

·论著·

伏硫西汀治疗抑郁障碍临床疗效评价

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摘要 目的:分析评价伏硫西汀治疗抑郁障碍的临床疗效及安全性。方法:纳入抑郁障碍患者118例,随机分为艾司西酞普兰组60例和伏硫西汀组58例。分别接受艾司西酞普兰片或伏硫西汀片10~20 mg/d治疗8周。分别于基线时,治疗2、4、8周末采用汉密尔顿抑郁量表(HAMD)17项版本和临床疗效总评量表(CGI)评价临床疗效。基线期及8周末使用席汉残疾量表(SDS)评估患者的社会功能恢复状况。采用副反应量表(TESS)记录治疗全过程发生的药物不良反应。结果:治疗8周后,CGI-GI评定结果显示,2组总有效率差异无统计学意义($P>0.05$)。治疗后各时间点,2组HAMD评分均显著低于同组基线期($P<0.01$),但2组各时间点间评分差异无统计学意义($P>0.05$)。治疗8周末2组SDS评分均低于治疗前($P<0.01$),且伏硫西汀组SDS评分低于艾司西酞普兰组($P<0.01$)。2组均未发生严重不良事件,且不良事件发生率差异无统计学意义($P>0.05$)。结论:伏硫西汀治疗抑郁障碍在安全性、有效性方面不劣于艾司西酞普兰,可快速有效治疗抑郁障碍患者症状,对社会功能恢复可以起到积极作用。
关键词 抑郁障碍;伏硫西汀;艾司西酞普兰;疗效;不良反应
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Clinical Efficacy of Vortioxetine in Treatment of Depressive Disorder WANG Shuo^{1,2}, WANG Gao-hua¹, LIU Xue-bing², JIANG Tao², DONG Xiao-jie². 1. Department of Psychiatry, People's Hospital of Wuhan University, Wuhan 430000, China; 2. Wuhan Mental Health Center, Wuhan 430000, China
Abstract **Objective:** To analyze and evaluate the clinical efficacy and safety of vortioxetine in the treatment of depressive disorder. **Methods:** A total of 118 patients with depressive disorder were randomly divided into the escitalopram group (n=60) and vortioxetine group (n=58). Patients were treated with either escitalopram or vortioxetine at 10~20 mg/d for 8 weeks. At baseline and at 2, 4, and 8 weeks after treatment, the 17-item Hamilton Depression Scale (HAMD) and the Clinical Global Impression Scale (CGI) were used to assess clinical efficacy. The recovery of social function was assessed by the Sheehan Disability Scale (SDS) at baseline and 8 weeks after treatment. Adverse reactions to drugs were assessed by the Treatment-Emergent Symptoms Scale (TESS) throughout the duration of the study. **Results:** CGI results at 8 weeks after treatment showed that there was no significant difference between the two groups ($P>0.05$). At each time point after treatment, the HAMD score of each group was significantly lower than that of the same group at baseline ($P<0.01$), but there was no significant difference between the two groups at each time point ($P>0.05$). SDS scores of the two groups after 8 weeks of treatment were significantly improved compared with that at baseline ($P<0.01$), and the SDS score of the vortioxetine group was significantly lower than that of the escitalopram group ($P<0.01$). No serious adverse events occurred in either group, and there was no significant difference between the two groups in the incidence of adverse events ($P>0.05$). **Conclusion:** Vortioxetine is not inferior to escitalopram in terms of safety and effectiveness in the treatment of depressive disorder. Vortioxetine can quickly and effectively treat the symptoms of depressive disorder and plays a positive role in the recovery of social function.
Key words depressive disorder; vortioxetine; escitalopram; efficacy; adverse reactions

抑郁障碍是一类以情绪或心境低落为主要表现的疾病总称,伴有不同程度的认知和行为改变^[1]。2015年全球抑郁障碍患者超过3.2亿^[2],中国抑郁障碍发病率为3.02%,目前全国有超过4000万抑郁障碍患者^[3]。
伏硫西汀片是一种多模式新型抗抑郁药,通过抑制5-羟色胺(5-hydroxytryptamine,

5-HT)转运体的再摄取和调节5-HT受体2种模式作用于6个药理学靶点发挥抗抑郁疗效^[4]。国外报道伏硫西汀治疗抑郁障碍效果好、安全性高,同时可改善认知功能、促进社会功能恢复^[5,6]。国内尚未见相关报道。本研究即比较伏硫西汀和艾司西酞普兰治疗抑郁障碍的疗效及安全性。

1 资料与方法

1.1 一般资料

选择2018年6月至2018年8月在我院就诊的抑郁障碍患者118例。入组标准:符合美国《精神疾病诊断与统计手册》第5版(The Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition, DSM-5)抑郁障碍诊断标准,由2名以上精神科医生诊断;汉密尔顿抑郁量表(Hamilton depression scale, HAMD)17项版本评分>17分;年龄18~65岁;患者或其法定监护人签署知情同意书。排除标准:妊娠期妇女;癫痫等惊厥性疾病患者或有既往病史的患者;肝脏病患者;肾功能损伤患者;药物性超敏反应患者;伴有脱水、营养不良症状等身体衰弱的患者。本研究获武汉大学人民医院及武汉市精神卫生中心医学伦理委员会审核批准。

1.2 方法

1.2.1 分组及治疗 118例患者随机分为2组。艾司西酞普兰组60例,男30例,女30例,平均年龄(26.1±6.9)岁,病程(10.1±6.1)月,已婚20例(33.3%),阳性家族史19例(31.7%);伏硫西汀组58例,男24例,女34例,平均年龄(25.6±7.1)岁,病程(10.3±5.8)月,已婚18例(31.0%),阳性家族史18例(31.0%);2组一般资料差异无统计学意义($P>0.05$)。2组分别接受艾司西酞普兰片(商品名:来士普,丹麦灵北制药有限公司)或伏硫西汀片(商品名:心达悦,丹麦灵北制药有限公司)10~20 mg/d治疗。共治疗8周。

1.2.2 疗效评价 分别于基线时,治疗2、4、8周末采用HAMD 17项版本和临床疗效总评量表(clinical global impression, CGI)评价临床疗效。HAMD总分>24分,可能为严重抑郁;总分>17分,可能有轻至中度抑郁;总分<7分,无抑郁症状。CGI中疗效总评(global improvement, GI)评分0、4、5、6、7分者为“无效”(0分为未评),评分3分为“稍进步”,评分2分为“进步”,评分1分为“显著进步”。总有效率/%=(稍进步例数+进步例数+显著进步例数)/总例数×100%。

1.2.3 社会功能评价 基线期及8周末使用席汉残疾量表(Sheehan disability scale, SDS)评估患者社会功能恢复状况。该量表由工作、社交生活、家庭生活/家庭责任3个自评项目组成,每个项目按照症状由轻到重评为0~10分,3个项目相加评价功能缺陷情况。

1.2.4 安全性评价 使用副反应量表(treatment emergent symptom scale, TESS)记录治疗全过程发生的药物不良反应。

1.3 统计学处理

采用SPSS 22.0软件处理数据。符合正态分布以及方差齐性的计量资料以($\bar{x}\pm s$)表示, t 检验;计数资料以率表示, χ^2 检验; $P<0.05$ 为差异有统计学意义。

2 结果

2.1 疗效评价

治疗8周后,CGI-GI评定显示2组总有效率差异无统计学意义($P>0.05$),见表1。治疗后各时间点,2组HAMD评分均显著低于同组基线期($P<0.01$),但2组差异无统计学意义($P>0.05$),见表2。

2.2 SDS评分比较

基线时艾司西酞普兰组和伏硫西汀组SDS评分分别为(20.93±5.97)分和(21.56±6.28)分,差异无统计学意义($P>0.05$);治疗8周末2组SDS评分分别为(12.18±3.69)分和(9.36±3.28)分,均低于治疗前($P<0.01$),且伏硫西汀组低于艾司西酞普兰组($P<0.01$)。

2.3 安全性评价

2组均未发生严重不良事件。艾司西酞普兰组不良事件发生率为41.67%(25/60, 132例次),伏硫西汀组为34.48%(20/58, 105例次),多为轻、中度,且差异无统计学意义($P>0.05$),见表3。艾司西酞普兰组和伏硫西汀组分别出现3例和2例谷丙转氨酶和谷草转氨酶升高超出正常3倍以上,可能与个体差异或药物对肝功能的影响有关。血常规、血糖、血脂未发现有意义的变化。艾司西酞普兰组发生心电图异常2例次

表1 2组CGI-GI评分比较

组别	例数	无效/例	稍进步/例	进步/例	显著进步/例	有效率/%
艾司西酞普兰组	60	10	13	22	15	83.33
伏硫西汀组	58	9	11	25	13	84.48

表2 2组治疗不同时点HAMD评分比较(分, $\bar{x}\pm s$)

组别	例数	基线期	2周末	4周末	8周末
艾司西酞普兰组	60	24.77±3.09	18.13±3.08	12.16±3.41	6.82±3.03
伏硫西汀组	58	25.20±3.23	18.23±3.23	11.93±3.39	6.74±3.01

(心动过速、过缓各1例),伏硫西汀组发生3例次(心动过缓、房室传导阻滞1例、室性早搏各1例)。

表3 2组治疗导致的常见不良事件比较[例(%)]

组别	例数	恶心	体重增加	焦虑	失眠
艾司西酞普兰组	60	11(18.3)	5(8.3)	6(10.0)	7(11.7)
伏硫西汀组	58	10(17.2)	6(10.3)	5(8.6)	5(8.6)
组别		嗜睡	便秘	口干	疲劳
艾司西酞普兰组	4(6.7)	5(8.3)	9(15.0)	10(16.7)	
伏硫西汀组	3(5.2)	4(6.9)	7(12.1)	6(10.3)	

3 讨论

抑郁障碍患者在一定程度上存在认知损伤和社会功能受损^[7]。目前大部分抗抑郁药的临床疗效相对单一,疗效有限^[8,9]。伏硫西汀具有多模式作用机制,可治疗抑郁症更为广泛的临床症状谱系,安全性和耐受性良好。2017年获国家食品药品监督管理总局批准,用于成人抑郁症的治疗。

本研究提示伏硫西汀治疗抑郁障碍在2周末已起效,8周末较基线期显著好转,与艾司西酞普兰比较临床疗效无明显差异,与国外相关结果一致^[10]。伏硫西汀药理效应复杂,可升高5-HT、去甲肾上腺素、多巴胺、谷氨酸、乙酰胆碱及组胺的释放,以及减少γ-氨基丁酸的释放^[11-13]。上述效应通过3个机制实现:阻断5-HT再摄取,类似于SRIs类药物;与G蛋白相关受体结合,完全激动5-HT1A受体,部分激动5-HT1B受体,拮抗5-HT1D受体及5-HT7受体;与离子通道相关受体结合,拮抗5-HT3受体^[14-16]。这些效应可抗抑郁及认知改善,还可减少与5-HT能再摄取抑制相关的恶心、呕吐、失眠、性功能障碍等副作用^[17]。

本研究SDS评分较基线时明显降低,提示伏硫西汀可使患者在工作、社交生活、家庭生活/家庭责任方面得到显著改善。社会功能的恢复是降低抑郁症患者伤残调整寿命年的重要环节^[18]。伏硫西汀开启了多模式作用机制、多维度全面改善症状抗抑郁药治疗的新时代^[19]。

本研究显示伏硫西汀不良反应轻微,多发生在开始治疗的前2周内,最常见的不良反应为恶心、口干和体重增加。多为一过性、可逆性的。与艾司西酞普兰相比无明显差异性。这有助于提高患者的服药依从性,使症状得到更好的改善。

综上所述,伏硫西汀治疗抑郁障碍在安全性、有效性方面不劣于艾司西酞普兰,可快速有效治疗抑郁障碍患者症状,对社会功能恢复可以起到积极作用。

参考文献

[1] Thase ME, Mahableshwarkar AR, Dragheim M, et al. A meta-analysis of randomized, placebo-controlled trials of vortioxetine for the treatment of major depressive disorder in adults[J]. Eur Neuropsychopharmacol, 2016, 26: 979-993.

[2] Naismith SL, Longley WA, Scott EM, et al. Disability in major depression related to self-rated and objectively-measured cognitive deficits: a preliminary study[J]. BMC Psychiatry. 2007, 7: 32.

[3] Mahableshwarkar AR, Zajecka J, Jacobson W, et al. A Randomized, Placebo-Controlled, Active-Reference, Double-Blind, Flexible-Dose Study of the Efficacy of Vortioxetine on Cognitive Function in Major Depressive Disorder[J]. Neuropsychopharmacology, 2016, 41: 2961.

[4] Lam RW, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Introduction and Methods[J]. Can J Psychiatry, 2016, 61: 506-509.

[5] Baldwin DS, Chrones L, Florea I, et al. The safety and tolerability of vortioxetine: Analysis of data from randomized placebo-controlled trials and open-label extension studies[J]. Psychopharmacol, 2016, 30: 242-252.

[6] 李凌江, 马辛. 中国抑郁障碍防治指南(第二版)解读:概述[J]. 中华精神科杂志, 2017, 50: 167-168.

[7] Katona C, Hansen T, Olsen CK. A randomized, double-blind, placebocontrolled, duloxetine-referenced, fixed-dose study comparing the efficacy and safety of Lu AA21004 in elderly patients with major depressive disorder[J]. Int Clin Psychopharmacol, 2012, 27: 215-223.

[8] McIntyre RS, Lophaven S, Olsen CK. A randomized, double-blind, placebo-controlled study of vortioxetine on cognitive function in depressed adults[J]. Int J Neuropsychopharmacol, 2014, 17: 1557-1567.

[9] Mahableshwarkar AR, Zajecka J, Jacobson W, et al. A randomized, placebo-Controlled, active-reference, double-blind, flexible-dose study of the efficacy of vortioxetineon cognitive function in major depressive disorder[J]. Neuropsychopharmacology, 2015, 40: 2025-2037.

[10] Beyer JL, Johnson KG. Advances in Pharmacotherapy of Late-Life Depression[J]. Curr Psychiatry Rep, 2018, 20: 34.

[11] Jacobsen PL, Mahableshwarkar AR, Palo WA, et al. Treatmentemergent sexual dysfunction in randomized trials of vortioxetine for major depressive disorder or generalized anxiety disorder: a pooled analysis[J]. CNS Spectr, 2016, 21: 367-378.

[12] Chen G, Lee R, Højer AM, et al. Pharmacokinetic drug interactions involving vortioxetine (Lu AA21004), a multimodal antidepressant[J]. Clin Drug Investig, 2013, 33: 727-736.

[13] Chen G, Zhang W, Serenko M. Lack of effect of multiple doses of vortioxetine on the pharmacokinetics and pharmacodynamics of aspirin and warfarin[J]. J Clin Pharmacol, 2015, 55: 671-679.

[14] Dudkowski C, Lee R, Wu R, et al. A phase 1 study to assess the effect of age, gender and race on the pharmacokinetics of single and multiple doses of Lu AA21004 in healthy subjects[J]. Clin Pharmacol Ther, 2012, 91(Suppl.): S69.

[15] Areberg J, Sogaard B, Hojer AM. The clinical pharmacokinetics of Lu AA21004 and its major metabolite in healthy young volunteers[J]. Basic Clin Pharmacol Toxicol, 2012, 111: 198-205.

[16] Uldam HK, Juhl M, Pedersen H, et al. Biosynthesis and identification of an N-oxide/N-glucuronide metabolite and first synthesis of an N-Oglucuronide metabolite of Lu AA21004[J]. Drug Metab Dispos, 2011, 39: 2264-2274.

[17] Hvenegaard MG, Bang-Andersen B, Pedersen H, et al. Identification of the cytochrome P450 and other enzymes involved in the in vitro oxidative metabolism of a novel antidepressant, LuAA21004[J]. Drug Metab Dispos, 2012, 40: 1357-1365.

[18] 张淑芳, 向东方, 申荷永, 等. 中国特色精神科日间医院的探索[J]. 神经损伤与功能重建, 2018, 13: 410-411.

[19] Pae CU, Wang SM, Han C, et al. Vortioxetine: a meta-analysis of 12 shortterm, randomized, placebo-controlled clinical trials for the treatment of major depressive disorder[J]. J Psychiatry Neurosci, 2015, 40: 174-186.

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