

Clinical Research Update Corner

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Researchers from Cincinnati, Ohio found that acetazolamide significantly improved Central sleep apnea and related daytime symptoms in patients with congestive heart failure. In this randomized controlled trial, patients with congestive heart failure and Obstructive Sleep apnea (RDI>15/hr) received acetazolamide or placebo, taken one hour before bedtime for six nights. Patient's receiving Acetazolamide showed decreased CSA, improved oxygenation and subjective perception of sleep quality. However questions persist over long term use of acetazolamide and development of tolerance.

Am. J. Respir. Crit. Care Med. 2006; 173: 234-237

BiPAP device is currently being used for patients with Sleep disordered breathing who do not tolerate CPAP or may have underlying neuro-muscular diseases. It is also approved by Medicare (USA) for treatment of Central Sleep Apnea. Now researchers have found that it may actually worsen central sleep apnea. In a retrospective analysis of 95 patients they assessed the incidence of and frequency of central events during baseline conditions, CPAP and BiPAP. BiPAP device was found to have significant worsening of Central apneas (both CSR and non-CSR). Author's hypothesized that since there is increased mortality with central apneas, BiPAP device would worsen overall prognosis. It would be interesting to know if this was a first night effect or would these central hypopneas persist on continuous use.

Chest 2005; 128; 2141-2150

It is well known that acute / chronic pain causes disturbed sleep. Researchers in Detroit, USA showed for the first time that modest reduction in sleep time and loss of REM sleep produces hyperalgesia the next morning. Healthy pain free individuals were enrolled in 1) sleep loss protocol 2) REM deprivation protocol.

Investigators showed that the latency to finger withdrawal to heat stimuli was reduced by 25% after 4 hours in bed compared to 8 hours. Similarly REM

deprivation caused 32% reduction in finger withdrawal latency relative to non- REM sleep. These findings may have clinical implications in treating patients with pain syndromes i.e. fibromyalgia.

Sleep 2006; 29; 145-151

Association between Sleep Disordered Breathing and arrhythmias has not been fully evaluated, though Javaheri et al have shown reduction in ventricular irritability by application of CPAP therapy overnight. Researchers recently looked into the prevalence of arrhythmias in patients with Sleep disordered breathing. Participants from Sleep Heart Health Study were taken and prevalence compared between those with SDB compared to those without SDB. Individuals with severe sleep-disordered breathing (AHI>30/hour) had two- to fourfold higher odds of complex arrhythmias than those without sleep-disordered breathing even after adjustment for potential confounders. This is generally attributed to the fact that alterations in sympathetic and parasympathetic nervous system activity occurring with SDB-associated hypoxemia, acidosis, apneas, and arousal.

Am. J. Respir. Crit. Care Med. 2006; 173: 910-916.

Use of Modafinil and wake promoting agent has been controversial. Recent study from Harvard University looked at use of Modafinil in shift-work sleep disorders. In this randomized double blind controlled trial 209 were randomized to receive either Modafinil or placebo for 3 months. Researchers reported improvement in sleep latency, reduction in lapse frequency on Psychomotor vigilance testing. They also found reduced number of accidents and near accidents and improvement in symptoms in the group taking modafinil. However patients treated with Modafinil continued to have excessive sleepiness and impaired performance at night. This is not very reassuring as these patients are under strictly monitored under the trial. In real life there is real possibility of misuse of medication to ward off

sleepiness due to sleep deprivation thus negating all the above benefits.

New England Journal of Medicine. 353(5):476-86, 2005 Aug 4.

After the study by Garrigue et al about the benefits of atrial pacing in Sleep Apnea syndrome there has been lot of interest in pacing as treatment for Sleep apnea. Subsequent studies however did not prove to be very encouraging. In a Recent randomized control trial with cross-over design by researchers in Greece 16 patients with Obstructive Sleep apnea with dual chamber pacemaker were randomly assigned to atrial over drive pacing or back-up atrial pacing. This latter group was initiated on nasal CPAP. After one month these two groups switched therapy and followed for another month. Atrial pacing was found to have no significant effect on any respiratory variables including apnea hypopnea index while CPAP was found to be highly effective in treatment of Sleep apnea. It appears that the controversy has at last been laid to rest.

New England Journal of Medicine. 353(24):2568-77, 2005 Dec 15.

Researchers at Mayo clinic reviewed the time of death by cardiac causes in patients with Obstructive Sleep apnea. Historically most deaths due to cardiac causes occur between 6AM to noon. The study revealed that in contrast to above most of the deaths in patients with

Obstructive sleep apnea due to cardiac causes occurred from midnight to 6AM. The relative risk of of sudden death in patients with OSA during sleeping hours was 2.57. It would be interesting to know if patients successfully treated for OSA will revert back to the time frame witnessed in general population.

New England Journal of Medicine. 352(12):1206-14, 2005 Mar 24.

There has been a controversy regarding the role of Sleep apnea in stroke. OSA has been implicated in stroke but many studies did not adjust for confounding factors. In a prospective trial done at Yale University researchers enrolled 1022 patients with 697 of them having obstructive sleep apnea (Mean AHI 35). The rest served as controls. Even after adjustment for age, sex, race, smoking alcohol, BMI and co-morbid conditions Sleep apnea retained a statistically significant association with stroke and death (Hazard Ratio 1.97). This large study together with previous smaller studies leaves little doubt that Obstructive sleep apnea independently increases risk of stroke and death.

New England Journal of Medicine. 353(19):2034-41, 2005 Nov 10.

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