ARIC Manuscript Proposal # 813S

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SHHS Manuscript Proposal

Full Title:
Susceptibility to sleepiness: factors associated with absence of sleepiness and fatigue in moderate to severe sleep-disordered breathing

Abbreviated Title:
SDB without symptoms

Lead Author:
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Timeline:
Start analysis immediately

Rationale:
Obstructive sleep apnea is defined as the presence of significant SDB accompanied by complaints resulting from disrupted sleep including sleepiness and fatigue. There appear to be individual differences in susceptibility to and/or awareness of sleepiness. It is not uncommon to encounter patients who have significant SDB, but little or no subjective complaints of sleepiness or fatigue. In the Wisconsin sleep cohort only a minority of men and women with RDI>5 had significant sleepiness.[1] Analyses by Gottlieb on the SHHS cohort show that only a minority of individuals with severe SDB have Epworth scores > 10. [2]

There are studies that have attempted to identify the predictors of objective and subjective sleepiness in sleep clinic patients.[3, 4,5,6,7] These studies indicate that sleep fragmentation, frequency of SDB, female gender are associated with sleepiness while hypoxemia does not appear to be an important factor. Gottlieb's analyses of snoring and sleepiness in the SHHS cohort indicates that RDI is associated with Epworth score and that snoring is an independent predictor of sleepiness at all levels of SDB.[2, 8] In addition, gender, usual sleep duration, sleep restriction on weekdays and symptoms of leg movements were associated with the Epworth score though they did not confound the relationship between the Epworth score and RDI or snoring

Many patients with sleep apnea complain of fatigue in addition to or instead of sleepiness. One study in a sleep laboratory population, patients more frequently complained of tiredness than sleepiness.[9] There are no community-based studies that have determined the prevalence of symptoms of fatigue relative to sleepiness in moderate to severe SDB. In addition, there are no community-based studies that have identified factors that are associated with the absence of fatigue and sleepiness in individuals with moderate to severe SDB.

The identification of factors associated with the *absence* of sleepiness and fatigue may important to identify individuals with significant SDB who do not have these complaints but still have increased

risk for the potential medical complications of SDB. In addition, the identification of factors associated sleepiness and fatigue in individuals with significant SDB may provide insights into individual susceptibility to sleepiness and the causal relationship between SDB and symptoms of non-restorative sleep. The SHHS has collected data that can address these issues.

Hypotheses:

1. A majority of subjects with moderate to severe SDB do not have complaints of sleepiness or fatigue. Fatigue is a more common complaint than sleepiness in this group.
2. The absence of fatigue and sleepiness in this population is associated with:
    a. Less disrupted sleep as assessed by EEG
    b. Longer usual sleep duration
    c. No evidence of weekday sleep restriction
    d. Female gender
    e. Lower educational level
    f. Lack of use of sedating medications
    g. Absence of self-report of awakenings due to legs
    h. Less frequent snoring
    i. Less comorbid illness

Data:

PSG: RDI, Arousal Index, Awakening Index, sleep efficiency, sleep stage %, lowest oxygen saturation, % time spent below 90% saturation

Sleep habits questionnaire: Questions on fatigue, sleepiness, sleep hours, snoring leg jerks

SF-36: Question on frequency of tiredness

Medications: Use of MAOI, TCA, benzodiazepine, antipsychotics. The chronic disease score calculated from medication list (see manuscript #27)

Demographic: Age, gender, BMI, race, education level

General Health: smoking caffeine, alcohol, self-reported cardiovascular and pulmonary disease

Type of Study:

Case-control study

Type of Publication:

Journal article

Analysis Responsibility:

Author

Introduction:

These analyses will determine the proportion of subjects with moderate to severe SDB (RDI $\geq$15) that have fatigue, sleepiness, both or neither and which factors are associated with the absence of symptoms.

Brief Analysis Plan:

1. Determine the prevalence of sleepiness, fatigue, both symptoms and no symptoms in subject with RDI≥15 using questions from sleep habits (#7E) and SF-36 (9i) on frequency of these symptoms. Compare characteristics of subjects with fatigue only, sleepiness only, both symptoms and no symptoms
2. Case control study:

Cases: RDI4%≥15 with rare or less frequent sleepy and "a little of the time" or less frequently tired
Controls: RDI4%≥15 with at least often sleepy or "a good bit of the time" tired

Independent variables: listed under data
Primary statistical method: logistic regression
Compare cases to controls and estimate odds ratios for factors associated sleepiness or fatigue. Identify and estimate odds ratios for independent risk factors using multivariate models.

Summary: The results of these analyses will add to our understanding of how individuals with moderate SDB perceive the effects of sleep disruption and what factors are associated with an awareness of the effects.

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3. Guilleminault C et al. Determinants of daytime sleepiness in obstructive sleep apnea. Chest 1988 Jul; 94(1):32-7.
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5. Furuta H et al. Epworth Sleepiness Scale and sleep studies in patients with obstructive sleep apnea syndrome. Psychiatry Clin Neurosci 1999 Apr; 53(2): 301-2.
6. Cot HG et al. Hypoxemia vs. sleep fragmentation as cause of excessive daytime sleepiness in obstructive sleep apnea. Chest 1991 Dec; 100(6): 1542-8.
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9. Chervin RD. Sleepiness, fatigue, tiredness and lack of energy in obstructive sleep apnea. Chest 2000 Aug; 118(2): 372-9.