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The Physician's Voice in Pain Medicine

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Sleep Apnea Associated with Methadone and Benzodiazepine Therapy
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Introduction: Prescription medications have been attributed to increased overdose deaths. Pain patients receiving methadone may be at an increased risk for sleep apnea which may contribute to overdose deaths. **Methods:** An IRB provided approval for this study. We retrospectively studied 152 consecutive patients on chronic opioid therapy. Overnight polysomnography was used to assess the relation between medications and the apnea-hypopnea index (AHI) as an overall measure of severity of sleep apnea and central sleep apnea index (CAI) as a measure of the severity of central sleep apnea. These data were adjusted for age, gender and BMI with generalized linear models. The mean age was 51 (range 22 to 86) years, the mean BMI was 29.7 (range 16 to 52.5) and female-male ratio was: 1.51:1. **Results:** Polysomnography showed abnormal AHI in 75% of patients, 42% had obstructive sleep apnea (OSA), 12 % central sleep apnea (CSA) 21% mixed OSA and CSA while 25% had no sleep apnea. Long acting opioids (LAOs) were prescribed to 96% of patients, 33% received methadone and LAOs, and 4% received methadone alone. Opioids were converted into morphine equivalents (ME) and benzodiazepines (36% of patients) converted to diazepam equivalents (DE). The use of muscle relaxants, anticonvulsants, antidepressants, antihistaminic, stimulants, proton pump inhibitors and non-steroidals were expressed as dichotomous variables. Log transformation was used for AHI, CAI, ME and DE. There was a direct relation between AHI and methadone ME ($p<0.005$) but not LAO ME. There was an inverse relation with use of muscle relaxants ($p<0.05$). There was a direct relation between CAI and methadone ME ($p<0.005$) and also DE ($p<0.05$). **Conclusion:** There is a dose response between methadone and benzodiazepines and the severity of sleep apnea. In addition the combinations of methadone and benzodiazepines have an additive effect on the severity of central sleep apnea.

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