

盐酸羟考酮在创伤性重型颅脑损伤术中的应用效果

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【摘要】 目的 探究盐酸羟考酮复合丙泊酚在创伤性重型颅脑损伤术中的麻醉效果及脑保护作用。方法 前瞻性选取 2020-01—2022-01 鹤煤总医院进行手术治疗的创伤性重型颅脑损伤患者 68 例为研究对象, 按照随机数字表法分为研究组与对照组各 34 例。2 组患者均行全身麻醉, 对照组麻醉维持给予丙泊酚+瑞芬太尼, 手术结束前 15~20 min 静脉注射舒芬太尼预镇痛; 研究组麻醉维持给予丙泊酚+盐酸羟考酮, 手术结束前 15~20 min 静脉注射盐酸羟考酮镇痛。比较 2 组麻醉效果、Ramsay 镇静情况、炎症因子 [肿瘤坏死因子- α (TNF- α)、白细胞介素-6 (IL-6)]、脑血流指标 [颈静脉血氧饱和度 (SjvO₂)、动脉-颈内静脉血氧含量差 (Da-jvO₂)、脑氧摄取率 (CERO₂)]、神经元特异性烯醇化酶 (NSE) 及 S-100 β 蛋白水平差异。结果 研究组患者的自主呼吸时间、苏醒时间、术后拔管时间、术中 MAP 及术后 HR 值均低于对照组 ($P < 0.05$), 且其麻醉 5 min、30 min 及 60 min 的 Ramsay 镇静情况评分分别为 (3.88 \pm 1.21) 分、(3.23 \pm 0.49) 分、(3.44 \pm 0.61) 分, 均低于对照组的 (5.59 \pm 1.42) 分、(4.68 \pm 0.64) 分、(5.00 \pm 0.49) 分 ($P < 0.05$)。组间比较, T1、T2 及 T3 时刻, 研究组 TNF- α 、IL-6、S-100 β 、NSE、SjvO₂ 值均低于对照组 ($P < 0.05$), Da-jvO₂、CERO₂ 值均高于对照组, 差异均具有统计学意义 ($P < 0.05$)。结论 盐酸羟考酮复合丙泊酚应用于创伤性重型颅脑损伤术中的镇静及镇痛效果均较好, 可降低脑组织应激及炎症反应, 具有更好的脑保护作用。

【关键词】 创伤性重型颅脑损伤; 盐酸羟考酮; 丙泊酚; 麻醉效果; 脑保护

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Application effect of oxycodone hydrochloride in traumatic severe craniocerebral injury

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【Abstract】 Objective To explore the anesthesia effect and brain protection effect of oxycodone hydrochloride combined with propofol in traumatic severe traumatic brain injury surgery. **Methods** A total of 68 patients with severe traumatic brain injury who underwent surgical treatment in our hospital from January 2020 to January 2022 were prospectively selected as the research objects, and were divided into the study group and the control group according to the random number table method, with 34 cases in each. Both groups of patients were given general anesthesia, the control group was given propofol + remifentanyl for maintenance anesthesia, and sufentanil was intravenously injected 15-20 minutes before the end of the operation for pre-analgesia. The study group was given propofol + oxycodone hydrochloride for maintenance anesthesia oxycodone hydrochloride was administered intravenously 15 to 20 minutes before the end of the operation for analgesia. The anesthesia effect, Ramsay sedation, inflammatory factors (tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6)), blood gas indexes (jugular vein oxygen saturation (SjvO₂), Differences in arterial-internal jugular vein oxygen content (Da-jvO₂), cerebral oxygen uptake rate (CERO₂)), neuron-specific enolase (NSE) and S-100 β protein levels. **Results** The spontaneous breathing time, recovery time, postoperative extubation time, intraoperative MAP and postoperative HR values of

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the study group were lower than those of the control group ($P<0.05$), and the Ramsay sedation scores at 5 min, 30 min and 60 min of anesthesia were respectively were (3.88±1.21) points, (3.23±0.49) points, (3.44±0.61) points, all lower than the control group (5.59±1.42) points, (4.68±0.64) points, (5.00±0.49) points ($P<0.05$). At T1, T2 and T3, the values of TNF- α , IL-6, S-100 β , NSE and SjvO₂ in the study group were lower than those in the control group ($P<0.05$), and the values of Da-jvO₂ and CERO₂ were higher than those in the control group, the differences were statistically significant ($P<0.05$). **Conclusion** Oxycodone hydrochloride combined with propofol has good sedative and analgesic effects in traumatic severe craniocerebral injury, can reduce brain tissue stress and inflammatory response, and has better brain protection

【Key words】 Traumatic severe traumatic brain injury; Oxycodone hydrochloride; Propofol; Anesthesia effect; Brain protection

重型颅脑损伤神经外科危重症,其致残率及病死率高,若未及时进行有效干预,可造成患者不同程度的残疾,严重影响其生命健康^[1]。急诊开颅手术为重型颅脑损伤的有效治疗方式之一,其可快速清除患者挫伤及血肿的脑组织,降低脑损伤^[2]。但颅脑的位置具有特殊性,其生理及解剖结构均较为复杂;且颅脑手术创伤较大,疼痛感强,可引起患者应激反应及全身炎症反应,对患者认知功能及预后造成不利影响^[3-4]。故做好围手术期间患者的麻醉镇痛至关重要。丙泊酚为常用短效麻醉制剂,其用于麻醉诱导及维持的效果确切;而盐酸羟考酮为半合成的阿片类受体激动剂,具有镇痛效果强且安全性高的特点^[5-6]。目前盐酸羟考酮复合丙泊酚应用于癌痛、内科及外科手术的镇痛效果已得到证实,但二者联合对重型颅脑损伤的研究报道偏少且二者联合对患者脑保护的影响尚缺乏系统性研究予以佐证^[7]。基于此,本研究探讨盐酸羟考酮复合丙泊酚在创伤性重型颅脑损伤术中的麻醉效果及脑保护作用。

1 资料和方法

1.1 一般资料 前瞻性选取 2020-01—2022-01 鹤煤总医院进行手术治疗的创伤性重型颅脑损伤患者 68 例为研究对象。纳入标准:①明确颅脑外伤史,经头部 CT、MRI,确诊者;②入院时间均 <6 h,且均进行开颅手术治疗者;③GCS 评分 ≤ 8 分者;④无中途退院,停止治疗者;⑤随访资料均完整者。排除标准:①重要脏器功能不全者;②合并颅脑外伤史;③合并血液系统疾病;④智力或精神障碍不能配合本研究者。治疗组中男 19 例,女 15 例,年龄 29~76(49.26±10.58)岁;入院时 GCS 评分(5.42±1.16)分。对照组男 21 例,女 13 例,年龄 26~74(49.46±11.48)岁;GCS 评分(5.69±1.21)分。2 组患者一般资料差异均无统计学意义($P>0.05$)。

1.2 方法 手术均由同一组医生进行。2 组患者术前均给予禁食、水(6 h)处理,常规开放上肢静脉通

道,连接心电监护仪严密监测患者的血压、心率、血氧等情况,同时控制患者颅内压。麻醉诱导:均给予丙泊酚(西安力邦制药有限公司,规格 100 mg×10 mL) 1.5 mg/kg,芬太尼 4~6 μ g/kg,罗库溴铵(浙江仙琚制药股份有限公司,国药准字 H20123188) 0.6 mg/kg,静脉推注。诱导后行气管插管及机械通气,维持潮气值范围为 8~10 mL/kg,呼吸频率 12~15/min, PETCO₂ 34~45 mmHg。

麻醉维持:对照组均给予丙泊酚 6~8 mg/(kg·h)、盐酸瑞芬太尼 0.15 μ g/(kg·min)(江苏恩华药业股份有限公司),手术结束前 15~20 min 静脉注射舒芬太尼 0.15 μ g/(kg·min)预镇痛处理,与 10 mg 脱烷司琼及生理盐水配置,持续泵入。研究组麻醉维持给予丙泊酚 6~8 mg/(kg·h)、盐酸羟考酮 0.1~0.15 mg/(kg·h),手术结束前 15~20 min 静脉注射盐酸羟考酮 0.08 mg/kg 镇痛处理,与 10 mg 脱烷司琼及生理盐水配置,持续泵入。

术中根据患者体征情况适当调整药物剂量,若患者出现低 BP 可给予适量的麻黄碱,若心率过低给予适量阿托品,术后送至恢复室。

1.3 观察指标 (1)麻醉效果:记录 2 组患者围手术期间呼吸恢复时间、苏醒时间、术后拔管时间、术中平均动脉压(MAP)及心率(HR)。(2)Ramsay 镇静:分别于麻醉 5 min、30 min 及 60 min 评估患者的镇静情况。其中 1 分:焦虑不安、焦躁状态;2 分:可配合,但为安静清醒状态;3 分:对指令有反应;4 分:反应迅速,常为睡眠状态;5 分:反应迟缓,多睡眠;6 分:深度麻醉或睡眠状态。(3)血清指标:术前(T0)、术中硬脑膜切开后(T1)、术后 12 h(T2)及术后 24 h(T3)时刻抽取患者肘静脉血 3 mL 进行离心,离心半径为 8 cm,速度 3 000 r/min,10 min,完成后取上层血清 -80 °C 保存备测。①炎症因子:肿瘤坏死因子- α (TNF- α)、白细胞介素-6(IL-6)均采用 ELISA 法测定。②神经功能:神经元特异性烯醇化酶(NSE)、S-100 β 蛋白(S-100 β)均采用 ELISA 法测定。(4)脑血

流指标:采用多功能血气检测仪检测颈静脉血氧饱和度(SjvO₂)、动脉-颈内静脉血氧含量差(Da-jvO₂)、脑氧摄取率(CERO₂)差值。

1.4 统计学处理 应用SPSS 22.0 进行数据分析。计数资料用百分率(%)表示,行 χ^2 检验;正态分布的计量资料用($\bar{x}\pm s$)表示,组间及组内比较分别行独立、配对样本 *t* 检验,不同时间的计量资料采用重复测量方差分析。*P*<0.05 为差异具有统计学意义。

2 结果

2.1 2组麻醉效果比较

研究组患者的自主呼吸时

间、苏醒时间、术后拔管时间、术中 MAP 及术后 HR 值均低于对照组(*P*<0.05)。见表 1。

2.2 2组 Ramsay 镇静情况比较 与对照组相比,研究组患者麻醉 5 min、30 min 及 60 min 的 Ramsay 镇静情况评分均偏低(*P*<0.05)。见表 2,图 1。

2.3 2组炎症因子比较 组间比较,T1、T2 及 T3 时刻,研究组 TNF- α 及 IL-6 水平均低于对照组(*P*<0.05)。组内比较,与 T0 时刻相比,2 组患者 T1 的 TNF- α 及 IL-6 水平均显著升高(*P*<0.05),而 T2 及 T3 的 TNF- α 及 IL-6 水平均出现降低(*P*<0.05)。见表 3,图 2。

表 1 2组麻醉效果比较 ($\bar{x}\pm s$)

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

组别	<i>n</i>	自主呼吸时间/h	苏醒时间/h	术后拔管时间/h	术中 MAP/mmHg	术后 HR/(次/min)
研究组	34	4.17±0.46	7.23±0.60	11.21±1.15	72.62±2.63	89.41±2.82
对照组	34	5.56±0.61	8.88±0.54	15.65±1.39	77.53±3.69	95.59±3.89
<i>t</i> 值		-10.533	-11.858	-14.360	-6.326	-7.492
<i>P</i> 值		<0.001	<0.001	<0.001	<0.001	<0.001

表 2 2组 Ramsay 镇静情况比较 ($\bar{x}\pm s$)

Table 2 Comparison of Ramsay sedation in two groups ($\bar{x}\pm s$)

组别	<i>n</i>	麻醉 5 min	麻醉 30 min	麻醉 60 min	<i>F</i> _{时点}	<i>F</i> _{交互}	<i>F</i> _{组间}
研究组	34	3.88±1.21	3.23±0.49	3.44±0.61	13.727	0.280	93.060
对照组	34	5.59±1.42	4.68±0.64	5.00±0.49			
<i>t</i> 值		-5.504	-9.549	-11.566			
<i>P</i> 值		<0.001	<0.001	<0.001	<0.001	0.598	<0.001

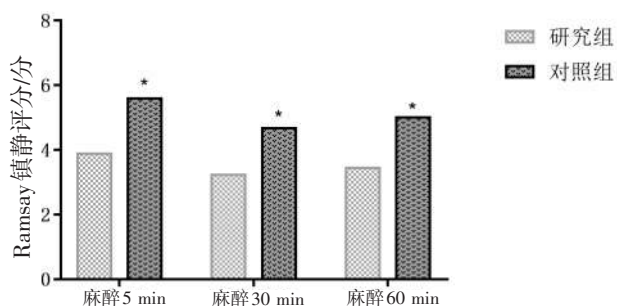


图 1 2组 Ramsay 镇静情况比较

Figure 1 Comparison of Ramsay sedation in two groups

2.4 2组NSE、S-100 β 水平比较 组间比较,T1、T2 及 T3 时刻,研究组 S-100 β 、NSE 水平均低于对照组(*P*<0.05)。组内比较,与 T0 时刻相比,2 组患者治疗 T1、T2 时刻的 S-100 β 、NSE 水平均显著升高(*P*<

0.05),而 T3 时刻均降低(*P*<0.05)。见表 4。

2.5 2组患者脑血流量比较 组间比较,T1、T2 及 T3 时刻,研究组 SjvO₂ 值均低于对照组(*P*<0.05), Da-jvO₂、CERO₂ 值均高于对照组(*P*<0.05)。组内比较,与 T0 时刻相比,2 组患者治疗 T1、T2、T3 的 SjvO₂ 值均显著升高(*P*<0.05),而 Da-jvO₂、CERO₂ 值均降低(*P*<0.05)。见表 5,图 4。

3 讨论

颅脑手术为重型颅脑损伤的有效治疗方法,其可快速解除患者脑血肿挤压情况,避免脑组织二次损伤,促进患者脑神经功能恢复^[8]。但颅脑创伤的位置及解剖结构特殊,手术时间长,患者经手术后可能会破坏其脑组织的血-脑屏障防御机制,在麻醉应激

表 3 2 组炎症因子比较 ($\bar{x}\pm s$)

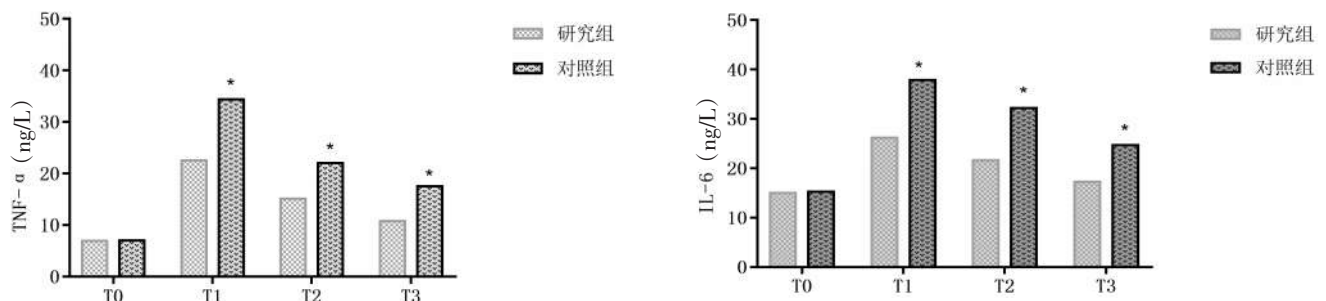
Table 3 Comparison of inflammatory factors in the two groups ($\bar{x}\pm s$)

指标	组别	n	T0	T1	T2	T3	F 值	P 值
TNF- α /(ng/L)	研究组	34	6.89 \pm 0.78	22.53 \pm 2.46	15.05 \pm 1.91	10.76 \pm 1.49	$F_{\text{时点}}=287.928$ $F_{\text{组间}}=119.742$ $F_{\text{交互}}=198.405$	$P_{\text{时点}}<0.001$ $P_{\text{组间}}<0.001$ $P_{\text{交互}}<0.001$
	对照组	34	7.03 \pm 0.78	34.35 \pm 5.55	21.98 \pm 2.71	17.53 \pm 1.62		
	t 值		0.740	11.353	12.188	17.935		
	P 值		0.462	<0.001	<0.001	<0.001		
IL-6(ng/L)	研究组	34	14.98 \pm 2.44	26.21 \pm 2.61	21.57 \pm 3.68	17.21 \pm 2.18	$F_{\text{时点}}=113.276$ $F_{\text{组间}}=78.689$ $F_{\text{交互}}=138.422$	$P_{\text{时点}}<0.001$ $P_{\text{组间}}<0.001$ $P_{\text{交互}}<0.001$
	对照组	34	15.21 \pm 2.59	37.90 \pm 4.74	32.18 \pm 3.84	24.64 \pm 3.91		
	t 值		0.377	12.597	11.632	9.678		
	P 值		0.707	<0.001	<0.001	<0.001		

表 4 2 组NSE、S-100 β 水平比较 ($\bar{x}\pm s$)

Table 4 Comparison of NSE and S-100 β levels between the two groups ($\bar{x}\pm s$)

组别	n	S-100 β 蛋白/(μ g/L)				NSE/(μ g/L)				
		T0	T1	T2	T3	T0	T1	T2	T3	
研究组	34	2.83 \pm 0.42	5.15 \pm 0.88	8.77 \pm 0.75	3.70 \pm 0.54	32.56 \pm 6.12	40.61 \pm 5.60	24.28 \pm 6.06	15.61 \pm 3.21	
对照组	34	2.87 \pm 0.53	8.46 \pm 1.02	11.63 \pm 1.14	5.61 \pm 0.74	33.56 \pm 5.89	48.22 \pm 5.42	34.12 \pm 5.12	22.56 \pm 5.12	
t 值		0.345	14.327	12.221	12.157	0.686	5.694	7.232	6.706	
P 值		0.731	<0.001	<0.001	<0.001	0.495	<0.001	<0.001	<0.001	
$F_{\text{时点}}, P_{\text{时点}}$			1335.293, <0.001				908.590, <0.001			
$F_{\text{交互}}, P_{\text{交互}}$			114.515, <0.001				28.051, <0.001			
$F_{\text{组间}}, P_{\text{组间}}$			183.263, <0.001				36.033, <0.001			



注:与研究组比较,* $P<0.05$

图 2 2 组炎症因子比较

Figure 2 Comparison of inflammatory factors in the two groups

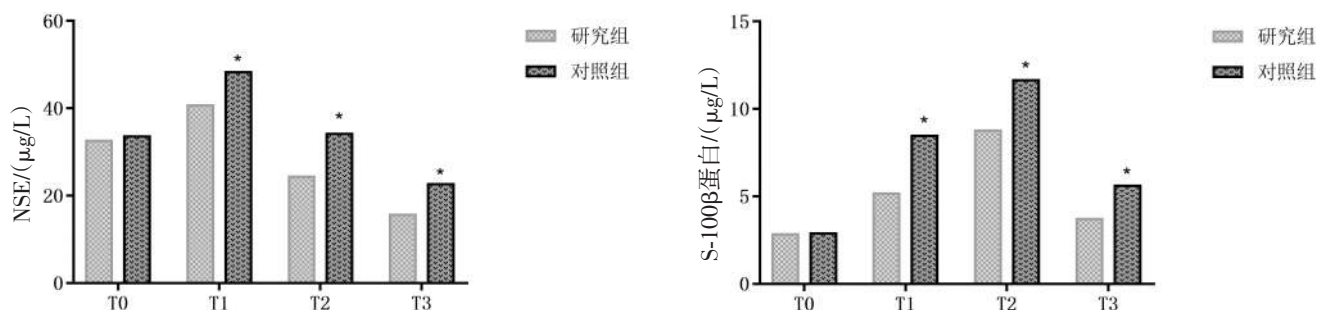


图 3 2 组NSE、S-100 β 水平比较

Figure 3 Comparison of NSE and S-100 β levels between the two groups

表 5 2 组患者脑血流量比较 ($\bar{x} \pm s$)

Table 5 Comparison of cerebral blood flow between the two groups ($\bar{x} \pm s$)

指标	组别	n	T0	T1	T2	T3	F 值	P 值
SjvO ₂ %	研究组	34	59.12±3.26	61.32±3.05	63.52±3.40	65.85±3.52	F _{时点} =577.028	P _{时点} =0.002
	对照组	34	59.36±3.06	64.58±3.42	68.21±3.86	72.88±4.21		
	t 值		0.313	4.148	5.316	7.470	F _{组间} =61.862	P _{组间} <0.001
	P 值		0.755	<0.001	<0.001	<0.001	F _{交互} =29.118	P _{交互} <0.001
Da-jvO ₂ %	研究组	34	48.60±3.42	45.62±3.02	42.28±2.85	39.52±2.42	F _{时点} =1 632.324	P _{时点} <0.001
	对照组	34	48.52±3.20	40.12±3.12	36.49±2.98	31.86±2.55		
	t 值		0.100	7.386	8.188	12.705	F _{组间} =121.471	P _{组间} <0.001
	P 值		0.921	<0.001	<0.001	<0.001	F _{交互} =68.037	P _{交互} <0.001
CERO ₂ %	研究组	34	34.12±2.62	33.12±2.20	32.20±2.13	30.12±2.08	F _{时点} =516.812	P _{时点} <0.001
	对照组	34	34.35±2.88	31.16±2.42	28.28±2.15	25.41±2.12		
	t 值		0.344	3.494	7.553	9.247	F _{组间} =80.111	P _{组间} <0.001
	P 值		0.732	0.001	<0.001	<0.001	F _{交互} =30.607	P _{交互} <0.001

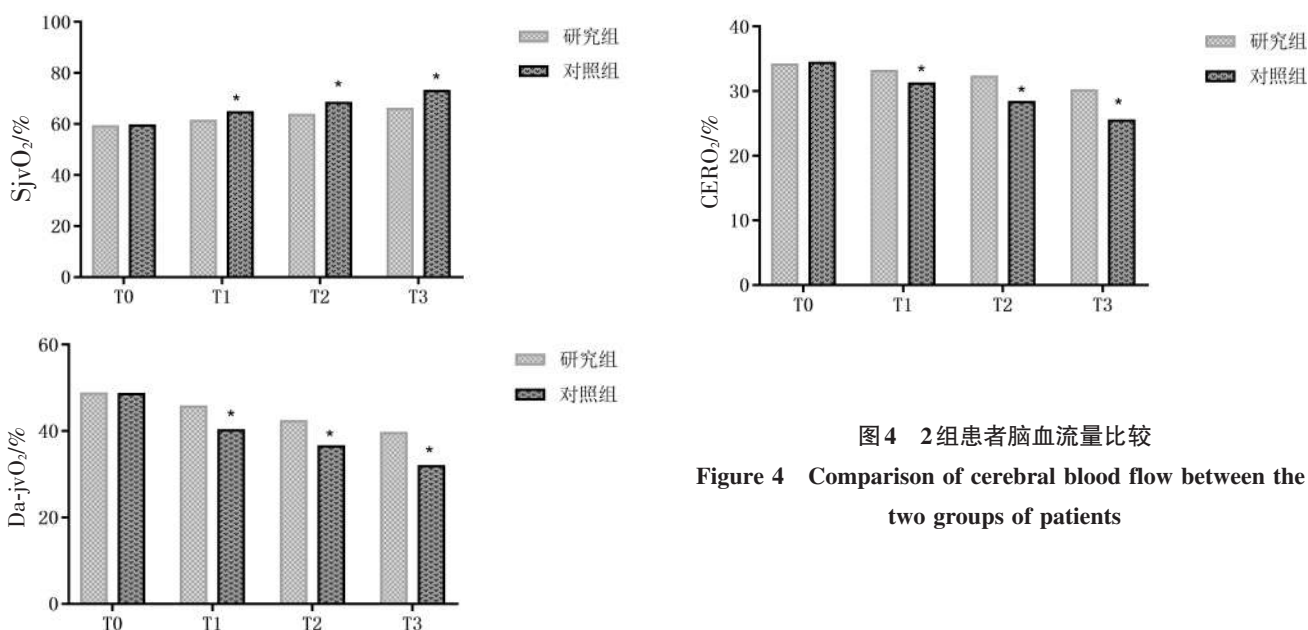


图 4 2 组患者脑血流量比较

Figure 4 Comparison of cerebral blood flow between the two groups of patients

反应作用下诱发机体炎症释放,影响患者的手术效果及预后^[9-12]。故围手术期间在保证麻醉效果的同时,降低患者应激反应至关重要。丙泊酚及瑞芬太尼为临床常用的麻醉维持方式,其镇痛效果确切,对患者血流动力学的稳定具有一定作用。但丙泊酚对患者的呼吸具有一定的抑制作用;而瑞芬太尼的代谢快,药效维持时间短,易造成患者痛觉恢复,引起术中应激反应及炎症释放,在影响患者手术效果的同时延缓其恢复进程,因此具有一定的弊端^[13-16]。盐酸羟考酮为半合成阿片类药物,具有与吗啡相似的药理机制,其对中枢神经系统中阿片 μ 及 κ 受体均具有激动作用而产生镇痛效果^[17-21]。且其可通多生物转运方式透过血脑屏障进入到中枢神经系统中,提高脑组织中的药物浓度,增强药效,发挥麻醉镇痛及维持效果,因此可利于脑组织血流动力学的稳定,降

低炎症,加快其术后恢复^[22-25]。本研究中,研究组患者术后自主呼吸时间、苏醒时间、术后拔管时间、术中 MAP 及术后 HR 值均低于对照组;且麻醉 5 min、30 min 及 60 min 的 Ramsay 镇静情况评分均低于对照组。该结果提示,盐酸羟考酮复合丙泊酚应用于创伤性重型颅脑损伤术中的镇静及镇痛明显。

颅脑手术虽能改善重型颅脑损伤患者的颅内压及水肿情况,降低原发性损伤对脑神经细胞的破坏^[26-31]。TNF- α 为促炎因子,可促使 T 淋巴细胞释放多种炎症细胞因子,参与脑组织炎症反应。IL-6 可介导炎症反应级联方法并诱导急性反应蛋白,可充当递质作用参与脑部炎症反应。而盐酸羟考酮不仅具有良好的镇静及镇痛效果,而且可调节细胞因子,维持机体抗氧-促炎因子平衡^[32-35]。本研究中,研究组 TNF- α 及 IL-6 水平均低于对照组,提示盐酸羟考酮

的炎症抑制作用。氧化应激为脑组织损伤过程中的重要生理表现。而NSE为神经元和神经内分泌细胞所特有的一种酸性蛋白酶,是糖酵解过程中的一种关键性烯醇化酶,其在脑组织细胞的活性最高,因此当神经元及血脑屏障受到损伤时,可迅速被释放。S-100 β 为神经胶质细胞分泌及合成的一种酸性钙结合蛋白,当中枢神经系统受到损伤时,S-100 β 蛋白大量释放进入脑脊液中,可透过血-脑屏障入血^[36-40]。本研究中,与T0时刻相比,2组患者治疗T1、T2时刻的S-100 β 、NSE水平均显著升高,而T3时刻均降低。提示颅脑手术对脑组织具有一定的损伤,但研究组T1、T2及T3时刻均低于对照组,说明盐酸羟考酮复合丙泊酚应用于创伤性重型颅脑损伤术具有更好的脑保护作用。

创伤性脑组织损伤缺血缺氧时,可对机体功能产生不可逆的影响,进一步造成脑血流异常。CERO₂为脑耗氧反映指标,其水平升高提示脑耗氧增加,而其水平降低提示脑组织耗氧量减少,可促进神经功能的恢复^[41-46]。SjvO₂主要体现脑氧代谢情况,可对全脑氧供需平衡具有一定的指示作用。另Da-jvO₂为脑耗氧指标,主要体现脑组织损伤情况。本研究中,研究组SjvO₂值均低于对照组,而Da-jvO₂、CERO₂值均高于对照组。该结果说明,盐酸羟考酮复合丙泊酚应用于创伤性重型颅脑损伤术可增加患者的脑血流量,改善患者脑组织水肿及氧合,利于患者术后的恢复。

盐酸羟考酮复合丙泊酚应用于创伤性重型颅脑损伤术中的镇静及镇痛效果均较好,可降低脑组织应激及炎症反应,具有更好的脑保护作用。

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