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Original Article

A cross-sectional analysis of daytime versus nocturnal polysomnographic respiratory parameters in cystic fibrosis during early adolescence☆

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Abstract

Background: In Cystic Fibrosis (CF), early detection and treatment of respiratory disease is considered the standard for respiratory care. Overnight polysomnography (PSG) may help identify respiratory deterioration in young patients with CF.
Methods: A prospective cohort study of 46 patients with CF, aged 8–12 years, from a specialist clinic in a tertiary paediatric hospital. Daytime pulmonary function, shuttle test exercise testing and overnight PSG were studied.
Results: Of 81 children aged 8–12 years, 46 (57%) agreed to participate. FEV_1 (% predicted, mean 74.6%) was normal in 23 (50%), mildly abnormal in 12 (26.1%), moderately abnormal in 10 (21.7%) and severely abnormal in 1 (2.2%). Amongst sleep study parameters, FEV_1 (% predicted) showed significant correlation with the respiratory rate (RR) in slow wave sleep (SWS), CO_2 change in REM, baseline SaO_2, and the arousal index (h^{-1}). Backward, stepwise linear regression modelling for FEV_1 (% predicted) included the entire group with a wide spectrum of clinical severity. From sleep, variables remaining in the multivariate model for FEV_1 ($F = 16.81$, $p < 0.001$) were the RR in SWS (min^{-1}) and the CO_2 change in REM ($p = 0.003$, and 0.014, respectively). When daytime tests were included, the variables remaining were RR in SWS and SD score for BMI (BMIsds) ($F = 18.70$, $p < 0.001$).
Conclusions: Respiratory abnormalities on overnight sleep studies included elevated respiratory rates during SWS and mild CO_2 retention in REM sleep, and these incorporated into a model correlating with FEV_1 (% predicted). Thus, mild mechanical impairment of ventilation is evident on overnight sleep studies in children with cystic fibrosis although the significance of this finding will require further investigation.

Keywords: Child; Adolescent; Sleep study; Exercise test; Pulmonary

1. Introduction

An array of daytime (awake) evaluations is established in Cystic Fibrosis, many of which are now incorporated into regular (particularly annual) clinical reviews. The annual review includes review of physical growth, pulmonary function testing, chest X-ray, sputum culture, blood count and liver function tests. These tests aim to detect complications of disease early so that treatment can be optimised to ensure the best prognosis for children attending the clinic. Amongst these, FEV_1 is the most common measure linked with risk factors and outcomes [1,2].

Respiratory complications of CF are the leading cause of mortality. While FEV_1 correlates with future outcomes in prognostic studies, other factors such as bacterial colonisation, the occurrence of pulmonary exacerbations and other manifestations of the disease also affect outcomes [3]. Thus, it is important to look at additional markers that may indicate changes in respiratory function not detected by usual pulmonary function testing, or that may provide more sensitive markers of disease progression [3–5].

☆ Conflicts of interest: None.

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Sleep is associated with reduced ventilation compared to wakefulness and these changes can exacerbate respiratory problems in patients with pulmonary or neuromuscular disease [6]. Contributors to the ventilatory abnormalities in sleep include reduced alveolar ventilation, lower airway tone, reduced airway calibre, and reduced sensitivity of the chemoreceptors to hypoxia and hypercapnia, which make the subject vulnerable to hypoxemia [7]. Pulmonary changes include increased ventilation/perfusion mismatch and a fall in functional residual capacity (FRC), changes that when coupled with the increased airflow resistance can lead to the pulmonary load exceeding the patient's capacity to increase ventilation, particularly during REM sleep [8].

Previous studies during sleep, in both children and young adults with CF, have identified overnight abnormalities including hypoxia in symptomatic children and those with reduced lung function [9–11], reduced sleep quality and sleep disruption measured both subjectively (questionnaires) and objectively (actigraphy) [12,13], sleep disordered breathing including snoring and OSA [14,15], and (particularly in adults), nocturnal respiratory failure [16,17]. These studies are summarised in Table 1.

The primary aim of this study was to determine whether overnight sleep studies could help detect early progression of lung disease in a cohort of pre-adolescent children with CF. In this study, we also examined associations between physiological parameters during polysomnography (PSG) and daytime markers of disease including nutrition, pulmonary function, and exercise testing. We hypothesised that sleep-associated PSG findings would show correlations with daytime measures, particularly with daytime respiratory function testing.

We targeted the age cohort of 8–12 year-olds from within our larger clinic population who were generally pre-pubertal but old enough to participate with an array of daytime tests.

2. Methods

This was a prospective, cross-sectional study of a cohort of children with CF who attended the CF clinic at the Children's Hospital at Westmead (CHW), Sydney Australia, which is a tertiary paediatric hospital. The primary method for diagnosing CF was neonatal screening, and for the majority the diagnosis was confirmed by sweat chloride testing.

The study comprised the Cystic Fibrosis Questionnaire (CFQ) and exercise testing using a shuttle test [18], followed by overnight PSG. Children who were aged between 8 and 12 years at the time the study commenced were eligible for inclusion and were invited to participate. There were no exclusion criteria.

Ethical approval was obtained from the Human Research Ethics Committee of the Sydney Children's Hospital Network. Informed consent was obtained from all participating children and/or their parents prior to participation in the study. Consent

Table 1
PSG studies in patients with CF.

Author, year	Patient group	Findings
Paranjape et al., 2015 [38]	13 CF 17 Cn 9.6 years. FEV_1 (CF only) 87% predicted (36–115%)	No sleep differences No ↑ in obstructive events No difference in CO_2 ↓ SaO_2 REM, NREM and nadir ↑ respiratory rates NREM ↑ flow limitation
Ramos et al. 2013 [9]	Age 2–14 years 67 of 85 eligible Clinically stable	6 (6%) had nocturnal hypoxemia: SpO_2 <90% for >5% of TST & nadir ≤85% Also had ↑ REM, ↑ AHI (NS), Correlates: FEV_1, FVC, Microarousal index, AHI
Fauroux et al., 2012 [12]	PSG in 11 adults 24 years, Actigraphy + overnight SpO_2 and $PtcCO_2$ in 55 adults (24 years), 25 children (13 years)	Mean FEV_1 44% predicted 18% had >10% night SaO_2 < 90% 24% TCO_2 > 50 mmHg ↑ sleep latency, ↓ sleep efficiency, ↑ night activity and ↑ sleep fragmentation Correlation: night SaO_2 with day FEV_1
Spicuzza et al., 2012 [15]	40 children CF (6 months–11 years), 18 Cn FEV_1 78% predicted in CF	↓TST, ↓sleep efficiency, ↓% REM sleep, ↑ arousal frequency, ↓ mean SaO_2, ↑ obstructive respiratory events, No correlation with FEV_1
Ramos et al., 2009 [14]	Questionnaire screening SDB PSG in 63 subjects Mean 7.6 years	Frequent sleep complaints 35 (55.6%) had AHI > 1 Correlate: chronic rhinosinusitis
Jankelowitz et al., 2005	Actigraphy: 20 CF, 20 Cn 25.9 years FEV_1, 65% predicted	↑ PSQI scores, ↓ Quality of life ↑ sleep fragmentation Correlate: FEV_1
Villa et al. 2001 [11]	19 infants, mean 13.1mo & 20 controls Equivalent sleep architecture,	7 with respiratory symptoms ↓ mean SaO_2, SaO_2 REM < NREM, ↑ % sleep with SaO_2 < 93%, ↓ SaO_2 nadir Correlates of lower SaO_2: RR, expiratory time constant
Milross et al., 2001 [16]	32 adults, 27 years, FEV_1 36% predicted	Evening PaO_2 morning $PaCO_2$ Correlates: Average min SaO_2, ↑CO_2 from NREM to REM, Muscle strength and RDI in REM

CF = cystic fibrosis, Cn = control, TST = total sleep time, REM = rapid eye movement sleep, NREM = non-REM sleep, AHI = apnea hypopnea index, RR = respiratory rate, TCO_2 = transcutaneous CO_2 (mmHg), PSQI = Pittsburgh sleep Quality Index.