Clinical study on sleep-regulating technique (TIP3–2) combined with medication of treating primary

W. Wang, L. Hong, Y. Lin, F. Wang, T. Li, W. Wang, G. Li
Psychology and Sleep Department in Guang-anmen Hospital, China Academy of Chinese Medical Sciences, China

Introduction: Cognitive behavioral therapy (CBT) and hypnotic medications are efficacious for short-term treatment of insomnia, but few patients achieve complete remission with any single treatment. In patients with persistent insomnia, the addition of medication to CBT produced added benefits during acute therapy. Sleep- regulating Technique (TIP3–2) is a Symptomatic treatment method of Low Resistance Thought Induction Psychotherapy (TIP). TIP is a psychotherapy of treating insomnia or other mental disorders accompanying with insomnia. TIP is a therapy developed based on low resistance theory and thought induction theory. It combines the eastern Guidance (Dao Yin) and Qigong with western suggestion and hypnotherapy. It is supposed that this can create a low resistance background. Then to treat the patients use some psychotherapy in this condition. Sleep-regulating Technique (TIP3–2) has standard operating procedures and induction word for different symptoms of the patients. The objective of this study is to observe the curative effect of primary insomnia using Sleep-regulating Technique (TIP3–2) combined with medication.

Materials and methods: 70 primary insomnia patients were randomly divided into two groups, TIP combined with medication and only medication, and 35 cases Each group. The patients in medication group were given 1¡«2 mg Estazolam half an hour before going to bed. On the basis of taking Estazolam, the patients in TIP combined with medication group were given Sleep-regulating Technique treatment twice a week. Observed the changes of Pittsburgh sleep quality index (PSQI) before and after treatment, and the period is 4 weeks.

Results: Comparison in group: In TIP combined with medication group, there are improvement in total score of PSQI, subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, daytime dysfunction in statistical significance ($P<0.05$). In medication group, the total score of PSQI, Subjective sleep quality, sleep duration have statistical significance improvement ($P<0.05$); Comparison between groups: Comparing the data after treatment, There were significant differences in the total score of PSQI, subjective sleep quality, medication use and daytime dysfunction ($P<0.05$). TIP combined with medication is better than only medication. Comparing the difference of PSQI values before and after treatment, there are significant difference between two groups in the total score of PSQI, subjective sleep quality, sleep latency, medication use and daytime dysfunction ($P<0.05$). TIP combined with medication is better than only medication.

Conclusion: The two methods have different degrees of improvement in primary insomnia. TIP combined with medication is better than only medication. It is suggested that psychological therapy combined with medication therapy is a more effective treatment of insomnia.

Study on clinical efficacy of treating primary insomnia by wen dan ning xin grain

W. Wang, Y. Liu, L. Hong, Y. Lin, F. Wang, W. Wang, G. Li
Psychology and Sleep Department of Guangán men Hospital, China Academy of Chinese Medical Sciences, China

Introduction: Wen Dan Ning Xin grain is a preparation which can only be prescribed in Guangán men Hospital in China. Its basic components comes from an ancient Chinese medical book called Zheng Zhi Zhun Sheng. It is developed by a Chinese famous doctor Rong-lin Gao, and has been used in clinical for about 10 years. It is said that this is an effective method of treating insomnia. This study is to observe the clinical efficacy of treating primary insomnia.

Materials and methods: 70 primary insomnia patients were randomly divided into two groups, Wen Dan Ning Xin Grain group and Estazolam group, and 35 cases each group. Patients in Wen Dan Ning Xin Grain group were given Wen Dan Ning Xin Grain, 6 g every time and 3 times a day.The patients in Estazolam group were given 1 < 2 mg Estazolam half an hour before going to bed. Observed the changes of Pittsburgh sleep quality index (PSQI) before and after treatment, and the observation period is 4 weeks.

Results: Wen Dan Ning Xin grain increased sleep duration, improved subjective sleep quality, reduced sleep disturbances and generally improved insomnia ($P < 0.05$); Estazolam only improved subjective sleep quality ($P < 0.05$). Comparison between groups, in terms of daytime dysfunction and total scores of PSQI, Wen Dan Ning Xin grain is better than Estazolam ($P < 0.05$). Additionally, effective rate of Wen Dan Ning Xin grain is higher than Estazolam.

Conclusion: Although there is selection bias in this study, it is inevitable in Traditional Chinese Medicine hospital in China. The data in this paper is suggested that Wen Dan Ning Xin grain is better than Estazolam for primary insomnia in Traditional Chinese medicine hospital, and further study is needed.

Evaluation of drug–drug interactions of sodium oxybate with divalproex: Results from a pharmacokinetic/pharmacodynamic study

M. Eller [1], Y. Wang [1], K. Wesnes [2], S. Alvarez-Horine [1], B. Benson [1], J. Black [1]
[1] *Jazz Pharmaceuticals, Inc., United States*
[2] *Bracket, United States*

Introduction: To evaluate drug-drug interactions of sodium oxybate (SXB) and divalproex sodium ER (DVP) with regard to PK, PD, and safety. SXB is the sodium salt of gamma-hydroxybutyrate (GHB), a substrate for monocarboxylate transporter and GHB dehydrogenase; both are inhibited by valproic acid.

Materials and methods: Healthy volunteers were randomized to one of 4 treatment sequences in a 5-period, double-blind, crossover design with washout between periods. During Periods 1 and 2, subjects received two 3g doses of SXB or placebo 4h apart in a crossover fashion (days 1 and 3). In Period 3 (days 5–14), subjects

received DVP 1250 mg, and continued DVP during Periods 4 and 5 (days 15–18), with two 3 g doses of SXB or placebo administered 4h apart in a crossover fashion on Days 15 and 18. Blood and urine samples were taken at predefined times for PK analysis. PD testing, performed during SXB treatment, included the Karolinska Sleepiness Scale, and several automated tests from CDR System (www.bracketglobal.com) including Simple Reaction Time, Digit Vigilance, Choice Reaction Time, Tracking, and Numeric Working Memory tasks. Safety was assessed throughout the study.

Results: 20 subjects enrolled and completed the study (all male, 65% white, mean age 33.9 ± 6.6 y). Geometric LS means of SXB with SXB + DVP relative to SXB alone were significantly higher for plasma AUC0-inf (349.7 vs. 275.6 μg * h/mL; $P < 0.0001$) and renal clearance (606.0 vs. 480.5 mL/h; $P < 0.001$), and upper bounds of the 90% CIs of the percent mean ratios exceeded the equivalence range of 80–125%. No changes in DVP PK were observed with SXB+DVP. SXB induced sleepiness and cognitive impairments. SXB + DVP produced significantly greater deficits ($P < 0.05$) at several time points than SXB alone in numeric working memory mean reaction time, simple reaction time mean, digit vigilance accuracy, choice reaction time accuracy, continuity of attention, and tracking distance from target. The most common adverse events (AEs) were consistent with the drug profiles. AEs in ≥2 subjects with SXB + DVP were somnolence, $n = 18$; euphoric mood, $n=10$; dizziness, $n = 7$; and nausea, $n = 4$.

Conclusion: SXB + DVP showed changes in SXB PK and renal clearance consistent with GHB dehydrogenase and monocarboxylate transporter inhibition. SXB produced sleepiness and cognitive impairments; some cognitive domains showed greater impairment with DVP co-administration, consistent with SXB PK changes. AEs with SXB + DVP reflect a combined drug effect.

http://dx.doi.org/10.1016/j.sleep.2013.11.741

What is known about the experience of CPAP for OSA from the users' perspective? A systematic integrative literature review

K. Ward [1,2], M. Gott [1,2]
[1] *The University of Auckland, Faculty of Medical & Health Sciences: School of Nursing, New Zealand*
[2] *The University of Auckland, Faculty of Medical & Health Sciences: School of Nursing & School pf Popu, New Zealand*

Introduction: The estimated economic, social and personal cost of untreated obstructive sleep apnoea (OSA) is high. Night time continuous positive airway pressure (CPAP) is a recommended, cost effective and popular treatment. The predicted global increase in obesity will lead to increasing prevalence of OSA. Exploring management of CPAP from the user perspective is crucial to successful administration of this therapy. The objective was synthesis of the international evidence base regarding users' experience of night time continuous positive airway pressure therapy for obstructive sleep apnoea.

Materials and methods: A systematic integrative literature review was conducted and quality assessment criteria applied.

Results: From 538 identified papers, 22 met inclusion criteria. Thematic analysis identified four themes: (1) evidence regarding experience of CPAP and issues of research design; (2) CPAP influenced by users' views and beliefs; (3) CPAP investigated using a language of difficulty; and (4) spouse and family impact on CPAP use. Overall, research relating to user experience of CPAP is limited. Understanding is incomplete because of problems of study design, for example the use of pre-determined checklists and survey questions. The problem oriented terminology adopted by most studies is also likely to set up the expectation that users will encounter difficulties with CPAP. There is evidence that personality and attitude impact expectations about CPAP prior to and during use, whilst engagement of spouse, family and colleagues also influence experience.

Conclusion: This comprehensive integrative review identified limited evidence about experiencing CPAP from the users' perspective. Current research is constrained by researchers' concern with non-compliance. Typically experiences of CPAP are not defined by the user, but from an 'expert' healthcare perspective, using language that defines CPAP as problematic. Family and social support is a significant, but underexplored, element of experiencing CPAP and warrants further investigation. Research that more comprehensively involves CPAP users is required to determine how patients manage this therapy successfully.

http://dx.doi.org/10.1016/j.sleep.2013.11.742

Repetitive transcranial magnetic stimulation enhances sleep quality of patients with comorbid major depressive disorder and insomnia

T. Li, W. Wang, L. Hong, Y. Lin, F. Wang
Sleep Medicine Committee of World Federation of Chinese Medicine Societies, Department of Sleep and Psychology, Guanganmen Hospital, China Academy of Chinese Medical Sciences, Beijing, PR China

Introduction: Insomnia impacts the course of major depressive disorder (MDD), obstructs response to treatment, and raises risk of depression relapse. This study approached how repetitive transcranial magnetic stimulation (rTMS) relieves depression and enhances sleep quality of patients with comorbid major depressive disorder and insomnia.

Materials and methods: A randomized, controlled, pilot study was conducted in our hospital. The study was approved by local Ethics Committee. All subjects signed informed consents. 30 patients, conforming to meet the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV–TR) criteria for MDD, and Montgomery–Asberg Depression Scale (MADRS) score between 12 and 29 were randomly chosen as the MDD group. Another 30 patients, meeting the DSM–IV–TR criteria for MDD and insomnia, MADRS score between 12 and 29, and Pitts-burgh Sleep Quality Index (PSQI) scores >7, were randomly selected as the MDD and insomnia group. Both groups received rTMS (10 Hz for 4 weeks) once per day. After treatment, patients' depression was assessed with MADRS, and their sleep quality was evaluated by PSQI. Raters were masked to treatment assignment.

Results: There were 30 subjects in MDD group (60% female, mean age 38.56 ± 12.13 s.d. mean course of disease 11.35 ± 7.53 months). MDD and insomnia group consisted of 30 subjects (66.67% female, mean age 32.72 ± 14.69 s.d. mean course of disease 9.23 ± 4.81 months). Although the rate of depression remission in MDD and insomnia group (59.36%) was higher than MDD group (57.21%), this difference was not significant. After 4 weeks treatment, both MDD group (12.56 ± 6.73) and MDD insomnia group (11.38 ± 7.16 s.d.) were significantly improved in MADRS scores (P<0.05). MDD and insomnia group was significantly improved (P<0.05) in PSQI sleep quality (1.40 ± 0.41), time for falling asleep (1.73 ± 1.21), sleep time (1.90 ± 1.28), sleep efficiency (0.90 ± 1.52), Function during the day-time (1.87 ± 0.84), total score (8.57 ± 3.74).