

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, "Association of Severe Obstructive Sleep Apnea and Elevated Blood Pressure Despite Anti-Hypertensive Medication Use," by Dr. Harneet K. Walia and colleagues from the Cleveland Clinic, Cleveland Clinic Learner College of Medicine of Case-Western Reserve University, Cleveland, OH, Center for Clinical Investigation, Case-Western Reserve University, Cleveland, OH, Brigham & Women's Hospital and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, VA Boston Healthcare System, Harvard Medical School, Boston, MA, Johns-Hopkins University, Baltimore, MD, Brigham & Women's Hospital Heart & Vascular Center, Harvard Medical School, Boston, MA. It is now generally accepted that obstructive sleep apnea is associated with elevations in blood pressure. However, there is limited data in individuals with resistant hypertension, particularly if they have cardiovascular disease. In this study, data from the HeartBEAT Study or Heart Biomarker Evaluation and Apnea Treatment Study was used to determine whether there was an association between severe obstructive sleep apnea and hypertension which was resistant to use of anti-hypertensive medication. HeartBEAT was a randomized controlled study to determine whether patients who had pre-existing cardiovascular disease or who were at high risk for cardiovascular disease had an improvement in 24-hour ambulatory blood pressure or other biomarkers of cardiovascular risk after treatment with CPAP, oxygen or lifestyle modification for sleep apnea. Participants were classified into four groups depending on their 24-hour blood pressure measurements performed at baseline. The groups were elevated blood pressure, that is a systolic blood pressure greater than or equal to 130 mm of mercury or a diastolic blood pressure greater than or equal to 80 mm of mercury, uncontrolled elevated blood pressure, that is a systolic blood pressure greater than or equal to 130 mm of mercury or a diastolic blood pressure greater than or equal to 80 mm of mercury without use of intensive anti-hypertensive therapy, resistant elevated blood pressure, that is a systolic blood pressure greater than or equal to 130 mm of mercury or a diastolic blood pressure greater than or equal to 80 mm of mercury with the use of three or more anti-hypertensive

medications including a diuretic, and controlled blood pressure, that is a systolic blood pressure less than 130 mm of mercury or a diastolic blood pressure less than 80 mm of mercury irrespective whether anti-hypertensive medications were being used. There were 284 participants included in this analysis. There were 175 participants with controlled blood pressure and 109 that had an elevated blood pressure. Of those with controlled blood pressure, 130 were controlled without an intensive anti-hypertensive regimen and there were 45 who were controlled with an intensive hypertensive regimen. Of those with an elevated blood pressure, there were 28 who had resistant hypertension and 81 who had uncontrolled hypertension without use of anti-hypertensive medications. The authors found that among participants who were prescribed an anti-hypertensive medication regimen that required three or more agents, including a diuretic, there was a 58.3% prevalence of resistant hypertension in those with severe obstructive sleep apnea compared to a 28.6% prevalence of resistant hypertension in those with moderate sleep apnea. Furthermore, individuals with severe obstructive sleep apnea had a more than four-fold higher odds of having resistant elevated blood pressures. These data suggest that untreated severe obstructive sleep apnea contributes to poor blood pressure control among individuals who have significant cardiovascular risk or underlying pre-existing cardiovascular disease, despite use of anti-hypertensive medications.

The next paper to be discussed in this podcast is entitled, "Sleep Disordered Breathing and Chronic Respiratory Failure in Patients with Chronic Pain on Long-Term Opioid Therapy," by Dr. Anand Rose and colleagues from Adelaide Institute for Sleep Health, Repatriation General Hospital, Daw Park South Australia, Australia, Department of Medicine, Flinders University, Bedford Park South Australia, Australia, Pain Management Unit, Flinders Medical Center, Bedford Park South Australia, Australia, Sleep & Circadian Research Group and NAHRC Centre for Integrated Research and Understanding of Sleep (CIRUS), Woolcock Institute of Medical Research, Central Clinical School, University of Sydney, Sydney, Australia. Over the past several years, there has been increasing emphasis on adequate treatment of pain in patients with a variety of diseases. Consequently, there has been increasing use of opioid medications in the treatment of these patients. Opioids cause central nervous system depression, including depression of central ventilatory drive. Therefore, it is possible that individuals on chronic long-term opioid therapy may have a greater prevalence of sleep disordered breathing. The purpose of this study was to assess the prevalence of sleep disordered breathing in a

population of chronic pain patients who were being prescribed opioid therapy. 24 patients age 18-74 years on long-term opioid therapy were prospectively recruited. Their data was compared to 20 healthy controls and 20 patients who were seen in the sleep clinic without opioid therapy. In addition to polysomnography, the patients underwent psychomotor vigilance testing and also had an awake daytime blood gas drawn. The authors found that 46% of individuals who were receiving opioids had severe sleep disordered breathing with an apnea-hypopnea index greater than or equal to 30. Central sleep apnea was particularly common in this group of individuals with central apnea being present in 17% of patients. However, the arousal frequency was significantly less in opioid treated patients in comparison to both healthy controls and those individuals with sleep apnea recruited from the sleep lab. In addition, opioid treated patients had worse performance on the psychomotor vigilance task with slower reaction times and more lapses. Arterial blood gas results in the patients with chronic opioid therapy showed that 45% had a PCO_2 greater than 45 mm of mercury. Finally, the morphine equivalent doses of opioids were found to positively correlate with the total apnea-hypopnea index in those individuals on opioid therapy. These data demonstrate that patients on chronic opioid therapy have a high prevalence of severe sleep disordered breathing which includes a high prevalence of central sleep apnea. Furthermore, performance on psychomotor vigilance testing is impaired and many individuals show evidence of chronic respiratory failure.

The final study to be summarized in this podcast is entitled, "A Novel Adaptive Servoventilation (ASVAUTO) for the Treatment of Central Sleep Apnea Associated with Chronic Use of Opioids," by Dr. Michelle Cao and colleagues from Stanford Sleep Medicine, Stanford University School of Medicine, Redwood City, CA, Willes Consulting Group, Inc., Encinitas, CA, ResMed Science Center, ResMed Corporation,

San Diego, CA. As noted in the introduction to the previous study, chronic pain frequently requires opioid therapy and as a consequence, many of these individuals have significant sleep disordered breathing. Because central sleep apnea frequently is observed as part of the sleep disordered breathing in these patients, it is unclear whether commonly used forms of positive airway pressure treatment will be effective in the treatment of these patients with chronic pain and who are on opioid therapy. Thus, it is possible that alternative methods of delivering positive airway pressure may be useful and more effective in treatment of these patients. The current study is a prospective, randomized cross-over study of 18 consecutive patients who were on long-term opioid therapy and who had previously documented central sleep apnea. They underwent testing on two separate nights with either adaptive servo ventilation or bi-level PAP in the ST mode. The authors found that use of ASV was significantly better in controlling the sleep disordered breathing than bi-level PAP. The apnea-hypopnea index and the central apnea index were markedly lower on ASV in comparison to bi-level PAP. The apnea-hypopnea index on ASV was 2.5 versus 16.3 on bi-level PAP. In addition, the central apnea index was 0.4 on ASV versus 9.4 on bi-level PAP. Finally, the patients were subjectively more alert and awake on ASV in comparison to bi-level PAP on a questionnaire that was administered on the morning after the study. These data suggest that ASV is a significantly more effective form of delivering positive airway pressure to individuals who are receiving chronic opioid therapy than use of bi-level PAP in the ST mode.

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*.