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瑞芬太尼联合丙泊酚对躁狂症患者电休克治疗后的 再定向时间和认知功能的影响*

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摘要 目的: 探究瑞芬太尼联合丙泊酚对躁狂症患者电休克治疗后的再定向时间和认知功能的影响。**方法:** 招募 2018 年 2 月至 2019 年 9 月在本院就诊的 150 例躁狂症患者,将患者分为对照组和观察组,各 75 例。通过简易精神状态检查(MMSE)评分系统比较电休克疗法(ECT)后的认知障碍。通过杨氏躁狂量表(YMRS)评分系统比较躁狂症患者的躁狂严重程度。通过 MMSE 评分系统比较躁狂症患者 ECT 后的时间定向能力。通过无创血压和心电图监测患者 ECT 前后的平均动脉压和心率。**结果:** 两组患者一般资料统计无差异($P>0.05$)。观察组术后 5 小时无碍率较对照组升高($P<0.05$),观察组术后 5 小时出现严重认知障碍率较对照组降低($P<0.05$),中度认知障碍率两组比较无差异($P>0.05$)。ECT 后 5 小时和 24 小时观察组与对照组的 YMRS 评分比较无差异($P>0.05$)。ECT 前,观察组时间定向评分与对照组比较无差异($P>0.05$),ECT 后,观察组时间定向评分较对照组升高($P<0.05$)。ECT 前和 ECT 后,观察组的平均动脉压和心率比较无差异($P>0.05$)。**结论:** 在接受 ECT 的躁狂患者中,瑞芬太尼补充丙泊酚诱导麻醉不影响 ECT 的疗效,并且能减少 ECT 后认知障碍的发生,缩短重定向时间。

关键词: 瑞芬太尼;丙泊酚;躁狂症;电休克治疗;认知障碍;再定向时间

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The Effect of Remifentanyl Combined with Propofol on the Reorientation Time and Cognitive Function of Patients with Mania after Electroconvulsive Therapy*

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ABSTRACT Objective: To explore the effect of remifentanyl combined with propofol on the reorientation time and cognitive function of patients with mania after electroconvulsive therapy. **Methods:** A total of 150 patients with mania treated in the our hospital from February 2018 to September 2019 were recruited and divided into control group and observation group, with 75 cases in each group. Cognitive impairment after electroconvulsive therapy (ECT) was compared by the MMSE scoring system. Young's Manic Scale (YMRS) score was used to compare the severity of mania in patients with mania. MMSE scoring system was used to compare the time orientation ability of patients with mania after ECT. Mean arterial pressure and heart rate before and after ECT were monitored by noninvasive blood pressure and electrocardiogram. **Results:** There was no difference in general data between the two groups ($P>0.05$). The barrier-free rate of observation group at 5 hours after operation was higher than that of control group ($P<0.05$), the rate of severe cognitive impairment at 5 hours after operation in observation group was lower than that of control group ($P<0.05$), the rate of moderate cognitive impairment in the two groups There was no difference ($P>0.05$). There was no difference in YMRS scores between the observation group and the control group at 5 hours and 24 hours after ECT ($P>0.05$). Before ECT, the time-oriented score of the observation group was not different from that of the control group ($P>0.05$). After ECT, the time-oriented score of the observation group was higher than that of the control group ($P<0.05$). Before ECT and after ECT, there was no difference in mean arterial pressure and heart rate of the observation group ($P>0.05$). **Conclusion:** In manic patients receiving ECT, remifentanyl supplementation with propofol-induced anesthesia does not affect the efficacy of ECT, and can reduce the occurrence of cognitive impairment after ECT and

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shorten the redirection time.

Key words: Remifentanyl; Propofol; Mania; Electroconvulsive therapy; Cognitive impairment; Reorientation time

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前言

躁狂症是心境障碍的一种表现形式,特点为心境高涨、活动增多以及思维奔逸等^[1]。目前尚不清楚 I 型双相情感障碍和躁狂症的病因。有证据表明其病因包括遗传、心理和社会因素的综合作用^[2]。治疗躁狂症患者最有效的疗法之一是电休克疗法 (Electroconvulsive therapy, ECT)^[3]。认知障碍已被认为是 ECT 中的一个常见问题。具体而言,注意力和执行功能领域,包括再定向时间、抑制控制、认知灵活性和目标导向行为,变得极其脆弱。最常用于诱导麻醉的注射麻醉剂包括硫喷妥钠、依托咪酯、丙泊酚等,偶尔还有瑞芬太尼^[4-6]。丙泊酚已被广泛应用于麻醉诱导、维持以及术中及重症监护室镇静等。具有起效快、镇痛镇静效果好、苏醒恢复迅速等特点。该药物可降低恶心和呕吐的发生率以及不良血流动力学反应^[7]。意识丧失和适当水平的肌肉松弛是 ECT 麻醉的主要目的。然而,通过引入不同的药理药物,科研人员已考虑麻醉剂对患者认知功能结果的可能影响^[8]。瑞芬太尼是一种有效的短效 μ -阿片受体激动剂,被组织和血浆酯酶迅速代谢,恢复效果较快。多项研究评估了瑞芬太尼对 ECT 患者的影响^[9]。一些科研工作者在重度抑郁症中提出了麻醉剂(包括在麻醉诱导药物中添加瑞芬太尼)影响 ECT 的假设^[10]。但迄今为止,尚未有已发表的文章在躁狂症中进行相关麻醉剂影响 ECT 这个问题。本研究旨在探讨瑞芬太尼联合丙泊酚对躁狂症患者电休克治疗后的再定向时间和认知功能的影响。

1 资料与方法

1.1 一般资料

招募 2018 年 2 月至 2019 年 9 月在本院就诊的 150 例躁狂症患者,其中男性 86 例,女性 64 例,平均年龄(32.57 ± 4.25)岁。所有患者入院均接受 ECT 治疗。根据研究目的,将 150 例患者分为对照组和观察组,对照组(ECT 治疗初用丙泊酚麻醉, $n=75$),观察组(ECT 治疗初使用瑞芬太尼联合丙泊酚麻醉, $n=75$)。

纳入标准:根据《精神疾病诊断和统计手册》第四版标准,患有双相 I 型障碍(躁狂发作)^[11];同意签署知情同意书;本研究经省人民医院研究伦理委员会批准。

排除标准:前 6 个月有 ECT 病史,最近一周使用非苯二氮卓类抗惊厥药(丙戊酸钠、卡马西平、拉莫三嗪或托吡酯);精神分裂症或其他不属于情绪障碍患者;神经系统疾病或严重内科疾病的精神障碍患者;怀孕、过去 3 个月内中风史、脑部手术史、严重头部外伤、近 2 年内有吸毒或酗酒依赖性;排除心血管疾病控制不佳、心律失常、慢性阻塞性肺疾病、肾或肝功能衰竭和器质性脑疾病的患者。

1.2 方法

1.2.1 治疗流程 在接受 ECT 前,所有患者均接受了杨氏躁狂

量表(Young Mania Rating Scale, YMRS)和简易精神状态检查(Mini-mental state examination, MMSE)的评估。清除期(1 周未用药)后,开始双侧 ECT 治疗。在第三次、第六次和最后一次 ECT 治疗后对患者进行评估。若 YMRS 总分 ≤ 12 ,主治精神科医生可决定结束 ECT 治疗。通过测量治疗后重新定向时间来评估即时认知不良反应。

1.2.2 麻醉剂用药 观察组患者预先给药瑞芬太尼(宜昌人福药业有限责任公司;国药准字 H20030200;规格:1 mg)1 μ g/kg,复合丙泊酚(西安力邦制药有限公司;国药准字 H20010368;规格:10 mL)1 mg/kg(间隔为 1 min),对照组患者给予生理盐水加丙泊酚 1 mg/kg,所有患者在睫毛反射消失后静脉注射琥珀酰胆碱(上海旭东海普药业有限公司;国药准字 H31020599;规格:2 mL)0.5 mg/kg。对于初始剂量丙泊酚未达到睫毛反射的患者,进一步增加 1%的丙泊酚以确保达到这一点;所有患者在 ECT 期间均通过面罩进行了 100%氧气的手动通气。期间连续监测血压、心率和氧饱和度。

1.2.3 ECT 干预 在 ECT 中,两个电极的中点位于两侧轨道侧角上方约 2.5 cm 处。短脉冲 ECT 设备(胸腺电子管;伊利诺伊州布拉夫湖 somatics 有限责任公司)用于所有受试者,刺激脉冲宽度为 1.0 ms。在第一次 ECT 治疗中,使用改良的剂量滴定法测量总散射因子(Total scattering factor, ST),并使用带套囊的方法来确定运动持续时间。若 ECT 刺激不能客观地引起持续至少 25 s 的全身性惊厥活动,则在 30 s 后通过逐步增加刺激剂量重复癫痫诱导。每周进行 3 次电休克治疗。ECT 治疗是由不知情的同一位精神科医生安排的。根据精神科医生的决定,每位患者接受的第一次 ECT 剂量在最大刺激幅度的 30%下进行。

1.2.4 MMSE 评估认知障碍和再定向时间 使用 MMSE 检查患者以确定任何认知缺陷。该测试在第一次 ECT 治疗前、ECT 治疗后 5 小时和 24 小时进行。认知障碍以 30 分评分系统进行分类^[12]:24-30 分表示无任何认知障碍,18-23 分表示中度认知障碍,0-17 分表示严重认知障碍。依据时间在定向单项评分(5 分)比较患者的再定向时间能力。

1.3 统计分析

本研究中数据均通过 SPSS 20.0 统计分析软件(美国 IBM 公司)处理;计量资料按照($\bar{x} \pm s$)形式表示,采取单因素方差分析;计数资料以(%)形式表示,采用 χ^2 分析。 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 人口统计学分析

两组患者一般资料统计无差异($P > 0.05$),见表 1。

2.2 ECT 后认知障碍比较

通过 MMSE 评分系统比较 ECT 后的认知障碍,观察组术后 5 小时无障碍率较对照组升高($P < 0.05$),观察组术后 5 小时

出现严重认知障碍率较对照组降低($P<0.05$), 中度认知障碍率 两组比较无差异($P>0.05$), 见表 2。

表 1 人口统计学分析
Table 1 Demographic Analysis

Items	Control group (n=75)	Observation group (n=75)
Age (years)	31.98±5.23	33.14±5.79
Gender (MALE: Female)	41:34	45:30
BMI (kg/m ²)	22.85±1.84	23.21±1.46
Course of disease (years)	5.18±2.46	6.33±3.45
MMSE score	24.36±5.29	25.71±5.74
YMRS scores	28.15±6.22	28.63±6.83
Hypertension, diabetes (%)	3(4.00 %)	4(5.33 %)

表 2 ECT 后 5 小时认知障比较
Table 2 Comparison of cognitive impairment at 5 hours after ECT

Groups	No cognitive impairment 5 hours after ECT (n/%)	Moderate cognitive impairment 5 hours after ECT (n/%)	Severe cognitive impairment 5 hours after ECT (n/%)
Control group (n=75)	10 (13.33 %)	29 (38.66 %)	36 (48.00 %)
Observation group (n=75)	28 (37.33 %) [#]	32 (42.66 %)	15 (20.00 %) [#]

Note: compared with the Control group, [#] $P<0.05$.

2.3 YMRS 评分比较

通过 YMRS 评分系统比较躁狂症患者的躁狂严重程度发

现,ECT 后 5 小时和 24 小时观察组与对照组的 YMRS 评分比较无差异($P>0.05$), 见表 3。

表 3 YMRS 评分比较($\bar{x}\pm s$)
Table 3 Comparison of YMRS scores ($\bar{x}\pm s$)

Groups	5 hours	24 hours
Control group (n=75)	22.68±3.18	23.06±3.58
Observation group (n=75)	23.49±3.44	23.75±4.05

2.4 时间定向评分

通过 MMSE 评分系统比较躁狂症患者 ECT 前后的时间定向能力,ECT 前, 观察组时间定向评分与对照组比较无差异

($P>0.05$),ECT 后, 观察组时间定向评分较对照组升高($P<0.05$), 见表 4。

表 4 时间定向评分($\bar{x}\pm s$)
Table 4 Time-oriented scoring ($\bar{x}\pm s$)

Groups	Before the ECT	After the ECT
Control group (n=75)	4.36±0.35	2.15±0.18
Observation group (n=75)	4.28±0.31	3.36±0.24 [#]

Note: compared with the Control group, [#] $P<0.05$.

2.5 血流动力学测量

通过无创血压和心电图监测患者 ECT 前后的平均动脉压

和心率,ECT 前和 ECT 后,观察组的平均动脉压和心率比较无差异($P>0.05$), 见表 5。

表 5 MMSE 评分分析($\bar{x}\pm s$)
Table 5 MMSE score analysis ($\bar{x}\pm s$)

Groups	Arterial pressure		Heart rate	
	Before the ECT	After the ECT	Before the ECT	After the ECT
Control group (n=75)	94.26±8.51	88.45±7.39	91.26±10.37	87.45±9.41
Observation group (n=75)	96.38±7.23	85.22±8.34	93.59±8.65	84.14±7.33

3 讨论

精神疾病是常见的健康问题,造成卫生系统高昂的成本。躁狂症是一种具有较大危害性的心理疾病。患者发病后,易出现攻击行为,其后果十分严重,因此积极治疗十分必要^[13,14]。ECT已被公认为是安全有效的选择,通过将电极放置于头皮上,并利用不同频率的电刺激引起癫痫发作^[15,16]。ECT虽是一种非常安全的治疗方法且无绝对的禁忌症,但具有一些不良反应如认知障碍(在大多数情况下会迅速消退)、罕见癫痫发作、短期并发症,并发症包括头痛、肌肉疼痛、恶心、呕吐和疲劳^[17,18]。ECT诱发的癫痫发作可导致认知和记忆功能受损,其对脑生理的影响仍存在争议^[19]。短期治疗副作用之一是ECT发作后躁动导致运动功能障碍、时间定向障碍及对语言的反应不佳^[20,21]。ECT进行麻醉的目的为:提供意识丧失和适当程度的肌肉松弛。但经引入不同的药理学药物,科研人员已考虑到麻醉剂对患者认知功能可能的影响^[22]。认知障碍的强度和持续时间,除短期疗效外,还可能直接受所用麻醉剂的影响^[23]。但迄今为止,尚未有已发表的文章探讨在躁狂症中进行相关麻醉剂影响ECT这个问题。因此本研究旨在探讨瑞芬太尼联合丙泊酚对躁狂症患者电休克治疗后的再定向时间和认知功能的影响。

本文研究结果显示:通过MMSE评分系统比较ECT后的认知障碍,观察组术后5小时无障碍率较对照组升高,观察组术后5小时出现严重认知障碍率较对照组降低,中度认知障碍率两组比较无差异。表明瑞芬太尼联合丙泊酚可降低躁狂症患者ECT后出现的认知障碍损伤。这一结果与Heidarbeigi F等人^[24]的研究具有相似性。分析可知:认知障碍是因治疗手段或者麻醉所造成的神经功能减退,例如机体中麻醉药物代谢降低、血浆中游离药物相对增多,这些均会对神经功能产生不良影响。瑞芬太尼以及丙泊酚的药物代谢快,机体内无残留,且术后苏醒快,可降低患者在ECT后不良血流动力学反应,进而保护脑组织,降低脑代谢率,最终达到降低认知障碍损伤的目的,因此瑞芬太尼联合丙泊酚的使用可降低认知障碍损伤^[25];经YMRS评分系统比较躁狂症患者的狂躁严重程度,发现ECT后5小时和24小时观察组与对照组的YMRS评分比较无差异,表明瑞芬太尼不影响ECT对患者的治疗效果。但经MMSE评分系统比较躁狂症患者ECT前后的时间定向能力,ECT前,观察组时间定向评分与对照组比较无差异,ECT后,观察组时间定向评分较对照组升高,瑞芬太尼联合丙泊酚可缩短ECT后的再定向时间。这一结果与Rezaei F等人^[26]的研究具有一致性。进一步分析可知:ECT能够成功降低患者躁狂,并缓解其严重程度。且在接受ECT治疗的躁狂发作患者中,瑞芬太尼联合丙泊酚处理不仅对患者的疗效或总体认知状态无影响,并会减少重新定向恢复时间,有利于患者的进一步意识清醒和恢复^[27,28];通过无创血压和心电图监测患者ECT前后的平均动脉压和心率,ECT前和ECT后,观察组的平均动脉压和心率比较无差异,瑞芬太尼联合丙泊酚不影响患者ECT后生理血流动力学参数。这一结果与Erdil F等人^[29]的研究具有相似性。结合相关文献进一步分析及推测可知:瑞芬太尼联合丙泊酚处理,能够抑制血小板的产生,参与机体的免疫调节,以及保护机体器官,降低损伤,在治疗前后有利于维持患者平均动脉压和心

率的稳定,进而不会影响ECT前后的生理血流动力学^[30,31]。本研究虽获得了一些结果,但存在一定不足,如样本量不足,还需进行大量研究;以及未对瑞芬太尼联合丙泊酚对躁狂症患者ECT疗效影响的具体分子机制探究,将在后续研究中深入探究。

综上所述,在接受ECT的躁狂患者中,瑞芬太尼联合丙泊酚诱导麻醉不影响ECT的疗效,并且能减少ECT后认知障碍的发生,缩短重定向时间。

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