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Comparison of Cognitive–Behavioral Therapy and Clonazepam for Treating Periodic Limb Movement Disorder

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Summary: Many patients with periodic limb movement disorder (PLMD) display inadequate sleep hygiene, and others decline conventional pharmacologic intervention for their form of sleep disturbance. Nonetheless, the use of nonpharmacologic therapies with PLMD remains unexplored. The current study was designed to compare the short-term treatment effects of a cognitive–behavioral therapy (CBT) and conventional pharmacotherapy (clonazepam) among a group of insomniacs with PLMD. The 16 subjects participating in this study first underwent baseline assessment procedures, including completion of a sleep log for 2 weeks, an ambulatory polysomnogram (APSG) and an Insomnia Symptom Questionnaire (ISQ). They then were randomized either to CBT (n = 8) or standard clonazepam therapy (n = 8). Subjects maintained sleep logs throughout a 4-week treatment and then completed a second APSG and ISQ. Comparison of pre- and post-treatment data suggested that the two treatments led to equal improvements in sleep log measures of sleep–wake times and ISQ measures of subjective sleep concerns. Patients treated with CBT showed a decrease in daytime napping, whereas the clonazepam group reported increased napping. Conversely, those treated with clonazepam showed larger declines in periodic limb movement-arousals per hour of sleep than did the CBT group. Post-treatment interviews suggested that both CBT and clonazepam therapies were generally well tolerated by study participants. It is concluded that both treatments may be useful for PLMD but that the two treatments may have contrasting effects across selected measures of improvement. Additional research is needed to examine the long-term efficacy of CBT as a primary or adjunctive treatment for varying levels of PLMD severity. **Key Words:** Periodic leg movements—Treatment, nondrug—Clonazepam.

Periodic limb movement disorder (PLMD) (1), characterized by repetitive, stereotyped limb movements and associated arousals during sleep, is regarded as the primary cause of sleep disturbance in 12–17% of all insomniacs who present to specialty sleep disorders centers (2,3). Pharmacologic agents such as clonazepam, L-DOPA compounds and some opioids have proven effective for alleviating the sleep–wake complaints of PLMD patients (4–7). However, drug tolerance, over-sedation, rebound symptoms, toxic interactions with other needed medications or a reticence to start/continue medication may all confound PLMD pharmacotherapy (8–10). Although Spielman et al. (11) and Hoelscher and Edinger (12) have observed sleep improvements in isolated PLMD patients treated solely with nonpharmacologic, behavioral interventions, the efficacy of such treatments for PLMD requires further study. This pilot investigation was conducted to compare a common pharmacologic intervention, clonazepam, with a cognitive–behavioral therapy (CBT) for the treatment of sleep disturbances among PLMD patients.

METHODS

From a total of 20 individuals screened, the sample of 16 (9 women, 7 men) older adults (≥60 years of age) selected for this investigation included both sleep clinic patients (n = 4) and research study volunteers (n = 12). All subjects 1) had an insomnia complaint for at least 6 months [10.8 ± 9 years; mean ± standard deviation (SD)] prior to entering the study, 2) had a minimum of five periodic limb movement related-arousals per hour of sleep during diagnostic ambulatory polysomnography (APSG) (using Medilog® 9000 recorders) conducted in subjects' homes during screen-

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TABLE 1. *Means, standard deviations and statistics for improvements shown by treatments*

	Clonazepam group		CBT group		CBT vs. clonazepam		Pre- vs. post-treatment		Interaction effects	
	Baseline	Treatment	Baseline	Treatment	*F*	p	*F*	p	*F*	p
Sleep log data										
Total wake time	147.64 (72.2)	80.1 (31.8)	107.9 (52.0)	60.6 (48.2)	1.6	NS	17.4	<0.005	0.5	NS
Total sleep time	367.8 (83.4)	427.5 (46.9)	335.8 (70.3)	347.7 (78.7)	2.8	NS	5.2	<0.05	2.3	NS
Sleep efficiency (%)	71.4 (14.8)	83.6 (7.8)	75.2 (13.1)	84.4 (13.9)	0.3	NS	12.6	<0.005	0.1	NS
Insomnia symptom questionnaire (ratings)										
Nighttime sleep concerns	53.5 (15.9)	36.3 (18.7)	49.5 (11.1)	37.5 (22.5)	0.0	NS	5.6	<0.05	0.2	NS
Daytime fatigue	45.4 (19.4)	40.3 (21.5)	59.6 (14.0)	54.7 (23.3)	2.6	NS	0.7	NS	0.0	NS
Daytime napping	27.5 (21.2)	37.6 (20.5)	26.2 (23.0)	8.0 (8.4)	3.5	NS	0.3	NS	4.8	<0.02
PSG measures										
Total wake time	106.3 (36.4)	97.7 (31.1)	125.2 (67.5)	88.3 (51.3)	0.0	NS	1.9	NS	0.7	NS
Total sleep time	341.9 (55.5)	379.6 (60.1)	348.0 (58.2)	326.8 (44.6)	1.2	NS	0.2	NS	1.8	NS
Movement index (MI)	77.4 (21.6)	63.8 (34.7)	30.7 (15.2)	31.8 (10.7)			0.6	NS	1.6	NS
Arousal index (AI)	37.7 (16.8)	21.0 (22.4)	19.2 (11.4)	15.4 (11.7)			5.0	<0.05	1.4	NS

Values in parentheses are standard deviations. Results shown for sleep log, insomnia symptom questionnaire (ISQ) and polysomnographic (PSG) total sleep and wake times are taken from 2 (CBT vs. clonazepam) × 2 (pre- vs. post-treatment) ANOVAs. Results shown for the pre- to post-treatment changes in MIs and AIs are taken from a one-way ANOVA. The "interaction" effects shown for the MI and AI data represent the results of analyses of covariance performed on pre- to post-treatment change scores for MIs and AIs, respectively, adjusted for pre-treatment MI and AI values. The ISQ ratings were made on 100-point visual analogue scales, with higher scores reflecting greater nighttime sleep concerns, daytime fatigue and daytime napping.

ing and 3) met other diagnostic criteria (1) for PLMD. None of the subjects had previously received medications for PLMD, and none had symptoms or polysomnographic (PSG) evidence of significant sleep-related respiratory disturbances. Once enrolled, all subjects were kept free of sleep-inducing medications other than those prescribed in the study.

Subjects first completed baseline measures, which included 2 weeks of sleep log monitoring, an additional night of APSG and a 13-item Insomnia Symptom Questionnaire (ISQ) (11), which included three factor-analytically derived subscales reflecting perceived nighttime sleep concerns, daytime fatigue and daytime napping. Subjects were then randomly assigned either to clonazepam therapy (n = 8; 4 women, 4 men) or CBT (n = 8; 5 women, 3 men) treatment conditions. Those in the medication group (67.6 ± 4.1 years of age; mean ± SD) were initially prescribed a bedtime dosage of 0.5 mg clonazepam, but they were allowed to escalate this dosage in 0.5-mg increments every 3 days to a maximum dosage of 1.5 mg until efficacy was achieved. Subjects (64.5 ± 4.1 years of age; mean ± SD) assigned to CBT were provided sleep education and a combination of stimulus control and sleep restriction instructions in a fashion similar to those of subjects treated in our previous reports (12, 13). Subjects maintained sleep logs throughout 4 weeks of treatment, and at the conclusion of treatment they again completed the ISQ and another night of home APSG monitoring.

Nightly estimates of total wake time, total sleep time and sleep efficiency percentage were obtained from sleep logs completed during baseline and the final 2 weeks of treatment. In addition, pre- and post-treatment APSGs were scored by personnel who were kept blind to the objectives of the study, the treatment conditions to which subjects were assigned and when (baseline vs. post-treatment) the APSG had been conducted. Standard criteria (14) were used to derive measures of total sleep time and total wake time, whereas scoring criteria (15,16) proposed specifically for scoring periodic limb movements (PLMs) and electroencephalographic (EEG) arousals were used to derive measures of PLMs (MI) and PLM-related arousals (AI) per hour of sleep time.

RESULTS AND DISCUSSION

All eight subjects assigned to clonazepam completed the 4-week treatment trial, although one man assigned to this therapy declined to undergo an APSG study at the end of treatment. Of those assigned to CBT, one woman withdrew from treatment due to a family medical emergency; a second woman underwent eye surgery at the end of her treatment and, hence, did not complete her post-treatment APSG and ISQ. Despite these events, neither treatment resulted in any serious side effects. Of those patients assigned to clonazepam, 6 remained on the 0.5-mg dosage throughout treatment; the remaining two escalated their dosages to 1.0 mg by the end of treatment. Acceptance of pharmacotherapy was generally good, although one woman receiving this treatment complained of heightened anxiety at the minimum dose

(0.5 mg) of medication and accordingly indicated a desire to discontinue this treatment after completing the study. Similarly, five of the seven patients who completed CBT reported good tolerance for this treatment; two women reported that the strict behavioral regimen caused anxiety that led them to discontinue CBT after completing the study.

Preliminary one-way analyses of variance (ANOVAs) showed that the treatment groups initially differed only in regard to their mean baseline values of MIs and AIs. Hence, one-way repeated measures ANOVAs were used to test for improvements in MIs and AIs across treatment conditions, whereas one-way analyses of covariance (adjusting for pre-treatment values of MIs and AIs) applied to change scores for these indices were used to compare the two treatments. The remaining data were analyzed using 2 (CBT vs. clonazepam) × 2 (baseline vs. treatment) ANOVAs. Table 1 summarizes the findings of these analyses.

These data suggest that both treatments led to some sleep improvements, but admittedly the groups we treated were small and the treatment effects were clinically modest. In addition, CBT had no effect on the MI and produced only a 20% decline in the AI. Although clonazepam treatment produced a notably larger decline in the MI and AI, this finding is difficult to evaluate given our small sample, the high variability in the data, and the higher baseline MIs and AIs for the clonazepam group. Also, whereas CBT decreased log estimates of total wake time (i.e. onset latency plus wake after onset), these estimates remained greater than 60 minutes per night on average for both treatment groups at the end of treatment. Finally, post-treatment measures (log, PSG) of total sleep time remained under 6 hours for those treated with CBT. Nonetheless, in a prior study (13), we found that log estimates of total sleep time increased markedly between the end of treatment and a 3-month follow-up period among primary insomniacs who were provided a 4-week course of CBT similar to that used in this study. Thus, further tests of CBT, as a primary and adjunctive treatment for PLMD patients, seem warranted. Such future investigations would benefit by 1) the use of larger PLMD samples, 2) the inclusion of long-term follow-up assessments, 3) use of multiple PSGs both before and after treatment to compensate for inter-night variability in PLMD indices and 4) the use of a matched-groups design to assure the comparability of treatment groups at baseline.

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REFERENCES

1. Diagnostic Classification Steering Committee, Thorpy MJ, chairman. *International classification of sleep disorders: diagnostic and coding manual.* Rochester, MN: American Sleep Disorders Association, 1990.
2. Coleman RM, Roffwarg HP, Kennedy SJ, et al. Sleep–wake disorders based on polysomnographic diagnosis. *JAMA* 1982;242:997–1003.
3. Coleman RM, Bliwise DL, Sajben N, et al. Epidemiology of periodic movements during sleep. In: Guilleminault C, Lugaresi E, eds. *Sleep/wake disorders: natural history, epidemiology and long-term evolution.* New York: Raven Press, 1983.
4. Peled R, Lavie P. Double-blind evaluation of clonazepam on periodic leg movements in sleep. *J Neurol Neurosurg Psychiatry* 1987;50:1679–81.
5. Walters AS, Wagner ML, Hening WA, et al. Successful treatment of idiopathic restless legs syndrome in a randomized double-blind trial of oxycodone versus placebo. *Sleep* 1993;16:327–32.
6. Allen RP, Kaplan PW, Buchholz DW, Walter JK. Double-blinded, placebo controlled comparison of propoxyphene and carbidopa/levodopa for treatment of periodic limb movements in sleep. *Sleep Res* 1991;20:199.
7. Montplaisir J, Lapierre O, Warnes H, Pelletier G. The treatment of restless leg syndrome with or without periodic leg movements in sleep. *Sleep* 1992;15:391–5.
8. Dement WC, Miles LE, Carskadon MA. "White paper" on sleep and aging. *J Am Geriatr Soc* 1982;30:25–50.
9. Ray WA, Griffin MR, Schaffner W, Baugh DK, Melton J. Psychotropic drug use and the role of hip fracture. *N Engl J Med* 1987;316:363–9.
10. Montplaisir J, Godbout R, Pelletier G, Warnes H. Restless legs syndrome and periodic limb movements during sleep. In: Kryger MH, Roth T, Dement WC, eds. *Principles and practice of sleep medicine.* Philadelphia: WB Saunders, 1994.
11. Spielman AJ, Saskin P, Thorpy MJ. Treatment of chronic insomnia by restriction of time in bed. *Sleep* 1987;10:45–55.
12. Hoelscher TJ, Edinger JD. Treatment of sleep-maintenance insomnia in older adults: sleep period reduction, sleep education and modified stimulus control. *Psychol Aging* 1988;3:258–63.
13. Edinger JD, Hoelscher TJ, Marsh GR, Ionescu-Pioggia M, Lipper S. A cognitive–behavioral therapy for sleep-maintenance insomnia in older adults. *Psychol Aging* 1992;7:282–9.
14. Rechtshaffen A, Kales A. *A manual of standardized terminology, techniques, and scoring systems of sleep stages of human subjects.* Los Angeles: Brain Information Service/Brain Research Institute, UCLA, 1968.
15. Coleman R. Periodic limb movements in sleep (nocturnal myoclonus) and restless legs syndrome. In: Guilleminault C, ed. *Sleeping and waking disorders: indications and techniques.* Menlo Park, CA: Addison-Wesley, 1982:265–95.
16. ASDA Task Force, Guilleminault C, chairman. EEG arousals: scoring rules and examples. *Sleep* 1992;15:173–84.