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螺环酮联合帕罗西汀治疗焦虑症的疗效及安全性分析

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摘要 目的:研究螺环酮联合帕罗西汀治疗焦虑症的疗效及其安全性。**方法:**选取 2009 年 1 月至 2013 年 8 月我院收治的符合诊断标准的焦虑症患者 244 例,按照知情同意原则随机分为治疗组(122 例)和对照组(122 例),治疗组给予丁螺环酮联合帕罗西汀治疗,对照组仅给予螺环酮治疗。治疗 10 周后,运用汉密尔顿焦虑量表(HAMA)及 Montgomery -Asberg 抑郁量表(MADS)评价疗效,运用治疗过程中不良反应症状量表(TESS)评价其安全性,比较两组患者的疗效及安全性。**结果:**治疗后两组的 HAMA 及 MADS 评分均低于治疗前,且治疗组低于对照组,差异均有统计学意义(P<0.05);两组 TEES 评分在治疗第 2、4、6、8、10 周末均无统计学差异(P>0.05)。**结论:**螺环酮联合帕罗西汀在治疗焦虑症时可提高疗效,且安全性高,可考虑在临床推广。

关键词:焦虑症;螺环酮;帕罗西汀;疗效;安全性

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The Analysis of The Effect and Security of Buspirone Combined with Paroxetine in Treating Anxiety

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ABSTRACT Objective: To study the effect and security of buspirone combined paroxetine in the treatment of anxiety. **Methods:** 244 patients who were diagnosed with anxiety were chosen from 2009 January to 2013 Augst in our hospital, and were divided into treatment group (122 cases) and control group (122cases) randomly according to the principle of informed and consent, treatment group was treated with buspirone combined paroxetine, while the control group was treated with buspirone alone. after 10 weeks of treatment, Hamilton anxiety scale (HAMA) and Montgomery -Asberg depression scale (MADS) were used to evaluate the effect and treatment emergent symptom scale (TESS) was used to evaluate the security, the effect and security between two groups of patients was compared. **Results:** The score of HAMA and MADS of two groups after treatment were all lower than those before the treatment, and the scores of the treatment group were lower than the control group, the differences were all statistically significant(P<0.05). There were no statistically differences in the comparison of the scores of TEES between two groups in the 2, 4, 6, 8, 10 weeks of treatment (P>0.05). **Conclusions:** Buspirone combined paroxetine can improve the effect in treating anxiety and have high security, which could be considered to be widely applied in clinic.

Key words: Anxiety; Buspirone; Paroxetine; Effect; Security

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前言

焦虑症是一种常见的精神疾病,主要包括广泛性焦虑症和发作性惊恐状态,临床症状主要有头晕、胸闷、呼吸困难等[1-3]。焦虑症的全球发病率约为 4-6%左右,且呈上升趋势,焦虑症如不进行合理有效的治疗大部分患者会发展为抑郁症,患者被负面情绪及其所导致的生理反应所影响，影响患者的生存质量,引起了临床医生的重视[4-6]。焦虑症的治疗主要为药物治疗,丁螺环酮在以往的治疗上得到了良好的疗效,可缓解大部分病人的病情,但是也有少部分患者的疗效不理想[7,8],需要探讨疗效更理想的治疗方案,给临床焦虑症患者的治疗带来福音。本研究给 244 例焦虑症患者分别给予单独的丁螺环酮治疗和丁螺环酮联合帕罗西汀治疗，比较两种治疗方案的疗效及其安全性,从而指导临床用药。

1 临床资料

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1.1 一般资料

选取 2009 年 1 月至 2013 年 8 月我院门诊和住院部收治的符合诊断标准的焦虑症患者 244 例，入选标准：(1)符合 符合国际疾病分类第 10 版 I C D.1 0 中焦虑症的诊断标准；(2) HAMA 评分≥ 14 分，MMSE 评分在 8-22 分之间；(3)患者知情同意；(4)未曾系统使用过 丁螺环酮和帕罗西汀治疗 ；(5)年龄在 18-60 岁之间。排除标准为：(1)合并严重躯体疾病；(2)妊娠和哺乳期妇女；(3)酒精或药物依赖、药物过敏者。按照知情同意原则随机分为治疗组(给予丁螺环酮联合帕罗西汀治疗，122 例)和对照组(仅给予螺环酮治疗，122 例)，两组患者年龄、性别、既往治疗情况等方面的差异无统计学意义(P>0.05)，资料均衡可比。见表 1。

表 1 两组一般临床资料 [$\bar{x}\pm s$;n(%)]

Table 1 The clinical data of two groups [$\bar{x}\pm s$;n(%)]

指标 Indexes		治疗组(n=122) Treatment group (n=122)	对照组(n=122) Control group (n=122)	T/X^2	P
	年龄(岁)Age(years)	34.2± 7.5	35.8± 8.2	1.590	0.113
性别 Gender	男 Male	68	64	0.264	0.607
	女 Female	54	58		
	病程 Course of disease	7.7± 4.1	6.9± 2.4	1.860	0.064
既往治疗史 Previous treatment history	未治疗 Untreated	28	31	0.239	0.971
	不系统治疗 No treatment system	40	39		
	一种药物系统治疗 Treatment of one drug system	28	26		
	两种及以上药物系统治疗 Treatment of two or more drugs system	26	26		

1.2 方法

两组患者均停药清洗两周后进行给药治疗。治疗组给予丁螺环酮(江苏恩华药业，5 mg/ 片)联合帕罗西汀(中美天津史克制药，20 mg/ 片)治疗，给药方式为：丁螺环酮起始剂量10mg/d，按病情严重程度于两周内增至 20-30 mg/d， 平均 (20.4± 3.0) mg/d，帕罗西汀起始剂量 20 mg/d，两周增至 30-50mg/d，平均 (30.1± 7.3) mg/d；对照组仅给予丁螺环酮治疗，给药方式为：起始剂量为 10 mg/d， 按病情严重程度于两周内增至 20-30 mg/d，平均剂量为(24.2± 3.5) mg/d，与治疗组相比丁螺环酮剂量差异无统计学意义(P>0.05)。治疗过程中两组均不给予其他类型抗精神病药物等。治疗 10 周后， 运用汉密尔顿焦虑量表(HAMA)及 Montgomery -Asberg 抑郁量表(MADS)评价疗效，得分越高说明症状越重，得分减低越多说明治疗效果越好。运用治疗过程中不良反应症状量表(TESS)评价其安全性，得分越高说明不良反应越重，比较两组患者的疗效及安全性的差异有无统计学意义。采用双盲法进行评定。

1.3 统计方法

计量资料以均数± 标准差($\bar{x}\pm s$)表示；两组资料比较时采用 t 检验、卡方分析。采用 SPSS 18.0 统计软件建立数据库并进行统计分析，检验水准 α=0.05。

2 结果

2.1 两组 HAMA 和 MADS 评分比较

治疗后两组的 HAMA 及 MADS 评分均低于治疗前，且治疗组低于对照组，差异均有统计学意义(P<0.05)。见表 2。

表 2 两组 HAMA 和 MADS 评分比较

Table 2 Comparison of the scores of HAMA and MADS between two groups

指标 Indexes	时间点 Time point	治疗组(n=122) Treatment group(n=122)	对照组(n=122) Control group (n=122)	T	P
HAMA	治疗前 Before treatment	14.56± 3.54	14.68± 3.48	0.267	0.790
	治疗后 After treatment	6.58± 2.84[a)]	7.99± 2.95[a)]	3.803	<0.01
MADS	治疗前 Before treatment	27.68± 3.95	26.98± 3.84	1.403	0.162
	治疗后 After treatment	10.89± 2.10[a)]	15.87± 2.12[a)]	18.433	<0.01

* 注：[a)]与治疗前相比，P<0.05

*Note：[a)]compared with before treatment, P<0.05

2.2 两种治疗方案安全性评价

由表 3 可知：两组 TEES 评分在治疗第 2、4、6、8、10 周末均无统计学差异(P>0.05)。且治疗后两组血常规、尿常规、肝肾功能及心电图等无明显异常。两组出现恶心呕吐等不良反应一般均轻微，可迅速消失。

表 3 两组 TEES 评分比较

Table 3 Comparison of the scores of TEES between two groups

时间点 Time point	治疗组(n=122) Treatment group(n=122)	对照组(n=122) Control group (n=122)	T	P
2 周末 After 2 weeks of treatment	3.95± 1.20	3.87± 1.03	0.559	0.577
4 周末 After 4 weeks of treatment	3.56± 1.08	3.43± 1.04	0.958	0.339
6 周末 After 6 weeks of treatment	2.46± 1.05	2.50± 1.04	0.299	0.765
8 周末 After 8 weeks of treatment	2.45± 1.07	2.51± 1.05	0.442	0.659
10 周末 After 10 weeks of treatment	2.35± 1.08	2.41± 1.01	0.448	0.654

3 讨论

焦虑症是临床常见的情感障碍性疾病,主要治疗方式包括心理治疗、药物治疗等。其中治疗焦虑症的药物种类繁多,但是具有成瘾性且价格昂贵,不良反应多,因此选择出合适的治疗药物是临床医生的首要任务[9-12]。丁螺环酮是临床应用最广的一种治疗焦虑症的药物,其不良反应少,治疗有效率高,可有效缓解大部分焦虑症患者的病情[13],但是仍有少部分病例的疗效不理想,有研究者指出可在应用丁螺环酮的基础上探讨一种联合用药的方案从而提高治疗有效率,但是具体的方案仍未有定论。学者在参考临床已有研究的基础上设想帕罗西汀联合丁螺环酮治疗焦虑症或有良好疗效[14,15],因此实施此研究。本研究分别对两组焦虑症患者给予单独丁螺环酮治疗和丁螺环酮联合帕罗西汀治疗,比较两种治疗方案的疗效和安全性,为临床治疗提供参考。

本研究发现,治疗后两组的 HAMA 及 MADS 评分均低于治疗前,且治疗组低于对照组,差异均有统计学意义(P<0.05),提示两种治疗方案在治疗焦虑症时均有良好疗效,而且丁螺环酮联合帕罗西汀治疗焦虑症的疗效优于单独应用丁螺环酮,丁螺环酮通过选择性结合 5-羟色胺 1A 受体,调节血清素的运输发挥抗焦虑作用[16],帕罗西汀是一种 5-羟色胺回收抑制剂,能有效抑制神经元对 5-羟色胺的再摄取, 从而提高中枢神经系统 5-羟色胺的功能从而发挥抗焦虑抗抑郁作用[17-19],有研究者发现帕罗西汀对躯体性焦虑及精神性焦虑均有效,且对精神性焦虑更有效[20]。本研究还发现,两组 TEES 评分在治疗第 2、4、6、8、10 周末均无统计学差异(P>0.05),提示联合帕罗西汀治疗焦虑症并不会增加不良反应的发生,其安全性不会降低。

总而言之,螺环酮联合帕罗西汀治疗焦虑症可在单独应用螺环酮的基础上提高治疗有效率,且不会增高不良反应发生情况,可考虑在临床推广应用,但是此研究样本量小,所得研究结果仅供参考,如需更可靠的结果需进行进一步的研究认证后才能下结论。

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