



Original Article

Patient-reported pain and impaired sleep quality in adult patients with cystic fibrosis[☆]

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Received 12 May 2009; received in revised form 6 July 2009; accepted 14 July 2009

Available online 8 August 2009

Abstract

Background: Sleep impairment has been described in patients with cystic fibrosis (CF). Pain is a known cause of sleep disturbance and as pain is commonly reported in patients with CF, we sought to find an association between impaired sleep quality and pain.

Methods: Fifty adult CF patients completed surveys of pain and sleep quality. The results were analyzed with additional clinical data including age, sex, nutritional status, and lung function.

Results: Thirty-two patients (64%) reported recent pain and 33 patients (66%) reported abnormal sleep quality. The patients with pain report worse sleep quality than those without pain ($p=0.006$). There was a strong correlation between impaired sleep quality and pain ($p<0.0001$).

Conclusions: We found that pain and poor sleep quality are reported in a majority of adult CF patients and there is a strong correlation between the two. This will have important clinical implications in the evaluation and treatment of adult patients.

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Keywords: Pain; Sleep quality; Cystic fibrosis; Adult

1. Introduction

Sleep disruption is a common symptom described in patients with chronic disease and is thought to contribute to impaired daytime functioning and overall quality of life [1]. Sleep impairment has been described previously in patients with cystic fibrosis (CF). Reported sleep complaints have included insomnia, frequent awakening, and the lack of a good night sleep [2]. Exacerbations of CF pulmonary infections are associated with

worsening of sleep [3]. Patients with more advanced obstructive disease have greater sleep fragmentation, which is, in turn, associated with impaired sleep quality [4]. These abnormalities have been attributed to a number of causes including nocturnal hypoxemia and hypoventilation, chronic cough, and an adverse effect of medications, among others [5,6].

There are other well-known causes of sleep disturbance that may be relevant in patients with CF, such as pain and depression, which are often reported by patients with CF [2,7,8]. Similar to the association of impaired sleep quality and advanced lung disease noted above, there is an association between pain and the severity of lung disease, with pain increasing near the end of life [7]. It is notable, however, that there are reports of considerable pain occurring in younger patients [9,10]. Given the well-known correlation between pain and poor sleep quality in other chronic illnesses, [11–13], we sought to find a similar association between impaired sleep quality and pain in an adult population of CF patients using

[☆] Data have been presented at the North American Cystic Fibrosis Conference, Denver, CO, October 2006. Flume JE, Flume PA, Ahmed QA, Gray S, Lester MK, Wohlfeiler M, Wang W. Self reported sleep quality and pain in adult cystic fibrosis patients *Pediatr Pulmonol* 2006; S29: 404–405.

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instruments of self-reported sleep quality and pain. It was our hypothesis that patients with CF who report pain will also report impaired sleep quality.

2. Methods

The Institutional Review Board for the Protection of Human Rights at the Medical University of South Carolina (MUSC) approved all aspects of this investigation. Patients with CF who receive their care at the MUSC Adult Cystic Fibrosis Program were recruited for participation in this study. Patients completed two validated surveys: a modified Brief Pain Inventory [14] and the Pittsburgh Sleep Quality Index [15]. Both surveys were completed at one visit. Additional data collected at that visit included the patient's age, sex, nutritional status (body mass index, BMI), and measures of severity of lung disease (i.e. spirometric measures including the forced vital capacity (FVC) and the forced expiratory volume at one second (FEV₁); these values were recorded as a percent of predicted).

2.1. Modified brief pain inventory

The Brief Pain Inventory (BPI) is a pain assessment tool developed for use with cancer patients to measure both pain intensity and pain interference in the patient's life [14]. We modified the BPI by adding one question appropriate for CF patients (i.e. performance of therapies). The instrument asks patients to report whether they had any pain, aside from minor daily pains, in the past month, and to rate the severity of the pain on a scale of 0 ("no pain") to 10 ("pain as bad as you can imagine"). The patients were also asked to rate how much their pain interfered with such things as their enjoyment of life, level of activity, ability to walk, mood, sleep, work, relations with others, and performance of their CF therapies. These scales had the phrases "does not interfere" at the 0 and "interferes completely" at the 10.

2.2. Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire, which assesses sleep quality and disturbances over a 1-month time interval [15]. It is a brief, validated instrument that has been used successfully in a CF population [4,16]. Nineteen individual items generate seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction, and the sum of the component scores yields one global score. The range of possible global scores is 0 (best) to 21 (worst) to measure subjective sleep quality. A global PSQI score of >5 indicates impaired sleep quality.

2.3. Statistical analyses

Statistical analyses were performed using SAS 9.1 statistical software and SPSS for Windows 11.5. Descriptive statistics for variables of interest were calculated and reported. All assumptions for statistical analyses were tested where appropriate, and

results were confirmed using nonparametric analyses where applicable.

The PSQI and BPI each have a question that rates how much pain interferes with sleep. A weighted Kappa statistic and a test for symmetry both suggest that the patient responses to these questions were concordant.

Independent two sample *t*-tests were performed to compare age, BMI, FEV₁, FVC, and PSQI global score between pain groups. A chi-squared test for difference in proportions was performed for the proportion of patients reporting pain with abnormal PSQI and normal PSQI scores. Independent, two-sample *t*-tests were also performed to assess similarity of possible confounding variables between the normal and abnormal PSQI groups.

Spearman's rank correlation coefficient was calculated to evaluate the association between global PSQI score and rank (0–10) of how much pain has interfered with sleep in the last 30 days. Patients not responding to this question were given a rank of zero since they did not report any pain in the last 30 days. A subsequent simple linear regression analysis was conducted using global PSQI as the outcome variable and ranking of how much pain has interfered with sleep as the predictor. Additionally, logistic regression analysis techniques were used to predict the likelihood of a patient reporting pain given his or her global PSQI score.

ANOVA and Bonferroni simultaneous comparison techniques were used to compare mean global PSQI score between groups based on response to how often pain has resulted in difficulty sleeping. A *p*-value of less than 0.05 was considered significant.

3. Results

Fifty adult patients (27 male, 23 female) completed the study. The mean age was 31.1 years (± 8.1) with a range of 18–53 years. There was a wide range of severity of pulmonary impairment with a mean FVC of 77.4% predicted (SD 18.3, range 39–110) and a

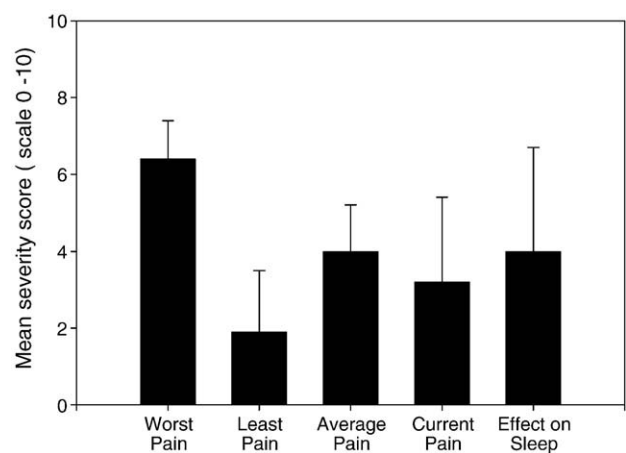


Fig. 1. Rated severity of pain and its effect on sleep. The BPI asked patients to describe the severity of pain they experienced in the previous month as well as rate the degree to which it affected their sleep. Mean values (\pm SD) are demonstrated for those patients who reported pain ($n=32$).

Table 1
Comparison of patients based on reporting of pain.

n	Pain		p	95% Confidence interval	
	32	18		Pain	No pain
Age (y)	30.6±6.5	32.1±10.5	0.574	28.2–32.9	26.9–37.3
BMI	21.3±3.0	21.2±3.0	0.852	20.2–22.4	19.9–22.6
FVC (% pred)	74.8±18.9	81.7±16.8	0.207	67.9–81.8	73.4–90.1
FEV ₁ (% pred)	59.1±23.5	57.2±21.3	0.786	50.4–67.7	46.6–67.8
<i>PSQI scores (higher scores are worse)</i>					
Subjective sleep quality	1.3±0.8	0.8±0.9	0.045		
Sleep latency	1.3±1.0	1.2±0.9	0.459		
Sleep duration	0.8±0.8	0.9±0.8	0.660		
Habitual sleep efficiency	0.9±1.0	0.4±0.8	0.053		
Sleep disturbances	1.8±0.6	1.2±0.5	<0.001		
Use of sleeping medications	1.1±1.4	0.4±1.0	0.083		
Daytime dysfunction	1.2±0.8	0.4±0.6	0.001		
Global PSQI	8.4±3.7	5.3±3.7	0.006	7.1–9.7	3.4–7.1

PSQI=Pittsburgh Sleep Quality Index.

mean FEV₁ of 58.4% predicted (SD 22.5, range 20–110). Their mean BMI was 21.3 (SD 3.0, range 17.5–28.6).

Thirty-two patients (64%) reported having had pain within the last month. The sites of pain were varied including abdomen (n=6), back (n=8), chest (n=3), extremities (n=2), head (n=11), and neck (n=2). The estimate of the severity of pain (on a scale of 0–10) was generally quite severe, as seen in Fig. 1. The range of the maximum pain was reported to be between 3 and 10.

Sleep quality was determined by the PSQI. The mean global score for the PSQI was 7.3 (SD 4.0, range 1–15). Thirty-three patients (66%) had an abnormal global PSQI (>5).

A comparison between patients who reported pain to those who did not is seen in Table 1. The groups were similar in age, nutritional status, and lung function. The patients who report pain have a higher PSQI global score (p=0.006), which indicates worse sleep quality in this group compared to those without pain. The component scores are also shown in Table 1. Patients who reported pain generally had higher scores for most of the component scores, and were the most significant for sleep disturbances and daytime dysfunction.

A similar analysis was made between patients based on sleep quality comparing those with a normal global PSQI (<5) to

Table 2
Comparison of patients by sleep quality.

n	Normal global PSQI		p	95% Confidence interval	
	17	33		Normal	Abnormal
Age (y)	30.0±9.4	31.7±7.4	0.487	25.2–34.8	29.1–34.3
BMI	21.1±2.5	21.4±3.2	0.770	19.8–22.4	20.2–22.5
FVC (% pred)	76.1±19.2	78.1±18.1	0.719	66.2–85.9	71.6–84.6
FEV ₁ (% pred)	57.1±21.0	59.1±23.6	0.777	46.3–67.9	50.6–67.6
Report pain (%)	41.2	75.8	0.016	17.8–64.6	61.1–90.4

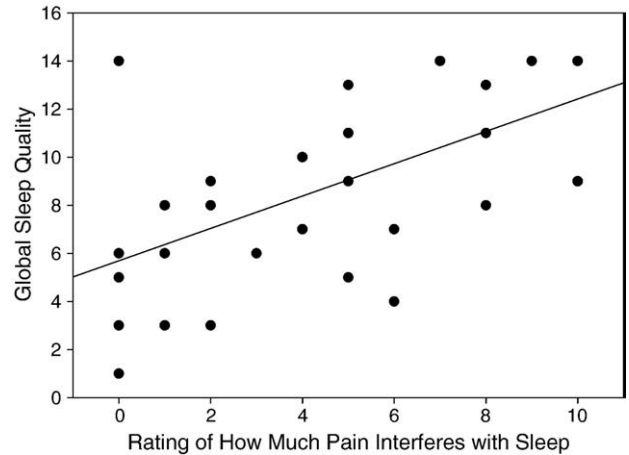


Fig. 2. Higher reports of pain interfering with sleep are associated with worse overall sleep quality. Each closed circle represents an individual patient and their survey results. The BPI recorded the degree to which pain interfered with sleep and this was correlated with the global PSQI score. Higher PSQI scores imply worse sleep quality and a score >5 is considered abnormal.

those with an abnormal score (Table 2). The groups are similar in age, nutritional status, and lung function. However, a greater percentage of patients with an abnormal global PSQI score also report pain, when compared to those with a normal global PSQI score (p=0.016).

The modified BPI asked those patients who reported pain to rate how much the pain interfered with sleep (on a scale of 0–10). Those patients who did not report pain were not asked this question, but we assumed that those patients would have answered this question with a score of 0, which allowed us to compare the global PSQI score with the rating of how much the pain interfered with sleep. There was a strong positive correlation between the global PSQI and the rating of pain interfering with sleep (Spearman Correlation 0.56, p<0.0001). No other variables (age, BMI, lung function) were correlated with the global PSQI

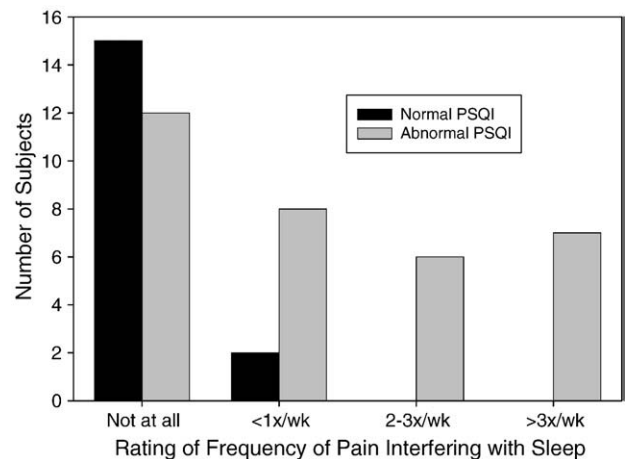


Fig. 3. Patients with poor sleep quality are more likely to report pain interfering with sleep. The PSQI asks how often the subject had trouble sleeping because of pain. This response contributes partially to the global PSQI score, but its contribution is limited to a maximum of 1. Nonetheless, patients with impaired sleep quality (PSQI>5) are more likely to report that pain interfered with sleep.

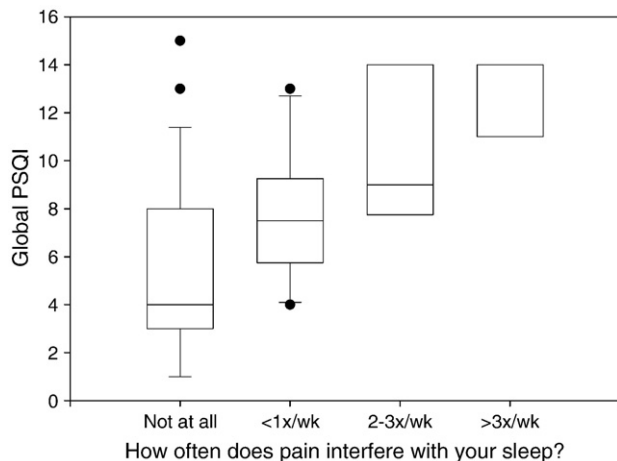


Fig. 4. A greater frequency of pain interfering with sleep causes worse sleep quality. The PSQI asks how often the subject had trouble sleeping because of pain. This response contributes partially to the global PSQI score, but its contribution is limited to a maximum of 1. The boxplot demonstrates the median global PSQI score, as the 10th, 25th, 75th, and 90th percentile for each group based upon the frequency with which pain interferes with sleep. ANOVA $p < 0.0001$.

score. A regression analysis of the relationship between the rating of the interference of pain with sleep and the global PSQI score can be seen in Fig. 2, where there is also a strong correlation ($p < 0.001$, $r^2 = 0.32$).

Those patients with an abnormal global PSQI score were more likely to report a greater frequency of pain interfering with their sleep when compared to those with a normal sleep quality (Fig. 3). The patients were to report how often in the last month that pain interfered with their sleep, with the choices of not at all (0), less than once per week (1), once or twice per week (2), or three or more times per week (3). There was a strong correlation between the reported frequency of pain interfering with sleep and the severity of abnormality of sleep quality (ANOVA $p < 0.0001$, Fig. 4). The significance of this analysis is due to the differences between those patients who reported pain either 2–3 times per week or >3 times per week compared to not at all.

Finally, we found significant evidence of a logistic relationship between the global PSQI score and whether or not a patient will report experiencing pain in the last 30 days ($p = 0.012$) with an odds ratio of 1.27 (95% CI: 1.05–1.52).

4. Discussion

There are three important findings in this study. First, pain is a commonly reported complaint in adults with CF and may be reported as severe. Second, sleep quality is impaired in most adult patients with CF. Finally, there is a strong correlation between impaired sleep quality and self reported pain scores in adult patients with CF.

Previous studies have demonstrated the importance of pain in patients with CF. More than 40% of adult patients reported pain in a recent survey [2]. The pain occurs in multiple sites suggesting multiple etiologies, and it appears to increase in intensity as patients have more advanced lung disease [7].

However, pain is also commonly reported in children and adolescents with CF [10] with an adverse effect on overall quality of life. This study was not designed to describe the epidemiology of pain in patients with CF, but our findings are consistent with what has been reported elsewhere.

There are also several studies that have demonstrated poor sleep quality in adults [5] and children [4,17,18] with CF. Although the results from these studies do not always agree, a reduction in sleep efficiency and frequent awakenings are common findings [5,17–19]. A number of factors that can adversely affect sleep in CF patients have been suggested including nocturnal cough, sleep related GERD, medications, and co-morbid sleep disordered breathing associated with nasal polyposis [5,6,20,21], but in none of these have there been a discussion of a role for pain.

Our finding of the association between pain and impaired sleep quality is not surprising. A significant number of patients with chronic pain, including patients with fibromyalgia, scleroderma and rheumatoid arthritis, report impaired sleep quality [12,13]. Studies that have demonstrated impaired sleep quality in other patients with chronic disease (e.g. systemic lupus erythematosus [22], idiopathic pulmonary fibrosis [23]), did not find an association between pain and sleep quality. However, the patients in these studies reported pain of low intensity and not different from control subjects; it has been suggested that only higher levels of pain intensity interfere with sleep quality [24].

Although we are able to demonstrate an association between pain and impaired sleep quality, we are unable to determine a cause and effect relationship. It is intuitive that pain adversely affects sleep, and there are both animal and human data that support this hypothesis. The injection of formalin into the tibialis muscles of freely moving cats, as a model for persistent nociception, was shown to impair sleep architecture, with a decrease in slow wave sleep percentages, increased arousals, and increased wakefulness implying painful symptoms acutely alter sleep architecture [25]. Longitudinal data examining pain and sleep quality in a fibromyalgia population reveals that pain intensity on the day prior influences subsequent sleep quality on the following night [26].

However, it may also be that impaired sleep quality heightens the sensitivity to pain. The function of sleep remains unknown but there appears to be specific analgesic properties found in consolidated sleep. Specifically, recent well-controlled human data shows that sleep deprivation leads to greater daytime hyperalgesia [27,28].

5. Conclusions

We have demonstrated a strong correlation between impaired sleep quality and pain in adult patients with CF. This finding is not surprising given similar results from studies of other chronic disease. However, there are important implications to these findings. First, the assessment of pain and sleep quality should be routine in the evaluation of adult patients with CF given the high frequency of reported symptoms in this study. Second, both pain and impaired sleep quality are associated with reduced quality of

life and this represents an opportunity to improve the lives of these patients. Third, although there may be several reasons for the patient with CF to have impaired sleep quality (e.g. cough), the clinician should recognize the potential role that pain may play. Finally, therapeutic maneuvers that address both pain and sleep architecture may be an important strategy of addressing these symptoms. Further studies are warranted to determine whether pain impairs sleep (or vice versa) and appropriate medications to treat these symptoms successfully.

Acknowledgements

The authors express their great appreciation to Jonathan E. Flume for his assistance with data collection and to Qanta Ahmed, M.D. for her insights into sleep disorders.

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