实验组高于对照组 ($P<0.05$), 详见表 2。

表 1 两组血流动力学指标比较 ($\bar{x} \pm s$)Table 1 Comparison of hemodynamic indexes between the two groups ($\bar{x} \pm s$)

Groups	Time points	HR (beats/min)	MAP (mmHg)	SpO ₂ (%)
Control group (n=65)	T0	77.43±5.28	84.90±5.13	92.06±6.14
	T1	84.98±6.36 ^a	95.72±6.25 ^a	81.08±5.73 ^a
	T2	93.29±4.47 ^{ab}	102.83±7.24 ^{ab}	74.29±6.68 ^{ab}
	T3	90.32±6.52 ^{abc}	96.62±6.51 ^{abc}	79.96±7.25 ^{abc}
	T4	86.89±5.65 ^{abcd}	91.67±5.95 ^{abcd}	85.23±6.94 ^{abcd}
Experimental group (n=65)	T0	77.16±6.02	85.14±6.79	91.93±6.36
	T1	80.39±5.87 ^{ac}	90.09±7.94 ^{ac}	87.31±6.69 ^{ac}
	T2	87.27±6.95 ^{abc}	95.98±5.87 ^{abc}	80.86±6.71 ^{abc}
	T3	82.04±6.35 ^{abcc}	91.60±6.21 ^{abcc}	86.32±5.31 ^{abcc}
	T4	78.23±5.36 ^{bcd}	86.80±5.14 ^{bcd}	90.34±5.29 ^{bcd}

Note: compared with T0, ^a $P<0.05$; compared with T1, ^b $P<0.05$; compared with T2, ^c $P<0.05$; compared with T3, ^d $P<0.05$; compared with control group, ^e $P<0.05$.

表 2 两组氧化应激指标比较 ($\bar{x} \pm s$)Table 2 Comparison of oxidative stress indexes between the two groups ($\bar{x} \pm s$)

Groups	Time points	SOD (U/mL)	MDA (nmol/mL)
Control group (n=65)	Before operation	447.32±24.93	9.88±0.72
	1d after operation	491.54±26.52 ^a	7.54±0.53 ^a
	3d after operation	553.20±25.07 ^{ab}	4.67±0.45 ^{ab}
Experimental group (n=65)	Before operation	446.19±22.83	9.83±0.58
	1d after operation	567.84±26.21 ^{ac}	5.35±0.89 ^{ac}
	3d after operation	626.83±25.12 ^{abc}	3.46±0.61 ^{abc}

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

2.3 两组炎症因子指标比较

两组术前 IL-6、TNF- α 、CRP 比较差异无统计学意义 ($P>0.05$), 两组术后 1d、术后 3d IL-6、TNF- α 、CRP 呈降低趋势, 且实验组低于对照组 ($P<0.05$), 详见表 3。

05), 两组术后 1d、术后 3d IL-6、TNF- α 、CRP 呈降低趋势, 且实验组低于对照组 ($P<0.05$), 详见表 3。

表 3 两组炎症因子指标比较 ($\bar{x} \pm s$)Table 3 Comparison of inflammatory factors between the two groups ($\bar{x} \pm s$)

Groups	Time points	IL-6 (pg/mL)	TNF- α (pg/mL)	CRP (ng/mL)
Control group (n=65)	Before operation	11.62±1.91	49.53±7.16	61.34±6.39
	1d after operation	37.29±3.87 ^a	128.21±9.82 ^a	88.91±8.26 ^a
	3d after operation	26.47±2.25 ^{ab}	83.86±8.65 ^{ab}	76.80±6.67 ^{ab}
Experimental group (n=65)	Before operation	11.93±2.04	49.27±7.49	62.07±7.19
	1d after operation	28.73±2.41 ^a	94.07±9.52 ^a	81.56±6.35 ^a
	3d after operation	19.76±2.37 ^{abc}	64.09±7.46 ^{abc}	68.51±5.39 ^{abc}

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

2.4 两组苏醒期躁动情况比较

两组拔管时 ~ 拔管后 10 min SAS 评分呈降低趋势, 且实验组低于对照组 ($P<0.05$), 详见表 4。

对照组发生呛咳的例数为 13 例, 呛咳发生率 20.00% (13/65); 实验组发生呛咳的例数为 4 例, 呛咳发生率 6.15% (4/65); 实验组的呛咳发生率明显较对照组低 ($\chi^2=5.482, P=0.019$)。

对照组发生呛咳的例数为 13 例, 呛咳发生率 20.00% (13/65); 实验组发生呛咳的例数为 4 例, 呛咳发生率 6.15% (4/65); 实验组的呛咳发生率明显较对照组低 ($\chi^2=5.482, P=0.019$)。

2.5 两组呛咳发生率比较

019)。

表 4 两组苏醒期躁动情况比较($\bar{x} \pm s$, 分)Table 4 Comparison of restlessness during awakening between the two groups($\bar{x} \pm s$, score)

Groups	Extubation	T4	10 min after extubation
Control group(n=65)	5.06±0.32	4.27±0.39 ^a	3.31±0.24 ^{ab}
Experimental group(n=65)	3.55±0.24	2.93±0.32 ^a	2.24±0.26 ^{ab}
t	12.657	11.082	9.731
P	0.000	0.000	0.000

Note: compared with extubation, ^a $P < 0.05$; compared with T4, ^b $P < 0.05$.

3 讨论

功能性鼻内镜鼻窦手术是鼻外科学的常见技术,在清除有效病变的同时,还可最大程度的保护患者的鼻粘膜结构和功能^[9,10]。尽管该手术创伤较小,但仍属于侵入性操作,故不良反应发生风险仍然存在。研究显示^[11],麻醉药物的选择与手术风险等因素有关。功能性鼻内镜鼻窦手术的高风险主要集中于拔管这一阶段,拔管时机体麻醉药物也逐渐衰减,患者逐渐感受到鼻部的不良刺激如吸取痰液及鼻腔内填塞物等,致使患者产生强烈的应激反应,诱发垂体肾上腺轴功能亢进,导致机体MAP、HR呈现不同程度的波动,若未能及时控制可出现术后不良心血管事件^[12-14]。此外,苏醒期躁动也是该类患者常见的不良反应之一,表现为躁动、兴奋以及程度不等的自主运动,有可能造成窒息、切口缝线断裂、手术部位出血、尿潴留等诸多严重后果^[15],同时也可导致MAP、HR出现波动,降低患者手术治疗效果^[16-18]。由于鼻腔内空间狭窄,手术器械、内窥镜、吸引器等同时操作难以满足,故而手术时间相对较长^[19,20]。全麻状态下患者血管可表现出扩张,导致出血量增加,不利于维持机体血流稳定,因此辅助麻醉药物适当应用,可使血流动力学维持稳定,机体应激反应减轻,确保了手术的安全性及术野质量^[21]。

地佐辛属阿片受体混合激动-拮抗剂,可激动 κ 受体,对 μ 受体有部分激动作用,是兼备阿片类激动剂和拮抗剂的药物,能缓解因疼痛引起的机体应激反应^[22,23]。右美托咪定属于肾上腺素受体激动剂,有助于保障围术期麻醉安全。有研究认为^[24],右美托咪定可使术后拔管时间延长,其原因与术中泵注剂量有关。也有研究证实小剂量右美托咪定可使由全麻药物使用后引起的苏醒期躁动、呛咳降低^[25]。本次研究结果显示,地佐辛联合小剂量右美托咪定辅助全身麻醉可有效维持功能性鼻内镜鼻窦手术患者的血流动力学稳定,减少呛咳发生率,减轻苏醒期躁动。小剂量右美托咪定作用于中枢神经系统,去甲状腺素释放降低,维持血流动力学稳定,同时能够在加深镇静镇痛效果的同时,减轻患者苏醒期躁动^[26]。联合地佐辛在镇痛的同时又不会引起镇静和呼吸抑制,同时地佐辛还可缓解全身麻醉药物镇痛作用后产生的不适感,进而维持机体血流动力学平稳^[27]。应激反应是外科手术患者围术期不可避免的身体反应,SOD是人体自然存在的超氧自由基的天敌,其水平越高,人体抗氧化能力越强;MDA的含量变化可间接反映组织中氧自由基含量^[28]。IL-6具有刺激及参与免疫反应细胞分化和增殖的能力;TNF- α 是炎症反应的介质之一,可促进机体炎症扩大级联化;CRP是一种急性时相反应蛋白,机体存在炎症反应时,其水平

迅速升高^[29]。本研究中,相对于单纯全身麻醉,地佐辛联合小剂量右美托咪定辅助全身麻醉可有效减轻应激反应,可能与地佐辛联合小剂量右美托咪定可充分镇静、镇痛,并减少了躁动、呛咳的诱发因素,同时较好的维持血流动力学波动,消除了中枢过敏化等因素有关^[30]。值得注意的是,右美托咪定存在心动过缓风险且起效较慢,临床使用剂量应严格控制,确保麻醉过程中的安全。

综上所述,地佐辛联合小剂量右美托咪定辅助全身麻醉用于功能性鼻内镜鼻窦手术患者,可减少苏醒期躁动,有效预防呛咳发生,血流动力学可维持平稳,并减轻机体应激反应。

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