Apnoea In Prematurity
R Sinha

Citation

Abstract
Apnoea of prematurity remains one of the most challenging problems faced by any neonatologist. Despite better understanding of neonatal physiology there is still not much consensus regarding its management. This PowerPoint tries to give a basic idea of its pathophysiology as well as discuss various management options available. It concludes with a brief review of various evidences available & a hope that a widespread consensus based on best evidences will be available soon.

Figure 1
APNOEA OF PREMATURETY
• Definition of apnoea and its incidence
• Apnoea of prematurity
  Types
  Principle of Management
  Outcome

Figure 2
DEFINITION

Figure 3
INCIDENCE

Figure 4
Apnoea of Prematurity
It is a diagnosis of exclusion
• Commonest cause of apnoea in NICU
• Usually occurs between D2 - D7

• Resolves by 37 weeks Post Conceptional Age though recent reports have shown its persistence beyond term
Apnoea In Prematurity

Figure 5

TYPES
- Central Apnoea
  - Failure of inspiratory muscle following exhalation
- Obstructive Apnoea
  - Presence of inspiratory muscle activity without airflow
- Mixed Apnoea
  - Central + Obstructive during same episode

Figure 6

DIAGNOSIS OF APNOEA OF PREMATURELY
- Monitoring
- Proper history
- Detailed physical examination
- Investigation

Figure 7

INVESTIGATIONS
- Lab studies
  - FBC, ABG, Sepsis screen
  - Biochemistry (glucose, electrolytes)
- Radiographic studies - CXR, AXR, CrUSS
- Other Studies - EEG
  4 Channel Pneumogram
  Polysomnography

Figure 8

PRINCIPLES OF THERAPY

Figure 9

(A) PRIMARY CENTRAL RESPIRATORY CENTER DEPRESSION
- Fewer neuronal synapses
- Decreased neurotransmitter level
- Decreased CO2 sensitivity
  Correct infection and metabolic problems
  CNS stimulants

Figure 10

(B) ALTERED AFFERENT INPUT
- Decreased cortical traffic
  Increase afferent input (Cutaneous & Vestibular stimulation)
- Sleep state (REM)
Apnoea In Prematurity

Figure 11

(C) ABNORMAL OR HYPERACTIVE REFLEXES
- Heads paradoxical reflex
- Posterior pharyngeal reflex
- Abnormal Hering Breuer reflex
- Hyperactive laryngeal receptors

Avoid triggering reflexes
- Vigorous suction
- Hyperinflation
- Hyperventilation
- Lung collapse
- GOR

Figure 14

SUGGESTED TREATMENT PROTOCOL
- Exclude other causes of apnoea
- Treat any precipitating factor
- Stimulation (vestibular, cutaneous)
- Trial of nasal prong air or oxygen
- Stimulant drugs
- Trial of nasal CPAP
- Mechanical ventilation
  
  Intervention should occur in order of invasiveness and risk.

Figure 12

(D) HYPOXEMIA
- Immature hypoxic response
- Lung disease
- Hypotension
- Anaemia
- CCF

Treat underlying pathology
- Oxygen
- CPAP
- Transfusion

Figure 15

WHEN TO INITIATE TREATMENT

<table>
<thead>
<tr>
<th>TYPES OF APNOEA</th>
<th>TREATMENT INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self resolving attack</td>
<td>Frequent episodes (at least 1 hr over a period of 12-24 hrs) with desaturation and or bradycardia</td>
</tr>
<tr>
<td>Mild attack (requiring light touch)</td>
<td>Multiple episodes (six or more over 12 hrs period or 12 or more over 24 hrs)</td>
</tr>
<tr>
<td>Moderate attack (requiring reposition + oxygen)</td>
<td>Two or more episodes over 24 hrs.</td>
</tr>
<tr>
<td>Severe (requiring vigorous stimulation, PPV + oxygen)</td>
<td>One or more episode over 24 hrs</td>
</tr>
</tbody>
</table>

Figure 13

RESPIRATORY CONTROL

Figure 16

EXCLUSION OF PRECIPITATING FACTORS
- Infection
- Temperature regulation
- GI
  - NEC, GOR
- CNS
  - IVH, Seizure, Asphyxia
- Drugs
  - Prenatal, Postnatal
Apnoea In Prematurity

Figure 17

EXCLUSION OF PRECIPITATING FACTORS
- Metabolic
  - $\text{Ca}^+$, $\text{Na}^+$, Acidosis, $\text{Glucose}$
- CVS
  - CCF, Pulmonary oedema (PDA, Coarctation)
- Haematological
  - Anaemia
- Pulmonary
  - Oxygenation, Ventilation

Figure 20

METHYLE XANTHINE THERAPY
Mechanism of action
- Inhibits adenosine action
  - $\text{O}_2$ sensitivity
  - 1 Minute ventilation
- Direct stimulation of diaphragm

Figure 18

SUPPLEMENTAL LOW FLOW O2


Has been shown to be beneficial.
- Increases the overall duration & percentage of total sleep time (TST) spent in quiet sleep
- Increase respiratory stability & less apnoea & bradycardias

Figure 21

METHYLE XANTHINE THERAPY
Adverse effects
1. Excessive diuresis
2. Cerebral, intestinal & retinal blood flow
3. Cardiac output, Heart rate & cerebral metabolic rate
4. Altered biochemistry
   - Blood sugar, glycerol
5. GI dysfunction

Figure 19

CNS STIMULANTS
- METHYLXANTHINES: Aminophylline, Caffeine
- DOXAPRAM

Figure 22

CHOICE OF METHYL XANTHINE

[McArdle BA Neonatal Netw Dec;19(8):33-6, 2000 (7)]
- Caffeine is the drug of choice.
- Longer half life → Easier dosing schedule
- Stable plasma levels → Wide therapeutic index
- Less side effects → less rigorous monitoring
- More stable brain haemodynamic
- Better CSF penetration
**Apnoea In Prematurity**

**Figure 23**

**DOXAPRAM**
- Second line add-on drug.
- Useful in apnoea of prematurity unresponsive to methylxanthine
- **SIDE EFFECTS**
  - Uncommon with low dose
  - Hyperactivity, jitteriness, seizure, hyperglycaemia

**Figure 26**

**OTHER TREATMENT OPTIONS**
1. Inhalation of low (<1%) CO2
   - ↓ Frequency of apnoea
   - Improved oxygenation & ventilation
2. Intermittent mandatory ventilation
   Should be reserved for recurrent resistant & significant apnoea.

**Figure 24**

**CPAP**

*Mechanism of action*
- Splints up airway & prevents pharyngeal collapse
- Alteration of Hering Breuer reflex
- Stabilisation of chest wall

*CPAP is helpful in obstructive and mixed apnoea*

**Figure 27**

**EVIDENCE BASED APPROACH**

A) Henderson-Smart DJ et al., Cochrane Database Syst Rev., 2001;(3):CD0001402 (11)
- Treatment with methylxanthine reduced the frequency of apnoeic attacks and the use of mechanical ventilation between D2-D7

- No supportive evidence for prophylactic methylxanthine. Further studies in high risk prematures recommended.

**Figure 25**

**CPAP**

*Side effects*
- Barotrauma
- Nasal irritation
- Abdominal distension

**Figure 28**

**EVIDENCE BASED APPROACH**

- Low dose doxapram does have positive benefit as an add-on in resistant cases

- Though blood transfusion significantly reduces tachycardia & tachypnoea, but it had a little effect on apnoea of prematurity even in mod to severe anaemia.

E) Henderson-Smart DJ et al., Cochrane Database Syst Rev, 2002;(2):CD000373 (15)
- Kinaesthetic stimulation is not recommended
**CORRESPONDENCE TO**

Dr Rajiv Sinha Flat 2 Block 2 St Peter's Hospital Chertsey KT16 0RN UK e-mail: rajivsinha_in@yahoo.com

**References**