Acute Wheezing Emergencies: From Young to Old!

Little Wheezers in the ED: Managing Acute Pediatric Asthma
Talk Outline

- Case
- Delivery of bronchodilators
  - Meter-dose inhalers and spacers
  - Continuous nebulization via large volume nebulizer
- Repeat ipratropium
- Early oral corticosteroids
  - Controversy in pre-school wheeze
- Asthma education after discharge

Alberta Childhood Asthma Pathway
{www.AHSchildhoodpathways.com}
Case

- 15 mo. old child with recurrent episodes of wheeze
- 48 hours URTI symptoms
- Progressively worse, now audible wheeze and indrawing at home
- At presentation
  - cough, rhinorrhea, audible wheeze at rest
  - moderately severe indrawing
  - decreased inspiratory breath sounds.
  - HR 170, RR 46, T 38.2°C, O₂ Sat RA 86%
Delivery of bronchodilators
MDI/Spacers

Evidence: Cochrane Review 2013

- **MDI with spacer vs. Nebulizer**
- 33 RCTs ED & Community Settings
  - 1690 children & 701 adults
- 6 RCTs in-patients with acute asthma

- Children in ED
  - Admission RR 0.71 (95% CI: 0.47 to 1.08)
  - ED LOS mean difference -33 min (95% CI: -43 to -24)
  - Peak flow & FEV1 were similar
  - Heart Rate mean difference -5% baseline (95% CI: -8 to -2%)
Delivery of bronchodilators
MDI/Spacers

- At least as effective
  - Shorter ED stay
- More efficient
  - Better drug delivery
- Fewer side effects
  - Less drug deposited at back of mouth
- Less of infection risk
  - Optimal in era of SARs/H1N1
- Parents like it better
Evidence: *Cochrane Review 2011*

- Continuous vs. Intermittent Aerosols
  - 8 RCTs (1 RCT in children)
    - 461 patients total
  - Hospital Admission = RR: 0.68; 95% CI: 0.5 to 0.9
  - Greater improvement in pulmonary function
  - No difference in side-effects
Large Volume Nebulizer

Efficient Hi-Flo (8 L/min)
30 mL reservoir
1 hour of nebulization at 8 L/min
Optimal 2-3 μm particles

Mix
- three 5 mg (>20 kg) or 2.5 mg (<20kg) ampules of salbutamol
- three 250 mcg ampules of ipratropium
- plus enough normal saline to make 20 ml total volume
Delivery of bronchodilators
When to use which type?

MDI and Spacer
- Mild
- Moderate
- Severe?

Continuous nebulization via LVN
- Severe?
- Impending Respiratory Failure
Repeat ipratropium

Evidence: Cochrane Review 2013

- Addition of ipratropium to β2 agonist in children (18 months to 17 years)
- 15 RCTs, 2497 patients
  - Greater improvement in PFT
  - Admission – RR 0.73 (95% CI 0.63 to 0.85)
  - NNT 16
- Trend towards greater effect with increased treatment intensity and asthma severity
Repeat Ipratropium
Who should receive?

- Severe
- Moderate?
Early oral corticosteroids

Evidence: Cochrane Review, 2008

- Early steroids in ED (< 60 minutes)
  - 12 RCTs, 863 patients
    - Admission RR 0.4 (95% CI 0.2 to 0.8)
    - NNT 8

- 6 RCTs, 409 children (3 RCTs Oral)
  - Admission RR 0.4 (95% CI .2 to 0.9)
Controversy in pre-school wheezy children

- RCT, mild to moderate wheezing induced by URTI, 10 mo – 6 yrs
- 687 children admitted to hospital were Rx’ed with Prednisolone vs Placebo
  - ~35% first episode of wheeze
  - Mean PRAM score 4.3 (Mild = 1-4 and Moderate = 5-8
- Hospital LOS – Pred 11.0 hrs vs Plac 13.9 hrs
  - No significant difference in LOS or any other outcome

NEJM 2009;360:329-38
Why the difference?

- Different study populations
  - NEJM RCT included just pre-school-aged children
    - Cochrane SR included majority < 5 years
  - NEJM included children with 1st wheeze (~35%)
    - Cochrane SR included only children with prior wheeze
  - NEJM RCT had mild to moderate resp distress
    - Cochrane SR included children with moderate to severe resp distress
- Differences in co-treatment
  - NEJM were not treated with standardized & frequent β-agonists
    - Cochrane SR were mostly given frequent, aggressive β-agonists
Is combination therapy synergistic?

- Effectiveness of LABA/ICS
- RCT bronchiolitis showed synergy with epinephrine and dexamethasone
  - Relative 1/3 reduction in hospitalization rate
  - Other smaller bronchiolitis RCTs (3/4) showed benefit with combination therapy
- Basic science studies suggest molecular mechanism for synergy
Both enhance each other
Analysis of 10 specific steroid-inducible genes

- glucocorticoid-inducible leucine zipper (GILZ)
- Aminopeptidase N
- FKBP51
- PAI-1
- Tristetraprolin
- DNB5*
- p57KIP2*
- metallothionein 1X*
- MKP-1*
- RGS2 *

*These 5 genes show enhancement with combination therapy; the others do not.
Salbutamol 1 μM absence (open circle) or presence (black circle)
Effect of LABA addition time on transcription

Time of formoterol addition (hours)

Luciferase Activity (Fold)

N=3-5
Corticosteroids
Who should receive?

- Severe/Impending respiratory failure
- Moderate
- Mild?
Asthma education after discharge


- 38 RCTs, 7,843 children, educational interventions directed at children and/or parents who present to ED
- Subsequent ED visit, RR 0.73, 95% CI 0.65 to 0.81
- Hospital admission, RR 0.79, 95% CI 0.69 to 0.92
- Unscheduled MD visit, RR 0.68, 95% CI 0.57 to 0.81
Asthma Education
Who should receive?

- All or just more severe?
Questions?