Acute Asthma: Therapeutic options after inadequate response to inhaled salbutamol.

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Objectives

• Review current practice
• for acute severe/life threatening asthma
  - recommended
  - actual
Objectives

Consider the common options.
1. Nebuliser versus MDI and spacer?
2. Anticholinergics?
3. Intravenous salbutamol?
4. Intravenous magnesium?
5. Intravenous aminophylline?
Objectives

Consider less common options.
1. Nebulised magnesium
2. Leukotriene receptor antagonists?
3. Helium/oxygen mix (Heliox)?
3. CPAP?
Figure 1

Asthma mortality 1960-2007
all age groups

Deaths per 100,000

Year


Age standardised death rates
3 year moving average
Patient

- 3 yo acute asthma
- Known asthmatic,
- Previous admissions with asthma, not PICU
- Urti last 2 days, increasing cough and difficulty breathing for 24 hours
- Not responding at home to ventolin
Patient

• Child is alert.
• Talking in words
• 88% saturations in air
• Resp rate at 45
• Pulse rate 170
Patient

- Obvious bilateral subcostal recession
- Tracheal tug
- Bilateral wheeze with reduced air entry
Patient

- Diagnosis
- Acute asthma episode
- ? Severity
### Table 5. Initial assessment of acute asthma in children

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe and life-threatening*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered consciousness</td>
<td>No</td>
<td>No</td>
<td>Agitated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Confused/drowsy</td>
</tr>
<tr>
<td>Oximetry on presentation (SaO₂)</td>
<td>94%</td>
<td>94–90%</td>
<td>Less than 90%</td>
</tr>
<tr>
<td>Talks in</td>
<td>Sentences</td>
<td>Phrases</td>
<td>Words</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Unable to speak</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>Less than 100 beats/min</td>
<td>100–200 beats /min</td>
<td>More than 200 beats /min</td>
</tr>
<tr>
<td>Central cyanosis</td>
<td>Absent</td>
<td>Absent</td>
<td>Likely to be present</td>
</tr>
<tr>
<td>Wheeze intensity</td>
<td>Variable</td>
<td>Moderate to loud</td>
<td>Often quiet</td>
</tr>
<tr>
<td>PEF**</td>
<td>More than 60% predicted or personal best</td>
<td>40–60% predicted or personal best</td>
<td>Less than 40% predicted or personal best</td>
</tr>
<tr>
<td>FEV₁</td>
<td>More than 60% predicted</td>
<td>40–60% predicted</td>
<td>Less than 40% predicted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Unable to perform</td>
</tr>
</tbody>
</table>

*Any of these features indicates that the episode is severe. The absence of any feature does not exclude a severe attack.

**Children under 7 years old are unlikely to perform PEF or spirometry reliably during an acute episode. These tests are usually not used in the assessment of acute asthma in children.
### Appendix B: Guidelines for Assessing Acute Severity in Children

<table>
<thead>
<tr>
<th>PRESENTATION</th>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
<th>LIFE THREATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered consciousness</td>
<td>No</td>
<td>No</td>
<td>Agitated</td>
<td>Agitated, confused, drowsy</td>
</tr>
<tr>
<td>Physical exhaustion</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Talks in...</td>
<td>Sentences</td>
<td>Phrases</td>
<td>Words</td>
<td>Words</td>
</tr>
<tr>
<td>Accessory muscle use</td>
<td>No</td>
<td>Minimal</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Pulsus paradoxus*</td>
<td>Not palpable</td>
<td>May be palpable</td>
<td>Palpable</td>
<td>Palpable</td>
</tr>
<tr>
<td>Wheeze intensity</td>
<td>Variable</td>
<td>Moderate - loud</td>
<td>Often quiet</td>
<td>Often quiet</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>&lt;100</td>
<td>Tachycardia</td>
<td>Marked tachycardia</td>
<td>Marked tachycardia or bradycardia</td>
</tr>
<tr>
<td>Central cyanosis*</td>
<td>Absent</td>
<td>Absent</td>
<td>Likely to be present</td>
<td>Likely to be present</td>
</tr>
<tr>
<td>Oximetry on presentation (SaO2)</td>
<td>&gt;94%</td>
<td>90-94%</td>
<td>&lt;90%</td>
<td>&lt;90%</td>
</tr>
<tr>
<td>PEF or FEV1 (% predicted)**</td>
<td>&gt;60% predicted or personal best</td>
<td>40-60% predicted or personal best</td>
<td>&lt; 40% predicted</td>
<td>&lt;40% predicted</td>
</tr>
</tbody>
</table>

The child should be assigned to the most severe grade in which any feature occurs. If the child has received treatment prior to arrival, manage as more severe than the clinical signs indicate.

* Cyanosis and paradoxical pulse may be absent, but when present indicate severe obstruction.

** Patient may be incapable of performing test.

Adapted and modified from NSW Department of Health Guidelines 2004 and Asthma Management Handbook 2002
Our patient

• Severe
• Management?
Severe- Management

- Salbutamol- nebuliser vs MDI vs IV?
- Ipratropium- nebuliser vs MDI?
  Single vs multiple dose?
- Steroids- oral vs IV?
Table 6. Initial management of children with acute asthma

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mild episode</th>
<th>Moderate episode</th>
<th>Severe and life-threatening episode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission necessary</td>
<td>Probably not</td>
<td>Probably</td>
<td>Yes: consider intensive care</td>
</tr>
<tr>
<td>Supplementary oxygen</td>
<td>Probably not required</td>
<td>May be required. Monitor SaO2</td>
<td>Required. Monitor SaO2. Arterial blood gases may be required.</td>
</tr>
<tr>
<td>Salbutamol*</td>
<td>4–6 puffs (under 6 years) or 8–12 puffs (6 years or over). Review in 20 mins</td>
<td>6 puffs (under 6 years) or 12 puffs (6 years or over). If initial response inadequate, repeat at 20-minute intervals for two further doses. Then give every 1–4 hours.</td>
<td>6 puffs (under 6 years) or 12 puffs (6 years or over) every 20 mins for three doses in first hour. If life-threatening episode, use continuous nebulised salbutamol. If no response, bolus IV salbutamol 15 mcg/kg over 10 mins then 1 mcg/kg/min thereafter.</td>
</tr>
<tr>
<td>Ipratropium14</td>
<td>Not necessary</td>
<td>Optional</td>
<td>2 puffs (under 6 years) or 4 puffs (6 years or over) every 20 minutes x 3 doses in first hour or nebulised ipratropium</td>
</tr>
</tbody>
</table>

*In children with severe acute asthma that does not respond to initial treatment with inhaled SABA, bolus IV salbutamol 15 mcg/kg over 10 mins is effective and can avoid the need for continuous IV salbutamol and ICU admission.*

14
Severe and life-threatening episode

**Salbutamol**

6 puffs (under 6 years) or 12 puffs (6 years or over) every 20 mins for three doses in first hour.

If life-threatening episode, use continuous nebulised salbutamol.

If no response, bolus IV salbutamol 15 mcg/kg over 10 mins then 1 mcg/kg/min thereafter.
Severe and life-threatening episode

Ipratropium

2 puffs (under 6 years) or 4 puffs (6 years or over) every 20 minutes x 3 doses in first hour or nebulised ipratropium
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Consideration</th>
<th>Oral Prednisolone 1 mg/kg daily for up to 3 days</th>
<th>Oral Prednisolone 1 mg/kg/dose daily for up to 5 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (consider)</td>
<td></td>
<td>Methylprednisolone IV 1 mg/kg 6 hourly on Day 1, 12 hourly on Day 2 then daily</td>
</tr>
<tr>
<td>Magnesium¹¹</td>
<td>No</td>
<td>No</td>
<td>Magnesium sulphate 50% 0.1 mL/kg (50 mg/kg) IV over 20 mins then 0.06 mL/kg/hr (30 mg/kg/hr): target serum Mg 1.5–2.5 mmol/L</td>
</tr>
<tr>
<td>Aminophylline¹²</td>
<td>No</td>
<td>No</td>
<td>Only in Intensive Care: loading dose 10 mg/kg. Maintenance 1.1 mg/kg/hour if under 9 years or 0.7 mg/kg/hour if 9 years and over</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Not necessary unless focal signs present</td>
<td>Not necessary unless focal signs present</td>
<td>Necessary if no response to initial therapy or pneumothorax is suspected</td>
</tr>
<tr>
<td>Observations</td>
<td>Observe for 20 mins after dose</td>
<td>Observe for 1 hour after last dose</td>
<td>Arrange for admission to hospital</td>
</tr>
</tbody>
</table>
Severe and life-threatening episode

Steroids

Oral prednisolone
1 mg/kg/dose daily for up to 5 days

Methylprednisolone IV 1 mg/kg 6 hourly on Day 1, 12 hourly on Day 2 then daily
CHW
Magnesium- NAC

- Give magnesium sulphate 50%
  50mg/kg(0.1ml/kg) IV over 20 minutes
- Then 0.06ml/kg/hr (30mg/kg/hr)
- Target serum magnesium 1.5-2.5 mmol/L
- Excellent safety profile
- “Its place is similar to aminophylline”
Aminophylline- NAC

- If used, only given in an ICU
- Loading dose of 10mg/kg
- Maintenance dose of 1.1mg/kg/hr (<9yrs)
- 0.7mg/kg/hr (9 yrs +)
Current practice- Australasia

- Babl FE et al (PREDICT collaborative).
- “Paediatric acute asthma management in Australia and New Zealand: practice patterns in the context of clinical practice guidelines.”
- Archives of Disease in Childhood 93(4):307-12, 2008 Apr
- Compared Clinical Practice Guidelines (CPG’s)
- Compared reported physician management
- 11 PREDICT sites (9 Australia, 2 New Zealand)
Babl et al 2008- CPG’s

- Mild to moderate asthma similar management
  - salbutamol MDI and spacer and oral prednisone
- Severe to critical asthma-
- Differences common
  - Ipratropium use
  - Salbutamol delivery- MDI versus neb
Babl et al 2008- CPG’s

Differences also in-

• Use of intravenous aminophylline,
• Use of intravenous magnesium
• Dose of intravenous salbutamol
Babl et al 2008-reported physician management

- Predict site Consultants
- 78/83 responded
- Severe or critical asthma
- 79% preferred nebulisers
Babl et al 2008-reported physician management

- In critical asthma
  - 45% used IV aminophylline
  - 55% IV magnesium
  - 87% IV salbutamol with
  - 39 different dosing regimens
In our patient

• Option 1.
• Salbutamol
• MDI and spacer?
• Nebuliser?
Spacers vs Nebulisers : Cochrane

- Cates CJ, Crilly JA, Rowe BH.
- “Holding chambers (spacers) versus nebulisers for beta agonist treatment of acute asthma.”
- Cochrane Database of Systematic Reviews 2006 Issue 2.
- up to date 21 July 2008
Spacers vs Nebulisers- Cochrane

• 27 trials.
• 2295 children, aged over 2 years
• 614 adults
• Does not include life threatening asthma
Spacers vs Nebulisers: Cochrane

1. Hospital admission rates SAME (in adults and children)
2. ED length of stay significantly SHORTER with SPACER
   (-0.53 hours (95% CI; -0.62 to -0.44 hours - in children)
3. Peak flow and FEV1 = SAME
4. Pulse rate was LOWER with spacer (in children)
   (mean -6.27%)
Graded Evidence

- Robinson PD, Van Asperen P
- “Asthma in Childhood.”
- Pediatr Clin N Am 56 (2009);191-226
- Graded evidence based approach.
Graded Evidence (ATS)

- American Thoracic Society (ATS)
- Am J Respir Crit Care Med 2006; 174:605-14
- Grade of recommendation-
  Strong vs weak
- Quality of supporting evidence
  Very low quality to high quality
Graded evidence

- Strong recommendation, high quality evidence
- Benefits clearly outweigh harms and burdens or vice versa
- Consistent evidence from well performed randomised controlled trials or exceptionally strong evidence from unbiased observational studies
- Recommendations can apply to most patients in most circumstances.
- Further research is very unlikely to change our confidence in the estimate of effect.
Graded evidence

• Strong recommendation
• Moderate quality evidence
• Benefits clearly outweigh harms and burdens or vice versa
• Evidence from randomised controlled trials with important limitations etc
• Recommendation can apply to most patients in most circumstances
• Further research likely to have an important impact
Option 1- MDI vs nebuliser

• Cochrane (2008) – Authors conclusion

• “Metered–dose inhalers with spacer produced outcomes that were at least equivalent to nebuliser delivery.

• Spacers may have some advantages compared to nebulisers for children with acute asthma.”
Graded Evidence

• “Spacer delivery of inhaled medications is recommended for all but life threatening acute asthma.”
• Strong recommendation
• High quality of evidence
In our patient

• Option 2.
• Anticholinergic agents
• Ipratropium?
Anticholinergic agents

• Mechanism of action
• Relieves cholinergic bronchomotor tone and secretions
• Beneficial effect when added to beta 2 agonist therapy.
Anticholinergic agents

Cochrane

• Plotnick LH, Ducharme FM.
• “Combined inhaled anticholinergics and beta 2 agonists for initial treatment of acute asthma in children.”
• Cochrane Database of Systematic reviews 2000.
• Up to date 2000
Anticholinergic agents
Cochrane

• 8 studies
• Overall
• No benefit from a single dose on hospital admission rate
Anticholinergic agents - Cochrane

- Severe exacerbations
- School age children
- **Multiple doses reduced admission rates** by 25% (NNT 7: 95% CI 5-20)
- Reduced additional bronchodilator use by 19%
Option 2- Anticholinergics

• Cochrane- Author’s conclusion
• “Multiple doses in severe asthma exacerbation in school aged children”
Option 2- Anticholinergics

- Graded evidence
- “Multiple doses beneficial in severe asthma”
- **Strong** recommendation
- **Moderate** quality evidence
In our patient

• Option 3.
• Oral vs IV steroid?
Steroids

• Rowe B, Spooner C, Ducharme F, et al.
• “Early emergency department treatment of acute asthma with systemic corticosteroids.”
• Cochrane Database of Systematic Reviews 2001
• Up to date 2002.
Steroids- Cochrane

- Oral corticosteroids in the first hour of arrival,
- Reduces admission rates for children
  (3 RCT’s OR 0.24; 95% CI, 0.11-0.53)
Steroids- other

- Becker JM, Aorora A, Scarfone RJ.
- “Oral versus intravenous corticosteroids in children hospitalised with asthma. “
  J Allergy Clin Immunol 1999; 103:586-90
- Oral corticosteroids as effective as parenteral.
- Oral corticosteroids are more cost effective
Option 3- oral vs IV steroids

- Cochrane
- Use of steroids within 1 hr of presentation to an ED
  - Reduces hospital admissions
  - Benefits greatest in more severe asthma
  - Children respond well to oral steroids
Oral vs IV steroids

- Graded evidence - oral steroids
- “Beneficial in acute asthma not responding to short acting beta2 agonist.”
- **Strong** recommendation
- **High** quality evidence
In our patient

• Not improved
• After 3 x 20 minutely salbutamol and ipratropium MDI and spacer, oxygen
• Oral prednisone 1mg/kg tolerated
• Now what?
In our patient

- Option 4
- Aminophylline IV?
Aminophylline

- Bronchodilator
- Improved diaphragmatic contraction
- Inotropic and chronotropic effects on myocardium
Aminophylline

- Therapeutic levels 10-20mg/dl
- Perhaps at levels below 10mg/dl
- Toxicity above these levels.
- Cardiac dysrhythmias, convulsions
- Sudden death
- Nausea and vomiting
Aminophylline

- Mitra AAD, Bassler D, Watts K, Lasserson TJ, Ducharme F.
- “Intravenous aminophylline for acute severe asthma in children over two years receiving inhaled bronchodilators.”
- Cochrane Database of Systematic Reviews 2005. Updated 8 February 2007
Aminophylline

- 380 children, 7 trials, 1 trial with 163
- mean age 5-9.
- 6 studies participants unresponsive to nebulised short acting beta agonist and steroids,
- 2 studies, spirometry performed
- baseline FEV 1 35-45% predicted
Aminophylline

• Significant **improvement** in FEV1% over placebo 6-8 hrs, 12-18 hours and 24 hours, PEF% improved at 12-18 hrs

• **No significant** difference in length of hospital stay, symptoms, frequency of nebulisations and mechanical ventilation rates.
Aminophylline

- Insufficient data on oxygenation and duration of supplemental oxygen
- 3 fold increase in vomiting
- No sign diff in hypokalaemia, headaches, tremor, seizures, arrhythmias and deaths.
Aminophylline

- Yung M, South M.
- “Randomised controlled trial of aminophylline for severe acute asthma.”
  Archives of Disease in Childhood 1998:79 (5) 405-10.
- 163 children vs usual treatment
Aminophylline

- 10mg/kg infusion over 1 hour
- Then 0.7 mg/kg/hr (>10yrs)
- 1.1mg/kg/hr <10 yrs
- Greater improvement in spirometry
- Improved oxygenation at 30 hrs
- None intubated vs 5 in placebo group
British Thoracic Society 2003

- IV aminophylline loading dose 5mg/kg over 20 minutes followed by continuous infusion of 1mg/kg should be considered.
- Over 2 years,
- unresponsive to b2 agonist and steroids.
Aminophylline Adults - Cochrane

- Parameswaran K, Belda J, Rowe BH
- “Addition of IV aminophylline to beta 2 agonists in adults with acute asthma”
- Cochrane Database of Systematic Reviews 2000. Up to date 2000
Aminophylline Adults-
Cochrane

• 15 studies,
• No additional bronchodilation
• More frequent adverse effects-
vomiting, palpitations/arrhythmias
Option 4 - Aminophylline

• Graded evidence
• “Alternative to IV salbutamol in severe or life threatening asthma.”
• Strong recommendation
• Moderate quality of evidence
In our patient

- Option 5
- IV salbutamol?
Beta 2 agonists

- Relaxes bronchial smooth muscle by stimulating beta 2 receptors
- Also affects skeletal muscle and cardiac muscle leading to tremor and tachycardia
Current Practice (Babli et al 2008)

- **Bolus dosage:** 1.5-15 mcg/kg/min
  **duration:** 1-60 minutes

- **Continuous infusion rates**

- **CPG’s:** 0.5-15mcg/kg/min

- **Physician report:** 0.5-20mcg/kg/min
Current Practice (Babli et al 2008)

• Most frequently used bolus and continuous infusion combination
• 5mcg/kg/min over 60 minutes followed by
• continuous infusion 1-2 mcg/kg/min (13 physicians, 22%).
IV Salbutamol

• Travers AA, Jones AP, Kelly KD, Camargo CA, Barker SJ, Rowe BH.
• “Intravenous beta 2 agonists for acute asthma in the Emergency Department”
• Cochrane Database of Systematic Reviews 2005
• Up to date 2000
IV Salbutamol- Cochrane

- 584 patients, 15 studies, 3 with children
- IV selective or non selective beta 2 agonists versus placebo or inhaled b2 agonists or others
- IV beta 2 agonists conferred no advantage over comparator regimens
IV Salbutamol- Cochrane

- 3 paed studies
- Brown 1997 – 29 patients,
- Hambleton 1979- randomised not blinded
- Hussein1986- used reproterol
IV Salbutamol- Cochrane

• “Efficacy in the paediatric population remains unclear since too few paediatric clinical trials were identified”
IV Salbutamol

• Browne G. Lam L.
• “Single dose intravenous salbutamol bolus for managing children with acute severe asthma in the Emergency Dept: Reanalysis of data.”
• Pediatr Crit Care Med 2002;Vol 3:117-123
IV Salbutamol

- 50 with IV salbutamol
- 34 controls
- Ready for discharge from ED at 3.7 hrs earlier than controls
- Ready for discharge from hospital 9.7 hrs earlier than controls
- No significant side effects
Option 5- IV Salbutamol

- Graded evidence
- “Beneficial in severe or life-threatening asthma”
- Strong evidence
- Moderate quality of evidence
Aminophylline vs Salbutamol

- Roberts G et al
- “Intravenous salbutamol bolus compared with an aminophylline infusion in children with severe asthma: a randomised controlled trial”
- Thorax 2003;58:306-310
- Aged 1-16 years
Aminophylline vs Salbutamol

- RCT: n=44
- IV salbutamol bolus of 15mcg/kg over 20 minutes (n=18) then saline infusion
  - versus
  - IV aminophylline infusion 5mg/kg over 20 mins then 0.9mg/kg/hr (n=26),
- Level at 1hr, adjusted to 7-15mg/l
Aminophylline vs Salbutamol

• No difference in first 2 hours of treatment
• 30% **reduction** in hospital stay in the aminophylline group
Aminophylline vs Salbutamol

- Adverse events
- Nausea, vomiting, abdominal pain
- Salbutamol 22.2% vs aminophylline 36% - not significantly different
- But was this fair?
In our patient

• Option 6
• Continuous nebulised beta 2 agonist?
Continuous Inhaled Salbutamol

- Camargo CA, Spooner C, Rowe BH.
- “Continuous versus intermittent beta-agonists for acute asthma.”
- Cochrane Database of Systematic Reviews 2003.
- Up to date 13 Feb 2008,
Continuous Inhaled Salbutamol

- 8 trials, only 1 with children
- Continuous nebulisation, or >4 hrs nebs/hr
- Admission rate reduced
- Most benefit in severe
- Small but significant improvements in lung function at 2-3 hrs.
Continuous Inhaled Salbutamol

- Only one study with children
- Khine H, Fuchs SM, Saville Al.
- Continuous vs intermittent nebulised albuterol for emergency management of asthma.
- (n=70)
- No difference in hospitalisation rates or time in ED
Continuous Inhaled Salbutamol

- No graded evidence comment
- Consider continuous nebulised salbutamol
In our patient

• Option 7
• Inhaled magnesium?
Magnesium

• Bronchodilator
• Relaxes smooth muscles
• Reduction of neutrophilic burst associated with inflammation-antiinflammatory
• Blocks calcium ion influx to smooth muscles
Inhaled magnesium- Cochrane

• Blitz M, Blitz S, Beasely R, Diner B, Hughes R, Knopp JA, Rowe BH.
• “Inhaled magnesium in the treatment of acute asthma.”
• Cochrane Database of Systematic Reviews 2005
• Up to date 21 August 2005
Inhaled magnesium - Cochrane

• 6 trials 296 patients,
• 2 paediatric (n=102)
• Overall,
• non significant improvement in lung function
Inhaled magnesium - Cochrane

- Severe asthma - significant lung function difference (SMD: 0.55; 95% CI: 0.12-0.98)
- No change in hospital admission rates
- No adverse events
- Used in addition to beta 2 agonists
- No advantage used alone
Inhaled magnesium- Cochrane

• “Benefits in pulmonary function in severe asthma.”
Option 7- inhaled magnesium

- Graded evidence
- “unclear role in severe asthma”
- Weak recommendation
- Moderate quality of evidence
In our patient

- Option 8
- IV magnesium?
IV Magnesium-Cochrane

- Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr
- “Magnesium Sulfate for treating exacerbations of acute asthma in the emergency department”.
- Cochrane Database of Systematic Reviews, 2000
- Up to date 2000
IV Magnesium- Cochrane

• 7 trials, 5 adult, 2 paediatric
• 665 patients, paed patients n=78
• Non significant improvements in peak expiratory flow rates – all studies
• Hospital admission rate not improved
IV Magnesium - Cochrane

- In severe acute asthma,
- Peak expiratory flow rate improved by 52.3 L/min (95% CI 27-77.5)
- FEV1 improved 9.8% (95% CI 3.8-15)
- Hospital admission rate reduced
- (OR: 0.10, 95% CI 0.04-0.27)
- No adverse effects
IV Magnesium- other

- Cheuk DK, Chau TC. Lee SL.
- “A meta-analysis on intravenous magnesium sulphate for treating acute asthma.”
- Arch Dis Child 2005; 90:74-7
IV Magnesium- other

- Meta analysis of 5 paediatric RCT’s
- N=182, age 1-18 years
- Decreased hospitalisations
- (OR, 0.29; 95% CI 0.14-0.59; NNT 4) 95%CI -3-8)
- Improved pulmonary function and symptom scores
- Dose range 25-75mg/kg
IV magnesium

- One study shows no benefit
- 2 studies by same author
Option 8- IV magnesium

- Graded evidence
- “Beneficial in severe or life-threatening asthma.”
- **Strong** recommendation
- **High** quality of evidence
In our patient

- Option 9
- Helium/oxygen mixture?
Heliox

- Helium oxygen mixture (70-80%/20-30%)
- Lower gas density (1/3rd that of air)
- Decreases flow resistance
- Enhancing airway penetration
- Greater percentage of lung particle retention
Heliox - Cochrane

• Rodrigo GJ, Pollack CV, Rodrigo C, Rowe BH.
• “Heliox for nonintubated acute asthma patients.”
• Cochrane Database of Systematic Reviews.
• Up to date 1 August 2006
• 10 trials, 7 adults, 3 paediatric 544 patients.
• Paed trials used 70:30 mix
Heliox - Cochrane

- Improved pulmonary function in the severe subgroup, small number of studies
- No difference in risk of hospital admission
- One patient hypoxic on 70:30 mix
- Overall doesn’t support use of heliox
Heliox- other

• Kim IK, et al
• “Helium/Oxygen driven albuterol nebulisation in the treatment of children with moderate to severe asthma exacerbations: a randomised controlled trial.”
• Pediatrics 2005;116:1127-33
Heliox- other

- N=30, aged 2-18 yrs
- Moderate to severe exacerbations
- Clinical scores significant improved at 2-4 hrs
- Improved discharge rates at 12 hrs
Option 9- Heliox

- Graded evidence
- “may have a role in medication delivery but insufficient evidence to recommend currently”
- **Weak** recommendation
- **Moderate** quality of evidence
In our patient

• Option 10
• CPAP?
Option 10- CPAP

- Unloads fatigued ventilatory muscles
- Recruits more alveoli
- Used in COPD
- Used in hypoventilatory syndromes
CPAP- Cochrane

- Rowe BH, Wedzicha JA
- “Non invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma.”
- Cochrane Database of Systematic Reviews.
- Up to date 9 May 2005
CPAP- Cochrane

- One trial, 30 patients, adults
- Some improvement versus usual care
CPAP- Cochrane

- All significantly improved
- Hospitalization rate
- ED discharge
- Pulmonary function
- Respiratory rate
CHW PICU

- 5 years 2003-2007
- About 22000 ED presentations in NSW
- About 2000 CHW ED presentations/yr
- Admission diagnoses asthma 198
- CPAP 22
- CPAP and intubated - 2
- Intubated - 2
Option 10- CPAP

- Graded Evidence
- “may have a role in life-threatening asthma to prevent intubation.”
- **Weak** recommendation
- **Low** quality of evidence
In our patient

• Option 11
• Leukotriene receptor antagonists?
• (LTRA’s)
LTRA’s

• Inhibit part of the inflammatory response that is unaffected by steroids
• Some degree of bronchodilation
LTRA’s

- Harmanci K et al
- “Oral montelukast treatment of preschool aged children with acute asthma.”
- Ann Allergy Asthma Immunol 2006;96:731-5
LRTA’s

• RCT preschool children
• Benefit in respiratory rate
• and symptom scores
• up to 4 hrs
• when given with SABA first dose
Option 11- LRA’s

• Graded evidence
• “may have a benefit in mild to moderate asthma but further studies are required”
• **Weak** recommendation
• **Low** quality of evidence
In our patient

- Option 12?
- If they are not worse,
- Continue current treatment
- Escalate if deteriorates
- Wait it out
Summary

• Our patient
• A range of therapeutic options
At CHW

Severe

- Oxygen
- Salbutamol cont neb
- Atovent 20 min x 3
- Steroids PO or IV if not tolerating PO
- Cardiac & SaO₂ monitor

Get senior help

Life Threatening

- Oxygen
- Salbutamol cont neb
- Atovent 20 min x 3
- Steroids IV Q 6hr
- IV Salbutamol bolus 15mcg/kg over 10 min
- EUC, VBG, CXR
- Cardiac & SaO₂ monitor

Get senior help

Reassess improving?

Reassess improving?

Yes

No
Reassess Improving?

Yes

No

- Salbutamol IV infusion  5mcg/kg/min x 2 hours - notify PICU
- Salbutamol nebs  1 hrly
- Atenolol  4 hrly
- Steroids IV Q6hr
- Oxygen
- PICU consult if in extremis or may require CPAP
If still not improving

- Consider
- Increase salbutamol infusion
- Adding magnesium
- Adding aminophylline
- CPAP
If improving

- Cut the IV salbutamol to 1mcg/kg/min
- For one hour
- If still improved cease, if not continue
- If worse go back to 5 mcg/kg/min
- Go to PICU
What did I learn from this

• Spacers in severe asthma
• IV Magnesium- safe, (strong, high)
• IV Salbutamol - not a lot of evidence
• Is it because it works?
• Further research is required
Current study-RCT

- IV Salbutamol 5mcg/kg/min for 20mins
- Versus
- IV Magnesium 40mg/kg for 20 mins
- Versus
- Both
What did I learn from this

• Heliox, inhaled magnesium, LTRA’s may all develop a role
• Should we ride the boundaries?
What did you learn from this

• Something I hope