Steroids in Neonatology

Lloyd Tooke
Neonatologist
Groote Schuur Hospital / University of Cape Town
Cape Town
Cape Town
Cape Town
Endogenous vs exogenous

- Exogenous (synthetic)
  - Dexamethasone
  - Betamethasone
Adverse effects

- Heart rate
- Movement

- Immune
- Hyperglycaemia
- Hypertension
- Osteoporosis
- Adrenal insufficiency

- Growth
- GI bleed/perf
- Neurological
Levels of evidence

- Level 1: Systematic Reviews and Randomized Control Trials
- Level 2: Cohort Studies
- Level 3: Case-controlled Studies
- Level 4: Case Series
- Level 5: Case-based Reasoning or Expert Opinion

*Based on the Oxford Centre for Evidence-based Medicine – Levels of Evidence*
<table>
<thead>
<tr>
<th>Condition</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory distress</td>
<td>0.59</td>
<td>0.38 - 0.91</td>
</tr>
<tr>
<td>Ventilation</td>
<td>0.68</td>
<td>0.56 - 0.84</td>
</tr>
<tr>
<td>IVH</td>
<td>0.55</td>
<td>0.40 - 0.76</td>
</tr>
<tr>
<td>NEC</td>
<td>0.50</td>
<td>0.32 - 0.78</td>
</tr>
<tr>
<td>Early systemic infections</td>
<td>0.60</td>
<td>0.41 - 0.88</td>
</tr>
<tr>
<td>NOT CLD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term: SAFE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Which gestational age?

- Conventional $24^{+0}-33^{+6}$
- Pushing boundaries on both sides
22-24 weeks
34+1-36+6 weeks

- Some experts have concerns: little long term data
- Hypoglycaemia
- Increased benefit with c/s

- Many guidelines
Elective Caesarean section 37-39 weeks

• Reduction in RDS from 6.7% (86/1281) to 2.7% (33/1217)
Timing

- Maximum efficacy 2-7 days after the first dose.
- Efficacy is incomplete <24 hours from administration
- Declines after 7 days
2017 France
4500+
24-31 weeks
Single course – at least one dose

Figure 2. Association Between Timing of Antenatal Corticosteroids (ANS) and In-Hospital Mortality in 4594 Very Preterm Infants

Association of Short Antenatal Corticosteroid Administration-to-Birth Intervals With Survival and Morbidity Among Very Preterm Infants
Results From the EPICE Cohort
Which one?

- Dexamethasone
- Betamethasone

- Cheaper
- More follow up studies
- Less injections
Repeat dosages (booster/salvage)

- **Single repeat**
  - Seem to be safe
  - 7-14 days
  - Single dose/course?

- **Multiple repeat**
  - Growth
  - Lack of follow up
6 countries including Kenya, India and Argentina

‘Should the Cochrane Logo be accompanied by a health warning’
Findings and questions:

• For every 1000 women: an excess of 3.5 neonatal deaths
• Increased maternal infection

• Are they effective (or harmful) where:
  a) gestational age is unsure
  b) infectivity is high
  c) neonatal care is inadequate

WHO has advised caution
Response to article

- Not level 1 evidence
- Steroids likely to work just as well in low income settings
- Can decrease the need for level 2 care
- No robust evidence of increased infection
- Preterm deaths 1 million per year
- Potential 370 000 babies saved
- Studies are underway
Second line management

- Not enough evidence for meningitis

Low platelets
Haemangiomat
Meningitis
Laryngeal oedema

- In neonates, trends towards reduced rates of re-intubation or stridor could be demonstrated only in high-risk patients

0.25 mg/Kg/dose given IV ~ 4 hours prior to scheduled extubation and then every 8 hours for 3 doses total.
Hypocortisolaemia

HPA and CAH

Endocrine

HPA Axis
Hypoglycaemia

- Hydrocortisone
- Gluconeogenesis
- >12mg/kg/min
- Measure cortisol and insulin
- Short course (<48hrs)
Blood pressure

- Relative or absolute adrenocortical insufficiency
- Sick prems lower cortisol
- Beta-adrenergic receptor expression
Conclusions

• 4 small studies
• May be as good as dopamine
• Effective in refractory hypotension
• Long term data
Steroids

BPD

Hypotension

Hypoglycaemia

Upper airway

Endocrine

Low platelets
Haemangioma
Meningitis
Post-natal steroids for BPD/CLD

- They work
- They are potentially harmful
Post-natal steroids for BPD/CLD

- They work
- They are potentially harmful
The good and the bad ...
Steroid use

<table>
<thead>
<tr>
<th>Birth Wgt 10 Levels</th>
<th>Center (2016)</th>
<th>Network (2016)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>N</td>
</tr>
<tr>
<td>&lt; 501</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>501-600</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>601-700</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>701-800</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>801-900</td>
<td>0</td>
<td>54</td>
</tr>
<tr>
<td>901-1000</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>1001-1100</td>
<td>0</td>
<td>62</td>
</tr>
<tr>
<td>1101-1200</td>
<td>1</td>
<td>63</td>
</tr>
<tr>
<td>1201-1300</td>
<td>0</td>
<td>65</td>
</tr>
<tr>
<td>1301-1400</td>
<td>1</td>
<td>60</td>
</tr>
<tr>
<td>&gt; 1400</td>
<td>0</td>
<td>51</td>
</tr>
<tr>
<td>All</td>
<td>3</td>
<td>488</td>
</tr>
</tbody>
</table>
 Recommendation for postnatal steroids for prevention or treatment:

- **Early**
  - Dexamethasone:
    - Not recommended
  - Hydrocortisone (Premiloc)
    - Survival without BPD
    - ‘Safe’
    - <28 weeks
    - 10 days

- **Late**
  - >8 days if on persistent ventilatory support (>14d)
  - Low dose (DART)
  - Hydrocortisone may be safer
  - Role of inhaled still to be defined
Asante sana

Thank you

Baie Dankie

Enkosi Kakhulu