

doi: 10.13241/j.cnki.pmb.2014.07.023

酒石酸唑吡坦对非器质性失眠症患者 Actigraphy 检测指标的影响 *

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摘要 目的:应用 Actigraphy 仪检测酒石酸唑吡坦对非器质性失眠症患者睡眠质量的影响。**方法:**选择非器质性失眠症患者 36 例,实验第二晚给予 10 mg 酒石酸唑吡坦,实验第一晚和第四晚采用 Actigraph 仪监测,观察用药后 Actigraph 指标的变化。同时设置正常对照组 24 名,进行基础 Actigraph 监测。**结果:**失眠组患者服用酒石酸唑吡坦后,夜间 Actigraphy 检测显示实际觉醒时间(AWT)、睡眠潜伏期(SL)、平均每次觉醒时间(MWB T)与服药前相比,显著缩短($P < 0.01$);睡眠效率(SE)、平均静息状态时长(MLI)与服药前相比,显著提高($P < 0.01$),同时反映身体活动的参数平均活动分数(MAS)和睡眠总体破碎程度的割裂指数(FI)与对照组相比,显著降低($P < 0.05$)。**结论:**酒石酸唑吡坦能明显改善非器质性失眠症患者睡眠,在非器质性失眠症的诊断治疗中 Actigraphy 仪是一种有效、便捷的方法。

关键词:失眠症;酒石酸唑吡坦;体动记录仪;睡眠障碍

中图分类号:R741.05 文献标识码:A 文章编号:1673-6273(2014)07-1294-03

Effect of Zolpidem Tartrate on Actigraphy Parameters in Patients with Insomnia*

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ABSTRACT Objective: To investigate the effects of Zolpidem tartrate on sleep quality of patients with functional insomnia tested by Actigraphy sleep instrument. **Methods:** All the patients received 10 mg Zolpidem tartrate before sleep on the second night, and actigraphy sleep instrument was employed for 36 patients with insomnia on the first night and the fourth night, obtaining changes of Actigraphy parameters. Another 24 participants without insomnia were recruited as the control group and tested by Actigraphy sleep instrument. **Results:** Compared with the parameters before treatment of Zolpidem tartrate, many parameters changed significantly, including reduced actual wake time, sleep latency, mean wake bout time ($P < 0.01$), and improved sleep efficiency, mean length immobility ($P < 0.01$), and reduced mean activity score, fragmentation index ($P < 0.05$). **Conclusion:** Zolpidem tartrate could significantly improve sleep quality of patients with functional insomnia, and Actigraphy sleep instrument was an effective and convenient tool in the diagnosis and treatment of patients with functional insomnia.

Key words: Insomnia; Zolpidem tartrate; Actigraphy; Sleep disorder

Chinese Library Classification(CLC): R741.05 **Document code:** A

Article ID:1673-6273(2014)07-1294-03

前言

目前,我国 45.4% 人群存在睡眠障碍,其中失眠症患者占 28%^[1]。酒石酸唑吡坦是新一代非苯二氮卓类安眠药,属于咪唑吡啶类化合物,是选择性的 Omega 受体激动剂,以不改变睡眠结构,吸收后血浓度达峰快、下降快为其作用特点,目前在临床上应用较为广泛^[2]。Actigraphy 仪是一种测量、记录并进行自动分析的便携式睡眠检测仪器^[3]。本研究采用 Actigraphy 仪来评价酒石酸唑吡坦治疗非器质性失眠症患者时其睡眠和活动指标的变化,以探讨酒石酸唑吡坦药物的作用特点,为临床上

合理用药提供客观依据。

1 材料与方法

1.1 研究对象

选择 2011 年 1 月 -2012 年 12 月北京市海军总医院及外院的非器质性失眠症患者,共 36 例。其中男 24 例,女 12 例;年龄 18~65 岁,平均(35.5±9.9)岁。病程 1 月~40 年。非器质性失眠症的诊断依据 ICD-10 F51.0 的标准^[4]:(1)主诉为入睡困难、易醒或睡眠质量差;(2)睡眠紊乱每周至少发生 3 次,同时持续 1 个月以上;(3)日夜专注于失眠而造成过分担心失眠的后

* 基金项目:全军后勤重大基金项目(AHJ2011Z001)

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(收稿日期:2013-07-15 接受日期:2013-08-10)

果;(4) 由于睡眠质和/或量的不满意造成了患者明显的苦恼或者影响了社会和职业功能;(5) 患者匹兹堡睡眠质量指数(Pittsburgh sleep quality index, PSQI) ≥ 14 分;以下情况需要排除:患有严重的躯体、神经精神系统疾病,以及孕期和哺乳期妇女;对照组 24 例,男 14 例,女 10 例。年龄 20~67 岁,平均(42.3 $\pm$ 15.9)岁,入组标准:身体和心理健全,无神经系统疾病和精神疾患,无饮酒史,无药物滥用史。

1.2 主要仪器

体动记录仪选用美国 MiniMitter 公司生产的腕式 Actigraphy 仪,加速度的敏感度 $< 0.01g$,采样时间设定为 0.25 s,对于所记录的睡眠和活动指标,由相应的 Actiware-Sleep v3.3 软件进行分析。酒石酸唑吡坦片为杭州赛诺菲安万特民生制药有限公司生产,剂量:每片 10 毫克。

1.3 试验方法

首先,使每名受试者了解试验过程,掌握 Actigraphy 仪的操作方法;其次,在受试者就寝前将 Actigraphy 仪激活,同时佩戴在腕部,连续进行记录 72 小时。在试验过程中每名受试者严禁口服催眠类药物以及饮酒。在记录开始时利用匹兹堡睡眠质量指数(Pittsburgh sleep quality index, PSQI)量表对每名受试者近期睡眠质量进行评定。

1.4 参数选择

本实验利用 Actiware-Sleep v3.3 分析软件所提供的睡眠参数进行统计分析:总睡眠时间(Assumed sleep, AS)、实际觉醒时间(Actual wake time, AWT)、实际睡眠时间(Actual sleep time,

AST)、睡眠潜入期(Sleep latency, SL)、睡眠效率(Sleep efficiency, SE)、觉醒次数(Wake bouts, WB)、睡眠次数(Sleepbouts, SB)、平均每次觉醒时间(Mean wake bout time, MWBT)、平均每次睡眠时间(Mean sleep bout time, MSBT)、平均静息状态时长(Mean length immobility, MLI)、割裂指数(Fragmentation index, FI)、平均活动分数(Mean activity score, MAS)等。

1.5 统计学处理

所有数据采用 SPSS15.0 统计软件包处理。失眠症组和正常对照组间参数指标比较采用独立样本 t 检验,失眠症组服药前后指标比较采用配对样本 t 检验,以 $P < 0.05$ 为表示差异有统计学意义。

2 结果

2.1 失眠组与正常对照组睡眠指标比较

失眠组与正常对照组在年龄、性别以及教育程度方面均无统计学差异($P > 0.05$)。但是与正常对照组比较,失眠组患者在实际觉醒时间(AWT)、睡眠潜入期(SL)、平均每次觉醒时间(MWBT)均有显著延长($P < 0.01$);同时睡眠效率(SE)、平均静息状态时长(MLI)与正常对照组比较显著降低($P < 0.01$);而反映睡眠总体破碎程度的割裂指数(FI)和身体活动的参数平均活动分数(MAS)与正常对照组相比,显著升高($P < 0.01$)。PSQI 评定结果显示失眠组患者 PSQI 达到(15.24 $\pm$ 2.86),正常对照组 PSQI 为(4.68 $\pm$ 1.92),两者比较有显著差异($P < 0.01$),见表 1。

表 1 失眠症组与正常对照组的 Actigraphy 指标($\bar{x} \pm s$)

Table 1 Actigraphy parameters of Insomnia group and the normal control group

Index	Normal control group(n=24)	Insomnia group(n=36)
Assumed sleep (AS, h)	6.72 $\pm$ 1.06	6.68 $\pm$ 1.24
Actual wake time (AWT, h)	0.38 $\pm$ 0.42	0.85 $\pm$ 0.43**
Actual sleep time (AST, h)	6.34 $\pm$ 0.94	5.82 $\pm$ 1.20
Sleep latency (SL, min)	2.50 $\pm$ 3.42	24.06 $\pm$ 21.56**
Sleep efficiency (SE, %)	92.36 $\pm$ 3.88	75.86 $\pm$ 9.52**
Wake bouts (WB)	42.12 $\pm$ 17.62	54.85 $\pm$ 27.92
Sleepbouts (SB)	43.06 $\pm$ 18.82	55.62 $\pm$ 27.96
Mean wake bout time (MWBT, min)	0.51 $\pm$ 0.18	0.97 $\pm$ 0.48**
Mean sleep bout time (MSBT, min)	9.88 $\pm$ 3.84	7.76 $\pm$ 4.52
Mean length immobility (MLI)	8.02 $\pm$ 3.16	5.46 $\pm$ 2.27*
Fragmentation index (FI)	8.68 $\pm$ 5.46	15.67 $\pm$ 8.38**

注:* 与对照组相比, $P < 0.05$; ** 与对照组相比, $P < 0.01$ 。

Note: Compare with Normal control group, * $P < 0.05$, ** $P < 0.01$.

2.2 失眠症组服药前后睡眠参数比较

失眠症组在治疗后,实际觉醒时间(AWT)明显缩短($P < 0.05$),睡眠潜入期(SL)、平均每次觉醒时间(MWBT)显著缩短($P < 0.01$),睡眠效率(SE)、平均静息状态时长(MLI)与治疗前相比,也显著降低($P < 0.01$),同时睡眠总体破碎程度的割裂指数(FI)显著减少($P < 0.01$),而反映身体活动的参数平均活动分数(MAS)夜明显减少($P < 0.05$),见表 2。

3 讨论

眠是一种睡眠障碍,主要指睡眠时间和质量不能满足正常睡眠要求,而出现的疲劳、注意力不集中、情绪不好等感觉。失眠虽然对人的器官不会造成直接损害,但会对人的精神造成伤害,影响到人的身心健康。长期的慢性失眠会增加大脑耗氧量,不利于脑细胞能量储存,容易引起患者出现心理失衡,表现为焦虑、抑郁等,进一步可导致患者精神活动效率降低,甚至妨碍其社会功能^[5,6]。

临床上诊断非器质性失眠症的方法主要依据 PSQI、ICD-10 等量表,这些量表虽然有较好内部一致性、构想效度、

表 2 失眠症组治疗前后的 Actigraphy 指标 ($\bar{x} \pm s$)

Table 2 Actigraphy parameters of Insomnia group before treatment and after treatment

Index	Insomnia group(n=36)	
	Before treatment	After treatment
Assumed sleep (AS, h)	6.68± 1.24	6.70± 1.26
Actual wake time (AWT, h)	0.85± 0.43	0.61± 0.42 [▲]
Actual sleep time (AST, h)	5.82± 1.20	6.10± 1.21
Sleep latency (SL, min)	24.06± 21.56	12.03± 5.46 ^{▲▲}
Sleep efficiency (SE, %)	75.86± 9.52	89.46± 9.43 ^{▲▲}
Wake bouts (WB)	54.85± 27.92	46.72± 27.36
Sleepbouts (SB)	55.62± 27.96	48.44± 26.38
Mean wake bout time (MWBT, min)	0.97± 0.48	0.74± 0.48 [▲]
Mean sleep bout time (MSBT, min)	7.76± 4.52	8.12± 4.52
Mean length immobility (MLI)	5.46± 2.27	7.62± 2.31 ^{▲▲}
Fragmentation index (FI)	15.67± 8.38	10.74± 6.38 ^{▲▲}

注:▲与治疗前组相比, $P < 0.05$; ▲▲与治疗前组相比, $P < 0.01$ 。

Note: Compare with Insomnia group before treatment, ▲ $P < 0.05$, ▲▲ $P < 0.01$.

再测信度以及实证效度,然而由于在这些量表主要依靠患者的主观表达,所以大多数对自身睡眠不满意的失眠症患者,容易对其失眠过度放大,评判自己睡眠障碍时打分过高,极易导致诊断和治疗评价标准不准确^[7,8]。在研究和临床上最常应用、最客观的依据是多导睡眠图,但是该方法比较复杂,需要连续记录脑电、肌电、眼动、体动、呼吸、心电等参数,很容易造成被检测者心理紧张,尤其对于失眠患者,干扰其日常就寝习惯,导致结果出现偏差^[9]。Actigraphy 仪使用比较简便,测量时不会影响检查者平时就寝睡眠习惯,该仪器应用感应腕部的加速度,来记录检查者身体的运动频次和幅度^[10],目前在国外临床上对相关疾病的诊断、评估等方面已有所应用^[11-14]。非快动眼期睡眠从深睡眠阶段逐渐转换到浅睡眠期时,往往会出现肢体活动,依据睡眠的这种特性对睡眠周期和睡眠质量进行鉴别和评估,这方面的研究发现其准确率为 90.2%^[15]。

本研究采用 Actigraphy 仪监测发现,非器质性失眠症患者在 实际觉醒时间、睡眠潜入期、平均每次觉醒时间显著延长,而平均静息状态时长、睡眠效率显著降低,同时反映频发睡眠分裂和身体活动的参数升高,依据上述参数指标特点,在客观数据上证实了非器质性失眠症患者存在不同程度的睡眠障碍。同时可依据 Actigraphy 仪监测的指标来评判睡眠障碍的临床分类,如:睡眠总时间、睡眠潜入期、睡眠质量以及睡眠维持情况等。本实验还发现,非器质性失眠症患者给予口服酒石酸唑吡坦片治疗后,实际觉醒时间、睡眠潜入期、平均每次觉醒时间显著缩短,睡眠效率、平均静息状态时长显著延长,同时反映身体活动的参数明显降低,睡眠分裂减少,睡眠障碍得到了改善。酒石酸唑吡坦是新一代的咪唑吡啶类催眠药物,主要药理作用能够特异性的激活中枢 γ -氨基丁酸受体,调节氯离子通道,选择性抑制神经元活动,具有快速、短时间的催眠作用^[16]。本研究表明酒石酸唑吡坦在治疗非器质性失眠症能明显缩短入睡时间,减少夜间醒觉次数,提高睡眠效率,次晨无明显后遗效应,显著改善了非器质性失眠症患者的睡眠质量,与国外 Roehrs TA、Kinnan S、Vijayan RS 等学者的相关研究相符合^[17-20],也同国内

曾报道的思诺思多中心开放式临床研究(北京、上海、广州、南京等地 15 家医院参加)结果基本一致^[21]。综上所述,酒石酸唑吡坦能明显改善非器质性失眠患者睡眠,在非器质性失眠症的诊断治疗中 Actigraphy 仪是一种有效、便捷的方法。

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