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重复经颅磁刺激联合阿普唑仑治疗失眠症伴焦虑患者的效果分析 *

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摘要 目的:研究重复经颅磁刺激以及阿普唑仑联用治疗失眠症伴焦虑患者的效果。**方法:**选择 2015 年 1 月～2019 年 12 月我院神经内科收治的 81 例失眠症伴焦虑患者,将其随机分为两组。对照组每晚在睡前 30 min 服用阿普唑仑 0.8 mg,观察组联用重复经颅磁刺激。比较两组的临床疗效,治疗前后焦虑评分、生活质量和睡眠质量评分的变化。**结果:**治疗后,观察组的有效率为 95.00 %,明显高于对照组(73.17 %,P<0.05);两组焦虑评分均较治疗前明显降低(P<0.05),心理领域、社会领域、环境领域和生理领域评分均较治疗前明显升高(P<0.05),且观察组的焦虑评分和心理领域、社会领域、环境领域、生理领域评分明显优于对照组(P<0.05);两组的睡眠持续性、主观睡眠质量、睡眠障碍、日间功能、睡眠潜伏期、安眠药物和入睡时间评分均较治疗前明显升高(P<0.05),且观察组以上指标均明显高于对照组(P<0.05)。**结论:**重复经颅磁刺激以及阿普唑仑联用治疗失眠症伴焦虑患者的效果明显优于单用阿普唑仑治疗,其能有效减轻其焦虑程度,提高患者生活质量及睡眠质量。

关键词:重复经颅磁刺激;阿普唑仑;失眠症;焦虑

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Analysis of the Efficacy of Repeated Transcranial Magnetic Stimulation Combined with Alprazolam in the Treatment of Insomnia with Anxiety*

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ABSTRACT Objective: To investigate the effect of repeated transcranial magnetic stimulation combined with alprazolam in the treatment of insomnia and anxiety. **Methods:** Eighty-one patients with insomnia and anxiety who were treated in the department of neurology in our hospital's from January 2015 to December 2019 were selected and randomly divided into two groups. The control group took 0.8 mg of alprazolam 30 min before going to bed every night, and the observation group was combined with repeated transcranial magnetic stimulation. Compare the clinical efficacy changes in anxiety score, quality of life and sleep quality score before and after treatment of the two groups. **Results:** After treatment, the effective rate of observation group was 95.00 %, which was significantly higher than that of the control group (73.17 %, P<0.05). The anxiety scores of the two groups were significantly lower than before treatment (P<0.05), and the scores of psychological, social, environmental and physiological fields were significantly higher than those before treatment (P<0.05), and the observation group's anxiety scores and psychological, social, environmental, and physiological fields were significantly better than the control group (P<0.05). The scores of sleep persistence, subjective sleep quality, sleep disorders, daytime function, sleep latency, sleeping drugs and time to fall asleep fall asleep were significantly higher than before treatment (P<0.05), and the above indicators in the above indicators in the observation group were significantly higher than those in the control group (P<0.05). **Conclusion:** The effect of repeated transcranial magnetic stimulation and alprazolam in the treatment of patients with insomnia and anxiety was significantly better than that of alprazolam alone, which could effectively reduce their anxiety and improve the quality of life and sleep quality of patients.

Key words: Repeated Transcranial Magnetic Stimulation; Alprazolam; Insomnia; Anxiety

Chinese Library Classification(CLC): R442.9; R749.72 Document code: A

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前言

失眠症主要表现为不能顺利的、快速的入睡或睡眠过程中容易醒、次日睡眠清醒后无法恢复为正常的精神状态以及睡眠时间短暂等[1,2]。随着社会经济的迅速发展,各种竞争日趋激烈,失眠症已成为一种比较常见的疾病[3]。失眠症患者常常伴有健

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忘、头昏、抑郁、心悸、多梦、焦虑和乏力困倦等症状，严重影响患者的身心健康以及日常工作[4]。中国失眠症的发病率高达42.5 %，且原发性失眠症患者伴发焦虑状态的发病率高达51 %~54 %[5]。苯二氮卓类等西药对于失眠症有显著的效果，但具有一定程度的残留效应和易依赖、易耐受等缺点，患者在服用时会出现一定的顾虑。

重复经颅磁刺激作为一种新型的物理治疗手段，具有定位相对准确和无创等优点，主要利用一定强度的时变磁场在患者脑内诱发电场，生成感应电流，进而有效改善大脑皮层局部神经元的功能[6,7]。临床上常常将重复经颅磁刺激用于抑郁症、认知功能障碍、帕金森病、精神分裂症和脑卒中的临床治疗[8]，但尚未见将重复经颅磁刺激应用于失眠症伴焦虑患者的相关研究。因此，本研究主要分析了重复经颅磁刺激以及阿普唑仑联用对于失眠症伴焦虑患者的效果，并探讨其对患者生活质量、焦虑症状和睡眠质量的影响。

1 资料与方法

1.1 一般资料

选择2015年1月～2019年12月我院神经内科收治的81例失眠症伴焦虑患者，纳入标准：(1)符合失眠症的诊断标准[9]，(2)近3个月内没有采取其他抗焦虑药物、镇静催眠药物和抗精神病药物治疗；(3)汉密尔顿焦虑量表(Hamilton Anxiety Scale，HAMA)评分大于7分；(4)均知情同意。排除标准：(1)目前癫痫发作的症状尚未得到有效控制或者有癫痫病史的患者；(2)有植入性的除颤器、心脏起搏器和其他的体内植入型仪器的患者；(3)患有脑出血、脑外伤、颅内感染以及脑梗死等脑器质性疾病的患者；(4)精神药物依赖和滥用和(或)酗酒所引起的失眠症患者；(5)伴有其他精神疾病的患者。

采用抽签法将患者随机分为两组。观察组40例，男17例，女23例；年龄25~64岁，平均(41.72± 5.48)岁；病程2~35个月，平均(13.97± 2.74)个月。对照组41例，男18例，女22例；年龄25~64岁，平均(40.93± 6.27)岁；病程2~35个月，平均(13.25± 2.68)个月。两组的基线资料比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 治疗方法

对照组：每晚在睡前30 min服用阿普唑仑0. 8 mg。观察组：采取丹麦Mag venture公司所生产的Magventure 30pro型经颅磁刺激仪，线圈为"8"字形，经颅磁刺激的具体治疗参数如下：采用高频率20 Hz，治疗部位为患者的双背侧前额叶，线圈两侧为F3以及F4位置，刺激的强度设置为80 %运动阈值，强度从50开始，然后慢慢增加，直至患者对侧手指和上肢位置抽动，每天20 min，持续治疗5 d为1个疗程，每个疗程之间间隔2 d，共治疗4个疗程。

1.3 观察指标

疗效标准[9]：① 治愈：失眠症伴焦虑患者白天的困倦感和不适感消失，焦虑症状基本消失，每天晚上的睡眠时间超过6 h或恢复至正常水平；② 显效：失眠症伴焦虑患者白天的困倦感和不适感消失，焦虑症状明显改善，每天晚上的睡眠时间增加4 h；③ 有效：失眠症伴焦虑患者白天的困倦感和不适感依旧存在，焦虑症状有所减轻，每天晚上的睡眠时间增加到2 h；④ 无效：失眠症伴焦虑患者的睡眠时间及质量没有改善。

治疗前后，采取SAS量表评估焦虑程度，评分50～59分表示轻度焦虑，评分60～69分表示中度焦虑，评分>70分表示重度焦虑；用WHO生存质量测定量表(WHOQOL-BREF)判断生活质量，包括心理、社会、环境和生理领域，总共包含26个条目，每项0～5分，分值越低，生活质量越差；采取PSQI量表[10]评估睡眠情况，包括入睡时间、睡眠质量、睡眠时间、睡眠障碍、睡眠效率、日间功能障碍和催眠药物等7个项目，评分值越低，表示其睡眠质量越好。

1.4 统计学分析

采用SPSS 21.0进行数据分析，两组间计量资料的采用t检验，计数资料组间比较采用x^2检验，以P<0.05为差异有统计学意义。

2 结果

2.1 两组临床疗效对比

治疗后，观察组失眠症伴焦虑患者的有效率为95.00 %(38/40)，明显高于对照组[73.17 %(30/41)](P<0.05)，见表1。

表1 两组临床疗效的比较[例(%)]

Table 1 Comparison of the clinical effect between two groups [n(%)]

Groups	n	Cure	Effective	Valid	Invalid	The total effect rate
Control group	41	11(26.83)	11(26.83)	8(19.51)	11(26.83)	30(73.17)
Observation group	40	13(32.50)	14(35.00)	11(27.50)	2(5.00)	38(95.00)*

Note: Compared with the control group, *P<0.05.

2.2 两组治疗前后焦虑评分和生活质量评分的对比

治疗前，两组的焦虑评分和生活质量评分比较无明显统计学差异(P>0.05)。治疗后，两组的焦虑评分较治疗前明显降低(P<0.05)，心理领域、社会领域、环境领域和生理领域评分较治疗前明显升高(P<0.05)，且观察组以上指标均明显优于对照组(P<0.05)，见表2。

2.3 两组治疗前后PSQI评分的对比

治疗前，两组的PSQI评分比较无明显统计学差异(P>0.05)，治疗后，两组的睡眠持续性、主观睡眠质量、睡眠障碍、日间功能、睡眠潜伏期、安眠药物和入睡时间评分明显升高(P<0.05)，观察组以上指标均明显高于对照组(P<0.05)，见表3。

3 讨论

失眠症的主要特征为睡眠障碍，具体的表现为睡眠较难维持或较难入睡，使得睡眠时间无法满足机体正常的生理需求，造成生活、学习和工作受到了影响[11-13]。现代研究认为失眠症的

表 2 两组治疗前后的焦虑评分和生活质量评分对比($\bar{x}\pm s$)

Table 2 Comparison of the anxiety score and quality of life score between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		SAS score	Environmental field	Psychological field	Psychosocial field	Physiological field	Total score of quality of life
Control group	41	Before treatment	63.24± 11.78	11.22± 1.59	10.51± 1.46	10.28± 1.34	10.35± 1.26	41.67± 4.38
		After treatment	57.13± 11.42#	14.42± 1.63#	13.73± 2.29#	13.64± 1.39#	13.48± 1.67#	47.14± 6.53#
Observation group	40	Before treatment	64.19± 12.45	11.21± 1.57	10.36± 1.47	10.17± 1.28	10.13± 1.49	42.37± 5.24
		After treatment	51.69± 10.38*#	18.69± 2.32*#	17.47± 3.38*#	17.25± 2.46*#	16.39± 1.27*#	56.24± 8.35*#

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

表 3 两组治疗前后的 PSQI 评分对比($\bar{x}\pm s$)

Table 3 Comparison of the PSQI scores between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		Sleep duration	Subjective sleep quality	Sleep disorders	Daytime function	Sleep latency	Sleeping drugs	Sleeping time
Control group	41	Before treatment	2.24± 0.65	2.19± 0.68	2.17± 0.75	2.18± 0.63	2.07± 0.64	2.25± 0.63	2.17± 0.54
		After treatment	1.59± 0.57#	1.72± 0.39#	1.63± 0.54#	1.54± 0.31#	1.60± 0.42#	1.57± 0.38#	1.47± 0.42#
Observation group	40	Before treatment	2.27± 0.68	2.20± 0.73	2.18± 0.69	2.19± 0.59	2.09± 0.58	2.27± 0.61	2.18± 0.58
		After treatment	0.92± 0.24*#	1.03± 0.35*#	0.87± 0.34*#	0.87± 0.11*#	0.92± 0.22*#	0.82± 0.19*#	0.73± 0.11*#

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

发生是因维持觉醒以及睡眠和神经受到了外界的刺激,造成机体中异常分泌 5- 羟色胺、多巴胺、肾上腺素等影响睡眠的神经递质,进而不利于正常的睡眠[14-16]。成人中大约有 25 %的人群存在不同程度的睡眠问题,这其中有 6 %~10 %的人群患有属于慢性失眠症,且随着人们压力的加大和生活节奏的加快,失眠症的发生率也日渐升高[17-19]。失眠症患者常常伴随有一系列的症状,以抑郁及焦虑最为常见。心烦意乱、紧张不安以及失眠多梦等焦虑症状常常困扰着多数的失眠症患者;严重者甚者有自杀的言行。目前,针对失眠症伴焦虑的治疗主要为镇静催眠类药物,虽有较好的效果,但是会引起比较突出的不良反应,如嗜睡、精神萎靡以及乏力等,长时间服用会对肝功能、肾功能造成严重的损伤[20,21]。

经颅磁刺激是一种在脑的特定部位进行刺激的疗法,具有无创、非侵入性、无痛、操作简单、耐受性和安全性高等优点,其作为一种无痛、快捷方便和无创的电生理技术,不仅对抑郁症、精神分裂症等多种神经精神科疾病具有确切的治疗效果,而且在改善脑卒中后吞咽功能、记忆功能以及言语功能等认知障碍方面有积极的作用[22-25]。经颅磁刺激主要通过一定强度的时变磁场在患者脑内诱发电场,生成感应电流,进而有效改善大脑皮层局部神经元的功能[26,27]。超过 1 Hz 者称作高频 rTMS,小于 1 Hz 者称作低频 rTMS。高频刺激可以有效激化患者局部的神经元活动,增强大脑皮质的可兴奋性;而低频刺激则会使局部的神经元活动受到抑制,从而降低大脑皮质的可兴奋性[28,29]。

本研究结果显示重复经颅磁刺激以及阿普唑仑联用能提高失眠症伴焦虑患者的疗效,与唐爱珠等[30]的研究结果类似。该学者研究重复经颅磁刺激应用在伴有失眠的焦虑症患者中的临床效果,研究组应用重复经颅磁刺激联合文拉法辛治疗,对照组采取伪线圈经颅磁刺激 + 文拉法辛治疗,所有患者每天均刺激 1 次,连续刺激 7 d 后,发现研究组疗效显著优于对照组。分析其原因为重复经颅磁刺激治疗失眠症伴焦虑患者可能通过调控机体内不同基因以及不同神经元的表达,促进具有生物活性的神经肽类以及神经递质甚至神经调质的表达和释放,进而发挥重要的生理效果[31,32]。但是也有学者探讨低频重复经颅磁刺激联合帕罗西汀治疗伴有焦虑症状抑郁障碍患者的疗效,发现治疗 6 周末帕罗西汀 +r TMS 治疗组、帕罗西汀 + 伪 r TMS 治疗组和帕罗西汀治疗组患者治疗总有效率比较差异均无统计学意义[33],可能与患者的个体差异有关。观察组的睡眠持续性、主观睡眠质量、睡眠障碍、日间功能、睡眠潜伏期、安眠药物和入睡时间评分明显更高,这与谢莉[34]的研究类似。该学者探究重复经颅磁刺激治疗伴有失眠的焦虑症患者的临床疗效分析,发现重复经颅磁刺激以及阿普唑仑联用能更显著的改善睡眠质量,效缩短睡眠潜伏期及觉醒时间,减少觉醒次数,其原因可能为重复经颅磁刺激能促进 5- 羟色胺以及γ- 氨基丁酸等抑制性神经递质的释放,明显降低神经元的活性,减慢神经传导的速度,有效增加非快速眼球运动睡眠,进而明显改善睡眠情况[35]。此外,观察组的焦虑评分和心理领域、社会领域、环境领域、生理领域评分明显优于对照组。谢莉的研究也发现重复经颅磁刺激能有效改善失眠症伴焦虑患者的负性焦虑情绪,有效减少觉醒时间和觉醒次数,缩短睡眠潜伏期时间,进而提高睡眠质量,减轻患者的焦虑情绪,提高生活质量。

综上所述,重复经颅磁刺激以及阿普唑仑联用对失眠症伴焦虑患者有较好的效果,能减轻其焦虑程度,提高其生活质量及睡眠质量。本研究虽取得一定的疗效,为失眠症伴焦虑患者的治疗提供了新的治疗方向,但是也存在一定的不足,如样本量少,也没有进行远期的随访研究,对其机制的研究较浅,后续需要扩大样本量,重点研究重复经颅磁刺激以及阿普唑仑联用对失眠症伴焦虑患者的治疗机制,为其治疗和预后提供新的作用靶点。

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