Apnoea In Prematurity

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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 PREMATURITY

- Definition of apnoea and its incidence
- Apnoea of prematurity
  Types
  Principle of Management
  Outcome

Figure 2

DEFINITION

(Coagulation factor activity in neonatal newborn 2002-2003 Paediatric Vol1 No 1; April 2003 pp 914-917 (1))
Cessation of breathing for at least 20s or for a shorter period of time if accompanied by bradycardia, desaturation, cyanosis or pallor

Figure 3

INCIDENCE

- 70%
- 20%
- 5%
- 1%

Figure 4

Apnoea of Prematurity

It is a diagnosis of exclusion

- Commonest cause of apnoea in NICU
- Usually occurs between D2 - D7

(Eckardt et al: Paediatrics Sep, 100(3 Pt 1):354-9 1997 (2))
- Resolves by 37 weeks Post Conceptional Age though recent reports have shown its persistence beyond term
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 8

**PRINCIPLES OF THERAPY**

Figure 6

**DIAGNOSIS OF APNOEA OF PREMATURITY**
- Monitoring
- Proper history
- Detailed physical examination
- Investigation

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 7

**INVESTIGATIONS**
(T.L. Gonzalez, Neonatology, Apnoea and periodic breathing, pp 494-8, Appleton & Lange, Connecticut, 1991)
- Lab studies
  - FBC, ABG, Sepsis screen
  - Biochemistry (glucose, electrolytes)
- Radiographic studies- CXR, AXR, Cranial USS
- Other studies - EEG
  - 4 Channel Pneumogram
  - Polysomnography

Figure 10

(B) ALTERED AFFERENT INPUT
- Decreased cortical traffic
  
Increase afferent input
(Cutaneous & Vestibular stimulation)

- Sleep state (REM)
(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

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

(D) HYPOXEMIA
- Immature hypoxic response
- Lung disease
- Hypotension
- Anaemia
- CCF
  - Treat underlying pathology
  - Oxygen
  - CPAP
  - Transfusion

WHEN TO INITIATE TREATMENT
- Types of apnoea
  - Self resolving attack
    - Frequent episodes (at least 1/hr over a period of 12-24 hrs) with desaturation and or bradycardia
  - Mild attack (requiring light touch)
    - Multiple episodes (six or more over 12 hrs period or 12 or more over 24 hrs)
  - Moderate attack (requiring reposition + oxygen)
    - Two or more episodes over 24 hrs.
  - Severe (Requiring vigorous stimulation, PPV + oxygen)
    - One or more episode over 24 hrs

RESPIRATORY CONTROL

EXCLUSION OF PRECIPITATING FACTORS
- Infection
- Temperature regulation
- GI
  - NEC, GOR
- CNS
  - IVH, Seizure, Asphyxia
- Drugs
  - Prenatal, Postnatal
Figure 17

**EXCLUSION OF PRECIPITATING FACTORS**

- Metabolic
  - \( [\text{Ca}], [\text{Na}], \text{Acidosis}, [\text{Glucose}] \)
- CVS
  - CCF, Pulmonary oedema (PDA, Coarctation)
- Haematological
  - Anaemia
- Pulmonary
  - Oxygenation, Ventilation

Figure 20

**METHYLE XANTHINE THERAPY**

**Mechanism of action**

- Inhibits adenosine action
  - \( \text{I}_2\text{O}_2 \) sensitivity
  - 1 Minute ventilation
- Direct stimulation of diaphragm

Figure 18

**SUPPLEMENTAL LOW FLOW O2**

*Stimac et al. N. Paediatrics. Nov; 110(6): p(1844-8), 2002 (5)*

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. \( \text{I}_2\text{Cerebral/intestinal & retinal blood flow} \)
3. \( \text{I}_3\text{Cardiac output, Heart rate & cerebral metabolic rate} \)
4. Altered biochemistry
   - Blood sugar, glycerol
5. GI dysfunction

Figure 19

**CNS STIMULANTS**

- METHYLXANTHINES: Aminophylline, Caffeine
- DOXAPRAM

Figure 22

**CHOICE OF METHYL XANTHINE**


- Caffeine is the drug of choice.
- \( \text{Rhee et al. Clinical Paed. June 29(9): p227-26,2000 (9)} \)
- Longer half life → Easier dosing schedule
- Stable plasma level → Wide therapeutic index
- Less side effects → Less rigorous monitoring
- More stable brain haemodynamic
- Better CSF penetration
DOXAPRAM

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

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.

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

EVIDENCE BASED APPROACH

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

B) Henderson-Smart et al., Cochrane Database Syst Rev. 2000;(2):CD0000432 (12)
   - No supportive evidence for prophylactic methylxanthine. Further studies in high risk preemies recommended.

CPAP

Side effects

- Barotrauma
- Nasal irritation
- Abdominal distension

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 et al., Cochrane Database Syst Rev, 2002;(2):CD000373 (15)
   - Kinaesthetic stimulation is not recommended
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References
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