

## Podcast of the *Journal of Clinical Sleep Medicine*

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Welcome to the regular podcast of the *Journal of Clinical Sleep Medicine*. I am Dr. Stuart Quan, editor of the *Journal*. These podcasts are a regular feature of each issue of the *Journal* and can be downloaded at the *Journal's* website. Each podcast features summaries of important articles published in the current issue of the *Journal*, as well as occasional interviews with authors of these papers.

The first paper to be highlighted in this podcast is entitled, "Efficacy and Safety of Adjunctive Modafinil Treatment on Residual Excessive Daytime Sleepiness among Nasal Continuous Positive Airway Pressure-Treated Japanese Patients with Obstructive Sleep Apnea Syndrome: A Double-Blind Placebo-Controlled Study," by Dr. Yuichi Inoue and colleagues from the Japan Somnology Center, Neuro-Psychiatric Research Institute, Tokyo, Japan, Department of Somnology, Tokyo Medical University, Tokyo, Japan, Yoyogi Sleep Disorders Center, Tokyo, Japan, Center of Sleep Medicine, Ohta Nishinouchi Hospital, Ohta General Hospital, Fukushima, Japan, and The Sleep Disorders Center, Ota General Hospital, Tokyo, Japan. Obstructive sleep apnea is highly prevalent in Asian populations, as well as Caucasian ones. It is estimated that over 20% of male factory workers in Japan have significant obstructive sleep apnea. Continuous positive airway pressure, or CPAP, continues to be the primary method of treatment for obstructive sleep apnea in Japan and other countries. However, some patients with obstructive sleep apnea continue to have excessive daytime sleepiness despite optimum use of CPAP. Previous studies have demonstrated that modafinil can be useful in the treatment of residual sleepiness in CPAP-treated patients who continue to have sleepiness. In fact, the Standard of Practice Committee of the American Academy of Sleep Medicine recommends the use of wake-promoting agents, such as modafinil, in such patients. However, there have been no studies on the use of modafinil in Asian populations. Therefore, the purpose of this study was to determine the efficacy of modafinil in the treatment of residual sleepiness in patients who are optimally treated with CPAP. In addition, the impact of modafinil on nocturnal sleep in these patients was evaluated. The subjects were 114 adult patients with obstructive sleep apnea who were being treated with CPAP and were judged to be compliant with therapy as evidenced by usage on more than 70% of nights for more than four hours per night for at least two weeks before their baseline visit and to have a residual apnea-hypopnea index less than 10 events per hour as determined by nocturnal polysomnography. Fifty-two participants were randomized to modafinil, 200 mg per day, and 62 to placebo

for four weeks. The outcome measures included changes in the Epworth Sleepiness Scale score, the sleep latency on a maintenance-of-wakefulness test, nocturnal polysomnography results, and scores on the Pittsburgh Sleep Quality Index. The authors found that the mean change in the Epworth Sleepiness Scale score was -6.6 in the modafinil group versus +2.4 in the placebo group. In addition, the maintenance-of-wakefulness test results showed that the modafinil group increased their sleep latency by 2.8 minutes versus -0.4 minutes in the control group. There were no significant differences in nocturnal polysomnography, changes in the Pittsburgh Sleep Quality Index, and the apnea-hypopnea index from baseline to the final assessment four weeks later. However, there were slightly more adverse reactions, 36.5% in the modafinil group versus 22.6% in the placebo group. However, this was not statistically significant. Nevertheless, the most common adverse event was headaches occurring in six out of the 52 patients in the modafinil group, or 11.5% of these individuals. These data provide additional evidence that modafinil is a relatively safe treatment alternative for patients with residual sleepiness who are adequately treated with CPAP therapy for their obstructive sleep apnea.

The next paper to be discussed in this podcast is entitled, "Impact of CPAP Use and Age on Mortality in Patients with Combined COPD and Obstructive Sleep Apnea: The Overlap Syndrome," by Dr. Michael L. Stanchina and colleagues from the Pulmonary, Critical Care & Sleep Medicine Sections, Alpert School of Medicine at Brown University, Providence, RI, and the Division of Sleep Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, MA. Both obstructive sleep apnea and chronic obstructive pulmonary disease are common medical conditions. When these conditions occur concurrently, the term "overlap syndrome," is frequently applied. Chronic obstructive pulmonary disease is a frequent cause of death in the United States and worldwide, and individuals with the overlap syndrome have been observed to have a greater risk of death in comparison to those with COPD alone. The purpose of this study was to determine whether the use of CPAP had any impact on mortality rates in patients with the overlap syndrome. This was a retrospective study of patients reviewed using an outpatient database from three sleep centers in Rhode Island. There were 10,272 patients in this database from the years 2007-2010. 1,112 COPD patients and 2,284 obstructive sleep apnea patients were identified using standard diagnostic codes. A comprehensive chart review was then undertaken and 227 of these patients were identified as having the overlap syndrome. Of these 227 patients, there were 17 who had died, or 7.4%

of the cohort. A multi-variate analysis revealed that hours of CPAP use and age were independent predictors of mortality. The hazard ratio for CPAP use was 0.71, indicating that greater usage was associated with a lower mortality rate. Conversely, the hazard ratio for age was 1.14, indicating that greater age was associated with greater mortality. As demonstrated by Kaplan-Meier survival curves, individuals who used CPAP only minimally, that is to say less than two hours per night, had a 40% survival rate over approximately 3.8 years. Whereas this was 80-100% in those individuals who used CPAP more regularly. These observations provide additional data indicating that treatment of obstructive sleep apnea in individuals with the overlap syndrome may have a significant impact in reducing their mortality. However, it should be stressed that this was a retrospective, uncontrolled study. It is possible that CPAP users were more motivated to use other forms of therapy to treat their chronic obstructive pulmonary disease or other co-morbidities. It is also possible that various other co-morbidities were not controlled for in the analysis, although the Charlson Index, which is a method of controlling for morbidity in these types of studies, was not different between the two groups. Nevertheless, clinicians at this time should probably stress to those individuals under their care who have the overlap syndrome that it would be to their marked benefit if they were adherent to the use of CPAP in the treatment of their obstructive sleep apnea.

The final study to be summarized in this podcast is entitled, "Delayed Diagnosis, Range of Severity, and Multiple Co-Morbidities: A Clinical and Polysomnographic Analysis of 100 Patients of the Innsbruck Narcolepsy Cohort," by Dr. Birgit Frauscher and colleagues from Innsbruck Medical University, Department of Neurology, Innsbruck, Austria. This paper is a review of the clinical presentation, co-morbidities and polysomnographic findings in 100 consecutive patients

in a narcolepsy cohort from Innsbruck, Austria. In general, the authors found that age of onset was young with a mean age of 20. However, one individual presented at age 69 years. There was a significant diagnostic delay, with an interval of 6.5 years between presentation of the first symptoms and the diagnosis. In one case, this delay was 39 years. Although all patients had sleepiness, the complete narcoleptic tetrad of excessive daytime sleepiness, cataplexy, hypnagogic hallucinations and sleep paralysis was only present in 36% of patients. 28% had three symptoms, 29% had two symptoms and only seven patients had excessive daytime sleepiness. The mean Epworth Sleepiness Scale score was 18. The range was 10-24. There were a large number of patients with other sleep co-morbidities, such as sleep-related movement disorders in 55% of patients, parasomnias in 34% of patients and sleep-related breathing disorders in 24% of patients. This study also demonstrated that REM sleep without atonia, or periodic limb movements, were present in most patients, 90% and 75% respectively. In addition, excessive fragmentary myoclonus was evident in 22% of patients. Furthermore, a large number of patients had evidence of REM-sleep behavior disorder on their Multiple-Sleep Latency Test during REM sleep. This study confirms previous observations that not all patients with narcolepsy have the classic narcoleptic tetrad and there is considerable delay in diagnosis. In addition, on polysomnography, many narcoleptic patients have evidence of REM sleep without atonia, periodic leg movements during the night and evidence for sleep fragmentation.

This concludes the regular podcast of the *Journal of Clinical Sleep Medicine*. The listener is encouraged to read the contents of the *Journal* for additional information regarding each of the articles summarized in this podcast, as well as other papers published in this issue of the *Journal*.