Perinatal bacterial infection: screening of vertical transmitted infections

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Portugal
Hospital Dona Estefânia, Lisbon. Founded in 1860
Summary

- The rational for screening
- Why some countries have a non-screening policy
- Risk factors: a very useful complement of screening
- Conclusions
The burden of the problem

- Incidence of early-onset neonatal infection may vary between 0.98 to 1.2 or 1.3/1000 live births (Stoll B, Kuhn P, Lin C-Y).
- Lethality vary between 1.8% and 16% ((Kuhn, Stoll).
- Mortality depends on gestational age and isolates: 30% in newborns 25-28 weeks; 33% in E. Coli vs 9% for GBS (Barbara Stoll, 2011).
Early-onset bacterial neonatal infection

Caused by bacteria colonising the birth canal

- **Gram positive isolates:**
  - Group B *Streptococcus*
  - but also *Streptococcus pneumoniae*,
  - *Enterococcus*, *Listeria*

- **Gram negative isolates:**
  - Enterobacteriaceae - *E. coli* but also
  - *Proteus* spp, *Klebsiella* spp, *Haemophylus*

- Vergnano S et al. Arch *Dis Child Fetal Neonatal* Ed 2011 UK
- Kuhn P et al. Paediatric and Perinatal Epidemiol 2010 France
- Stoll BJ et al. *Pediatrics* 2011 – USA
- Al-Taier A et al. International J Infectious Dis 2011 Kuwait
Early-onset bacterial neonatal infection

- In the past Enterobacteriacea, mostly *E. coli*, were accepted as the most common cause of early-onset (EOS) neonatal bacterial infection.
- In the 1970s GBS infections emerged as the leading cause of EOS and meningitis (and *E. Coli* was forgotten?)
### Portuguese National Prevalence Study
One day surveillance - 2010

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns in the postnatal ward</td>
<td>567</td>
<td><em>Enterococcus faecalis</em> – 1</td>
</tr>
<tr>
<td>Newborns in NICU</td>
<td>287</td>
<td><em>E. coli</em> – 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>GBS</em> – 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Streptococcus pneumoniae</em> – 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Proteus mirabilis</em> – 1</td>
</tr>
<tr>
<td>Patients &gt;28 days</td>
<td>20270</td>
<td><em>E. coli</em> - 320</td>
</tr>
<tr>
<td>Infections in patients admitted from home</td>
<td></td>
<td><em>GBS</em> – 22</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Listeria</em> -2</td>
</tr>
</tbody>
</table>
Incidence of early-onset infection caused by GBS and *E. coli* /1000 births

- Kuhn P: GBS 0.75, E. coli 0.3
- Al-Taiar A: GBS 0.48, E. coli 0.27
- Stoll B: GBS 0.41, E. coli 0.28
- Lin C-Y: GBS 0.43, E. coli 0.7
- Vergnano S: GBS 0.50, E. coli 0.18
Sepsis caused by possible mother-acquired bacteria in newborn infants admitted to NICUs
Portuguese surveillance system data

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>5369</td>
<td>5058</td>
<td>4911</td>
<td>15338</td>
</tr>
<tr>
<td>GBS</td>
<td>34</td>
<td>27</td>
<td>20</td>
<td>81 (5/1000)</td>
</tr>
<tr>
<td></td>
<td>6.3/1000</td>
<td>5.3/1000</td>
<td>4.1/1000</td>
<td></td>
</tr>
<tr>
<td>E. coli</td>
<td>37</td>
<td>39</td>
<td>24</td>
<td>100 (7/1000)</td>
</tr>
<tr>
<td></td>
<td>6.9/1000</td>
<td>7.7/1000</td>
<td>4.9/1000</td>
<td></td>
</tr>
<tr>
<td>Listeria</td>
<td>6</td>
<td>0</td>
<td>4</td>
<td>10 (0.7/1000)</td>
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<td></td>
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</table>
GBD early-onset infection

- Since 1992 AAP guidelines advise screening and prevention of GBS vertical transmission aiming to decrease early-onset infection.
- These guidelines were adopted by several countries and denied by others
- No studies on screening and prophylaxis for *E. coli* are known
The Portuguese studies
PPSU

• Group B streptococcal disease in Portuguese infants younger than 90 days
  Enrolling only septic newborn infants with positive cultures in sterile fluids * (2001-2004)
• Group B streptococcal disease - the hidden cases
  Enrolling newborn infants with proven and possible GBS infection (2006-2007)

** Neto MT Non-published data
## Compared data

<table>
<thead>
<tr>
<th></th>
<th>First study</th>
<th>Second study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of early-onset proven infection</td>
<td>0.44/1000LB</td>
<td>0.22/1000LB</td>
</tr>
<tr>
<td>Early-onset infection</td>
<td>83%</td>
<td>66%</td>
</tr>
</tbody>
</table>
Incidence

Per complete years, in the two studies

Proven infection only

Casualty or effects of screening and prophylaxis?

/1000LB

2002 2003 2004 2006 2007
GBS and *E. coli* positive blood cultures in Portuguese NICU in two different periods (in % of admitted newborn infants)

- **1999-2000**
  - GBS: 0.97%
  - E. coli: 0.44%

- **2008-10**
  - GBS: 0.77%
  - E. coli: 0.33%

5339 patients 10446 patients
Conclusions of two important studies on universal GBS screening and prophylaxis

- Rates of GBS infection declined but reflect a continued burden of disease. GBS continues the most frequent pathogen in term infants and *E. Coli* the most frequent in preterm infants.

  *Stoll BJ et al. Pediatrics 2011 - USA.*

- GBS screening and prophylaxis is effective in decreasing the incidence of GBS EOS; however an increase in EOS caused by *E. Coli* was noted.

Is there a reason to screen? Yes!

However, even today, against all grades of evidence, some countries do not have national guidelines

Why?
Bias related to carriers

- Colonization is intermittent
- Prevalence of carriers varies with geographic areas making obsolete national guidelines. In Portugal it is about 30% in the North and 12% in the South*

*Neto MT, 2009
Bias related to screening

- Screening should be done by 35/36 gestational week - preterm delivery is excluded
- Vaginal and rectal swabs should be done - many women only have a vaginal swab - false negative
- Specification on request should be done - false negative
- Transport and culture should be appropriate - false negative
- Once a national guideline is implemented it should be accomplished all over the country with uniform high quality
Bias related to prophylaxis

- Time before birth is needed
- Penicillin is the antibiotic of choice.
- *GBS* resistance to some of the alternatives have been reported - 10% to erythromycin in a Portuguese study*
- Early-onset infection may occur in newborn infants whose mothers were given correct prophylaxis

* Exposto F. Non-published data
Newborn infants with early-onset GBS infection
Screening and prophylaxis

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<thead>
<tr>
<th></th>
<th>Neto MT</th>
<th>Stoll B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened mothers</td>
<td>61%</td>
<td>58%</td>
</tr>
<tr>
<td>Negative screening</td>
<td>28%</td>
<td>81% in term and 26% in PT</td>
</tr>
<tr>
<td>Intrapartum Antibiotics</td>
<td>28%</td>
<td>53% all EOS</td>
</tr>
</tbody>
</table>
Newborns with early-onset infection and mother’s prophylaxis Proven and possible infection – n=57

<table>
<thead>
<tr>
<th>Positive</th>
<th>Complete prophylaxis</th>
<th>1 dose of antibiotics</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>7* (37%)</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

* One infant with positive blood culture
Bias related to those conditions supposed to protect that do not

<table>
<thead>
<tr>
<th>Proven and possible GBS early-onset infection</th>
<th>Caesarean section</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>24 (42%)*</td>
</tr>
</tbody>
</table>

* 14 (58%) with positive blood culture
Screening and prophylaxis

Screening and prophylaxis

Summarizing confounding factors

Reasons for non-screening policies

- Newborn infants with early-onset infection born to supposed negative mothers
- Newborn infants with early-onset infection born to mothers with complete prophylaxis
- Newborn infants with early-onset infection born by caesarean section
If screening has so many problems should prophylaxis be based on risk factors?
Non-screened mothers with risk factors | 57 (29%)
---|---
Term newborn infants with early-onset infection and risk factors | 35/160 (22%) *

Conclusion: Prophylaxis based on risk factors would have missed 71% of all newborn infants and 78% of term newborns with early-onset infection.
P.J. Steer and J Plumb found that only 60% of newborn infants with EOGBS disease had risk factors apparent at labour.

(Semin Fetal Neonatal Med 2011;16: 254-8)
Common-sense proposals

- Screening should be correctly performed - rectal and introit swabs, selective medium
- Women should know the meaning of carrier state in order to go to the maternity on time to start prophylaxis
- Antibiotics should be started as soon as possible instead of awaiting for a schedule
Common-sense proposals

- GBS carrier state should not be considered the only main risk for early-onset neonatal infection.
- Other risk factors have to be considered even if there is a negative GBS screening – maternal fever, prolonged rupture of membranes, laboratory signs of mother’s infection deserve attention and prophylaxis or treatment.
- In any case we know some cases will be missed.
Final conclusions

- Screening and intrapartum antibiotics, result in a significant decrease of EOGBS disease. However GBS infection still exists. Better screening and prophylaxis and avoidance of missed opportunities to prevent neonatal infection are desirable.

- *E. coli* is the second most common bacteria causing EOS and its importance should not be disregarded mainly in preterm infants.

- Monitoring of pathogens causing EOS continues an important issue.

- Adding screening to risk factors seems to be a valuable policy to improve prevention of EOS.