Sleep Disordered Breathing in Children with Chronic Lung Disease

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Sleep and Respiratory System

- Sleep is a vulnerable period for the respiratory system because of
  - reductions in minute ventilation,
  - lower lung volumes,
  - increased upper airway resistance, and
  - positional ventilation-perfusion mismatching

Chronic Lung Disease and Sleep Hypoxemia

- CLD patients are vulnerable to hypoxemia during sleep,
  - Reduced baseline arterial oxygen pressure that develops overtime with advancing lung disease
  - Ventilation-perfusion mismatching puts them closer to the steep-decline portion of the oxygen dissociation curve
    - Even the expected reduction in minute ventilation during sleep poses a risk for marked reductions in SpO_2

Chronic Lung Disease and Hypoventilation During Sleep

- Over time, progression of lung disease increases airway resistance and eventually results in alveolar hypoventilation
- Sleep is normally characterized by hypoventilation related to decreased drive to the upper and lower respiratory muscles
- Nocturnal hypercapnia may be present in CLD without nocturnal hypoxemia or daytime gas-exchange abnormalities

Chronic Lung Disease and Obstructive Sleep Apnea

- Increased upper airway resistance, including nasal obstruction, is a risk factor for OSA.
- CF and PCD are associated with a high incidence of chronic sinonasal disease including nasal polyps
- OSA is associated with considerable metabolic, cardiovascular, and neurocognitive morbidity
- Presence of OSA may put children with CLD at increased risk for growth failure and pulmonary hypertension

Outline

- Sleep in children with
  - Cystic fibrosis
  - Primary ciliary dyskinesia
  - Non-CF bronchiectasis
  - Bronchiolitis obliterans
  - Bronchopulmonary dysplasia

Subjective Sleep Problems in CF

- Disturbed sleep in more than 50% of CF patients (especially advanced lung disease)
- Common sleep complaints:
  - sleep-onset insomnia,
  - frequent awakenings,
  - night cough,
  - snoring,
  - excessive daytime sleepiness,
- Even when stable, CF patients report more frequent awakenings with cough

Objective Sleep Problems in CF

- CF infants have a sleep architecture similar to healthy controls
- CF children have lower sleep efficiency, reduced REM sleep, and increased electrocortical arousals
- Children with more severe pulmonary disease (lower FEV_1) have lower sleep efficiency and more nocturnal coughing
- There is an association between decreased sleep efficiency and decreased mood profile, including happiness

Subjective Sleep Problems in CF Exacerbations

- School-aged children have sleep disruption attributed primarily to coughing
- Patients report sleeping during the day as a consequence of inability to sleep at night
- When describing improvement following treatment, improvements in sleep are an important determinant of perceived resolution
- Treatment of a CF pulmonary exacerbation results in decreases in sleepiness and nocturnal cough

Objective Sleep Problems in CF Exacerbations

- Poor-quality sleep in CF pulmonary exacerbation
- Pulmonary exacerbations are associated with
  - more wakefulness after sleep onset,
  - less REM sleep, and
  - more hypoxemia,
- Improve following approximately 2 weeks of inpatient therapy

Hypoxemia During Sleep in CF

- Usually precedes diurnal hypoxemia and is generally unrecognized symptomatically
- Significant hypoxemia: SpO_2 <90% for 10% of the total sleep time or if minimal SpO_2 < 85%
- Primarily during REM sleep and has been associated with pulmonary hypertension
- Nocturnal hypoxemia is generally present when the FEV_1 is < 64% or if the baseline SpO_2< 93%-94%

Pediatric Pulmonology 42:716–722 (2007)

Factors That Correlate With Sleep Oxygenation in Children With Cystic Fibrosis

Z.S. Uyan, MD,[1]* N. Özdemir, MD,[2] R. Ersu, MD,[1] İ. Akpınar, MD,[3] S. Keskin, MD,[4] E. Çakır, MD,[1] B. Karadağ, MD,[1] F. Karakoç, MD,[1] and E. Dağlı, MD[1]

- 24 stable children with CF (mean age 9.5 years, FEV_1 >40%)
- Hypoxemia (SpO_2 <90% for >5% of the night) was not seen

Hypoxemia During Sleep in CF

- 95.8% of CF children with normal PFT or mild to moderate lung disease had desaturation during sleep
- Nocturnal oxygenation correlated with
  - S–K and Brasfield scores,
  - PaO_2 and SaO_2,
  - Z-score of weight and height and
  - CT scores
- Children with CF do tend to have lower SpO_2 and more frequent desaturations compared with control children

Hypercapnia During Sleep in CF

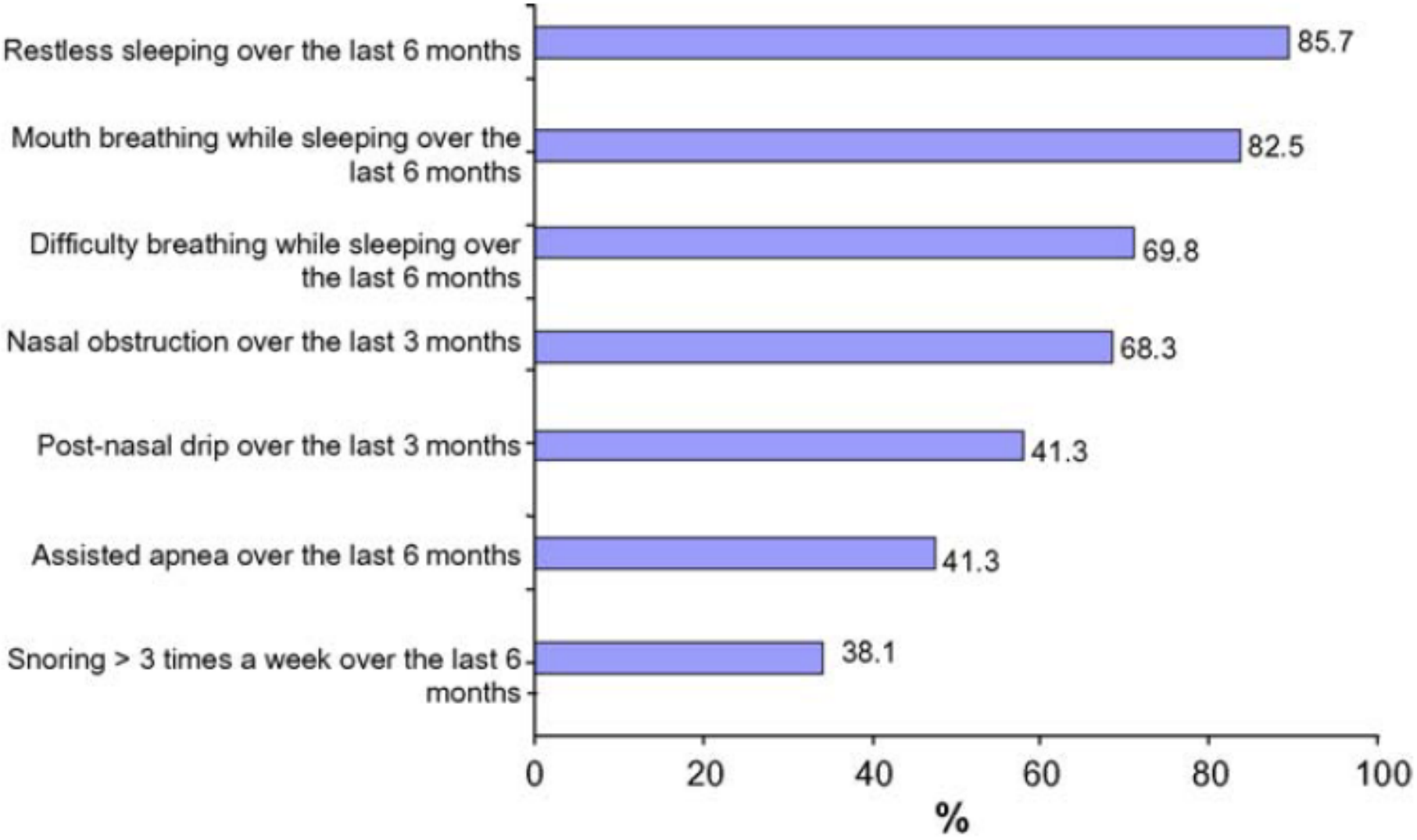
- The measurement of end-tidal CO_2 is not accurate in the setting of CF lung disease because of poorly plateaued waveforms
- Transcutaneous CO_2 has been suggested as an alternative measure of nocturnal CO_2 retention
- In CF patients with an FEV_1 <60%, 24% spent greater than 10% of sleep with a PCO_2 >50 torr
- Administration of supplemental oxygen in hypoxemic CF patients may lead to hypercapnia

Obstructive Sleep Apnea in CF

- OSA is very prevalent in children with CF
- In a study of 63 children with CF 56% had OSA syndrome (apnea index >1/h) and 26% had moderate to severe OSA (apnea index >5/h)
- OSA symptoms:
  - mouth breathing during sleep (83%),
  - difficulty breathing during sleep (70%),
  - and snoring greater than 3 times/week (38%)

Int J Pediatr Otolaryngol 2009;73:1780-5

Sleep and sinus complaints are common in CF



Int J Pediatr Otolaryngol 2009;73:1780-5

Oxygen Therapy in CF

- Balancing the
  - risks of developing pulmonary hypertension related to nocturnal hypoxemia
  - against the costs, psychological impact, logistical difficulties, discomfort, and potential for limiting mobility.
- Consensus guidelines in adult CF patients recommend supplemental oxygen
  - “if oxygensaturation is less than 88% to 90% for 10% of the total sleep time.”

Oxygen Therapy in CF

- Supplemental oxygen may decrease the severity of pulmonary hypertension
- No effect on cognition, sleep quality, exacerbation frequency, disease progression, or quality of life
- However, a long-term randomized trial reported an improvement in school and work attendance in hypoxemic CF patients receiving nocturnal supplemental oxygen

Oxygen Therapy in CF

- Sufficient supplemental oxygen to maintain saturations >93% during acute exacerbations and >90% over the long term in chronically hypoxemic patients
- Follow trends in the transcutaneous CO_2 and serum levels of bicarbonate during oxygen initiation

NIV in CF

- Non-invasive ventilation may be a useful adjunct to other airway clearance techniques, particularly in people with CF who have difficulty expectorating sputum.
- Non-invasive ventilation, used in addition to oxygen, may improve gas exchange during sleep to a greater extent than oxygen therapy alone in moderate to severe disease.
- These benefits of NIV have largely been demonstrated in single treatment sessions with small numbers of participants.
- The impact of this therapy on pulmonary exacerbations and disease progression remain unclear.

Cochrane Database Syst Rev 2012

NIV in CF

- NIV is an option for CF patients with symptomatic nocturnal hypoventilation, which typically precedes daytime hypoventilation.
- NIV avoids the considerable morbidity associated with tracheostomy or an endotracheal tube.
- NIV is recommended:
  - if there is a 10-torr increase in PCO_2 on supplemental oxygen,
  - a 10-torr increase in PCO_2 during sleep, or
  - an absolute PCO_2 of at least 60 torr

NIV in CF

- Symptoms of nocturnal hypercapnia include dyspnea and headaches that may result in sleep fragmentation.
- A 6-week trial of NIV was reported to improve nocturnal PCO_2, quality of life, and exercise performance.
- NIV has also been reported to decrease morning headaches and to subjectively improve sleep quality
- Cross-sectional studies indicate that NIV is used in 7.6% of adults and 1.2% of children with CF
- NIV is typically started during a CF respiratory exacerbation. In stable CF patients, diurnal hypercapnia is the primary indication for NIV.

NIV in CF

- Patients with advanced CF lung disease have an increased work of breathing, which can be reduced by 60% to 80% with NIV
- NIV increases the tidal volume and minute ventilation during sleep and therefore improves gas exchange and patient comfort
- The use of spontaneous-mode NIV in CF patients (mean age 25 years, FEV1 16% predicted) was accompanied by a reduction in PCO_2 from 91 to 67 torr

NIV in CF

- For dyspnea, the usual practice is to start bilevel ventilation with an inspiratory positive airway pressure (IPAP) of 10 to 12 cm H_2O and an expiratory positive airway pressure (EPAP) of 4 to 6 cm H_2O
- The support levels are titrated upward toward IPAP 16 to 18 cm H_2O and EPAP 4 to 8 cm H_2O, in increments of 1 cm H_2O, until the dyspnea is relieved
- The spontaneous pressure support mode is preferable initially, as respiratory drive is normal in CF and patients may adjust the tidal volume and rate to whatever feels most comfortable

Facial Side Effects during Non-invasive Positive Pressure Ventilation in Children

- 16 pts w/ OSAS, 14 pts w/ NMD, 10 pts w/ CF
- Clinical evaluation of facial tolerance to PAP
- Skin injury %

AGE >10 years (OR=16)

Use of commercial masks (OR=15)

Less common in OSAS pts

- Global face flattening %

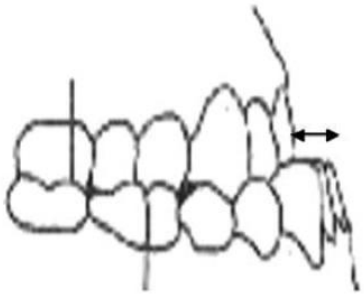
More common in OSAS & NMD pts

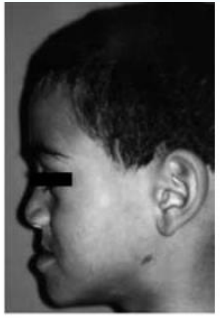
- Maxillary retrusion %

Longer daily use of PAP (>10 hr/day, OR=6.3)

Fauroux, B. et al. Intensive Care Med 2005;31:965-9

Side Effects





Although most adverse efffects are minor, they need to be addressed to ensure adherence

- **Heated humidification, saline nose drops, nasal steroids**
- **Well fitting masks, alternating between different masks, avoiding equipment that is too tight, using a dressing to protect the bridge of the nose**
- **Using a mask that fits properly**
- **Risk increases with the use of full facemask**

Pediatric Pulmonology 46:919–926 (2011)

Effect of Night Symptoms and Disease Severity on Subjective Sleep Quality in Children With Non-Cystic-Fibrosis Bronchiectasis

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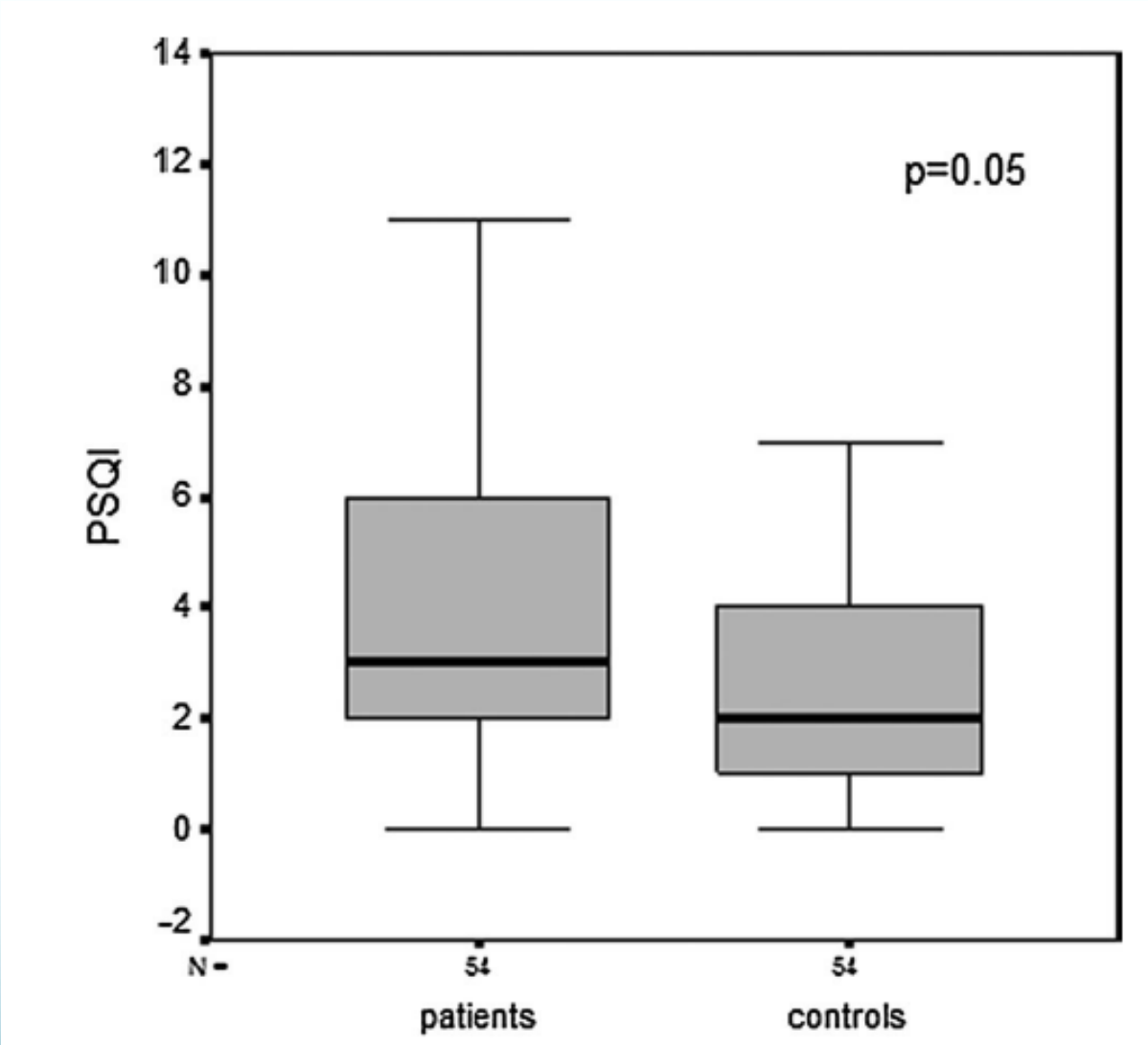
Sleep Quality in Children with Bronchiectasis



Sleep Quality in Children with Bronchiectasis

- 37% BE and 17% control children had poor sleep quality ($p < 0.05$)
- Patients with sputum and wheezing had poorer sleep scores ($p=0.003$ and 0. 0.005)
- The association of wheezing and breathlessness during night time with sleep quality tended to be significant ($p= 0.05$)
- 22% BE and 9% controls had sleep disordered breathing ($p=0.003$)
- BE patients who snored had poorer sleep quality ($P < 0.001$) and patients with wheezing had significantly higher rate of snoring ($p= 0.04$)
- Children with worse HRCT scores also had worse sleep quality ($r=0.28$, $p=0.04$).

OPEN ACCESS Freely available online

PLOS ONE

Sleep Disturbances and Health-Related Quality of Life in Adults with Steady-State Bronchiectasis

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- In adults with steady-state bronchiectasis, sleep disturbances are more common than in healthy subjects and related to poorer QoL.
- Determinants associated with sleep disturbances include depression, aging, nighttime cough and increased sputum volume.
- Assessment and intervention of sleep disturbances are warranted and may improve QoL.

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Sleep Disordered Breathing in Patients With Primary Ciliary Dyskinesia

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Sleep Disordered Breathing in PCD

- 29 PCD patients
- Eleven PCD patients reported themselves to be “poor” sleepers, compared to only one subject in the control group ($p=0.002$).
- Sixty-five percent of PCD patients had habitual snoring
- 52% of the PCD patients had OSAS in polysomnography.
- OSAS rate was higher in PCD patients who snored ($p=0.008$).
- Habitual snoring and OSAS were more common in PCD patients who had cigarette smoke exposure in their homes ($p < 0.001$ and $p=0.02$)

Sleep Disordered Breathing in PCD

- 16 PCD children had higher
  - obstructive apnoea (4.7 vs 0.2, $p < 0.001$),
  - central apnoea (0.8 vs 0.2, $p < 0.001$),
  - hypopnoea (1.8 vs 0.2, $p < 0.001$),
  - apnoea–hypopnoea (7.8 vs 0.6, $p < 0.001$),
  - oxygen desaturation indexes (ODI; 0.7 vs 0.2, $p = 0.002$), and mean oxygen desaturation (4% vs 1%, $p< 0.001$),
  - mean and nadir oxygen saturation (97.1% vs 98.1, $p < 0.001$) (93% vs 97.2%, $p < 0.001$) were lower
- Oxygen saturation was associated with bronchiectasis severity score ($r = -0.6$, $p = 0.02$).

Santamaria F. et al. Respirology 2014;19:570-5

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Sleep Disordered Breathing and Sleep Quality in Children With Bronchiolitis Obliterans

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Sleep in Children with BO

- Twenty-one patients (14 male, median age: 8.3 years)
- 25% had a PSQ score of >0.33, predictive of a SDB.
- 48% had poor sleep quality.
- 19% had an OAHI of >1/hr.
- 90% had a high desaturation index.
- 19% had a mean oxygen saturation of <93%.

Sleep in Children with BO

- Median central apnea time was 7.5 (IQR: 6.9–9.1) seconds.
- Central apnea index of the patients correlated positively with R5, R10, R15, R20, Z5, and negatively with X10 and X15 at IOS.
- There was a positive correlation between the lowest oxygen saturation and FVC, FEV1, X5, X10, X15, X20 while
- There was a negative correlation between lowest saturation and the central apnea index at PSG, R5, R10, and Z5 at IOS.
- Mean oxygen saturation during PSG correlated positively with FVC, FEV1, FEF25–75, X5, X10, X15, X20 results.

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Sleep Disordered Breathing and Sleep Quality in Children With Bronchiolitis Obliterans

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- The risk of nocturnal hypoxia is increased in patients with BO and correlated to the severity of lung disease determined by pulmonary function tests.
- Although BO patients have a shorter duration of central apneas, they are more prone to desaturate.

Sleep and BPD

- Infants with BPD are at risk for:
- Hypoxemia during sleep that is not predicted by waking oxygen saturation or respiratory rate
- Tachypnea and paradoxical breathing (thoraco-abdominal asynchrony)
- Obstructive and central apneas
  - Even brief events result in desaturation
- Maladaptive responses to hypoxemia with apnea and bradycardia despite arousal from sleep

Sleep and BPD

- Hypoxemia and tachypnea during sleep correlate with poor growth
- Treatment of sleep related hypoxemia enhances growth and reduces the risk of pulmonary hypertension
- Sleep related abnormalities improve with time, presumably with growth and resolution of lung disease

BPD and Sleep

- Seek and you will find:
  - Hypoxemia during sleep
  - Frequent central and obstructive apneas and hypopneas
  - Improved growth with treatment of hypoxemia
  - Chronic lung disease in infants born prematurely who present with ALTE
  - Improvements in sleep disordered breathing as lung disease improves with treatment, growth, and time

Conclusion

- Patients with chronic lung disease experience both subjective and objective sleep disruption and gas-exchange abnormalities during sleep.
- Sleep problems are usually underestimated in these patients.
- Noninvasive ventilation and supplemental oxygen may be helpful in mitigating the adverse effects of nocturnal hypercapnia and hypoxemia