Effect of Adenotonsillectomy (T&A) on the Lung Function of Children with Obstructive Sleep Apnea (OSA) and Asthma

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Disclosure

I have nothing to disclose.

Learning Objectives

1. To describe the pathophysiologic characteristics common to OSA and asthma

2. To recognize the importance of an objective measurement in the management of asthma

Background

Sleep tech calling the fellow at 3 am re: patients being evaluated for OSA

> Test is interrupted because of coughing. Patient has asthma, forgot to bring his meds.

> Another patient with OSA, possibly needs to be admitted for asthma exacerbation.

Background

- In the clinic:

- Mom says, “my child did not have asthma after his tonsils were taken out!”

- OSA - now recognized as prevalent in children
  - FTT, pulmonary HTN, neurocognitive impairment

- Asthma - highly prevalent in children known to be a major cause of disability

** Both are considered major public health burden
**Background**

**OSA and asthma**
- can worsen each other’s clinical course
- When one is present, entertain the presence of the other.
- Adult OSA- asthma improves with CPAP

**OSA in children**
- Adenotonsillectomy (T&A) – first line of treatment
- Does T&A improve asthma???

**Background**

- Review of Children's Hospital & Research Center Oakland (CHRCO) sleep lab census
- 37% of referred patients with OSA have asthma
- 48% of asthmatics with confirmed OSA needed T&A

**Objective:**
To determine if T&A improves the lung function of children with OSA and asthma

**Hypothesis:**
T&A improves the FEV1 of these children

**Predictor variable:**
T&A

**Outcome variables:**
FEV1, FEV1/FVC

**Secondary outcome variables:**
Airway reversibility
Asthma score

> Two pediatric studies showing improvement in asthma symptoms after T&A.

> But No data in the literature about looking at lung function in children with OSA and asthma

**OSA and Asthma Link**

- Neural receptors
- GERD
- Inflammation
- Leptin
- VEGF
- Weight gain

OSA

Upper airway collapse
from sleep disruption

Cross sectional area of pharynx

Nasal obstruction

Asthma
**Methods:**

> Combined prospective and retrospective cohort study

> IRB approved

**Criteria**

**Inclusion Criteria**
- 7-21 years old
- Physician diagnosed asthma
- Sleep study-diagnosed OSA
- Able to do spirometry

**Exclusion Criteria**
- Major medical illness
- Craniofacial anomalies
- Sickle cell disease
- CF, bronchiolitis obliterans, bronchiectasis
- Tracheostomy

**Polysomnographic Criteria of OSA**
- Apnea Hypopnea Index (AHI) $\geq 1$
- Multiple events of snoring, retractions, paradoxical breathing with either:
  - PET CO2 $>53$mmHG or
  - O2 sat $<92$

**Diagnostic Criteria for Asthma**
- Asthma symptoms (according to NAEPP guideline)
- Improvement with beta-agonist
- Use of asthma controllers
- Airway reversibility $\geq 12$

**Prospective**

**Treated**
- Repeat spirometry 6 weeks after T&A

**Untreated**
- Repeat spirometry

**Prospective**

- 34 recruited
- 18 eligible
- 1 dropped
- 17 completed
**Statistical Analysis**

- Sample size: N=34 Study has 35 patients. Power of 80% Detect 10% difference

Chi- Square, T-test
Logistic regression analysis, Paired T-test

**Baseline Characteristics**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>T&amp;A (+)</th>
<th>T&amp;A (-)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Rhinitis</td>
<td>12 (41.4%)</td>
<td>17 (58.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mean tonsil size Mallampati Class</td>
<td>1.83 (0.83)</td>
<td>1.94 (0.78)</td>
<td>0.702</td>
</tr>
<tr>
<td>Smoke exposure</td>
<td>3 (66.7%)</td>
<td>2 (33.3%)</td>
<td>0.567</td>
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<tr>
<td>Asthma classification</td>
<td>1 (25%)</td>
<td>3 (75%)</td>
<td>0.252</td>
</tr>
<tr>
<td>Intermittent Mild persistent Moderate persistent Severe persistent</td>
<td>1 (100%)</td>
<td>8 (42.1%)</td>
<td>5 (62.5%)</td>
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<tr>
<td>Age (years/SD)</td>
<td>10.33 (2.69)</td>
<td>11.65 (3.39)</td>
<td>0.224</td>
</tr>
<tr>
<td>Male</td>
<td>11 (52.4%)</td>
<td>10 (47.6%)</td>
<td>0.296</td>
</tr>
<tr>
<td>Ethnicity African American Hispanic Others</td>
<td>5 (38.5%)</td>
<td>5 (38.5%)</td>
<td>5 (55.6%)</td>
</tr>
<tr>
<td>8 (61.5%)</td>
<td>8 (61.5%)</td>
<td>4 (44.4%)</td>
<td></td>
</tr>
<tr>
<td>BMI (&gt;85%/SD)</td>
<td>89.6 (19.83)</td>
<td>87.15 (12.02)</td>
<td>0.653</td>
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<tr>
<th>Demographics</th>
<th>T&amp;A (+) N=15</th>
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<th>P-value</th>
</tr>
</thead>
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<tr>
<td>Airway reversibility</td>
<td>20.63 (26.24)</td>
<td>10.56 (24.07)</td>
<td>0.358</td>
</tr>
<tr>
<td>FEV1</td>
<td>82.73 (19.15)</td>
<td>85.35 (15.13)</td>
<td>0.654</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>80.27 (6.63)</td>
<td>81.05 (6.91)</td>
<td>0.738</td>
</tr>
<tr>
<td>Asthma score</td>
<td>5.29 (1.7)</td>
<td>3.40 (2.54)</td>
<td>0.109</td>
</tr>
</tbody>
</table>

### Is there improvement of asthma and lung function with T&A?

<table>
<thead>
<tr>
<th>Logistic Regression</th>
<th>OR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 improvement</td>
<td>0.197</td>
<td>0.127</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>7.59</td>
<td>0.662</td>
</tr>
<tr>
<td>Airway reversibility</td>
<td>0.86</td>
<td>0.138</td>
</tr>
<tr>
<td>Asthma score</td>
<td>2.41</td>
<td>0.684</td>
</tr>
</tbody>
</table>

### Is there improvement of OSA with T&A?

<table>
<thead>
<tr>
<th>Pediatric Sleep Score</th>
<th>Mean score change</th>
<th>P-value</th>
</tr>
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<tr>
<td>-0.315</td>
<td>-</td>
<td>0.019</td>
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### Course over time

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<tr>
<td>N=15</td>
<td>N= 20</td>
</tr>
<tr>
<td>Poorly controlled</td>
<td>9 (60%)</td>
</tr>
<tr>
<td>Well controlled with controller</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>No information on record</td>
<td>5 (33%)</td>
</tr>
</tbody>
</table>

### Discussion

**Two Previous retrospective pediatric studies:**

- OSA occurred in 65% of poorly controlled asthmatics
  
  Gozal LK et al Pediatric Pulmonol 2011;46:913-918

- T&A improves asthma (asthma score, frequency of hospital visits, use of asthma medications, acute exacerbations)
  
  Gozal LK et al Pediatric Pulmonol 2011;46:913-918
  Buscino RS et al Laryngoscope 2010; 120 Suppl S4 p221

### Conclusion

- T&A does not significantly improve lung function in asthma.

- There is continued risk of poor asthma control after T&A.

- Exacerbation occurred as early as 2 months up to 2 years post T&A.

- Why?
  - Asthma controller was discontinued.
  - Patients lost to follow after T&A and was seen again in the ED.
• Perception of symptom – unreliable
• Need for more objective assessment
• NAEPP’s goal for asthma:
  – Achieve adequate control
  – Treat co-morbid illnesses
  – Reduce consequence and severity over time

Limitation and Recommendations
1. Retrospective collection of data limits uniform assessment and measurements.
2. A prospective cohort study and a more extended observation period is recommended.

Discussion
• Mechanical Effects of OSA on the lower airways
  Upper airway resistance
  \[ \uparrow \text{Lung resistance} \quad \uparrow \text{Elastance (\downarrow \text{Compliance})} \]
  \[ \downarrow \text{Outward stretching of the airways} \] (narrowing of the airways)

  Bijouei et al (AJRRC 2002; 1165: 1055)

• Points against this:
  This mechanical load should improve once source of upper airway resistance is removed (T&A)
  CPAP only improved night time asthma symptom scores, but no significant improvement in the lung function. (Ciftci. Respiratory Medicine 2005; 99:529-534)

Discussion
• Systemic Inflammation
• United Airway Concept
  OSA \rightarrow upper airway inflammation \rightarrow activation of inflammatory mechanisms in the lower respiratory tract.
• OSA is associated with systemic inflammation and increased oxidative stress

Discussion
OSA
• TNF alpha, IL-6 and IL-1alpha were seen to be highly expressed in OSA-derived tonsils of children
  (Rakesh, Pediatric Research 2009 66 (4), 423)
• Increased levels of CRP in OSA
  (Ryan. Thorax 2009 64:631-636)
• Increased IL-8 in sputum of untreated OSA , correlated with AHI
  (Boulet. Eur Resp J 2009; 33:897)
**Discussion**

**Asthma**
- Elevated concentration of Leukotrienes
- Elevated CRP, IL-6 and IL-8
  
  (Wood. Chest 2012 11:1838)
- IL-6 elevated in mild to moderate allergic asthma and contributes to impaired lung function.
  
  (Neveu. Respiratory Research 2010, 11:28)

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**OSA**
- TNF-alpha
- IL-6
- IL-1 alpha
- IL-8
- CRP
- Leukotrienes

**Asthma**
- TNF alpha, IL-1
- IL-1 beta, IL-3
- IL-4, IL-5
- IL-8, IL-11
- IL-13, Eotaxin
- NGF, GMCSF
- RANTES, PGE-2
- CRP, NO
- Leukotrienes

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**Effect of treatment of OSA**
- Surgical treatment of the upper airway significantly decreased the levels of TNF alpha
- CPAP did not decrease CRP and IL-6.

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**OSA**
- TNF-alpha
- IL-6
- IL-1 alpha
- IL-8
- CRP
- Leukotrienes

**Asthma**
- TNF alpha, IL-1
- IL-1 beta, IL-3
- IL-4, IL-5, IL-6
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REFERENCES:

Thank you for your attention!