Should parenteral nutrition solutions for preterm infants be photoprotected?

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Introduction (1)

**Weak anti oxidant system**
- Immaturity
- Low maternal milk intakes

**High oxidant load**
- \( O_2 \)
- Transfusion
- Sepsis
- Parenteral Nutrition

Preterm infant
Introduction (2)

- Multivitamins are the main source of peroxides in parenteral nutrition solutions (Lavoie 1997).
- Peroxides are cytotoxic and bactericidal in vitro.
Photoprotection of parenteral nutrition solutions

1. peroxides content \((\text{Lavoie 1997, Laborie 1998})\)
2. biochemical benefices \((\text{Lavoie 2002, Chessex 2010})\)
3. nutritional benefices \((\text{Khashu 2006})\),
4. histological benefices in an animal model \((\text{Lavoie 2004})\)
5. no effect on bronchopulmonary dysplasia or death in very low birth weight infants \((\text{Laborie 2014})\)
Hypothesis and aim

- **Hypothesis**: For some preterm infants, death is induced by the imbalance between the oxidant load and the antioxidant defenses.
- **Photoprotection may decrease mortality in very low birth weight infants.**

- **Aim**: To evaluate the consequences of photoprotection of parenteral nutrition solutions on mortality of very low birth weight infants.
Methods

1. Identification of eligible trials through electronic databases


3. Meta-analysis of mortality data at 36 wks GA or hospital discharge
Results (3)

34 publications identified

→ 17 titles excluded due to absence of relevance

17 abstracts examined

→ 5 reviews excluded

12 studies assessed

→ 7 titles excluded due to multiple publications (same population)

5 studies retained

→ 1 title excluded due to absence of randomization

4 publications included in meta analysis
### Results: Population

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Randomization</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sample size (n)</td>
<td>77</td>
<td>80</td>
<td>56</td>
<td>587</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>56</td>
<td>54</td>
<td>53</td>
<td>50</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>$27 \pm 2$</td>
<td>$31 \pm 2$</td>
<td>$26 \pm 1$</td>
<td>$28 \pm 1$</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>$915 \pm 240$</td>
<td>$1588 \pm 366$</td>
<td>$775 \pm 161$</td>
<td>$969 \pm 238$</td>
</tr>
<tr>
<td>Days of TPNa/PNb</td>
<td>$9 \pm 8a$</td>
<td>$11 \pm 8a$</td>
<td>$11 \pm 1a$</td>
<td>$28 \pm 14b$</td>
</tr>
<tr>
<td>Mechanical Ventilation (%)</td>
<td>70</td>
<td>72</td>
<td>66</td>
<td>82</td>
</tr>
<tr>
<td>Mortality at 36 weeks (%)</td>
<td>5</td>
<td>32</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Light exposed</td>
<td>Light protected</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>---------------</td>
<td>----------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 36 weeks or hospital discharge</td>
<td>Dead</td>
<td>Alive</td>
<td>Dead</td>
<td>Alive</td>
</tr>
<tr>
<td>J Pediatr, 2007</td>
<td>3</td>
<td>36</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>JPGN, 2009</td>
<td>17</td>
<td>23</td>
<td>9</td>
<td>31</td>
</tr>
<tr>
<td>FRBM, 2010</td>
<td>7</td>
<td>31</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>JPEN, 2014</td>
<td>25</td>
<td>269</td>
<td>16</td>
<td>277</td>
</tr>
<tr>
<td>Total</td>
<td><strong>52</strong></td>
<td><strong>359</strong></td>
<td><strong>28</strong></td>
<td><strong>361</strong></td>
</tr>
</tbody>
</table>
Results

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LP Events</th>
<th>Total Events</th>
<th>LE Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>J Pediatr 2007</td>
<td>1</td>
<td>38</td>
<td>3</td>
<td>39</td>
<td>6.6%</td>
<td>0.32 [0.03, 3.26]</td>
</tr>
<tr>
<td>Free Radic Biol Med 2010</td>
<td>2</td>
<td>18</td>
<td>7</td>
<td>38</td>
<td>9.2%</td>
<td>0.55 [0.10, 2.98]</td>
</tr>
<tr>
<td>J Pediatr Gastro Ntr 2009</td>
<td>9</td>
<td>40</td>
<td>17</td>
<td>40</td>
<td>30.2%</td>
<td>0.39 [0.15, 1.04]</td>
</tr>
<tr>
<td>JPEN 2014</td>
<td>16</td>
<td>293</td>
<td>25</td>
<td>294</td>
<td>54.1%</td>
<td>0.62 [0.32, 1.19]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>389</strong></td>
<td><strong>411</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>0.53 [0.32, 0.87]</strong></td>
</tr>
</tbody>
</table>

Total events: 28, 52

Heterogeneity: $\chi^2 = 0.77$, df = 3 ($P = 0.86$), $I^2 = 0\%$

Test for overall effect: $Z = 2.51$ ($P = 0.01$)
Discussion

- Udge decrease in mortality
- Mechanisms?
  - Balance oxidant anti oxidant?
  - Bioavailability of nutrient and vitamins?
  - Direct toxicity?
- Long term outcome of survivors?
Discussion

Methods

- Opposite with Sherlock study (*pediatrics*, 2009)
- Complete versus partial photoprotection
- Complexity of total photoprotection

- Feasibility?
Conclusion

- Is it **ethical** to infuse now **unprotected** parenteral nutrition solutions to the **most immature** preterm infant?
- What happened in other populations with compromised oxidant/antioxidant balance???
Perspectives

- Can we find a way to minimize the infused oxidant load which is less time consuming and less expensive?

- Can we optimize the antioxidant defenses of the most immature preterm infants?