How Well Do Children with Cystic Fibrosis Sleep? An Actigraphic and Questionnaire-Based Study

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Objective To measure sleep patterns and quality, objectively and subjectively, in clinically stable children with cystic fibrosis (CF) and healthy control children, and to examine the relationship between sleep quality and disease severity.

Study design Clinically stable children with CF and healthy control children (7-18 years of age) were recruited. Sleep patterns and quality were measured at home with actigraphy (14 days). Overnight peripheral capillary oxygen saturation was measured via the use of pulse oximetry. Daytime sleepiness was evaluated by the Pediatric Daytime Sleepiness Scale (PDSS) and subjective sleep quality by the Sleep Disturbance Scale for Children and Obstructive Sleep Apnea-18.

Results A total of 87 children with CF and 55 control children were recruited with no differences in age or sex. Children with CF had significantly lower total sleep time and sleep efficiency than control children due to frequent awakenings and more wake after sleep onset. In children with CF, forced expiratory volume in 1 second and overnight peripheral capillary oxygen saturation nadir correlated positively with total sleep time and sleep efficiency and negatively with frequency of awakenings and wake after sleep onset. Patients with CF had significantly greater Sleep Disturbance Scale for Children (45 vs 35; $P < .001$), Obstructive Sleep Apnea-18 (35 vs 24; $P < .001$), and PDSS scores (14 vs 11; $P < .001$). There was a negative correlation between PDSS and forced expiratory volume in 1 second ($r = -0.23$; $P < .05$).

Conclusions Even in periods of clinical stability, children with CF get less sleep than their peers due to more time in wakefulness during the night rather than less time spent in bed. Objective measures of sleep disturbance and subjective daytime sleepiness were related to disease severity. In contrast, parents of children with CF report high levels of sleep disturbance unrelated to disease severity. *(J Pediatr 2017;182:170-6).*

Despite improvements in life expectancy, patients with cystic fibrosis (CF) continue to experience a considerable daily treatment burden. Adults with CF have a high prevalence of sleep disturbance,[1-4] but there are limited studies in children with CF. Some studies that use subjective measures, such as parental questionnaire, show a high prevalence of sleep problems[5,6]; however, objective sleep studies that use one night of polysomnography (PSG) show conflicting results.[7-12] Whereas a single in-laboratory PSG may not reflect sleep quality in the home environment accurately, actigraphy is a validated method to measure sleep/wake patterns for extended continuous periods.[13]

Sleep duration and the stability of sleep/wake schedules have been shown to have significant impacts on daytime functioning and mood in healthy children.[14-16] Although time-consuming, daily treatments might be expected to impact significantly on sleep opportunity in children with CF, there are very few studies of sleep patterns in this group. In one study of preschool children with CF, parents reported an average of 30 minutes less sleep than control children.[6] Another study that used actigraphy to quantify sleep demonstrated shorter sleep duration and more sleep disturbance than control children but did not report sleep schedules.[7]

BMI	Body mass index
CF	Cystic fibrosis
DI3	The number of dips in saturation of ≥3%/h of sleep
FEV_1	Forced expiratory volume in 1 second
MFI	Movement fragmentation index
OSA	Obstructive sleep apnea
OSA-18	Obstructive Sleep Apnea-18
PDSS	Pediatric Daytime Sleepiness Scale
PSG	Polysomnography
SDSC	Sleep Disturbance Scale for Children
SEIFA	Socio-Economic Indices for Areas
SES	Socioeconomic status
SpO_2	Peripheral capillary oxygen saturation
TST	Total sleep time
WASO	Wake after sleep onset

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The aim of the current study was to examine in detail the sleep of children with clinically stable CF compared with control children. We hypothesized that children with CF would have reduced sleep quantity due to later bedtimes and would display more variability in their sleep patterns than age-matched, healthy control children. We also aimed to compare objective and subjective measures of sleep quality in these children and to investigate the association between sleep patterns, sleep quality, and the severity of CF. We hypothesized that disease severity would contribute to disturbed sleep patterns and subjective and objective sleep quality in children with CF.

Methods

Children and adolescents aged 7-18 years attending the CF outpatient clinics at the 2 tertiary pediatric hospitals in Melbourne, Australia, were recruited. The exclusion criteria for children with CF included the presence of acute pulmonary exacerbation requiring therapy with intravenous antibiotics in the last 4 weeks; a history of lung transplantation; and residing more than 50 km from either tertiary care center. Healthy control subjects aged 7-18 years were recruited from the community via poster advertisements in the same 2 pediatric hospitals. Control children had been free from any acute respiratory tract infection in the preceding 4 weeks and did not have any other chronic medical, psychiatric, or sleep disorder, including habitual snoring, defined as snoring on ≥3 nights per week. The study was approved by the ethics committees at both institutions, and written informed consent was obtained from parents and verbal assent from all participants.

All participants underwent a medical history and examination on the day of enrollment. Height and weight were recorded and body mass index (BMI) and BMI z score calculated.[17] Socioeconomic status (SES) was defined by matching each child's postcode with the corresponding Australian Bureau of Statistics Socio-Economic Indices for Areas (SEIFA) measure.[18] This is a composite measure including household income, occupation, highest education level, and ethnicity. Low SEIFA values indicate an area of social disadvantage and high values indicate an area of advantage. Subjects were classified into 3 groups of socioeconomic disadvantage according to the SEIFA index of deciles: most disadvantaged decile range 1-3 (SEIFA ≤ 960), mid-range decile range 4-7 (SEIFA 961-1029), and least disadvantaged decile range 7-10 (SEIFA ≥ 1030).

All children with CF underwent pulmonary function testing at the time of enrollment. Spirometry was performed (Master Screen Diffusion or Master Screen Body; Erich Jaeger, Hoechberg, Germany) according to the standards of the American Thoracic Society/European Respiratory Society.[19] Forced expiratory volume in 1 second (FEV_1) was recorded as a measure of disease severity and classified as normal (FEV_1 ≥90% predicted), mildly reduced lung function (FEV_1 70%-89% predicted), moderately reduced (FEV_1 40%-69% predicted), or severely reduced (FEV_1 <40% predicted).[7,20] Values are expressed as percentages of the predicted normal values, with adjustments made for age, sex, and height.

Subjective Measures of Sleep

Parents were asked to complete 2 validated questionnaires regarding their child's usual sleep and any sleep disturbance: the Sleep Disturbance Scale for Children (SDSC)[21] and the Obstructive Sleep Apnea-18 (OSA-18).[22] Children completed the Pediatric Daytime Sleepiness Scale (PDSS).[23]

The SDSC is a 26-item Likert-type rating scale that assesses sleep behaviors and disturbances in the previous 6 months based on parental report. The questionnaire measures 6 domains: initiating and maintaining sleep, sleep-disordered breathing, arousal, sleep-wake transition, excessive daytime sleepiness, and hyperhydrosis. A SDSC total score greater than 39 in the original study identified children with disturbed sleep.

The OSA-18 is health-related quality of life survey used to determine the quality of life impact of obstructive sleep apnea (OSA) in children based on parental report. Scores < 60 suggest a small impact on health-related quality of life, scores between 60 and 80 suggest a moderate impact, and scores > 80 suggest a large impact.[22]

The PDSS is an 8-item self-report questionnaire that measures daytime sleepiness. Mean total score values in the original study of healthy children in the community were 15.3 ± 6.2 (range 0-32), with greater scores indicating greater sleepiness.

Objective Measures of Sleep

Children wore an actigraph (Actiwatch 2, MiniMitter, Philips Healthcare, Andover, Massachusetts) continuously on their nondominant wrist for 14 days, and data were downloaded onto commercially available software (Actiware Software Package, version 5.5, MiniMitter; Philips Healthcare) for analysis. Measures calculated included sleep onset and sleep offset, time to fall asleep (sleep latency), wake after sleep onset (WASO; the number of minutes scored as wake in the sleep period [the available time for sleep]), the number of periods of wakefulness, total sleep time (TST; number of minutes scored as sleep in the sleep period), sleep efficiency (sleep duration divided by sleep period, expressed as a percent), and movement fragmentation index (MFI). The MFI or sleep fragmentation index is a measure of sleep disturbance.[24]

Actigraphic sleep measures were averaged across weekdays (Sunday to Thursday) and weekends (Friday and Saturday) during a school term.[14] Participants were asked to complete a daily sleep diary documenting sleep onset, awakenings during sleep, and morning awakening time to aid in the interpretation of the actigraphy data. To assess variability in sleep patterns, 4 variability measures were calculated[14]: (1) "sleep onset variability": the difference between the earliest and latest time the child went to sleep, calculated separately for week nights and weekends; (2) "week/weekend shift sleep onset": difference between the usual sleep onset on a week day vs a weekend; and similarly, for (3 and 4) "wake time variability" and "week/weekend shift wake time."

Overnight Oximetry

One night of overnight oximetry recording was performed at home during the 14 days of the study (Masimo Radical