Update on Neonatal Resuscitation

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Exercise: The Golden Minute

1st. Global Congress for Consensus in Pediatrics & Child Health
Paris, February 19th 2011
Birth Asphyxia- the Global Burden

136 mill newborn babies each year (WHO World Report)

Resuscitation

- 5-8 mill newborn infants need resuscitation
  - 5% moderate and
  - 1% (1.3 million) extensive resuscitation

- Optimal resuscitation methods may substantially reduce mortality
Maternal, and intrapartum related deaths

1.02 million intrapartum stillbirths

814,000 (0.56 – 0.99 million) neonatal deaths related to intrapartum events

Newborns with neonatal encephalopathy related to acute intrapartum events*

Children and adults long term impairment subsequent to acute intrapartum events*

Inadequate coverage and quality of intrapartum care
60 million births at home each year

Interventions in term or near term newborn in the delivery room

INTERVENTION

Assess baby’s response to birth

Keep baby warm
Position, clear airway, stimulate to breathe by drying
Give oxygen only if necessary

Establish effective ventilation
• bag & mask ventilation
• endotracheal intubation

• Provide chest compressions
• Adrenaline

Volume expansion

FREQUENCY

3 – 5/100
1/100-1/700

< 1/1000
6/10 000

1/12000
Neonatal Resuscitation

The following questions should be answered after every birth:

- Is the amniotic fluid clear of meconium?
- Is the baby breathing or crying?
- Is there a good muscle tone?
- Is the color pink?
- Was the baby born at term?

*If the answer is no to any of these consider resuscitation*
ILCOR Guidelines Newborn Resuscitation
Changes from 2000 -2005

• More freedom to choose any \( \text{O}_2 \) concentration at initiation of resuscitation

• Less need for routine intrapartum suctioning for infants born with meconium staining of amniotic fluid

• Occlusive wrapping of very low birth weight infants < 28 weeks to reduce heat loss

• Preference for the IV vs endotracheal route for adrenaline/epinephrine

• Increased parental autonomy at the threshold of viability
Birth

Term Gestation? Amniotic fluid clear? Breathing or crying? Good muscle tone? Color pink?

No

Evaluate respirations, heart rate and color

A

Apneic or HR <100 HR > 100

B

Provide positive pressure ventilation

HR < 60 HR > 60

C

Continue positive pressure ventilation
Administer chest compression

HR < 60

D

Administer Adrenaline and/or volume

Yes

If the baby is crying

Provide routine care
Provide warmth
Clear airway if needed
Dry
Assess color

Saugstad 2006
Adapted from ILCOR 2005
Is 30 seconds sufficient time before you move from ventilation to chest compressions?

Pulm. Gas Exchange in term infants delivered vaginally or by caesarean section

Palme-Kilander, Tunell
Arch Dis Childhood, 1993
ILCOR Guidelines Newborn Resuscitation
Changes from 2005 - 2010

• Timing the first 60 seconds only
• Progression to the next step following initial evaluation is defined by heart rate and respiration
• For babies born at term it is best to begin resuscitation with air rather than 100% oxygen
• Evidence does not support or refute routine endotracheal suctioning of infants born through meconium-stained amniotic fluid, even when the newborn is depressed
• Chest compression- ventilation ratio 3:1 unless the arrest is known to be of cardiac etiology. Then higher ratio should be considered (15:2)
• Hypothermia in moderate to severe HIE
ILCOR Neonatal Resuscitation Guidelines 2011

3 questions:
Term, Breathing, Tone

Timing: First 60 seconds only

Start with air, consider SpO2

Perlman J et al, Circulation 2010;122 (Suppl 2) S516-538
<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Airways</td>
<td>Initial steps of stabilisation (assess the airways, positioning, stimulating, dry and provide warmth)</td>
</tr>
<tr>
<td><strong>B</strong> Breathing</td>
<td>Ventilation (including bag-mask or bag-tube ventilation)</td>
</tr>
<tr>
<td><strong>C</strong> Circulation</td>
<td>Chest compressions</td>
</tr>
<tr>
<td><strong>D</strong> Drugs</td>
<td>Medications or volume expansion</td>
</tr>
</tbody>
</table>

ILCOR/AHA 2005

*Four Categories*
A: Airways  
Stabilisation and suctioning

• A vigorous newborn who starts to breath within 10-15 seconds does not need suctioning routinely

• Deep suctioning should be avoided especially the first 5 min of life. It may induce apnea, bradycardia and bronchospasm

• If suctioning, always suction the mouth before through the nose to minimize risk of aspiration
Suctioning of upper airways

• Routine intrapartum oropharyngeal and nasopharyngeal suctioning for infants born with clear or meconium stained amniotic fluid is no longer recommended

ILCOR 2010
The most important is to ventilate the lungs. Training is needed.

Increasing heart rate is the primary sign of effective ventilation during resuscitation.

What is an adequate heart rate?

Observe also:

- Improving color
- Spontaneous breathing
- Improving muscle tone

Check these signs of improvement after 30 seconds of PPV. This requires the assistance of another person.

The 50th percentile for heart rate is 99 bpm at one minute. Dawson et al, 2010.
Assessment if resuscitation is stepped up

3 vital characteristics

• Heart rate
• Respirations
• State of oxygenation

"The most sensitive indicator of successful response to each step is an increase in heart rate"
Sustained inflation (SI) ?

- In babies with GA < 29 weeks SI is tested out
- Different models for instance 5 seconds x 3 or 15 seconds with increasing PIP
- Still experimental
Initial breaths and pressures

• Initiation of intermittent positive-pressure ventilation at birth can be accomplished with either shorter or longer inspiratory times.

• Initial peak inflating pressures needed are variable—start with 20 cm H2O may be effective but 30–40 cm H2O may be needed.

• PEEP is likely to be beneficial.

Heart rate increase is more important to observe than chest rise.
Assisted ventilation devices

Ventilation of the newborn can be performed effectively with a flow-inflating, a self inflating bag or a pressure limited T-piece resuscitator.
Is it easy to ventilate a newborn with bag and mask?

< 32 weeks
Face mask (Laerdal) PPV
Mask PPV by either
T-Piece (Neopuff)
Or self inflating (Laerdal) bag
Florian Respiratory Monitor
(Pressure and flow)

Schmolzer G et al ADC-FN 2010
Face mask leaks % of inspired tidal volume

Schmolzer G et al ADC-FN 2010
C: Circulation

Neonatal Resuscitation

Chest compressions - indication

Chest compressions should be performed if the heart rate is < 60 beats/minute, despite adequate ventilation for 30 seconds. 3:1 ratio - that is 90:30

ILCOR 2005

0.8 per 1000 term or near term infants
2-10% in preterm infants

No Human data have identified an optimal compression to ventilation ratio for cardiopulmonary resuscitation in any age

2 thumb technique is more efficient than the 2 finger technique
Lower 1/3 of sternum, pressure to one third of posterior anterior diameter to generate pulses

Goals: Reperfuse the heart (obtain diastolic pressure)
Reperfuse the Brain

Wyckoff et al, Pediatrics 2005;115:950-955
Finer et al Pediatrics 1999;104:428-34
Wyckoff and Berg Seminars Fetal and Neonatal Med 2008;13:410-415
Newborn hypoxic piglets with cardiac arrest:

Time to return of spontaneous circulation after cardiac arrest

Solevaag A et al Neonatology 2010
D: Drugs

Neonatal Resuscitation
Adrenaline/Epinephrine dose

If adequate ventilation and chest compressions have failed to increase heart rate to > 60 bpm, then it is reasonable to use adrenaline despite the lack of human neonatal data.

The recommended dose of adrenaline is 0.1 to 0.3 mL/kg IV of a 1:10,000 solution (0.01 to 0.03 mg/kg) repeated every 3 to 5 minutes as indicated. – Not evidence based

Higher doses cannot be recommended and may be harmful.
If the Endotracehal route is chosen use higher doses (0.05-0.1 mg/kg)

*No different dose for premature infants*
Adrenaline for newborn resuscitation

- 6:10 000 newborns
- 0.1-0.3 mL/kg 1:10 000 adrenaline solution
- 1st dose at earliest at 6 min of life

*Barber et al Pediatrics 2006;118:1028-1034*
Volume expansion

Volume expansion may be accomplished with (1) isotonic crystalloid such as normal saline or Ringer’s lactate or (2) O-negative blood. 10ml per kg, can be repeated

Needed in 1:12000 term or near term infants (Perlman et al)

Insufficient evidence to support routine use

In infants with no blood loss.
Treatment Recommendation

In term infants receiving resuscitation at birth with positive pressure ventilation, it is best to begin with air rather than 100% oxygen. If despite effective ventilation there is no increase in heart rate or if oxygenation (guided by oximetry) remains unacceptable, use of a higher concentration of oxygen should be considered.
Before 1998

Resuscitation World Map
Term or Near Term infants

100% O2

Resuscitation of Asphyxiated Newborn Infants With Room Air or Oxygen: An International Controlled Trial: The Resair 2 Study
Ola Didrik Saugstad, Terje Rootwelt and Odd Aalen
Pediatrics 1998;102:e1
A changing attitude to the use of oxygen for newborn resuscitation

1992 (ILCOR): 100% $O_2$ should be used, it is not toxic- no reason to be concerned

2000 (ILCOR/AAP): 100% $O_2$ should be used, however if $O_2$ is not available use room air

2005 (ILCOR/AAP): The optimal $O_2$ conc is not known for newborn resuscitation
There is no reason to change the initial $O_2$ concentration

2010 (ILCOR/AAP) ...that adverse outcomes may result from even brief exposure to excessive oxygen during and following resuscitation (AAP)

In term infants receiving resuscitation at birth with positive-pressure ventilation, it is best to begin with air rather than 100% $O_2$ (ILCOR)
ILCOR and AAP October 18th 2010
Low oxygen approach
American Academy of Pediatrics 2010

FIGURE.
Newborn Resuscitation Algorithm.

Targeted Preductal $\text{SpO}_2$
After Birth

- 1 min: 60%-65%
- 2 min: 65%-70%
- 3 min: 70%-75%
- 4 min: 75%-80%
- 5 min: 80%-85%
- 10 min: 85%-95%

Term gestation? Breathing or crying? Good tone?

- Yes, stay with mother
- No

Warm, clear airway if necessary, dry, stimulate

HR below 100, gasping, or apnea?

- Yes
- No

Labored breathing or persistent cyanosis?

- Yes
- No

PPV, $\text{SpO}_2$ monitoring

HR below 100?

- Yes
- No

Take ventilation corrective steps

- Consider: Hypovolemia, Pneumothorax

HR below 60?

- Yes
- No

Consider intubation Chest compressions Coordinate with PPV

Postresuscitation care

IV epinephrine
Development in SaO2 after birth

- At 5 minutes 50% have SaO2 90%
- Preductal values are approx 9% higher than postductal the first 10 minutes of life

Lower saturations in:
- Preterm
- C-section

Development of SaO2 first 10 min of life

Dawson et al, Pediatrics 2010
FIGURE
Newborn Resuscitation Algorithm.

Targeted Preductal $\text{SpO}_2$
After Birth

<table>
<thead>
<tr>
<th>Time</th>
<th>Percentile Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 min</td>
<td>60%-65%</td>
</tr>
<tr>
<td>2 min</td>
<td>65%-70%</td>
</tr>
<tr>
<td>3 min</td>
<td>70%-75%</td>
</tr>
<tr>
<td>4 min</td>
<td>75%-80%</td>
</tr>
<tr>
<td>5 min</td>
<td>80%-85%</td>
</tr>
<tr>
<td>10 min</td>
<td>85%-95%</td>
</tr>
</tbody>
</table>

FIGURE 1
Third, 10th, 25th, 50th, 75th, 90th, and 97th $\text{SpO}_2$ percentiles for all infants with no medical intervention after birth.
Meta analysis
Air Vs 100% O₂ in newborn resuscitation

• All studies show better outcome with 21% O₂
  N= 10, Infants 2134
  Neonatal Mortality 12.8 Vs 8.2% p < 0.001
  RR Neonatal death 0.69 (0.54-0.82)

• Randomised studies better outcome with 21% O₂
  N= 4, Infants 449
  Neonatal Mortality 3.9 Vs 1.2 % p < 0.01
  RR Neonatal death 0.32 (0.12- 0.82)

Saugstad, Ramji, Soll, Vento, Neonatology 2008
Neonatal Mortality after 21% or 100% O2 resuscitation
10 studies including 2134 infants

814,000 asphyxic deaths:
252,000 (95% CI: 146,000 - 374,000) saved lives

# Effect of Some Therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Estimated Potential Saved Lives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal steroids</td>
<td>500,000</td>
</tr>
<tr>
<td>Surfactant*</td>
<td>250,000</td>
</tr>
<tr>
<td>Respirator**</td>
<td>625,000</td>
</tr>
<tr>
<td>Air resuscitation</td>
<td>250,000</td>
</tr>
<tr>
<td>Hypothermia***</td>
<td>40,000</td>
</tr>
<tr>
<td>Oral Rehydration Therapy</td>
<td>2000,000</td>
</tr>
</tbody>
</table>

*0.5% < 29 weeks, 50% survival without surfactant, 90% survival with
** 1% in need of ventilator 50% survival
*** 1 per 10000 needs hypothermia, 30% reduction in mortality
Metabolomic Analyses of Plasma Reveals New Insights into Asphyxia and Resuscitation in Pigs

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¹ Department of Pediatric Research, Oslo University Hospital, Rikshospitalet, University of Oslo, Norway, ² Department for Surgical Research, Oslo University Hospital, Rikshospitalet, University of Oslo, Norway, ³ BIOCRATES Life Sciences AG, Innsbruck, Austria, ⁴ Innsbruck Medical University, Department of Pediatrics IV, Division of Neuropediatrics and Inherited Metabolic Disorders, Innsbruck, Austria, ⁵ Department of Pediatrics I, Neonatology, University Essen, Essen, Germany

Background: Currently, a limited range of biochemical tests for hypoxia are in clinical use. Early diagnostic and functional biomarkers that mirror cellular metabolism and recovery during resuscitation are lacking. We hypothesized that the quantification of metabolites after hypoxia and resuscitation would enable the detection of markers of hypoxia as well as markers enabling the monitoring and evaluation of resuscitation strategies.

Methods and Findings: Hypoxemia of different durations was induced in newborn piglets before randomization for resuscitation with 21% or 100% oxygen for 15 min or prolonged hyperoxia. Metabolites were measured in plasma taken before and after hypoxia as well as after resuscitation. Lactate, pH and base deficit did not correlate with the duration of hypoxia. In contrast to these, we detected the ratios of alanine to branched chained amino acids (Ala/BCAA; $R^2_{adj}=0.58$, q-value<0.001) and of glycine to BCAA (Gly/BCAA; $R^2_{adj}=0.45$, q-value<0.005), which were highly correlated with the duration of hypoxia. Combinations of metabolites and ratios increased the correlation to $R^2_{adjust}=0.92$. Reoxygenation with 100% oxygen delayed cellular metabolic recovery. Reoxygenation with different concentrations of oxygen reduced lactate levels to a similar extent. In contrast, metabolites of the Krebs cycle (which is directly linked to mitochondrial function) including alpha keto-glutarate, succinate and fumarate were significantly reduced at different rates depending on the resuscitation, showing a delay in recovery in the 100% reoxygenation groups. Additional metabolites showing different responses to reoxygenation include oxysterols and acylcarnitines ($n=8–11$, q<0.001).

Conclusions: This study provides a novel strategy and set of biomarkers. It provides biochemical in vivo data that resuscitation with 100% oxygen delays cellular recovery. In addition, the oxysterol increase raises concerns about the safety of 100% O₂ resuscitation. Our biomarkers can be used in a broad clinical setting for evaluation or the prediction of damage in conditions associated with low tissue oxygenation in both infancy and adulthood. These findings have to be validated in human trials.
Alpha keto-glutarate
Succinate
Fumarate

Normalised faster in room air than in O2
Indicating poor mitochondrial function
In 100% O2
Asphyxia

End of asphyxia

Resuscitation

End of resuscitation

Increase during asphyxia
Alpha-ketoglutarate 266%
Succinate 8000%
Fumarate 587%
Lactate 850%

Higher Fumarate, Succinate and alpha keto-glutarate in O2 groups indicate mitochondrial dysfunction
<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>0</td>
<td>&lt;100</td>
<td>≥100</td>
</tr>
<tr>
<td>Respiration</td>
<td>0</td>
<td>Weak, irregular</td>
<td>Good cry</td>
</tr>
<tr>
<td>Reaction*</td>
<td>0</td>
<td>Slight</td>
<td>Good</td>
</tr>
<tr>
<td>Colour</td>
<td>Blue or pale</td>
<td>All pink, limbs blue</td>
<td>Body pink</td>
</tr>
<tr>
<td>Tone</td>
<td>Limp</td>
<td>Some movement</td>
<td>Active movements</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>limbs well flexed</td>
</tr>
</tbody>
</table>

* Reaction to suctioning
Newborn resuscitation

Current challenges

• Optimal heart rate response not established
• Ratio ventilation:chest compession not established
• Sustained inflation?
• Optimal PEEP not established
• Optimal pCO₂ not established
• Optimal adrenaline dose not established
• Optimal FiO₂ and other procedures for ELGANS not established
• Better biochemical asphyxiation indicators needed
• Time for a revised Apgar Score?
Thank you for your attention!

Comments – Questions?