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Factors associated with sleep apnea in men with spinal cord injury: a population-based case-control study

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Objective: To characterize a population of spinal cord injury (SCI) patients with sleep apnea, and to determine associated factors and comorbidities
Study Design: Population-based retrospective case-control study.
Subjects: 584 male patients served by a Veterans Affairs SCI service.
Measures: Medical records were reviewed for sleep apnea diagnosis, demographic information, neurologic characteristics, and treatments received. Sleep study reports were not available to determine the nature of abnormal respiratory events (ie central, obstructive, hypoventilation). For each case with tetraplegia, a control tetraplegic subject without sleep apnea diagnosis was selected.
Results: We identified 53 subjects with diagnosed sleep apnea: 42 tetraplegic, 11 paraplegic. This represented 14.9% of all tetraplegic and 3.7% of all paraplegic patients in the population ($P<0.0001$ for comparison of tetraplegic and paraplegic proportions). In tetraplegic subjects, sleep apnea was associated with obesity and more rostral motor level, but not with ASIA Impairment Scale. Medical comorbidities associated with sleep apnea in non-SCI patients, such as hypertension, were more common in case subjects. Less than half of case subjects were receiving some form of treatment. For motor-complete tetraplegics, long-term positive airway pressure treatment was less common with motor level C5 and above compared to C6 and below.
Conclusion: In this population, sleep apnea has been frequently diagnosed, particularly in tetraplegic subjects. The true prevalence is likely to be considerably higher, since this study considered only previously diagnosed cases. Sleep apnea was associated with obesity and higher neurologic level, but not ASIA Impairment Scale. Medical comorbidities were more frequent in this group, and treatment acceptance was poor with higher level motor-complete injuries. Since the type of sleep apnea (central or obstructive) was not distinguished, we cannot comment on the prevalence and associations based on specific types of sleep apnea.
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Keywords: spinal cord injuries; quadriplegia; sleep apnea syndromes; case-control studies; obesity; baclofen

Introduction

Sleep apnea has become recognized as a common complication of spinal cord injury (SCI). Investigators have determined a 9–45% prevalence in randomly selected SCI patients, depending on the screening method used and the neurologic characteristics of the population studied.[1–8] Studies using more sensitive testing methods, such as full polysomnography or limited cardiopulmonary sleep studies, have established that the prevalence is significantly greater than in the general population. These studies indicate that the majority (75%) of cases have predominantly obstructive sleep apnea, although a significant prevalence of central sleep apnea has also been noted.[4,5,8] Prior studies have either excluded paraplegic subjects[2,5–7] or included a small number of them.[1,3,4,8] The majority of studies have excluded subjects with American Spinal Injury Association (ASIA) Impairment Scale (AIS) scores[9] or Frankel scores[10] of D[1,2,4,5,7] or have not reported ASIA or Frankel scores.[3]

Published studies on sleep apnea in SCI are of limited use in understanding clinical characteristics of the disorder for a number of reasons. These studies have included only small numbers of cases. In total, these studies have reported on approximately 50

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subjects with sleep apnea. Since these studies were performed on different populations, with a variety of inclusion criteria and screening methods, it is difficult to generalize about characteristics of SCI patients with sleep apnea. Predictive factors for sleep apnea in SCI have been examined, but the studies have had limited power to define these associations due to the small number of cases. Contradictory results have been obtained on the role of neurologic status and baclofen use as risk factors.[5,6,8] In addition, these studies identify all cases in the screened population, regardless of sleep apnea severity. It may be of greater use to understand the clinical characteristics of moderate and severe cases. It also remains unclear how frequently sleep apnea is being diagnosed in clinical practice in the population of persons with SCI.

In order to understand the clinical characteristics of SCI patients with sleep apnea, we identified all individuals in our SCI patient population with a diagnosis of sleep apnea. We sought to determine the proportion of our population carrying a diagnosis of sleep apnea (obstructive or central sleep apnea), to describe them with respect to neurologic classification and clinical characteristics, and to determine the treatments received, such as continuous positive airway pressure (CPAP) therapy. Using the tetraplegic subjects with sleep apnea as cases, we then performed a case-control analysis to identify factors predictive of diagnosed sleep apnea, and we determined whether medical comorbidities were more frequent with sleep apnea. We hypothesized that diagnosis of sleep apnea would be associated with higher neurological level of injury, motor-complete injury, and higher doses of antispasticity medications.

Methods

Subjects and setting

The study received approvals from institutional review boards at the University of Washington and the VA Puget Sound Health Care System (VAPSHCS), which included a waiver of consent for retrospective medical records review. Subjects were drawn from the population served by the SCI Service of the VAPSHCS, which provides primary care and specialty care to veterans with acute and long-term SCI residing in urban and rural locations over a large geographic area. The population served has a mean age of 55 ± 13 years and is 99% male. Approximately 95% of these individuals have been injured for greater than 1 year. At the start of the study, a patient list was generated from an administrative database to include all living patients who had received services from our facility during the preceding 4-year period. This procedure identified a population of 584 actively served patients that was used for the remainder of the study.

In order to identify as many subjects as possible with sleep apnea, multiple strategies were used. Initially, all available discharge summaries for a 4-year period were reviewed for any notation of a diagnosis of sleep apnea. Since most annual medical evaluations had been performed on an inpatient basis, the majority of patients had at least one discharge summary available for review. For those patients who did not have discharge summaries available, we reviewed outpatient records for any notation of sleep apnea diagnosis. We reviewed a list of all sleep studies performed by our Respiratory Therapy department over the prior 6 months to identify patients served by the VAPSHCS SCI Service, and we selected those patients with studies confirming sleep apnea. Additionally, we used an administrative database to identify all patients who had receive CPAP or bilevel positive airway pressure (Bi-PAP) equipment for home use from VAPSHCS, and we cross-referenced this with our study population list. Finally, we asked practitioners on the SCI service to identify any additional patients they could recall with sleep apnea diagnosis.

Since the overwhelming majority of our cases were tetraplegic, a control group of tetraplegic subjects was created. We generated a list of all tetraplegic patients without a prior diagnosis of sleep apnea and used a random number generator to select control subjects in an equal number to the case tetraplegic subjects.

Data abstraction

Data were abstracted from medical records by study investigators with experience in SCI medicine and familiarity with medical records maintained by the institution. Characteristics abstracted from records included age, years since injury, etiology of injury, neurologic classification, height, weight, total daily baclofen and diazepam dosage, and medical comorbidities that are associated with sleep apnea in the general population (hypertension, cerebrovascular disease, cardiovascular disease, arrhythmias, depression). For subjects with tetraplegia, we determined whether cervical spine surgery was performed following SCI, and if so, which levels were involved and whether the surgical approach was anterior, posterior, or combined anterior and posterior. For subjects with prior diagnosis of sleep apnea, charts were reviewed for information pertaining to date of diagnosis of sleep apnea, reason for work-up, and treatment currently received, such as CPAP or Bi-PAP. For most cases, the sleep study report was not available to determine severity or type of sleep apnea (central or obstructive) present.

The neurologic classification for case and control subjects was determined by a single investigator (SPB) from review of all available neurologic examination records. Subjects were classified for motor levels, sensory levels, and ASIA Impairment Scale scores using the 1996 revision of the International Standards for Neurological and Functional Classification of Spinal Cord Injury,[9] which resulted in reclassifications for some subjects, compared with classifications noted in the medical records. For the purpose of analysis, a single motor level was then designated for each subject. For subjects with asymmetric motor levels, the more caudal of the two levels was designated as the motor level. We chose the more caudal of the two levels because, based on our prior study,[8] we were interested in the relationship between hand function and CPAP/Bi-PAP acceptance in motor-complete tetraplegia, and presence of at least unilateral grasp and release function was expected to improve the ability to manipulate a CPAP/Bi-PAP mask.

Data analysis
Differences between subpopulations for normally distributed continuous variables were compared using the Student *t*-test. Non-normally distributed continuous data and ordinal data were analyzed using the Mann–Whitney U-test, and the Chi-Square test and Fisher's exact test were used for categorical data. Z-scores were calculated to compare differences in proportions between populations. A logistic regression analysis was performed using those variables that showed significant differences between case and control groups on univariate analysis. For this analysis, level of injury was dichotomized into C5 and above or C6 and below, BMI (body mass index) was dichotomized into $>=30$ or <30, and baclofen dose was dichotomized into <80 or $>=80$ mg/day. All three indicator variables were included in the multivariate logistic regression model. We considered age as a potential confounder, but the model did not change significantly when it was included. It should be noted that, given the high prevalence for the associated factors of interest in our study population, the calculated odds ratio significantly overestimates the risk ratio.[11] All statistical analyses were performed using SPSS statistical software version 7.5 (SPSS, Inc.; Chicago, IL, USA). A P value of less than 0.05 was considered significant.

Results

Case identification
Of the 584 patients whose medical records were reviewed, 53 had a prior diagnosis of sleep apnea. This represents 9.1% of the population followed by the service. Most charts contained information pertaining to location and date of sleep apnea work-up and treatment received, but information on indication for work-up was frequently absent. Sleep apnea had been diagnosed a mean (SD) of 2.5 ($\pm$2.1) years previously for the 40 subjects with date of diagnosis. The majority of cases had been diagnosed using limited sleep studies (respiratory effort, airflow, oxygen saturation, and heart rate, without electroencephalographic monitoring) and not full polysomnography. In most cases, sleep study data were not available to allow classification of the types of sleep apnea (obstructive, central or hypoventilation) present. Excluding eight subjects who had sleep apnea diagnosed as part of screening for a concurrent research study, the reason for the work-up was noted in the reviewed medical records for only 27% of subjects. The most common reason for work-up was patient complaints of sleepiness. The second most common reason for a work-up was observed apneas, either observed by an inpatient clinician or by a bed-partner of the subject. Only one subject had been diagnosed with sleep apnea prior to SCI.

Neurologic characteristics
Of the 53 subjects with prior diagnosis of sleep apnea, 42 had tetraplegia, and 11 had paraplegia. This represents 14.9% of the 282 tetraplegic patients and 3.7% of the 302 paraplegic patients in the population served ($P<0.0001$ for comparison of tetraplegic and paraplegic proportions).

The neurologic classification of the 42 tetraplegic case subjects was compared with 42 randomly selected control tetraplegic subjects without prior diagnosis of sleep apnea. Motor level was found to differ significantly between the two groups, while ASIA Impairment scores did not differ. Tetraplegic sleep apnea subjects had an overall higher motor level than tetraplegic control subjects ($P<0.001$; Mann–Whitney U-test), with the majority of subjects with apnea having motor level of C4 or C5. The distribution of motor levels between case and control subjects is shown in Figure 1. In contrast, the distribution of ASIA Impairment scores did not differ between tetraplegic subjects with and without sleep apnea ($P=0.995$; Mann–Whitney U-test). ASIA Impairment scores for case and control subjects are depicted in Figure 2. Of the 11 paraplegics with sleep apnea, neurological level was between T2–T6 in four, T7–T12 in five, and L1 or below in two.

Other associated factors
Age, years injured, etiology of injury, and spine surgery history did not differ between tetraplegic subjects with

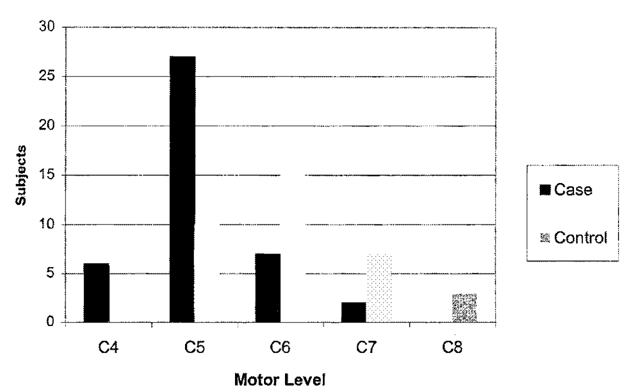

Figure 1 Motor level differed significantly between tetraplegic sleep apnea cases and controls ($P<0.001$)

and without sleep apnea. The mean age of tetraplegic subjects with apnea was 54.5±11.1 years and for controls it was 50.0±14.5 years ($P>0.05$; two-sided *t*-test). The mean number of years injured for case tetraplegic subjects was 16.4±12.6 years and for controls was 14.2±12 years ($P>0.05$; two-sided *t*-test). Proportions of subjects with SCI secondary to MVA and due to non-traumatic etiologies were similar in tetraplegic subjects with and without sleep apnea. The type of spine surgery received by case and control subjects was similar, whether considered as proportion receiving surgery, proportion receiving surgery through an anterior approach, or number of vertebral levels fused.

Obesity was common in paraplegic and tetraplegic subjects with sleep apnea. Height and weight were available for greater than 80% of subjects, allowing calculation of body mass index (BMI). Tetraplegic subjects with sleep apnea had a significantly greater BMI than control tetraplegic subjects (27.5±6.9 *vs* 23.9±4.6 kg/m^2 for apnea and control, respectively; $P=0.01$, Mann–Whitney U-test). A greater proportion of tetraplegic subjects with sleep apnea met criteria for obesity (BMI >30) and overweight (BMI >25) than did control tetraplegic subjects (obesity: 37.8% of cases *vs* 8.6% of controls; overweight: 67.6% of cases *vs* 40.0% of controls; $P=0.003$ and $P=0.02$, respectively). We also determined BMI for paraplegics with sleep apnea and compared them to tetraplegics with sleep apnea. Paraplegics with sleep apnea had a greater mean BMI (34.6±9.2) than tetraplegics with sleep apnea ($P=0.032$; Mann–Whitney U-test), and a greater proportion of paraplegics were overweight (88%; $P=0.017$, Fisher's Exact Test).

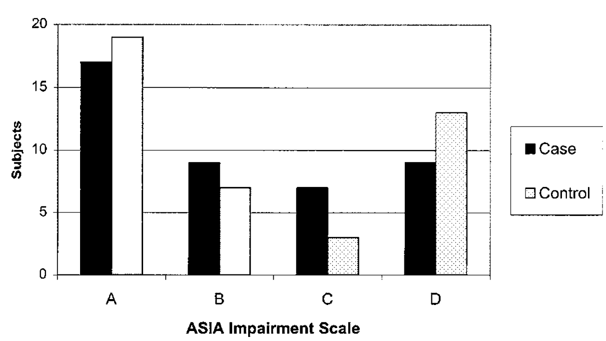

Figure 2 ASIA Impairment Score did not differ significantly between tetraplegic sleep apnea cases and controls ($P>0.05$)

Although mean daily baclofen doses were not statistically different for tetraplegic subjects with and without sleep apnea, a larger proportion of case subjects were receiving high daily doses of baclofen. The mean daily dose of baclofen in tetraplegic subjects with sleep apnea was 53.7±51.3 mg and for control subjects was 36.8±42.2 mg ($P>0.05$; Mann–Whitney U-test). However, 19/42 (45.2%) of case subjects *vs* 10/42 (23.8%) controls subjects were receiving a daily dosage of 80 mg or greater of baclofen ($P=0.039$; Chi-Square test). Daily diazepam dose did not differ significantly between case and control subjects.

We performed a logistic regression analysis for tetraplegic subjects after dichotomizing data for three factors associated with sleep apnea: motor level, obesity, and baclofen dose. This multivariate analysis showed significant associations with both obesity and high (C4 or C5) motor level (odds ratios [95% confidence intervals] of 9.2 [1.7–49] and 15.2 [3.9–59.5], respectively). High (> =80 mg/day) baclofen dose was no longer found to be significantly associated with sleep apnea (odds ratio 1.7 [0.46–6.5]) when the covariates of motor level and obesity were considered. Performing the analysis using ASIA Score as an additional covariate (motor-complete versus motor-incomplete) did not significantly change the associations, and ASIA Score remained without significant association with sleep apnea. Odds ratios for high motor level, obesity, and high baclofen dose are shown in Table 1, with values listed for univariate and multivariate analyses.

Medical comorbidities associated with sleep apnea in the general population were more common in subjects with sleep apnea than in controls. The chance of having at least one of the reviewed comorbidities (hypertension, cerebrovascular disease, cardiovascular disease, arrhythmias, or depression) was significantly greater in subjects with apnea ($P<0.0001$). Hypertension was present in 21% of case subjects versus 5% of control subjects ($P=0.024$).

Sleep apnea treatment

Treatment information was available on 49 tetraplegic and paraplegic subjects with sleep apnea. Slightly less

Table 1 Odds ratios for association with sleep apnea

Associated factor	*Odds ratio (95% CI) (Univariate analysis)*	*Odds ratio (95% CI) (Multivariate analysis)*
High motor level (C5 or above)	7.1 (2.7–18.7)	15.2 (3.9–59.5)
Obesity (BMI > =30)	6.4 (1.7–25.2)	9.2 (1.7–49)
High baclofen dose (> =80 mg/day)	2.6 (1.04–6.7)	1.7 (0.46–6.5)

Abbreviations: CI, confidence interval; BMI, body mass index than half (47%) were receiving some form of treatment. Eighteen subjects were receiving CPAP, three were receiving Bi-PAP, and two were receiving nocturnal oxygen due to intolerance of CPAP treatment. Two subjects had been treated with uvulopalatopharyngoplasty but continued to require CPAP. The majority of patients not receiving treatment had either been intolerant of CPAP/Bi-PAP treatment or had refused a CPAP/Bi-PAP trial. The most common reason noted for CPAP/Bi-PAP intolerance was facial or nasal discomfort from the mask.

We analyzed CPAP/Bi-PAP usage in motor-complete tetraplegic patients as a function of motor level. CPAP/Bi-PAP usage was significantly less likely for motor-complete patients with motor level of C5 or above *vs* C6 and below. Excluding one subject receiving nocturnal oxygen and two subjects without treatment information, three out of 13 subjects with motor level C5 and above were using CPAP/Bi-PAP, compared with seven out of 10 subjects with motor level C6 and below ($P=0.04$, Fisher's Exact Test).

Discussion

Prior screening studies have generally confirmed a higher prevalence of sleep apnea, particularly obstructive sleep apnea, in SCI than in the general population. The prevalence of central sleep apnea is also likely to be markedly elevated in this population, although fewer than 10 cases have been reported in prospective studies of SCI patients.[4,5,8] Numerous factors could be responsible for the high prevalence of obstructive apnea, including weakness of respiratory muscles, impaired chest wall afferent feedback, medications, supine sleeping position, and neck muscle hypertrophy, as well as more typical risk factors such as obesity. This population may be predisposed to central apnea due to high cervical and brainstem pathology, including syringomyelia and syringobulbia, as well as medications that interfere with respiratory drive. In this study, we were unable to classify sleep apnea cases on the basis of predominant type of sleep-disordered breathing.

Despite this limitation, this study provides useful information as we were able to identify a large number of SCI patients with sleep apnea from a single population. This study identified more SCI subjects with sleep apnea than had been reported in all prior published studies, and it allowed us to analyze associated factors using a case-control design.

This study demonstrates that sleep apnea is being recognized clinically in a substantial proportion of males with long-term SCI. While the case population does include some subjects diagnosed through a screening study (3% of our population was screened),[8] 85% of cases in the present study were clinically diagnosed outside of any research study. In our population, sleep apnea has been diagnosed in a significantly larger proportion of tetraplegic *vs* paraplegic subjects. This most likely represents an increased prevalence in tetraplegics, but the study design prevents us from ruling out a bias toward testing for the disorder more frequently in tetraplegic *vs* paraplegic patients. The prevalence of sleep apnea in higher level paraplegics could be similar to lower level tetraplegics, but too few paraplegic patients have been included in prior studies to assess this.[1,3,4,8]

This study examined the relationship between sleep apnea and neurological classification for motor level and ASIA Impairment Scale. The case-control portion showed a motor level of C5 or above to be associated with sleep apnea. The increased risk of sleep apnea associated with high motor level was comparable or greater than the risk associated with obesity, which is the major risk factor for sleep apnea in non-SCI patients. McEvoy and coworkers[5] found no difference in mean respiratory disturbance index (apneas plus hypopneas per hour) between groups with high (C4–C5) *vs* low (C6–C8) level in a study of 40 Frankel A–C tetraplegic subjects. However, they classified level using older definitions, while the current study considered only motor level and used the clarified definition for lowest motor level with intact innervation.[9,12] Motor level has been shown to correlate more highly with upper extremity motor impairment and function than a single neurological level that considers both sensory and motor function.[13] Klefbeck and coworkers[6] demonstrated a correlation between ASIA motor scores (sum of muscle strength test scores for 10 key muscles bilaterally)[9] and rate of desaturation episodes for tetraplegics subjects with complete injuries, but no correlation existed when incomplete injuries were also considered. In that study, an elevated number of desaturations only occurred in subjects with complete injuries if the ASIA motor score was 10 or less. These subjects would correspond to the C4 and C5 ASIA A and B subjects in our current study. In patients with central cord injuries, the majority of total motor score comes from the lower extremity motor score, so in motor-incomplete tetraplegia the total motor score may not reflect respiratory muscle strength.

It has been assumed that sleep apnea has a greater prevalence with increasing neurologic impairment as measured by the ASIA Impairment Scale. Many prior screening studies have excluded subjects with a neurologic classification of ASIA D, and some have been limited to motor-complete injuries.[1,2,4,5,7] A prior study from our center failed to show a higher prevalence of sleep apnea in motor-complete injuries, and in fact demonstrated a somewhat higher prevalence in motor-incomplete injuries.[8] The case-control portion of the current study showed no association between ASIA Impairment Scale and presence of sleep apnea for tetraplegic subjects. A potential cause for sleep apnea in motor-incomplete tetraplegics may be diaphragmatic weakness, based on the association of C4 and C5 motor levels with sleep apnea and the likelihood of some neurologic compromise of diaphragm strength in these patients. It is also possible that this group may be predisposed to hypoventilation and central apneas. Based on our findings, it is likely that a significant proportion of motor-incomplete tetraplegic patients with sleep apnea are undiagnosed cases, since the clinical suspicion of sleep apnea for this group has been low.

Obesity, as determined by BMI, is the most strongly associated risk factor for sleep apnea in the general population, but prior studies have had contradictory findings for persons with SCI. One prior study with tetraplegic subjects found a relation between BMI and percentage of time with oxygen saturation below 90%,[2] while three studies found no relation between BMI and sleep apnea.[4,6,8] In this study, case tetraplegic subjects had a significantly greater mean BMI than control subjects, and greater proportions of the case population met criteria for both overweight and obesity. However, nearly one third of case tetraplegic subjects did not meet criteria for overweight, and less than 40% were considered obese. In contrast, nearly all paraplegic subjects with sleep apnea met criteria for obesity. This implies that for paraplegics, as in the general population, obesity is frequently a primary risk factor, while in tetraplegics additional risk factors, such as respiratory muscle weakness, also contribute significantly.

A confounding factor in determination of obesity in SCI is that lean body mass is decreased following SCI.[14] Published guidelines for ideal body weight in persons with SCI recommend adjustment of ideal body weight by 4.5–7 kg lower for paraplegia and 7–9 kg lower for tetraplegia.[15] However, these formulas were derived empirically, and the correction factors do not take into account the variable degree of muscle atrophy in motor-incomplete injuries and pure lower motor neuron injuries, and they do not adjust for height. An estimate of total body fat corrected for SCI neurologic classification would show a greater proportion of tetraplegic subjects with apnea to have excessive body fat. Obesity is thought to contribute to obstructive sleep apnea through adipose deposition near the upper airway and through an effect on breathing pattern from abdominal mass loading, and thus total body fat, rather than BMI, may be a better predictor for obstructive sleep apnea in SCI patients. Additionally, both waist and neck enlargement have been documented following tetraplegia.[16] These changes in body habitus could be due to total body fat increase or a redistribution of fat to these areas, and neck enlargement could be secondary to neck muscle hypertrophy.

Antispasticity medications have been hypothesized to be contributors to sleep apnea in SCI, either due to a general sedative effect or a specific relaxation of pharyngeal muscles. In non-SCI subjects with mild sleep-disordered breathing, a single nighttime 25 mg dose of baclofen produces no significant change in the rate of apnea events.[17] Prior studies on SCI patients have generally not supported a relationship between baclofen and apnea, but some studies have had small sample sizes, and the rate of baclofen use in the study populations has varied widely.[3–6] A prior study from our center showed an association with baclofen, but the study lacked the power to control for confounding factors.[8] In this study we demonstrated an association between high (80 mg or greater per day) doses of baclofen and sleep apnea in univariate analysis, but the relationship was not significant when other associated factors were considered. We were not able to show a relationship between daily diazepam dose and sleep apnea, but a relatively low proportion of subjects used this medication.

As in the general population, sleep apnea in SCI appears to be associated with significant medical comorbidities. In the non-SCI population, the association with hypertension has been shown to be independent of other known confounding factors such as obesity.[18] Since borderline hypotension is common in SCI due to autonomic dysfunction, it was of interest that our study confirmed that a significant association between sleep apnea and hypertension exists in SCI. After adjustment for obesity, the odds ratio relating hypertension and sleep apnea remains considerably greater than 1 (3.5) though it is no longer statistically different than 1. This is likely attributable to our limited sample size. McEvoy and coworkers[5] had previously demonstrated a correlation between respiratory disturbance index and blood pressure in SCI subjects, but only 5% of their subjects met criteria for hypertension. Our finding of comorbidities similar to non-SCI patients suggests that the pathophysiology and consequences of sleep apnea in SCI are comparable to those seen in the general population.

Few prior studies have addressed treatment of sleep apnea in SCI patients. Biering-Sorensen and coworkers[19] reported on treatment of three cases, two of which were successfully treated with CPAP and one with weight loss. A prior study from our center showed poor acceptance of CPAP/Bi-PAP in SCI patients, and we suggested that treatment acceptance may be less likely in patients with markedly impaired hand function, such as higher level motor-complete tetraplegics.[8] The current study confirms a lower rate of CPAP/Bi-PAP acceptance in motor-complete tetraplegic patients with C5 or higher motor level, as compared to C6 and lower motor level. It should be noted that three of the subjects in this treatment analysis were described in our prior study (two higher level, one lower level motor-complete tetraplegic, none of whom tolerated treatment), and that treatment acceptance may be higher in cases presenting clinically than in those diagnosed through screening. In addition, the rate of CPAP/Bi-PAP acceptance in higher level motor-complete tetraplegic patients (23%) was less than the 60–80% acceptance that has been described in non-SCI patients.[20,21] Mask intolerance was the most commonly reported reason for failure to accept treatment in this population, as is the case for non-SCI patients.[21] Alternatively, these higher level patients with motor-complete injuries may be rejecting treatment because of discomfort or the ineffectiveness of the prescribed type of airway pressure. It has been the practice at our institution to trial CPAP for all cases of obstructive sleep apnea, and to only use Bi-PAP if obstructive apneas and hypopneas are not adequately reduced on CPAP. The ventilatory dysfunction seen commonly in SCI, with profound expiratory weakness, may cause CPAP to be less effective and more uncomfortable than for neurologically intact sleep apnea patients. In addition, in central sleep apnea patients, Bi-PAP (sometimes with a timed back-up rate) is required for resolution of sleep-disordered breathing.

The study design introduces a number of significant limitations to generalization of the findings. One weakness is that we were unable to ascertain whether the cases had predominantly central or obstructive sleep apnea or whether significant hypoventilation occurred during sleep. We have several reasons to believe that the majority of cases have primarily obstructive sleep apnea. Prior studies of similar SCI populations have found that the majority of individuals with sleep-disordered breathing had predominantly obstructive sleep apnea, though a significant minority (25%) had central sleep apnea or rapid eye movement sleep related hypoventilation.[4,5,8] Nevertheless, we would expect that there was a significant proportion of our cases who had central sleep apnea or nocturnal hypoventilation, given the weakness of respiratory muscle that can occur with cervical spinal cord injury and potential respiratory depressant effects of medications used to treat spasticity. The heterogeneity of the case group with respect to type of sleep apnea would tend to decrease the strength of association for any factor that predisposed to only obstructive or only central sleep apnea. The fact that the strongest factor associated with sleep apnea was higher motor level (C5 or above) could indicate that this was associated with both obstructive and central sleep apnea.

Additionally, case subjects were primarily those who had presented clinically, and thus this is an underestimation of the true prevalence of sleep apnea for this population. There may be diagnostic bias toward evaluating for sleep apnea in obese subjects and in those who experience sedation due to medications such as baclofen. We do not feel that our clinicians would have been biased toward testing patients with C4 and C5 motor levels, since most prior data did not support a higher prevalence in this group, and the more recent study of Klefbeck and coworkers[6] was published after most of these cases were diagnosed. An advantage of the case selection method used in this study is that cases diagnosed clinically are likely to be more severe than those diagnosed through random screening, and thus the associated factors may be of greater relevance.

A further limitation from the unavailability of sleep study data is that we were not able to confirm the diagnoses, and therefore the case group may include a few subjects without obstructive or central sleep apnea. Additionally, the control group is likely to contain a few subjects with undiagnosed sleep apnea, given the high prevalence in this population. However, any control subjects with undiagnosed sleep apnea would probably have milder symptoms and less frequent apnea events than clinically identified case subjects. These two conditions, resulting in misclassification of case and control subject with respect to true diagnosis, would bias the results toward weaker associations for the analyzed factors. Our study may overestimate treatment acceptance, since notation of a prior sleep apnea diagnosis could be more likely to be omitted from subsequent medical records in patients who rejected treatment. Finally our study population was almost entirely male, and all identified cases were male. It remains to be determined whether sleep apnea is more common in SCI males than females, as is the case in the general population.[22]

Conclusion

At our study center, sleep apnea has been clinically diagnosed in a substantial proportion of males with tetraplegia. Obesity and higher cervical motor level are associated with sleep apnea, but there is no association with ASIA Impairment score. Medical comorbidities are more common in SCI patients with sleep apnea, and treatment acceptance appears to be suboptimal, especially with higher level motor-complete tetraplegia. Future studies should address the prevalence of sleep apnea in paraplegic, female, and acutely injured SCI populations, distinguish the predisposing factors for sleep apnea in these patients and the types of sleep-disordered breathing present, and most importantly evaluate the treatment of sleep apnea in SCI.

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