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氯胺酮麻醉的 MECT 对难治性抑郁症患者认知功能的影响*

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摘要 目的:探讨氯胺酮麻醉下的 MECT 治疗难治性抑郁症的安全性和治疗前后的认知功能变化。**方法:**入组 60 例需要 MECT 治疗的难治性抑郁症患者,随机分为氯胺酮组(30 例)使用氯胺酮诱导麻醉的 MECT 治疗;异丙酚组(30 例)使用异丙酚诱导麻醉的 MECT 治疗。入组患者在基线期及 MECT 治疗 8 次后完成汉密尔顿抑郁量表(HAMD)评定及连线测验 A&B、威斯康星卡片分类测验、汉诺塔测试,出组时评定副反应量表。**结果:**两组患者治疗结束后认知功能均较治疗前明显降低,异丙酚组较氯胺酮组降低更明显。**结论:**氯胺酮 MECT 治疗难治性抑郁症安全有效,对患者的认知功能损害较异丙酚组轻,未出现严重副作用。

关键词:改良性电抽搐治疗;难治性抑郁症;氯胺酮;认知功能

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The Cognitive Effects of Ketamine as Anesthesia on MECT in Patients with Refractory Depressive Disorder*

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ABSTRACT Objective: To investigate the cognitive function defect of patients with TRD after ketamine-MECT. **Methods:** 60 TRD inpatients were randomly divided into two groups: propofol-MECT group, and ketamine-MECT group. Both patients were assessed HAMD, Trail Making Test A&B, WCST, Tower of Hanoi before and after the eighth time of MECT, and TESS was examined at the end of MECT treatment. **Results:** HAMD score of the two groups were lower after MECT treatment respectively and reach the clinical recovery criterion. The cognitive function of patients in two groups were deteriorated remarkable, while which in propofol-MECT group were worse than that in ketamine-MECT group. **Conclusion:** Ketamine-MECT in treatment of TRD is safe and effectively, which cause the cognitive function damage of TRD patients is milder than propofol-MECT, and no serious side effect was observed.

Key words: MECT; TRD; Ketamine; Cognitive function

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前言

难治性抑郁症(Treatment Resistant Depression, TRD)是指对两种及两种以上抗抑郁药物足剂量、足疗程治疗无效的一些抑郁症患者。TRD 的治疗目前主要采用抗抑郁药和改良电抽搐治疗(Modified electroconvulsive therapy, MECT)^[1]。MECT 抗抑郁起效快,治疗重性抑郁障碍的有效率为 79%,完全缓解率为 75%^[2]。现今 MECT 术中常用的全身麻醉药物是硫喷妥钠、异丙酚、美索比妥钠、依托咪酯等,这些药物存在抗癫痫作用,在 MECT 中作为麻醉剂使用的同时也会部分拮抗 MECT 术中以电流诱发的癫痫发作,以至影响 MECT 疗效^[3]。氯胺酮是 N-甲基-D-天冬氨酸受体阻断剂,已作为麻醉剂在临床使用数十年,临床发现该药能快速有效的治疗单相抑郁症和双相障碍的抑郁相^[4],并可快速削弱自杀观念^[5]。作为 TRD 的强化治疗方

案,氯胺酮也显示出了良好的疗效^[6,7]。有部分文献报道以氯胺酮作为 MECT 麻醉剂可以强化 MECT 的治疗效果^[8,9]。

在临床应用中,MECT 由于对患者认知功能的损害被某些患者、家属及医生排斥。国外有学者研究提出^[10],用氯胺酮作为 MECT 的麻醉剂可导致较少的认知功能损害。为了验证外国学者的研究并探索更好的治疗难治性抑郁症的方法,本研究比较了以氯胺酮和异丙酚为麻醉剂的 MECT 治疗下对难治性抑郁症患者认知功能的影响。

1 对象与方法

1.1 研究对象

来自 2012 年 6 月~2013 年 3 月于广州市精神病医院住院的患者。入组标准:① 18~45 岁;② 符合 DSM-IV 中抑郁发作的诊断标准;既往对二种以上的抗抑郁剂足剂量、足疗程治疗无

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效,(足量是指最大推荐剂量的 2/3 以上,足程是指足量治疗 4 周以上,慢性重性抑郁障碍需治疗 8 周以上,无效是指 HAMD 减分率 < 30%);③ HAMD 评分(17 项) ≥ 20 分;④ 无 MECT 禁忌证;⑤ 无色盲及影响认知功能测试的各种肢体残疾;⑥ 小学以上文化程度。所有入组患者获患者及家属知情同意。

入组共 60 例,按照入院时间先后随机分组。氯胺酮组 30 例:其中男 12 例(40%),女 18 例(60%),年龄 28~45 岁(平均 46.74 ± 10.61 岁),病程 2~25 年(平均 8.8 ± 6.7 年);复发性抑郁 20 例,双相抑郁 10 例;初中 3 例(10%),高中 9 例(30%),大学以上 18 例(60%);入组时 HAMD 评分为 26.70 ± 1.58 ;异丙酚组 30 例:其中男 11 例(36.7%),女 19 例(43.2%),年龄 26~45 岁(平均 43.67 ± 13.55 岁),病程 4~23 年(平均 8.2 ± 6.1 年);复发性抑郁 19 例,双相抑郁 11 例;初中 5 例(16.7%),高中 8 例(26.7%),大学以上 17 例(56.6%);入组时 HAMD 评分为 26.17 ± 2.70 。二组在年龄、病程、疾病组成、受教育年限方面差异均无显著性($P > 0.05$)。

1.2 研究方法

1.2.1 治疗方法 氯胺酮组使用氯胺酮(1mg/kg 体重)作为麻醉剂进行 MECT 治疗;异丙酚组使用异丙酚(2mg/kg 体重)作

为麻醉剂进行 MECT 治疗。

1.2.2 MECT 操作程序 (1)病人治疗前 8 小时禁食禁水,治疗前测体温、脉搏、呼吸、血压,排空大小便。(2)电极放置两侧颞部。(3)MECT 共 8 次,隔 1-2 日上午进行一次,3 周内完成。(4)使用美国醒脉通电抽搐治疗仪,根据病人年龄设定治疗剂量。(5)MECT 过程中监测心电图、脑电图、血氧饱和度、呼吸。(6)治疗期间禁用精神科药物。

1.2.3 观察指标 (1)量表评定:入组前、治疗 8 次末(第三周)进行 HAMD、认知功能评定、副反应量表(TESS)评定。(2)认知功能评定:由 1 位专业认知评定人员进行评定,按照连线测验 A&B、威斯康星卡片分类测验、汉诺塔的顺序测验。

1.3 统计学处理

全部数据采用 SPSS 17.0 统计软件包进行分析。

2 结果

2.1 两组治疗后 HAMD 分值及减分率比较

MECT 治疗前后相比,两组患者 HAMD 评分均降低,差异有统计学意义($P < 0.01$)。两组间相比,氯胺酮组的减分率大于异丙酚组,差异有统计学意义差异更为显著($P < 0.01$)。

表 1 两组治疗后 HAMD 分值及减分率比较

Table 1 The comparison of two groups' HAMD scores and points rate after treatment

Group	Befor treatment	Evaluation after treatment				
		First	Twice	Fourth	Sixth	Eighth
K.T. group	26.70 ± 1.58	$21.13 \pm 1.31^*$	$16.67 \pm 1.24^{**\#}$	$10.97 \pm 0.96^{**\#\#}$	$5.63 \pm 0.72^{**\#\#}$	$6.00 \pm 0.69^{**\#\#}$
Ratio of points(%)		$20.79 \pm 3.42^*$	$37.47 \pm 4.63^{**}$	$58.8 \pm 4.01^{**}$	$67.60 \pm 2.90^{**}$	$77.48 \pm 2.70^{**}$
Propofol group	26.17 ± 2.70	22.59 ± 2.57	19.24 ± 2.08	$14.03 \pm 1.80^{\#\#}$	$11.24 \pm 1.55^{\#\#}$	$8.17 \pm 1.91^{\#\#}$
Ratio of points(%)		13.54 ± 4.41	25.86 ± 6.19	45.6 ± 7.60	56.60 ± 7.11	68.23 ± 7.77

Note: Using t test, #compared with before treatment, $P < 0.05$, ## $P < 0.01$; *VS propofol group, $P < 0.05$; ** $P < 0.01$.

2.2 两组治疗前后认知功能比较

两组患者治疗前 WCST、汉诺塔及连线测验 A&B 各项分值比较无统计学差异。两组患者治疗后在 WCST 完成分类数上比治疗前明显减少,总错误数、随机错误数比治疗前明显增加;汉诺塔总分及完成步数比治疗前明显减少。治疗后,氯胺酮

组在 WCST 完成分类数方面较异丙酚组好($t=2.125$, $P=0.038^*$);在 WCST 总错误数与随机错误数方面二组间差异接近统计意义($P=0.08$),异丙酚组比氯胺酮组错误数多,其余各项两组间差异无统计学意义。

表 2 两组患者前后 WCST、TOH 分数比较

Table 2 The comparison of two groups' WCST and TOH scores points rate after treatment

	WCST		WCST		WCST		TOH		TOH		TOH	
	Complete categories	Total mistakes	Continue mistakes	Random mistakes	Total scores	Complete setps	total time	Mean thinking time of one step	Mean operating time of one step			
K.T. group	4.00 ± 1.51	16.17 ± 9.33	6.33 ± 8.45	9.83 ± 4.72	35.20 ± 15.83	5.93 ± 2.64	381.46 ± 206.89	6.77 ± 3.33	32.39 ± 15.46			
Before	$3.13 \pm 1.28^{**}$	$18.93 \pm 8.69^{**}$	$7.43 \pm 7.46^*$	$11.50 \pm 4.71^{**}$	$28.97 \pm 14.26^{**}$	$5.03 \pm 2.41^{**}$	$336.33 \pm 180.03^{**}$	7.53 ± 4.03	34.66 ± 16.52			
After												
Popofol group	3.70 ± 1.93	18.27 ± 11.44	7.00 ± 7.07	12.17 ± 6.75	36.67 ± 18.02	6.17 ± 2.99	367.63 ± 220.84	7.61 ± 6.68	27.65 ± 14.12			
Before	$2.30 \pm 1.73^{\#\#}$	$23.53 \pm 11.11^{\#\#}$	8.97 ± 5.68	$14.23 \pm 6.26^{\#}$	$27.33 \pm 20.67^{\#}$	$4.63 \pm 3.40^{\#}$	286.25 ± 197.35	6.72 ± 4.78	28.06 ± 16.97			
After												

Note: Using t test, compared between before and after treatment, K.T. group, ** $P < 0.01$, * $P < 0.05$; propofol group, ## $P < 0.01$, # $P < 0.05$; compared with two groups, * $P < 0.05$.

表 3 两组患者前后连线测验 A&B 比较

Table 3 The comparison of two groups' Trail Making Test A&B scores

	Trail Making Test A Finish time	Trail Making Test A Mistakes	Trail Making Test A Interruptions	Trail Making Test B Finish time	Trail Making Test B Mistakes	Trail Making Test B Interruptions
K.T. group	50.48± 15.43	0.133± 0.43	0.267± 0.69	89.25± 20.52	0.43± 1.01	0.83± 0.99
Before	51.60± 15.82**		0.33± 0.48	88.47± 17.23	0.57± 0.50	1.27± 0.58*
After		0				
Popofol group	54.75± 23.91	0.10± 0.40	0.333± 0.71	95.08± 52.10	0.47± 0.82	0.90± 1.06
Before	54.88± 11.42	0	0.40± 0.50	93.32± 19.98	0.60± 0.56	1.13± 0.78
After						

Note: Using t test, compared between before and after treatment, K.T. group, **P<0.01, *P<0.05;

propofol group, ## P<0.01, #P<0.05; compared with two groups, *P<0.05.

2.3 两组治疗参数及副作用比较

氯胺酮组治疗使用电量明显小于异丙酚组,抽搐持续时间明显长于异丙酚组。术后呼吸恢复时间两组间无统计学差异;

氯胺酮组意识恢复时间明显短于异丙酚组。研究期间二组患者均未出现严重不良反应。

表 4 两组治疗参数对照

Table 4 The comparison of two groups' treatment parameters

	K.T. group	Popofol group	t	P
Electric quantity(mC)	140.47± 41.09	195.30± 69.73	2.737	0.008**
Convulsion last time(s)	60.17± 12.44	33.03± 11.11	20.438	0.000**
Exponent(%)	87.67± 2.07	86.27± 3.68	0.141	0.889
Breathing recovery time (minute)	3	3	0	1
Consciousness recovery time (minute)	18.73± 1.74	27.33± 20.67	17.569	0.000**

Note: Using t test, *P<0.05, ** P<0.01.

3 讨论

氯胺酮是 N- 甲基 -D- 天冬氨酸 (NMDA) 受体阻断剂, 2009 年被世界卫生组织列入“基本药物目录”, 已作为麻醉剂在临床使用数十年, 目前作为新型滥用物质亦受到社会各界重视, 并且由于其抗抑郁作用近来成为精神医学研究的热点。有研究发现氯胺酮作为难治性抑郁的强化治疗方案也显示出了良好的疗效^[1]。

执行功能是指个体在完成认知任务时, 对各种认知过程进行协调, 以灵活、优化的方式实现特定目标的能力, 执行功能受大脑前额叶皮质以及丘脑和基底核各区域组成的神经环路控制^[2]。大量研究证实, 抑郁症患者伴有执行功能改变和注意缺陷^[3]。许多研究报道改良电抽搐治疗对患者认知功能及记忆存在损害, 对近记忆的影响甚于远记忆, 损害程度有限且为可逆性, 停止治疗后一段时间可以恢复^[4]。也有研究显示少部分患者的逆行性遗忘可持续 6 个月以上^[5,16]。

一项关于氯胺酮和依托咪酯的小样本对照研究^[7]发现, 使用氯胺酮诱导 MECT 麻醉的个体伴随较少的短期记忆功能损害; Krystal 等^[18]报道以氯胺酮为麻醉剂的 MECT 后意识恢复的比对照组快。有研究对比美索比妥钠和氯胺酮作为 MECT 麻醉剂在抽搐持续时间、发作期脑电图和认知功能影响三方面的区别^[19,20], 发现氯胺酮引起的抽搐持续时间更长, 发作期脑电图慢波波幅更大, 认知副反应更少。本研究发现, 使用氯胺酮诱导麻醉的电抽搐治疗可以用较小的电量引起较长的抽搐时间, 而且术后生命体征平稳, 苏醒较快; 经过 3 周共 8 次 MECT 治

疗后, 患者的短时和持续性注意力、工作记忆、认知的敏感性和灵活性、执行功能都有显著下降。氯胺酮麻醉组与异丙酚麻醉组相比, 氯胺酮组术后认知功能稍好。

综上所述, 氯胺酮 MECT 治疗难治性抑郁症是安全、有效的, 且与异丙酚相比对患者的认知功能损害较轻, 未出现严重副作用, 是临床上值得推广用于难治性抑郁症的治疗方法。

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