Sleep Disordered Breathing in Special Population

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Sleep Disordered Breathing in...
- Neuromuscular Disorder
- Sickle Cell Disease
- Down syndrome
- Obesity Hypoventilation Syndrome

Disclosure
I have no conflict of interest to declare

Abbreviations
- NMD: Neuromuscular disorders
- OSA: Obstructive sleep apnea
- CSA: Central sleep apnea
- NIPPV: Non-invasive positive pressure ventilation
- CPAP: Continuous positive pressure ventilation
- Bi-PAP: Bi-level positive pressure ventilation
- SMA: Spinal muscular atrophy
- DMD: Duchene muscular dystrophy
- SCD: Sickle cell disease

Neuromuscular Disorder

Diseases which affect Neuromuscular function in Children
- Muscle
  - Dystrophy
    - Congenital muscular dystrophy
    - Duchenne Muscle dystrophy
    - Becker Muscular dystrophy
  - Myopathy
    - Myotubular myopathy
    - Central core myopathy
    - Myotonic dystrophy
    - Type I and II
- Neuromuscular Junction
  - Congenital myasthenia gravis
- Peripheral nerve
  - Hereditary sensory-motor neuropathy (Type 1-2)
- Motor neuron disease
  - Classic spinal muscular atrophy
  - SMA with respiratory distress (SMARD)
Acquired NM disorders
- Muscle
  - Dermatomyositis
- NM junction
  - Myasthenia gravis
- Peripheral nerve
  - Guillain-Barré Syndrome
- Anterior Horn Cell
  - Polio

Sleep disordered breathing in children with NMD
- Quite common in NMD
- Full spectrum of abnormalities seen
  - OSA, central apneas, hypoxemia, hypoventilation
- Healthy children:
  - 2-3%
- Neuromuscular patients:
  - Adults: 36-53%
  - Varies with different types of NMD (DMD vs. SMA)

Disorders | Respiratory muscle affected | Type of SDB
--- | --- | ---
Cerebral Palsy | Upper airways | OSA
Arnold Chiari Syndrome | Upper airways, diaphragm | Central apnea
Spinal cord (C2-3) | Upper airways | OSA
Spinal cord (C4-5) | Diaphragm, intercostals, abdominals | Hypoventilation
Spinal Muscular Atrophy | Generalized | OSA, Hypoventilation
Charcot-Marie-Tooth | Upper airways, diaphragm | OSA, Hypoventilation
Leukodystrophies | Generalized | Hypoventilation
Guillain-Barré | Generalized | Hypoventilation
Duchenne Muscular Dystrophy | Generalized | OSA, Hypoventilation
Myotonic Dystrophy | Upper airways, central drive | OSA, CSA, Hypoventilation
Myopathies | Upper airways, general | OSA, CSA, Hypoventilation
Mitochondrial myopathies | Upper airways, gen, central drive | OSA, CSA, Hypoventilation

Respiratory drive during sleep
- Normal patients:
  - Relative hypoventilation: Decrease in hypoxic and hypercarbic respiratory drive to breathe
  - Tidal volume by 25%
  - PaO2 by 3-5 mm Hg
  - PaCO2 by 3-6 mm Hg
  - Maximum attenuation in phasic REM
- NMD patients:
  - Normal changes are amplified → frank hypoventilation
  - Re-breathe CO2 – unable to increase ventilation
  - Usually the drive is normal but mechanical system is weak

Respiratory failure in NMD
- Lung failure
  - First hypoxemia, later hypercarbia (VQ mismatch, V6 vent)
  - Aspiration / GERD
  - Recurrent infections
- Pump failure
  - Manifested by hypercarbia
  - Respiratory muscle weakness, kyphoscoliosis, central control
  - Alveolar hypoventilation

Symptoms of SDB in NMD patients
- Symptoms are subtle and insidious in onset, may be asymptomatic
  - Snoring – usually soft
  - Frequent nocturnal awakenings
  - Excessive daytime sleepiness
  - Morning headaches
  - Fatigue
  - Exertional dyspnea
  - Weak cough
  - Weight loss
  - Frequent respiratory infections
  - Restless leg symptoms
Progression of Hypoventilation

- Initial compensation for hypoventilation is arousal response
- Prevents prolonged desaturation and hypercarbia
- Sleep fragmentation → daytime fatigue, hypersomnia
- As disease progress → ventilatory response is reset
- Arousal response becomes blunted
- Longer periods of alveolar hypoventilation
- Eventually → respiratory drive becomes depressed → severe hypoventilation (first night and then also during daytime)

Hypoventilation (AASM 2007)

- Adult
  - $\geq 10$ mm Hg increase in PaCO2 during sleep compared to awake supine value
  - Persistent desaturation is NOT sufficient to document hypoventilation
- Pediatrics
  - $> 25$ % of total sleep time CO2 $> 50$ mm Hg
  - Measured by ETCO2 or TcCO2 sensors
  - Signals unreliable:
    - Mouth breathers
    - Nasal congestion

Routine respiratory function evaluation

- Pulmonary function test (FVC, FEV1, mid flows)
- Lung volumes (RV/TLC ratio)
- Peak cough flows
- MIP and MEP
- Pulse oximetry
- ETCO2
- CXR
- Blood gases (VBG)
- HCO3
- Hematocrit
Visit to Pulmonologist
ATS task force 2004

- Twice per year
  - Wheel chair bound
  - Age > 12 years
  - FVC < 80% predicted
- 3-4 times per year
  - Mechanical ventilation
  - Tracheostomy
  - FVC < 40

Indication for sleep study in NMD
- Gold standard
- Overnight oximetry: pattern of desaturation
  - Positive predictive value of 97%
  - Does not correlate with severity
  - Normal oximetry does not rule out SOM [1]
- Screening PSG
  - Annually if asymptomatic
  - SMA: usually first decade
  - DMD: usually second decade
- Clinical indications for PSG
  - Clinically symptomatic
  - Low daytime saturation
  - Blood gas: elevated PaCO2 and HCO3
  - PFT are reduced (FVC, FEV1, MIP)

Management
- Airway Clearance
- Non-Invasive Nocturnal Ventilation
  - Daytime Noninvasive Ventilation
  - Continuous Invasive Ventilation
- Oxygen therapy
- Corticosteroids and neuromuscular patients (DMD)
- Patient Education
- Long-term Care Issues
- End of Life Care

Oxygen therapy
- May be used only during acute respiratory infections/hypoxemia if there is no associated hypoventilation
- Oxygen treatment for nighttime use for hypoventilation can be dangerous and SHOULD NOT be used alone as it was worsen hypoventilation

Positive pressure ventilation
- Non-Invasive Positive Pressure Ventilation (NIPPV)
  - CPAP: OSA
  - Bi-level: OSA and hypoventilation
  - Bi-level S/T: severe hypoventilation, central apneas
  - Ventilator
- Invasive Positive Pressure Ventilation (IPPV)
  - Tracheostomy
    - Progressive respiratory failure & need for daytime vent

Indication of nighttime ventilatory support
- Daytime symptoms of CO2 retention
  - Headaches, excessive tiredness, frequent respiratory tract infections, difficulty with attention
- PSG: Nocturnal hypoventilation
- Physiological criteria (Medicare criteria in adults)
  - PCO2 > 45 mm Hg (daytime)
  - Nocturnal SaO2 < 88% for > 5 minutes
  - PFT Criteria:
    - MIP < 60 cm H2O
    - FVC < 50% predicted
Indication of daytime ventilatory support

- Self extension of nocturnal ventilation into wake time
- Inability to speak in full sentence without being breathless
- Abnormal deglutition
- Symptoms of daytime hypoventilation
- Daytime testing
  - SaO2 < 95% RA
  - PaCO2 > 50 torr

Indication for tracheotomy

- Patient and caregiver preference
- Requiring 24 hours ventilatory support
- Cannot successfully ventilate using NIPPV
- ≥ 3 failures to achieve extubation after acute illness
- Failure of pulmonary toileting measures

One big happy family with a little help from technology of today!

Sickle Cell Disease (SCD)

SCD: Prevalence & Burden of the Problem

- SCD is the most prevalent genetic hemoglobinopathy
- 1 in 600 African Americans
- Autosomal recessive disorder
- Sickle cell trait affects 8% of African Americans

Rees DC et al 2010

Pulmonary Complications of SCD

- Acute chest syndrome
- Pulmonary hypertension
- Pulmonary embolism
- Obstructive lung defect (asthma)
- Restrictive lung defect (pulmonary fibrosis)
- Interstitial lung disease
- Atelectasis
- Daytime hypoxemia
- Sleep disordered breathing
Oxyhemoglobin saturation curve

Slippery slope - showing stable Hb saturation in spite of ↓ PaO₂ & stable PaO₂ in spite of falling Hb O₂ saturation

Limitation of Pulse Oximetry in SCD (high)

- Since pulse oximetry measures oxyHb and carboxyHb similarly, it may over-estimate Hb saturation by 3-7% in SCD due to the presence of carboxy Hb & methHb in these patients
- Similar high pulse oximetry values are seen in patients with CO poisoning

Nocturnal Hypoxemia in SCD

- Seen in up to 40% of subjects with SCD
  - secondary to intrinsic lung disease
  - impaired diffusion capacity
  - VQ mismatch
  - asthma
  - OSA
- Can leads to painful crises, acute chest syndrome, & pulmonary hypertension
- Daytime SpO₂ < 94% in children with SCD is a reasonable threshold to screen for SDB by PSG

Co-oximetry

- Can separate by several wavelengths oxyHb from carboxyHb
- Hence it detects true oxygen saturation in patients with SCD, and should be considered for use in any sleep lab with a referral from an active SCD program

SDB in Sickle cell disease

- OSA
- Hypoventilation
- Nocturnal hypoxemia

Sleep-Disordered Breathing in SCD

- OSA in the general population
  - 2-3%, more so in the African American population
- OSA in SCD
  - 11%
- OSA in the Sleep Laboratory
  - 30%
- OSA in SCD in the Sleep Laboratory
  - 63%
- High risk:
  - Enlarged adenoids and tonsils
  - Facial bone remodeling: extra medullar hematopoiesis

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OSA in SCD

- OSA: hypoxemia, respiratory acidosis & hypercarbia
- May further precipitate polymerization of Hb S
- Polymerization in SCD without OSA occurs at PaO₂ of 60, but with respiratory acidosis & shift of the HDC to the right in SCD with OSA, this can occur at higher PaO₂
- Strokes and OSA in SCD both occur with a higher frequency in the 3-6 year age range
- Snoring is associated with ↑ CBF
- Nocturnal desaturations and ↑ CBF are associated with increased risk for stroke, which may be reversed after T&A

Consider sleep studies in SCD

- Clinical history suggestive of OSA
- Hypoxemia (SaO₂ < 94%)
- Pulmonary hypertension
- Systemic hypertension
- Too much opioids for pain control — ? hypoventilation
- Recurrent chest syndrome — ? Hypoventilation — ? Sleep hypoxemia

Pulm-sleep evaluation of children with SCD

- High risk SCD patient
  - Frequent acute chest, hypoxemia (SaO₂ < 94%)
- History and Exam
  - Snoring, mouth breathing, restless sleep
  - Daytime fatigue, tired and attention deficits
  - Adeno-tonsillar hypertrophy, crowded airways
- Pulmonary function testing
  - Obstructive, restrictive, diffusing defects
- ETCO₂
- Chest X-ray: atelectasis
- ECHO: Pulmonary pressures
- Trans-cranial & carotid Doppler
- Sleep study

BTS Guidelines for O₂ Therapy

Thorax, 2009

- Increased risk of stroke (Kirkham)
  - Maintain SpO₂ ≥ 96%
- Increased risk of pain (Hargrave)
  - Maintain SpO₂ ≥ 94%
- UK Guidelines for SCD (2006):
  - Treat chronic sickle cell lung disease with supplemental O₂
    - ? evidence base
    - More controversial
    - Reduced erythropoietin, reticulocytes, followed by rebound followed by rebound in irreversibly sickled cells and pain crisis reported
  - O₂ did not provide additional relief over iv or po narcotics and did not shorten the duration of severe pain compared to the placebo

Treatment

- Oxygen
- CPAP
- BiPAP

Effects of CPAP


PEP comparable to incentive spirometry

Effects of CPAP

Hsu et al, Respiratory Care, 2005

ETCO₂ comparable to incentive spirometry

no bone marrow suppression or rebound pain
**Down Syndrome**

- Trisomy 21
- Most common chromosomal cause of mental retardation
- Prevalence in the US
  - 1/660 live birth
- OSA:
  - Healthy children: 2-3%
  - Down syndrome:
    - children: 30 - 100%
    - Adults: 50 – 75%

**Predisposing factors in DS for OSA**

- Mid-facial hypoplasia
- Mandibular hypoplasia
- Glossoptosis/macrogllossia
- Abnormal small upper airway
- Hypertrophied tonsils / lingual tonsils
- Hypotonia
- Laryngomalacia / Pharyngomalacia (43%)
- Hypothyroidism (12%)
- Obesity
- GERD

**Etiology of dynamic UAW collapse in DS**

- Cine MRI studies in 27 children age 4-19 years with DS and persistent OSA after adeno-tonsillectomy
  - 20 (74%) - Macroglossia
  - 17 (63%) - Glossoptosis,
  - 17 (63%) - adenoidal regrowth
  - 8 (30%) - Enlarged lingual tonsils
  - 6 (22%) - Hypopharyngeal collapse

**Treatment options of OSA children with Down Syndrome**

- Adeno-tonsillectomy
  - Increased risk for post AT complications (5 times)
  - Only 27 – 35% had full resolution
- Positive airway pressure therapy
  - CPAP or BiPAP with in-lab PAP titration
  - Needs habituation and desensitization
- Other options:
  - Rapid maxillary expanders
  - Lingual tonsillectomy
  - Tongue base reduction
  - Supraglottoplasty, UPPP, tracheostomy
**Obesity Hypoventilation Syndrome**

*Pickwickian syndrome*

- Obesity (BMI > 30)
- Sleep disordered breathing
  - OSA, Sleep hypoventilation
- Chronic daytime hypoventilation
  - PaCO2 > 45 mm Hg, PaO2 < 70 mm Hg
  - r/o other causes of hypoventilation
- Prevalence:
  - BMI > 35: > 20% have OHS
  - BMI > 40: > 25% have OHS

**OHS**

- Not all morbidly obese patient develop OHS
  - Distinct phenotype
  - Higher central fat distribution
  - Marked leptin resistance
  - Reduced ventilatory response to CO2
  - High morbidity and mortality
- Arises from complex interaction between
  - Obesity related respiratory impairment
  - Sleep disordered breathing
  - Diminished respiratory drive

**Complications**

- Hypoxemia
- Pulmonary hypertension
- Cor pulmonale
- CHF

**Treatment**

- Oxygen
- NIPPV: CPAP, BiPAP, AVAPS
- Tracheostomy
- Weight reduction
- Bariatric surgery

**Thank you**