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百乐眠胶囊联合艾司西酞普兰片对失眠伴抑郁焦虑患者睡眠质量、不良情绪以及神经递质水平的影响*

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摘要 目的:探讨百乐眠胶囊联合艾司西酞普兰片对失眠伴抑郁焦虑患者睡眠质量、不良情绪以及神经递质水平的影响。**方法:**选取 2017 年 7 月~2019 年 12 月期间我院收治的失眠伴抑郁焦虑患者 117 例,将上述患者根据随机数字表法分为对照组(n=58,艾司西酞普兰片治疗)和研究组(n=59,百乐眠胶囊联合艾司西酞普兰片治疗),比较两组患者睡眠质量、不良情绪、多导睡眠图(PSG)参数、神经递质水平及不良反应。**结果:**研究组治疗 2 个月后的临床总有效率为 93.22%(55/59),高于对照组的 79.31%(46/58)($P<0.05$)。两组治疗 2 个月后汉密尔顿焦虑量表(HAMA)、汉密尔顿抑郁量表(HAMD)以及匹兹堡睡眠质量指数(PSQI)评分、睡眠潜伏期、P 物质(SP)均较治疗前降低,且研究组低于对照组($P<0.05$)。两组治疗 2 个月后睡眠总时间、睡眠效率、神经肽 Y(NPY)、5-羟色胺(5-HT)升高,且研究组高于对照组($P<0.05$)。治疗期间研究组不良反应发生率较对照组降低($P<0.05$)。**结论:**失眠伴抑郁焦虑患者经百乐眠胶囊联合艾司西酞普兰片治疗后,睡眠质量、不良情绪得到显著改善,同时还有效改善血清神经递质水平,减少不良反应,临床应用效果确切。

关键词:百乐眠胶囊;失眠伴抑郁焦虑;艾司西酞普兰片;睡眠质量;不良情绪;神经递质

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Effect of Bailemen Capsule Combined with Escitalopram Tablet on Sleep Quality, Bad Mood and Neurotransmitter Level of Insomnia Patients with Depression and Anxiety*

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ABSTRACT Objective: To investigate the effect of Bailemen capsule combined with escitalopram tablet on sleep quality, bad mood and neurotransmitter level in insomnia patients with depression and anxiety. **Methods:** 117 insomnia patients with depression and anxiety who were admitted to our hospital from July 2017 to December 2019 were selected, they were randomly divided into control group (n=58, treated with escitalopram tablet) and study group (n=59, treated with Bailemian capsule and escitalopram tablet) by random number table method. The sleep quality, bad mood, polysomnography (PSG) parameters, neurotransmitter level and adverse reactions of the two groups were compared. **Results:** The total clinical effective rate of the study group was 93.22%(55/59), which was higher than 79.31%(46/58) of the control group ($P<0.05$). The scores of Hamilton anxiety scale (HAMA), Hamilton depression scale (HAMD) and Pittsburgh sleep quality index (PSQI), sleep latency and substance P (SP) of the two groups were lower than those before treatment, and the study group was lower than the control group ($P<0.05$). The total sleep time, sleep efficiency, neuropeptide Y (NPY), 5-hydroxytryptamine (5-HT) in the two groups increased at after 2 months of treatment, and the study group was higher than the control group ($P<0.05$). The incidence of adverse reactions in the study group was lower than that in the control group ($P<0.05$). **Conclusion:** After the treatment of insomnia patients with depression and anxiety with baile mian capsule and esitalopram tablet, the quality of sleep and bad mood are improved significantly, and the levels of serum neurotransmitter are also improved effectively, and the adverse reactions are reduced, the effect of clinical application is accurate.

Key words: Bailemen capsule; Insomnia with depression and anxiety; Escitalopram tablet; Sleep quality; Bad mood; Neurotransmitter

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前言

睡眠是人体正常生理活动之一，与人类的健康息息相关，当人体长期无法获得充足的睡眠时，可引起失眠现象^[1]。近年来，随着人们遭受的外界压力逐渐增加，失眠的发病率呈逐年升高趋势。据统计^[2]，我国存在睡眠障碍的人群中约有 28% 患有失眠症。长期的失眠可引起疲乏、精力及日间警觉性下降、抑郁焦虑、认知以及行为情绪障碍等并发症，其中以抑郁焦虑最为常见^[3,4]。既往的研究结果显示^[5]，失眠症患者中约有 50% 可伴有抑郁焦虑情绪。艾司西酞普兰片是治疗抑郁焦虑的常用药^[6]。但近年来的研究证实，长期使用艾司西酞普兰片易产生药物依赖性，导致患者产生抵触情绪，停药后极易复发^[7]。百乐眠胶囊是一种中成药，是治疗失眠的中成药，具有养心安神、清热滋阴的效果，无依赖性，安全性高^[8]。本研究通过对我院收治的部分失眠伴抑郁焦虑患者在艾司西酞普兰片的基础上联合百乐眠胶囊治疗，疗效显著，现报道如下。

1 资料与方法

1.1 一般资料

选取 2017 年 7 月~2019 年 12 月期间我院收治的失眠伴抑郁焦虑患者 117 例，纳入标准：(1) 诊断标准参考《精神障碍诊断与统计手册》第 5 版中谱系障碍的变化^[9]；(2) 患者及其家属知情本研究且签署了同意书；(3) 汉密尔顿抑郁量表 (HAMD)^[10]评分 ≥ 17 分，汉密尔顿焦虑量表 (HAMA)^[11]评分 ≥ 7 分，匹兹堡睡眠质量指数 (PSQI)^[12]评分 ≥ 10 分；(4) 对本次研究用药方案无禁忌者；(5) 近一个月内未服用过抗抑郁、焦虑情绪药物。排除标准：(1) 妊娠及哺乳期妇女；(2) 合并有严重心脑血管疾病者；(3) 存在抑郁焦虑情绪病史者；(4) 合并有严重躯体性疾病者。将上述患者根据随机数字表法分为对照组 (n=58) 和研究组 (n=59)，其中对照组男 31 例，女 27 例，年龄 25~57 岁，平均 (41.27 ± 4.39) 岁；病程 6~18 月，平均 (12.39 ± 1.82) 月；体质指数 20.9~26.7 kg/m²，平均 (23.46 ± 0.86) kg/m²。研究组男 33 例，女 26 例，年龄 27~60 岁，平均 (41.96 ± 5.24) 岁；病程 7~20 月，平均 (13.06 ± 1.95) 月；体质指数 21.3~27.5 kg/m²，平均 (23.82 ± 0.97) kg/m²。两组一般资料比较无统计学差异 (P>0.05)，具有可比性。此次研究已获取我院医学伦理学委员会批准进行。

1.2 方法

对照组患者给予口服艾司西酞普兰片 (国药准字 H20080788, 四川科伦药业股份有限公司, 规格: 按艾司西酞普兰计 10 mg) 治疗, 初始剂量为 5 mg/次, 1 次/d, 2 周内逐渐加量至 10~20 mg/次, 1 次/d。基于对照组, 研究组口服百乐眠胶囊 (国药准字 Z20020131, 扬子江药业集团有限公司, 规格: 每粒装 0.27 g) 治疗, 2 粒/次, 2 次/d。两组疗程 2 个月。

1.3 观察指标

(1) 治疗 2 个月后记录两组患者临床疗效, 疗效判定标准如下^[13]: 痊愈: 抑郁焦虑情绪消失, 夜间睡眠时间 > 6 h 或睡眠恢复正常; 显效: 抑郁焦虑情绪有所好转, 睡眠时间增加 3 h 以上或者睡眠明显好转; 有效: 抑郁焦虑情绪症状稍有缓解, 睡眠时间增加不足 3h; 无效: 失眠、抑郁焦虑等均未见显著改善甚至加重。总有效率 = 痊愈率 + 显效率 + 有效率。(2) 于治疗前、治疗 2 个月后采用 HAMA、HAMD 以及 PSQI 评价患者焦虑、抑郁及睡眠情况。其中 HAMA 包含 14 个项目, 总分 56 分, 分值越高, 焦虑症状越严重。HAMD 包含 5 个项目, 总分 30 分, 分数越高, 抑郁症状越严重。PSQI 包括 7 个项目, 总分 18 分, 分值越高表明睡眠质量越差。(3) 于治疗前、治疗 2 个月后用多导睡眠图 (Polysomnography, PSG) 监测患者睡眠情况, 包括睡眠总时间 (入睡至最后觉醒时间)、睡眠效率 (睡眠总时间与总记录时间之比)、睡眠潜伏期 (从关灯上床到出现任何睡眠分期的时间间隔)。(4) 记录两组治疗期间不良反应状况。(5) 采集患者治疗前、治疗 2 个月后的清晨空腹静脉血 5 mL, 离心半径 15 cm, 3300 r/min 离心 10 min, 取上清液, 置于冰箱 (-30℃) 中待测。采用上海基免生物科技有限公司生产的试剂盒, 参考试剂盒说明书步骤, 采用酶联免疫吸附试验检测血清神经肽 Y (Neuropeptide Y, NPY)、5-羟色胺 (5-hydroxytrypt amine, 5-HT)、P 物质 (Substance P, SP) 水平。

1.4 统计学方法

用 SPSS25.0 进行统计分析, 计量资料经正态性检验符合正态分布, 采用 ($\bar{x} \pm s$) 描述, 采用 t 检验; 计数资料用 [n(%)] 描述, 组间比较行 χ^2 检验; $\alpha=0.05$ 为检验水准。

2 结果

2.1 两组疗效比较

治疗 2 个月后, 研究组临床总有效率为 93.22% (55/59), 高于对照组的 79.31% (46/58) (P<0.05); 详见表 1。

表 1 两组疗效比较 [例(%)]

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

Groups	Cure	Markedly effective	Valid	Invalid	Total effective rate
Control group (n=58)	10 (17.24)	19 (32.76)	17 (29.31)	12 (20.69)	46 (79.31)
Study group (n=59)	15 (25.42)	26 (44.07)	14 (23.73)	4 (6.78)	55 (93.22)
χ^2					4.794
P					0.029

2.2 两组相关量表评分比较

治疗前两组 HAMA、PSQI 以及 HAMD 评分比较无差异 (P>0.05), 治疗 2 个月后, 两组 HAMA、PSQI、HAMD 评分较治疗前降低, 且研究组较对照组降低 (P<0.05), 详见表 2。

2.3 两组 PSG 相关指标比较

两组治疗前睡眠总时间、睡眠效率、睡眠潜伏期比较差异无统计学意义 (P>0.05), 两组治疗 2 个月后睡眠总时间、睡眠效率升高, 且研究组高于对照组 (P<0.05), 睡眠潜伏期下降, 且

研究组较对照组降低($P<0.05$), 详见表 3。

表 2 两组相关量表评分比较($\bar{x} \pm s$, 分)

Table 2 Comparison of scores of related scales between the two groups($\bar{x} \pm s$, scores)

Groups	HAMA		HAMD		PSQI	
	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment
Control group(n=58)	18.62± 3.19	12.95± 2.87 ^a	27.64± 4.25	21.19± 3.67 ^a	15.42± 2.57	11.35± 2.07 ^a
Study group(n=59)	18.73± 4.08	7.64± 2.36 ^a	27.16± 3.82	15.62± 3.72 ^a	15.16± 2.61	7.24± 1.97 ^a
t	0.162	10.939	0.643	8.152	0.543	11.003
P	0.871	0.000	0.522	0.000	0.588	0.000

Note: compared with before treatment, ^a $P<0.05$.

表 3 两组 PSG 相关指标比较($\bar{x} \pm s$)

Table 3 Comparison of PSG related indexes between two groups($\bar{x} \pm s$)

Groups	Total sleep time(min)		Sleep efficiency(%)		Sleep latency(min)	
	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment
Control group(n=58)	319.32± 11.14	358.27± 17.65 ^a	67.28± 7.42	73.21± 6.73 ^a	37.18± 4.62	29.42± 3.15 ^a
Study group(n=59)	320.35± 12.17	396.92± 21.32 ^a	66.41± 6.45	80.84± 7.45 ^a	37.02± 3.65	23.81± 3.73 ^a
t	0.477	10.672	0.677	5.810	0.208	8.782
P	0.634	0.000	0.500	0.000	0.836	0.000

Note: compared with before treatment, ^a $P<0.05$.

2.4 两组血清神经递质水平比较

治疗前两组 NPY、5-HT、SP 比较无差异($P>0.05$), 两组治

疗 2 个月后 NPY、5-HT 升高, 且研究组高于对照组($P<0.05$), SP 下降, 且研究组低于对照组($P<0.05$), 详见表 4。

表 4 两组血清神经递质水平比较($\bar{x} \pm s$)

Table 4 Comparison of serum neurotransmitter levels between the two groups($\bar{x} \pm s$)

Groups	NPY(pg/mL)		5-HT(mg/mL)		SP(ng/mL)	
	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment	Before treatment	After 2 months of treatment
Control group(n=58)	108.25± 16.19	129.20± 15.27 ^a	10.73± 1.65	14.37± 1.83 ^a	108.08± 11.24	86.27± 12.27 ^a
Study group(n=59)	109.92± 15.41	141.69± 20.23 ^a	10.24± 1.53	18.93± 1.74 ^a	107.27± 13.27	61.87± 9.25 ^a
t	0.572	3.764	1.666	13.814	0.356	12.159
P	0.569	0.000	0.098	0.000	0.723	0.000

Note: compared with before treatment, ^a $P<0.05$.

2.5 不良反应比较

治疗期间研究组不良反应发生率为 5.08%(3/59) 低于对照

组 18.97%(11/58), 差异有统计学意义($P<0.05$), 详见表 5。

表 5 两组患者不良反应情况比较 [例(%)]

Table 5 Comparison of adverse reactions between the two groups [n(%)]

Groups	Nausea	Sweating	Dry mouth	Constipation	Total incidence rate
Control group(n=58)	2(3.45)	3(5.17)	4(6.90)	2(3.45)	11(18.97)
Study group(n=59)	1(1.69)	1(1.69)	1(1.69)	0(0.00)	3(5.08)
χ^2					5.350
P					0.021

3 讨论

睡眠是人类正常生命活动中不可缺少的一部分生理过程,

充足的睡眠可使脑组织及其他脏器组织更好的发挥能量储存、体温调节以及组织修复等作用,进而促进机体的整合和复原^[14,15]。当机体睡眠不足时则会造成失眠,失眠的主要症状为易惊醒、入睡困难、睡眠不深、多梦、醒后难以再入睡等^[16]。由于失眠患者长时间睡眠质量较差,无法维持正常的日间功能,因此患者担心睡眠质量,从而引发抑郁焦虑等^[17-19]。艾司西酞普兰片是临床常见的苯二氮类药物,是抗抑郁治疗的一线用药^[20]。但失眠伴抑郁焦虑的治疗过程为长期过程,长期大量的西药治疗易增加记忆损害、药物依赖、内分泌失衡等副作用的发生风险^[21]。近年来,中西医结合治疗失眠伴抑郁焦虑获得了较大进展^[22]。其中中医认为该病的主要治疗方向为疏肝解郁、养血安神。而百乐眠胶囊包含首乌藤、百合、酸枣仁、五味子、丹参、远志、合欢花、珍珠母等 15 种中药,既往常用于失眠症的治疗中,效果确切^[23]。

本次研究结果显示,研究组治疗 2 个月后的临床总有效率高于对照组,睡眠质量及抑郁焦虑情绪等改善情况优于对照组,表明失眠伴抑郁焦虑患者经百乐眠胶囊联合艾司西酞普兰片治疗后,可迅速改善临床症状。究其原因,艾司西酞普兰片主要通过提高脑细胞外的 5-HT 浓度,抵抗抑郁,改善焦虑^[24]。联合百乐眠胶囊中的丹参、酸枣仁、镇静抗惊厥、催眠,珍珠母、首乌、百合藤祛风通络、安神宁心,合欢花镇静催眠,五味子滋阴养血,远志安神益智,诸药合用,共奏养血安神、疏肝解郁之效,进一步提高治疗效果^[25]。既往研究显示^[26],失眠症的主要病因与睡眠觉醒功能紊乱息息相关,而 NPY、5-HT、SP 等神经递质在睡眠的开始及维持中发挥重要作用。本研究中上述血清神经递质水平均有所改善,且百乐眠胶囊联合艾司西酞普兰片治疗者的改善效果更佳。现代药理研究证实^[27-29],百合、合欢花、丹参可增加睡眠总时间,提高睡眠质量,发挥不同程度的助眠作用,同时上述药物成分还可提高机体对外界有害刺激的抵抗能力。酸枣仁具有镇静催眠、抗抑郁、改善记忆、抗焦虑等作用。另本研究还显示联合治疗安全性较好,这可能是由于百乐眠胶囊作为中成药,本身毒副作用相对较小,同时还可一定程度上缓解艾司西酞普兰片的大量用药带来的不良反应,有效降低总体不良反应发生率^[30]。

综上所述,失眠伴抑郁焦虑患者经百乐眠胶囊联合艾司西酞普兰片治疗后,睡眠质量、不良情绪得到显著改善,同时还可有效改善血清神经递质水平,减少不良反应,临床应用效果确切。

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