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ORIGINAL ARTICLE

Respiratory sleep disturbance in children and adolescents with cystic fibrosis

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Abstract Sleep disturbance has been described in cystic fibrosis (CF) patients as relevant to clinical and lung function predictive factors helping to improve the diagnosis and early intervention. Related paediatric studies are scarce.

Objective: To describe respiratory sleep disturbance (RSD) and its association with spirometric indices in a population of CF children. A second aim was to determine if spirometric indices and wake-time SpO_2 are predictors of sleep disturbance.

Methods: A cross-sectional study involving 33CF paediatric patients. All participants underwent in-lab polysomnography (PSG), pulse oximetry and spirometry. A standardized sleep questionnaire was completed for each patient. Two subgroups were considered: I – Normal ($FEV_1 > -1.64$ z-score); II – Obstructed ($FEV_1 \leq -1.64$ z-score).

Results: Participant's median age was 12 (6–18) years, 16 (48.5%) were male. Twenty-nine patients (87.9%) presented sleep complaints. Sleep efficiency was reduced; sleep latency and waking after sleep onset (WASO) increased. N1 increased, N2, N3, REM and awakenings were normal. The apnoea–hypopnoea index was 0.6/h (sd 0.9); respiratory disturbance index (RDI) was 6.6/h (sd 5.2). Mean awaking (97% (sd 1.1)) and sleep SpO_2 (95% (sd 2.7)) were normal;

Abbreviations: AHI, apnoea/hypopnoea index; BMI, body mass index; CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane condutance regulator; ERS, European Respiratory Society; FEF_{25-75}, forced expiratory flow between 25% and 75% of maximal expiratory flow; FEV_1, forced expiratory volume in 1 s; FL, flow limitation; FVC, forced vital capacity; HSM, Hospital de Santa Maria; N1, sleep stage 1; N1%TST, time in N1 as a percentage of total sleep time; N2, sleep stage 2; N2%TST, time in N2 as a percentage of total sleep time; N3, sleep stage 3; N3% TST, time in N3 as a percentage of total sleep time; NREM, non REM sleep; ODI, oxygen desaturation index; PSG, polysomnography; RDI, respiratory disturbance index; REM, rapid eye movement; REM%, time in REM as a percentage of total sleep time; REML, REM latency; RSD, respiratory sleep disturbance; SE, sleep efficiency; SL, sleep latency; SQ, sleep questionnaire; SpO_2, pulse oximetry; SpO_2mean, mean pulse oximetry value; SpO_2min, minimal pulse oximetry value; $tcCO_2$, transcutaneous CO_2; TST, total sleep time; W, wake; WASO, wake after sleep onset.

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mean nocturnal oximetry desaturation index was 2.36/h; minimal nocturnal SpO_2 was 89% (sd 4.1).

We found associations between mean nocturnal SPO_2 and mean values of FEV_1 ($r = 0.528$; $p = 0.002$) and FEF_{25-75} ($r = 0.426$; $p = 0.013$). There were significant differences in nocturnal SpO_2 between normal and obstructed patients ($p < 0.000$). PSG data correlated with the questionnaire answers for night awakenings and WASO ($p = 0.985$) and difficult breathing during sleep and RDI ($p = 0.722$).

This study points to most CF children having sleep complaints, and highlights the correlation between subjective assessment of sleep and PSG and spirometric results. Awake-time SpO_2 and spirometric values are possible risk predictors for nocturnal desaturation.
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Introduction

Sleep disturbance in cystic fibrosis (CF) patients has been increasingly recognized in all ages.[1–6] Respiratory sleep disturbance (RSD), with nocturnal desaturation[4,7] and hypoventilation[6] has been described in association with chronic lung disease and respiratory failure[1,8] as well as with cough[9,10] and upper airway obstruction.[11,12] Sleep fragmentation and poor sleep quality are also reported.[6,11,13]

It is not clear in what way RSD modulates the clinical course of children with CF,[14] but it interferes with quality of life.[11] Other factors contributing to poor sleep quality in CF patients are night anguish, fear of death, drug effects and the need for nocturnal therapies.[11,14,15]

Lung function measures, in particular spirometric indices, are critical for the assessment and management of CF patients; they are a primary diagnostic, therapeutic and prognostic endpoint.[16–20] Few reports have evaluated lung function tests and awake pulse oxymetry (SpO_2) as predictors of sleep disturbance in children with CF and the results are contradictory.[6,14,15,21]

Our main objective was to describe respiratory sleep disturbance in a population of clinically stable children and adolescents with CF. Our aim was also to identify if spirometric indices (FEV_1, FEF_{25-75}, FEV_1/FVC) and awake-time SpO_2 could be predictors of sleep disturbance.

Methods

This was an observational, prospective, cross-sectional and descriptive–analytical study. Children were recruited from the Paediatric Unit of a Specialized Centre for Cystic Fibrosis of a Tertiary Care Hospital, between February and October 2013. Written informed consent was obtained from parents of children under 16 years-old and from patients above that age.

All but one patient had CF confirmed by the presence of two transmembrane regulator (CFTR) mutations; one child had one CFTR mutation with a sweat chloride test >60 mmol/l, associated with characteristic phenotype; twenty-one (63.6%) were homozygote for the mutation DelF508.

Clinical stability, defined as the absence of respiratory exacerbations and increased tiredness, maintenance of weight gain and stable FEV_1, for a month previous to the study was required for inclusion. Exclusion criteria were chronic respiratory failure or being unable to cooperate during spirometry.

Body mass index (BMI) was assessed and reported as z-score.

All participants or their parents completed a standardized sleep questionnaire (SQ) before polysomnography (PSG); daytime SpO_2 and spirometry were performed the following day.

SQ is a non validated but routinely applied questionnaire at the Paediatric Sleep Laboratory. SQ has been developed as a rapid screening tool based on the Paediatric Sleep Questionnaire[22] and the Sleep Apnea Questionnaire.[23] It includes questions about sleep quality, night-time and daytime symptoms and signs of RSD and sleep disturbance, and associated events like parasomnias.

In-lab PSG (SomnoScreen® Plus TM Domino Software, v.2.3.1) was performed for a minimum of 7 h. The following parameters were recorded at the same time: six channel electroencephalogram, bilateral electrooculogram, anterior tibialis and chin electromyogram, electrocardiogram, oronasal thermistor airflow detection, nasal cannula transducer, body position, tracheal microphone, thoracic and abdominal movements using respiratory effort bands and pulse oximetry.

A desaturation event was defined as a decrease of $SpO_2 \geq 3\%$. Mean and minimum SpO_2 were determined as well as the percentage of total sleep time with $SpO_2 < 90\%$. Analysis of sleep stages, arousals, movements and respiratory events was performed according to the American Academy of Sleep Medicine manual.[24–26] Flow limitation was defined as a flattening of the inspiratory portion of the flow waveform detected by nasal cannula pressure during sleep without criteria of hipopnoea. The sleep data included were: time in bed, defined as time from lights out to lights on; sleep efficiency (SE), calculated as total sleep time divided by the total time in bed; sleep latency (SL), defined from lights out until the first epoch of any sleep stage; wake after sleep onset (WASO), defined as time spent awake between the sleep onset and the end of sleep; REM latency (REML)

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