#403 Obstructive Sleep Apnea in Children
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Sleep Disordered Breathing

- **Primary Snoring:**
  - Snoring without intermittent hypoxia, hypercarbia or repeated arousal
- **Upper airway resistance syndrome (UARS):**
  - Snoring with labored breathing
  - Repeated arousals
  - No gas exchange abnormalities
- **Obstructive sleep apnea/hypopnea syndrome (OSAS):**
  - Snoring with apnea
  - Intermittent hypoxia
  - Hypercarbia
  - Repeated arousals

SDB & OSAS

- SDB affects up to 12% of prepubertal children.
- OSAS is estimated to occur in 2-3% of children.

OSAS Pathophysiology

- Poorly understood
- Multiple factors play a role:
  - T&A hypertrophy
  - Obesity
  - Neuromuscular disorders
  - Craniofacial disorders
  - Inflammation
- Likely that the pathophysiology involves both structural and neuromotor abnormalities.

SDB & OSAS

- Cardiovascular complications
- Poor quality of life
- Failure to thrive
- Behavioral disturbances
- Excessive daytime sleepiness
- Poor learning
- Enuresis
- Systemic inflammation

OSAS Sequelae
Upper Airway Obstruction Physiologic Sequelae

- Hypoxia
- Alveolar hypoventilation
- CO\(_2\) retention
- Secondary pulmonary edema
- Pulmonary hypertension
- Right heart failure

OSAS Adversely Affects QOL

- Started with 19, included 10.
- Clinical or PSG documentation of SDB.
- QOL instruments:
  - Child Health Quest (CHQ): generic instrument, measures global QOL
  - OSA-18: validated disease-specific instrument

OSAS Adversely Affects QOL

- Divided studies into 3 groups:
  - Gp I: n=3, CHQ to compare OSAS to healthy children and JRA
  - Gp II: n=5, QOL before and after T&A with short term FU (at least 4 wks)
  - Gp III: n=2, QOL before and after T&A with long term FU (at least 6-12 mos)

QOL: OSAS vs Healthy

- First grade, public school children.
- Academically ranked in the lowest 10th percentile of their class.
- An OSA childhood questionnaire was administered.
- All children underwent an overnight recording of pulse oximetry and transcutaneous CO\(_2\) tension at home.
- Considered to have sleep associated gas exchange abnormality (SAGEA):
  - Questionnaire score \( \geq 5 \)
  - More than 2 desat episodes/hr: 6 secs >5% Sp\(_{O2}\) reduction from baseline or Sp\(_{O2}\) <90%.
  - And/or sustained elevation of TcCO\(_2\) >8mm Hg vs waking values for >60% of total recording time.

Sleep-Disordered Breathing and School Performance

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**Sleep-Disordered Breathing and School Performance**

- 297 first grade children were studied.
- 66 (22.2%) had primary snoring (questionnaire > 5 but no desats or increased TcCO₂).
- 54 (18.1%) had SAGEA:
  - 24 underwent T&A ± topical steroids (TR)
  - 30 had no intervention (NT)
- School performance was compared before and after the overnight recording.


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**Inattention, Hyperactivity and SDB**

- Inattentive and hyperactive behavior are common among children with OSA or UARS.
- Treatment of SDB is often associated with improved behavior and decreased need for stimulant medications.
- Frequency of SDB among inattentive and hyperactive children has received little study.


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**Inattention, Hyperactivity and SDB**

- Administered a validated instrument, the Pediatric Sleep Questionnaire (PSQ) to a large sample of parents who brought their children to either of 2 general pediatric clinics.
- Parents also completed 2 validated measures of inattention and hyperactivity.
- Compared the frequency of SDB sx's among hyperactive and nonhyperactive children.


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**Sleep-Disordered Breathing and School Performance**

- Habitual snoring was reported in 16% of the participants.
- High HI scores (>60) were found in:
  - 13% of all participants
  - 22% of habitual snorers
  - 12% of nonsnorers

0= never, 3= always snores

Enuresis in Children with OSAS

- Purpose:
  - Determine the prevalence of nocturnal enuresis in a group of children referred for suspected sleep-disordered breathing (SDB).
  - Examine whether the presence of enuresis is related to the severity of SDB


A total of 66 children (41%) currently described enuresis


Enuresis in Children with OSAS

- Children referred to the sleep center (n=160) underwent a detailed H&P.
- Severity of enuresis was determined as follows:
  - Frequently: > 3x/wk
  - Sometimes: 1-2x/wk
  - Rarely: < 1x/wk
  - Never
- All patients underwent a full overnight polysomnogram.


Enuresis in Children with OSAS

- Proposed causes:
  - Insufficient arousal response
  - Impaired urodynamics (increased intra-abdominal pressure caused by respiratory efforts against an obstructed airway can be transmitted to the bladder)
  - Insufficient vasopressin production during sleep


OSAS

Inflammation
CRP in Pediatric OSAS

- CRP is an important serum marker of inflammation with implications for CV morbidity.
- Levels are elevated in adults with SDB.
- 81 consecutive children being evaluated for SDB by PSG had blood drawn the morning after the PSG.


CRP and NG Dysfunction in OSAS

- To assess magnitude of systemic inflammatory response (serum hsCRP) which may identify children with OSA and higher susceptibility of cognitive morbidity.
- Habitual snoring and non-snoring children were recruited.
- N=278, Age range= 5-7 yrs.
- Underwent PSG, neurocognitive testing and blood draw the next morning.

**CRP and NG Dysfunction in OSAS**

GCA = General Conceptual Ability, Subjects considered to have an abnormal neurocognitive assessment if GCA < 85%

**CRP and NG Dysfunction in OSAS**

- hsCRP levels are higher in children with OSA, particularly in those who develop neurocognitive deficits.
- This suggests that the magnitude of the inflammatory responses elicited by OSA is a major determinant of increased risk for neurocognitive dysfunction.

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**Clinical Presentation**

**Upper Airway Obstruction/OSA**

*Clinical Presentation*

- Snoring, mouth breathing
- Sleep pauses, apneas (>10 secs)
- Frequent awakenings
- Hypersomnolence
- Behavioral problems
- Enuresis
- Growth retardation

**Physical Examination**

- Large tonsils and adenoids
- Possible obesity
- Neuromuscular disorders (Floppy)

**Lateral Neck Film**

- Obstructive adenoids
- Soft palate
- Tracheal air column
Upper Airway Obstruction Assessment

- Careful parental observation with documentation of presence and length of apneic episodes.
- Audiotape or videotape of sleep.
- Polysomnography if:
  - High risk for respiratory compromise post-op
  - Unreliable history
  - History not commensurate with physical findings
- CXR, EKG, Echocardiogram if necessary.

Polysomnography

- Golden standard in evaluating OSA
- Monitors:
  - Duration and efficiency of sleep
  - EKG and EEG
  - Number of obstructive apneas and hypopneas
  - Changes in pulse oximetry
  - Number of arousals
  - End tidal CO₂
- AHI, REM AHI, ETCO₂, arousals, and lowest desaturations help determine severity of OSA.

Severity of Pediatric OSA

- Most pediatric sleep experts agree to the following definitions:
  - Mild OSA: 1< AHI<5
  - Moderate OSA: 5< AHI<10
  - Severe OSA: AHI>10

PSG before T&A: for Whom???

- If patients exhibit certain complex medical conditions:
  - Obesity
  - Down syndrome
  - Craniofacial abnormalities
  - Neuromuscular disorders
  - Sickle cell disease
  - Mucopolysaccharidoses
- In children for whom the need for surgery is uncertain or when there is discordance between tonsillar size on physical examination and the reported severity of sleep-disordered breathing.


OSAS Medical Treatment

OSAS Medical Treatment

- Randomized, triple-blind, placebo-controlled, parallel-group trial.
- Inclusion criteria:
  - Adenoid hypertrophy by X-ray or 2-3+ tonsillar hypertrophy on exam
  - S/S of OSA: loud snoring, difficulty breathing, OSA witnessed by parents, parental concern about sleep or restless sleep
  - RDI (apneas + hypopneas)>1 by lab/home PSG
- Fluticasone administered at 1 spray/nostril twice daily x 1 week and once daily for the remaining 5 weeks.
- PSG, clinical and radiographic assessment at baseline and after 6 wks of Rx.

Fluticasone in OSA


Fluticasone in OSA


Fluticasone in OSA


Fluticasone in OSA


Release of IL-6 from Adenoid Cells

- Spontaneous CD3-induced over spont
  *p=0.05

Leukotrienes in OSAS

- Also studied T/A tissue from OSA and patients with chronic tonsillitis and showed enhanced expression of LT receptors 1 and 2 and elevated levels of leukotrienes in OSA pts.
Anti inflammatory Rx

SA= sleep apnea
RI= recurrent infectious tonsillitis


Montelukast in OSAS


Surgical Treatment

Adenotonsillectomies in 2003-2004

Postoperative Care

Respiratory Compromise After Adenotonsillectomy in OSA

- Retrospective review of children undergoing T&A for OSA.
- Of 69 patients with PSG-documented OSA, 16 (23%) had severe respiratory compromise (RC) post T&A:
  - $\text{SaO}_2 \leq 70\%$ &/or hypercapnea ($\text{PaCO}_2 > 45$ mm Hg) requiring nurse or physician intervention
- Intervention included:
  - Supplemental $\text{O}_2$ (n=16)
  - Nasopharyngeal airway (n=2)
  - Helium-oxygen mixture (n=2)
  - Intubation (n=2)

Respiratory Compromise After Adenotonsillectomy in OSA

- Children with RC vs those without RC:
  - Were younger: 3.4±4 yrs vs 6.1±4 yrs (p<0.01)
  - Had higher OEI: 49±41 vs 19±30 (p<0.01)
- The following were significantly more frequent in children with RC:
  - OEI >10 (OR=16.8)
  - Age < 3 yrs (OR=12.1)
  - Weight < 5th percentile for age
  - Presence of a craniofacial abnormality
  - Cardiac disease documented by EKG/Echocardiogram
  - CXR abnormalities


Recurrent Hypoxia and Increased Respiratory Sensitivity to Fentanyl

- Low O2 sat nadir and young age associated with reduced total analgesic morphine dose.
- Animal experiment to explain these findings.
- Two groups of rats:
  - Recurrent hypoxia (Days 17-33) (n=7)
  - Control (n=6)
  - Given SQ fentanyl (120 μg/kg) and monitored


Recurrent Hypoxia and Increased Sensitivity to Opiates in OSAS

- Prospective study in 22 children (Av age=3.8 yrs) undergoing T&A for OSAS:
  - Sat nadir: <85% or ≥85%
  - Postop morphine regimens:
    - Standard: 50% of 0.1 mg/kg
    - Calculated: based on sat nadir and age (reduced)
  - Morphine administered every 7 min in PACU until:
    cessation of crying, moaning, grimacing, restlessness and verbal reports of pain.
  - Total analgesic morphine dose calculated.


Recurrent Hypoxia and Increased Sensitivity to Opiates in OSAS

- In patients with OSA and significant hypoxemia on preoperative sleep study, the total analgesic opiate dose that will be sufficient to ensure adequate analgesia will be one half of that required in patients with no such history.

Admission after T&A

- Clinicians should admit children with obstructive sleep apnea documented on polysomnography for inpatient, overnight monitoring after T&A if they are:
  - Younger than age 3 or
  - Have severe obstructive sleep apnea:
    - AHI >10 events/hour
    - Oxygen saturation nadir less than 80%
    - Or both


Postoperative Pain Management

Between 1969-2012, 10 deaths and 3 overdoses identified in children treated with codeine:
- 8/13 occurred in children after T&A
- 3/13 involved children with URI
- A Boxed Warning, FDA’s strongest warning, will be added to the label of codeine-containing products about the risk of codeine in children post T&A (updated 2/20/13).

Codeine and T&A

- After ingestion, codeine is converted to morphine in the liver by cytochrome P450 2D6 (CYP2D6).
- Some people have genetic variations in CYP 2D6 that alter the metabolism:
  - Two nonfunctional alleles: poor drug metabolism
  - One or two functional alleles: extensive metabolism
  - Duplicated or amplified active genes: ultrarapid metabolism
- About 7-10% of whites have poor CYP2D6 metabolism
- 1-7% of whites and more than 25% of Ethiopians have gene duplications and are ultrarapid metabolizers.

Post T&A Pain Management

- Pain medication every 3 hours while awake.
- Alternate between:
  - Tylenol 15 mg/kg/dose
  - Ibuprofen 10 mg/kg/dose
- Meta-analysis shows no increased bleeding risk with ibuprofen.

QOL: Short Term After T&A

N=369
Age:
6.3 yrs (5.3-7.1)
Post op:
1.6-5.5 mos

### QOL: Long Term After T&A

N=91, Postop: 6-16.4 mos


### Improved Behavior After T&A

- Prospective study in 117 consecutive pts with SDB (clinical Dxn) undergoing T&A
- 61 boys, 56 girls
- Mean age 6.5 ± 3.1 yrs
- Quest day of surgery and 6 mos postop
- Complete data available on 71 pts


### Improved Behavior After T&A

- Conner’s Parent Rating Scale-Revised Short Form (CPRS-RS): 27 item questionnaire
- Pediatric Sleep Questionnaire (PSQ): 22 items, validated
  - PSQ includes 6 behavioral items
  - PSQm6: 16 non behavioral items


### Enuresis in OSA: Effect of T&A

- Aim of the study:
  - Determine the incidence of nocturnal enuresis (NE) among children with UAO
  - Evaluate the relationship between UAO and NE
  - Determine the effect of T&A on NE in patients with UAO


### Enuresis in OSA: Effect of T&A

- 321 children who underwent surgery for UAO
- 174 males, 147 females
- Age range: 5-16 years
- UAO diagnosis made on clinical basis
- Patients and their parents were interviewed 3 mos post-op and asked about enuresis

Enuresis in OSA: Effect of T&A

- 111/321 children (35%) had NE.
- 74/111 children with NE were evaluated post-op:
  - 47/74 (63%) reported complete relief of NE
  - 3/74 (4%) reported partial relief of NE (a min of 50% decrease in frequency of NE compared to pre-op)
  - 24/74 (33%) reported no change in NE


Residual OSAS after T&A

Retrospective Multicenter

AT Outcomes in OSAS


AT Outcomes in OSAS


AT Outcomes in OSAS

AT Outcomes in OSAS

- AHI <1/hr
  - 157/578, 27.2% (residual apnea 72.8%)
- AHI <5/hr
  - 453/578, 78.4% (residual apnea 21.6%)
- Hi risk (suggest repeat PSG post T&A):
  - Older children (>7yrs)
  - Obese children
  - Non obese with severe OSAS or asthma


Residual OSAS after T&A

Young children

Study Design

- Retrospective chart review of children under 3 who underwent T&A between October 1, 2002 and June 30, 2010.
- 283 patients underwent a preoperative PSG, with 70 of these patients having both a pre and postop PSG.
- Examined pre and postop PSGs and patient characteristics to measure residual OSA and identify predictors of incomplete resolution.

Demographics of Children < 3y with PSG

Characteristics of Children with Both Pre and Post-op PSG

Pre and Postop AHI
Pre and Postop Minimal O₂ Sats

Residual OSAS
- 15/70 (21%) had residual OSAS as defined by AHI>5.
- 41/70 (59%) had residual OSAS as defined by AHI>1.
- Compared preoperative characteristics between the children with complete resolution and those who had residual OSAS (defined by AHI>5).
- Similar results obtained if residual OSAS was defined as AHI>1.

Summary
- Our data shows that between 20-60% of children <3 yo had residual OSA after T&A.
- Severity of preop OSA was found to predict persistent disease after surgical intervention.

Preoperative Parameters with Residual OSAS defined by AHI >5

Residual OSAS after T&A
Obese children

T&A for OSAS in Obese Children
- 110 children
- Mean age= 8.4 yrs

**T&A for OSAS in Obese Children**


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**Anti-inflammatory Rx for Residual OSAS**

- Open label, non placebo controlled study.
- Children with AHI>1 but ≤5/hour 10-14 wks after T&A.
- Active Rx (n=22) received Montelukast and intranasal budesonide for 12 weeks.
- Control (n=14) received no Rx.


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**Residual OSAS after T&A**

- Other Medical Rx:
  - CPAP
  - Supplemental O₂
- Other Surgical Rx:
  - UPPP
  - Lingual tonsillectomy
  - Hyoid advancement
  - Somnoplasty of BOT
  - Repose suture advancement of BOT
  - Tracheotomy

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Thank you for your attention