The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynyk and Fineout-Overholt (2011).

I Evidence obtained from a systematic review of all relevant randomised control trials.

II Evidence obtained from at least one well designed randomised control trial.

III Evidence obtained from well-designed controlled trials without randomisation.

IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case-series

V Evidence obtained from systematic reviews of descriptive and qualitative studies

VI Evidence obtained from single descriptive and qualitative studies

VII Expert opinion from clinicians, authorities and/or reports of expert committees or based on physiology


<table>
<thead>
<tr>
<th>Reference</th>
<th>Evidence level (I-VII)</th>
<th>Key findings, outcomes or recommendations</th>
</tr>
</thead>
</table>
• Differential diagnosis  
• Clinical examination  
• Pharmacology                                                                                           |
• Further potential causes of apnoea                                                                                                                               |
| Doherty Chantal, MD. Causes and management of apnoea in the newborn. Powerpoint presentation.                        | VII                    | • Differences between apnoea in preterm and term infants  
• Potential causes of apnoea  
• The 3 types of apnoea  
• Expected onset of apnoea of prematurity and duration  
• Treatment and management possibilities after recognizing the type and cause of apnoea                             |
• High-dose caffeine reduces the need for respiratory support over the standard dose regimen of 5mg/kg/day, without apparent adverse outcomes in infant development, temperament or behavior at 2 years of age |
| Henderson-Smart, D.J., Steer, P.A. (2010). Caffeine versus theophylline for apnea in preterm infants. *Chochrane Database Syst Rev*. Jan 20; (1) | I                      | • Caffeine has similar short term effects on apnea/bradycardia as theophylline but caffeine has certain therapeutic advantages over theophylline.  
• Theophylline associated with higher rates of toxicity  
• Possibility that higher dose caffeine might be more effective in extremely preterm infants- needs further evaluation in randomized controlled trials |
• Examines benefits of caffeine citrate  
• Review of pharmacology and pharmacokinetics of caffeine  
• Review of current evidence-based practice for the use of caffeine citrate in treating apnoea of prematurity                              |
| Mohammed, S., Nour, I., Shabaan, A.E., Shouman, B., Abdel-Hady, H., Nasef, N. (2015). High vs low-dose caffeine for apnea of prematurity: a randomized controlled trial. *Eur J Pediatrics*. Jul; 174(7): 949-956 | II | • Shows that a higher dose of caffeine (40mg/kg load and 20mg/kg/day compared to the current standard of 20mg load and 10mg/kg/day) can decreases the chance of extubation failure and frequency of apnoeas in the preterm infant. |
• At flows of 2.5L/min in infants <2kg, HFNC can generate positive distending pressure which is as effective as NCPAP in the management of AOP |