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Original Article

What keeps children with cystic fibrosis awake at night?☆,☆☆

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Abstract

Background: Sleep disturbance is common in children with cystic fibrosis (CF) however there are limited studies investigating the causes for poor sleep quality. In a cross sectional observational study we aimed to evaluate the clinical correlates of sleep disturbance in this population.
Methods: Children with CF (7–18 years) free from pulmonary exacerbation completed medical review, overnight oximetry, the OSA-18 and 14 days of actigraphy recordings with a sleep diary.
Results: In addition to FEV_1 <80% and low baseline SpO_2, CF-related diabetes, PEG feeding and co-morbid behaviour disorder were associated with lower objective sleep quantity. Paternal smoking and a family member with a mood disorder were also associated with sleep disturbance. The use of electronic devices before bedtime was associated with lower sleep quantity and quality. FEV_1, nocturnal cough, age and a behaviour disorder predicted sleep duration. FEV_1, nocturnal cough, SpO_2 nadir and asthma predicted sleep efficiency. Conversely, sleep efficiency independently predicted FEV_1.
Conclusions: Reduced sleep quality in children with CF is related to lung health and co-morbidities. However, family characteristics and poor sleep hygiene in the child were also associated with sleep disturbance. Optimal management of CF would seem to be the primary intervention to alleviate children's sleep disturbance, however our data raises additional targets for attempts to improve sleep.

Keywords: Sleep; Actigraphy; Oximetry; Sleep hygiene

1. Introduction

Sleep problems are common in patients with cystic fibrosis (CF). Studies of children and adults with CF report subjective sleep problems in more than 50% of patients [1–3]. We have recently reported that even clinically stable children with CF sleep less than their peers, due to more time awake during the night rather than less time in bed [4]. In that study, objective measures of sleep disturbance using actigraphy in the home environment, as well as self-reported sleepiness, were related to lung function. However, parents reported a high prevalence of subjective sleep disturbance in their children that was unrelated to lung function. Whilst adult studies in CF have demonstrated a relationship between disease severity and objective sleep quality, likely mediated by nocturnal

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hypoventilation [5], there are limited studies investigating the causes for poor sleep in children with CF, who generally have milder lung disease.

In addition to lung disease, studies in the adult population with CF have shown that several other clinical features are associated with sleep disturbance including chronic pain [6], low mood [5] and haemoptysis with iron deficiency [7]. Based on evidence from other clinical populations, various CF co-morbidities; asthma, gastro-oesophageal reflux disease (GORD) and PEG feeds are hypothesised to impact on sleep quality [8]. CF is associated with chronic sino-nasal disease and whilst young children with CF have been shown to have a higher incidence of obstructive sleep apnoea (OSA) compared to healthy controls, by contrast, in older children and adults the incidence is generally low [9–11]. Factors that impact on sleep in otherwise healthy children such as poor sleep hygiene and the family environment could also be expected to affect sleep in CF.

Sleep disturbance is associated with a number of adverse cardiovascular, immune, metabolic and neurocognitive sequelae [12,13]. Patients with CF are at risk for CF related diabetes (CFRD), recurrent respiratory tract infections and mood disorders, all of which may be exacerbated by poor sleep. Studies in adults with CF provide evidence that impaired sleep quality is also associated with poorer quality of life [5,14]. Understanding the relationship between sleep disturbance and health in children with CF could have important implications for clinical management and outcomes.

The aim of the current study was to evaluate the clinical correlates of sleep disturbance in a cohort of children with stable CF, specifically which individual co-morbidities, family and sleep hygiene characteristics were associated with objective sleep problems. The primary outcome measure for sleep disturbance was total sleep time, which we have previously shown to be significantly reduced in children with CF compared with healthy children [4]. Secondary outcomes were sleep efficiency, wake after sleep onset (WASO) and time to fall asleep (sleep onset latency, SOL). We also aimed to investigate whether sleep disturbance impacted on lung function, the primary measure of disease severity. We hypothesised that in addition to lung function, there would be other disease co-morbidities, family and sleep hygiene characteristics associated with sleep disturbance. Furthermore we expected there to be a bidirectional relationship between sleep quality and lung function.

2. Methods

2.1. Subjects

We aimed to recruit all eligible children aged 7 to 18 years attending the two paediatric CF centres in Melbourne, Australia (n = 108). Exclusion criteria included the presence of a pulmonary exacerbation requiring intravenous antibiotics in the last four weeks and residing over 50 km from either centre. The study was approved by the ethics committees at both institutions and written informed consent was obtained from a parent of all participants.

2.2. Medical history and demographics

All children underwent a medical history focussed on sleep and family factors that may impact directly or indirectly on a child's health e.g. the presence of a "doctor diagnosed" mood or sleep disorder and parental smoking. Sleep history included questions about sleep habits and bed-time practices. Physical examination was performed and height and weight recorded. The presence of key respiratory and non-respiratory co-morbidities hypothesised to impact on sleep quality [8] was recorded. Children were asked specifically about nocturnal cough: "how often in the past 2 weeks did you wake up during the night because you were coughing?" [15]. Possible responses were "always", "often" (grouped as frequent), "sometimes" or "never" (grouped as infrequent). Socio-economic status (SES) was defined using the Australian Bureau of Statistics Socio-Economic Indices for Areas (SEIFA) measure [16] (lower score indicates greater social disadvantage).

All children underwent spirometry at the time of enrolment (Master Screen Diffusion or Master Screen Body, Jaeger, Hoechberg, Germany) according to American Thoracic Society/European Respiratory Society standards [17], with results expressed as percentages of the predicted normal values. The forced expiratory volume in 1 s (FEV_1) was grouped as normal ($\geq$ 80% predicted) or abnormal.

2.3. Objective measures of sleep and sleep quality

Children wore an actigraph (Actiwatch 2, MiniMitter, Philips) continuously on their non-dominant wrist for 14 days and data were downloaded (Actiware Software Package, version 5.5, MiniMitter, Philips) for analysis. Measures calculated included sleep onset and offset, time to fall asleep (sleep onset latency, SOL), 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 (wake bouts/night), total sleep time (TST; number of minutes scored as sleep in the sleep period) and sleep efficiency (SE; sleep duration divided by sleep period, expressed as a percent). Actigraphic sleep measures were averaged across weekdays (Sunday to Thursday) and weekends (Friday and Saturday) separately. Participants also completed a daily sleep diary documenting sleep onset, awakenings during sleep and the reason for these, and morning awakening time, to aid in the interpretation of the actigraphy data.

2.4. Subjective measure of sleep quality

Given previously reported high rates of snoring and obstructive sleep apnoea (OSA) in young children with CF [9], we assessed this possible contributor to poor sleep quality using a parent-completed OSA-18 questionnaire [18]. The OSA-18 is an OSA-specific health-related quality of life (HRQL) instrument. Scores <60 suggest a small impact of OSA on HRQL [18].

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