Naveen Bajaj
DM (Neonatology) – Seth GS & KEM Mumbai
Neonatal - Perinatal Medicine Fellow (UWO, Canada)
MD (Ped), GMC Patiala
Presently working as Neonatologist In Charge Deep Hospital, Ludhiana, Punjab.
Beating the bugs: what works and what does not against nosocomial infections?

DR NAVEEN BAJAJ
DM (NEONATOLOGY)
NEONATAL PERINATAL MEDICINE FELLOW
NEONATOLOGIST, DEEP HOSPITAL, LUDHIANA, PUNJAB
Nosocomial Infections in Neonates

- Sepsis claims > 1 million neonatal deaths/year worldwide
- Nosocomial sepsis 100 times more common than EO sepsis
- 7-24% of NICU patients
  - Blood stream infections 55%
  - Pneumonia 30%
- Incidence varies inversely with gestational age
- Huge burden of mortality, morbidity and cost
Common Organisms

Developed world
- Gram +ve – 70%, mainly CONS
- Gram –VE – 18%
- Fungi – 15%
- Staph Aureus
- Enterococci
- Viruses – RSV and Rotavirus
- Fungal

Developing world
- Klebsiella
- Staph Aureus
- Acenatobacter
- E coli
- Fungal
- Enterococci
- Gram +ve
Hand Hygiene

- Simplest Most effective method for reducing nosocomial infections
- High compliance lowers rate of blood stream infection
- Antiseptic Hand wash vs Alcohol hand rub (*Larson et al 2005*)
  - No significant differences
    - Any Neonatal infections (*OR 0.98 95% CI 0.77-1.25*)
    - Mean microbial counts on nurses’ hands (*3.21 and 3.11 log10 CFU for handwashing and alcohol, respectively; P=.38*)

Hand Hygiene

- AAP Perinatal Care Guidelines 6th ed (2007) recommends
  - When hands are visibly contaminated, they should first be washed

Antiseptic Hand Wash and Alcohol Hand Rub equally effective
Gowning by Staff and visitors

- No significant effects on (Cochrane review 2013)
  - Incidence of systemic nosocomial infection
  - Colonization
  - Length of hospital stay
- Not required routinely in NICU’s
- Wear doing procedures or handling neonate for isolation

Webster J, Pritchard MA. Gowning by attendants and visitors in newborn nurseries for prevention of neonatal morbidity and mortality. Cochrane Database of Systematic Reviews 2013
Central Venous Catheter Related Infections

- CRBSI - Most common nosocomial infection
- Usually because of
  - Breach of asepsis during insertion
  - Poor insertion technique
  - Lack of Ongoing care of catheter
  - Hub manipulation and contamination
- After 2 weeks odds of infection ↑ *(Advani et al 2011)*
  - Extraluminal – 1st week
  - Intraluminal and hub colonization - > 1st week
Risk factors for CVC-associated bloodstream infections in NICU

- ELBW \((OR = 5.13, CI = 2.1 \text{ to } 12.5)\)
- Catheter hub colonization \((OR = 44.1, 95\% \ CI = 14.5 - 134.4)\)
- Exit site colonization \((OR = 14.4, CI = 4.8 - 42.6)\)
- Duration of parenteral nutrition \((OR = 1.04, CI = 1.0 - 1.08)\)
- Catheter insertion after 1st week of life \((OR = 2.7, CI = 1.1 - 6.7)\)

CVC Protocol

- Maximal sterile barrier precautions during insertion (cap, mask, glove, gown) reduce infection (*Raad et al 1995*)

- Asepsis by Chlorhexidine vs Povidone –Iodine
  - Equally efficacious (*Garland et al 1995*)
  - Chlorhexidine impregnated dressing (*Garland et al 2001*)

- In line filters (*Jack et al 2012*)
  - No impact on sepsis
Antimicrobial-impregnated CVC for prevention of CRBI - Cochrane review 2015

- 1 small trial (N=98)

Silverzeolite impregnated UVC reduced the incidence of bloodstream infection in very preterm infants (RR 0.11, 95% CI 0.01 to 0.87; risk difference -0.17, 95% CI -0.30 to -0.04; NNT for benefit 6)

Needs more data before Routine use
Proactive Management of CVC

- Dedicated task force for CVC management – 2/3rd reduction in CRBSI (Golombek et al 2002)

- Standardization of CVC placement and maintenance had 49% lower risk of CRBSI in patients who had a central line in place for more than 30 days (Taylor et al 2011)
Antibiotic lock for prevention of catheter related infection - Cochrane Review 2015

- 3 trials (271 infants)
- ↓ confirmed CRI’s (RR 0.15, 95% CI 0.06 - 0.40)
- ↓ suspected CRI’s (RR 0.65, 95% CI 0.22 to 1.92)
- ↓ Co-infected and suspected infection rates (RR 0.25, 95% CI 0.12 0.49)
- ARR was 20.5% and the NNTB was 5
- However, No difference for mortality due to sepsis

Appears to be effective but concern of antibiotic resistance
Needs more data before routine recommendations

Taylor JE, Tan K, Lai NM, McDonald SJ. Antibiotic lock for the prevention of catheter-related infection in neonates. Cochrane Database of Systematic Reviews 2015
Antibiotics Use and Misuse

- Use is universal and Misuse is very common
- Alteration of neonatal microflora
- Development of antibiotics resistance
- Use of 3rd Gen cephalosporin as empirical therapy increase drug resistance
- Increase fungal infections
Prophylactic Antibiotics

- Central Catheters - ↓ rate of proven bacterial sepsis but no effect on overall mortality (Cochrane Review 2008)

DON’T Use Prophylactic Antibiotics

- UAC - Insufficient evidence (Cochrane Review 2010)
- ICD - Insufficient evidence (Cochrane Review 2010)
- Ventilation - Insufficient evidence (Cochrane Review 2010)
- Proph Vancomycin - Not recommended (Cochrane Review 2010)
Prolonged Initial Empirical Antibiotic Treatment is Associated with Adverse Outcomes in Premature Infants

Venkata S Kuppala, MD1, Jareen Meinzen-Derr, PhD1,2,3, Ardythe L. Morrow, PhD1,2,3, and Kurt R. Schibler, MD1,3

Results—Of the 365 premature infants surviving 7 days free of sepsis or NEC, 36% received prolonged initial empirical antibiotics, which was independently associated with subsequent outcomes: LOS (odds ratio [OR] 2.45, 95% confidence interval [CI] 1.28–4.67) and the combination of LOS, NEC, or death (OR 2.66, 95% CI 1.12–6.3).

Conclusions—Prolonged administration of empirical antibiotics to premature infants with sterile cultures in the first week of life is associated with subsequent severe outcomes. Judicious
Probiotics for prevention of NEC in preterm infants - Cochrane Review 2014

- Significantly ↓ severe NEC (≥stage II) (RR 0.43, 95% CI 0.33 to 0.56) and mortality (RR 0.65, 95% CI 0.52 to 0.81)

Probiotics prevents Severe NEC and Mortality
Recommended, if right preparation is available

Concerns
- Most effective preparations
- Timing, Dose and duration
- Preparations available in India
80 patients received pagibaximab at 90 (n=22) or 60 (n=20) mg/kg or placebo (n=46) for three once-a-week 90 or 60 mg/kg pagibaximab infusions in high-risk neonates, seemed safe and well tolerated. No staphylococcal sepsis occurred in infants who received 90 mg/kg. Not enough data for recommendation.

Promising Future
Immunoprophylaxis

- IVIG – No Role *(INIS 2011)*
- Antistaph Immunoglobulin – No Role *(Cochrane 2009)*
- Oral Immunoglobulins for Prevention of NEC – No role *(Cochrane 2011)*
- G-CSF and GM-CSF – No role *(Cairo et al 1999)*
- Glutamine Supplementation – No Role *(Cochrane 2012)*
Prophylactic Fluconazole in VLBW – Cochrane Review 2013

- 7 trials involving 880 infants compared systemic antifungal prophylaxis vs placebo or no drug

- Significant difference of invasive fungal infection (RR - 0.41, 95% CI 0.27 - 0.61)

- Risk of death not different

- High Incidence of Fungal infection in control

- Concerns
  - Emergence of fluconazole resistant strains of Candida

Can be considered in settings of high incidence of fungal infections and in neonates with multiple risk factors

95% CI 0.27 - 0.61) Risk of death not different

Austin N, McGuire W. Prophylactic systemic antifungal agents to prevent mortality and morbidity in very low birth weight infants. Cochrane Database of Systematic Reviews 2013,
Breast Milk

- Anti-infective properties – Lactoferrin, lysozyme, IgA, IgG, cytokines interferons, bifidogenic factors, PAF

- BM feeding associated with decreased gut permeability

- Reduction of Late onset Sepsis and NEC (*Schanler et al, Pediatrics 1999*)

- Fresh Breast milk of > 50 ml/kg/day reduces sepsis by 0.27 (*Furman 2003*)
Always Use Breast Milk – Fresh whenever possible

ORIGINAL ARTICLE
Impact of early human milk on sepsis and health-care costs in very low birth weight infants

AL Patel1,2, TJ Johnson2,3, JL Engstrom2,4, LF Fogg2, BJ Jegier2, HR Bigger1 and PP Meier1,2

OBJECTIVE: To study the incidence of sepsis and neonatal intensive care unit (NICU) costs as a function of the human milk (HM) dose received during the first 28 days of life for very low birth weight (VLBW) infants.

RESULTS: Mean HM intake expressed as maternal milk volume (ml) and milk expressed (ml) for VLBW infants was 54 ± 39 ml kg⁻¹ day⁻¹ (range 0–135). Binary logistic regression analysis controlling for propensity score revealed that increasing ADDHM-Days 1–28 was associated with lower odds of sepsis (odds ratio 0.981, 95% confidence interval 0.967–0.995, P = 0.008). Increasing ADDHM-Days 1–28 was associated with significantly lower NICU costs.

CONCLUSION: A dose–response relationship was demonstrated between ADDHM-Days 1–28 and a reduction in the odds of sepsis and associated NICU costs after controlling for propensity score. For every HM dose increase of 10 ml kg⁻¹ day⁻¹, the odds of sepsis decreased by 19%. NICU costs were lowest in the VLBW infants who received the highest ADDHM-Days 1–28.
Oral lactoferrin for prevention of sepsis and NEC in preterm infants – Cochrane 2015

- ↓Late onset Sepsis
- ↓NEC > Stage II
- ↓All Cause mortality

Low to Moderate quality evidence Favors its use
Large Ongoing trials results and Long term outcome data awaited

PammiM, Abrams SA. Oral lactoferrin for the prevention of sepsis and necrotizing enterocolitis in preterm infants. Cochrane Database of Systematic Reviews 2015
KMC and nosocomial infection – Cochrane Review 2014

- ↓ Nosocomial infection/sepsis ($RR \ 0.45$, $95\% \ CI \ 0.27-0.76$)

KMC should be encouraged

- ↓ Length of hospital stay ($MD \ 2.2 \ days$, $95\% \ CI \ 0.6 \ to \ 3.7$)

- Better infant growth, breastfeeding, and mother-infant attachment

Conde-Agudelo A, Díaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database of Systematic Reviews 2014
Use of H2 Blockers

- Impairs Acid gastric barrier
- ↑Risk of infections
- 7 times greater risk of LO Sepsis (Bianconi et al, J P Med 2007)
Ranitidine is Associated With Infections, Necrotizing Enterocolitis, and Fatal Outcome in Newborns

H2 Blockers are Harmful

exposed to ranitidine and 18 (9.8%) of the 183 not exposed to ranitidine had contracted infections (odds ratio 5.5, 95% confidence interval 2.9–10.4, \( P < .001 \)). The risk of NEC was 6.6-fold higher in ranitidine-treated VLBW infants (95% confidence interval 1.7–25.0, \( P = .003 \)) than in control subjects. Mortality rate was significantly higher in newborns receiving ranitidine (9.9% vs 1.6%, \( P = .003 \)).
Ventilator Associated Pneumonia - VAP

- **Risk Factors (Garland 2009)**
  - <28 weeks/ELBW
  - Duration of venti
  - No of reintubations
  - ET Suction
  - Opiate use

- **Position (Torres 1992)**
  - Lateral vs Supine – Lateral better

- **Suctioning systems**
  - Closed vs suction – Equal
Sustained reductions in neonatal nosocomial infection rates following a comprehensive infection control intervention

RL Schelonka, S Scruggs, K Nichols, RA Dimmitt and WA Carlo

- Baseline infection rate was 8.5 /1000 hospital days
- NI rate fell 26% ($P=0.002$) from baseline in 1st year and 29% ($P<0.001$) in 2nd and 3rd years after the CIC intervention
- CIC measures can reduce bacterial and fungal NI rates. This effect has been sustained for 3 years following the intervention
Efficacy of an infection control programme in reducing nosocomial bloodstream infections in a Senegalese neonatal unit

C. Landre-Peigne\textsuperscript{a,b}, A.S. Ka\textsuperscript{b}, V. Peigne\textsuperscript{c}, J. Bougere\textsuperscript{d}, M.N. Seye\textsuperscript{b}, P. Imbert\textsuperscript{e,*}

Table 1
Main results of the infection control programme in the neonatal unit of Hôpital Principal de Dakar, Senegal

<table>
<thead>
<tr>
<th>Variable</th>
<th>Period 1</th>
<th>Period 2</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of neonates</td>
<td>Jan–Feb 2005\textsuperscript{a}</td>
<td>Jun–Jul 2005\textsuperscript{b}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of neonates with birth weight $&lt;2500$ g (%)</td>
<td>125</td>
<td>148</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>No. of neonates with birth weight $&lt;1500$ g (%)</td>
<td>32 (25.6)</td>
<td>36 (24.3)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Median birth weight (g)</td>
<td>3050</td>
<td>3140</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of NI (%)</td>
<td>11 (8.8)</td>
<td>3 (2.0)</td>
<td>0.23</td>
<td>0.07–0.81</td>
<td>0.01</td>
</tr>
<tr>
<td>NI/1000 patient-days</td>
<td>10.9</td>
<td>2.9</td>
<td>0.27</td>
<td>0.08–0.97</td>
<td>0.03</td>
</tr>
<tr>
<td>No. of deaths (%)</td>
<td>4 (3.2)</td>
<td>8 (5.4)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>No. of deaths after 48 h (%)</td>
<td>3 (2.4)</td>
<td>3 (2.1)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>No. of NI-related deaths</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of infants treated with antibiotics for suspected early-onset sepsis</td>
<td>88 (100)</td>
<td>64 (51)</td>
<td>0.5</td>
<td>0.43–0.61</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(% of admissions for suspected early-onset sepsis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of infants with proven or possible early-onset sepsis (% of admissions)</td>
<td>41 (33)</td>
<td>45 (30)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Ratio of drug-resistant bacteria/all positive cultures (%)</td>
<td>34/43 (79)</td>
<td>4/33 (12)</td>
<td>0.15</td>
<td>0.06–0.39</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval; NI, nosocomial bloodstream infections; NS, non-significant.
\textsuperscript{a} Immediately before implementation of the infection control programme.
\textsuperscript{b} Immediately after implementation of the infection control programme.
- Identify high risk
- Increase host defence
- Reduce exposure to pathogens

NICU CARE BUNDLES
Potentially Best Practices – PBP’s

- **Hand Washing**
  - Initial hand wash till elbows with soap and water
  - Follow 6 steps of Hand Washing
  - Soap and water/Alcohol hand rub for routine asepsis
  - Hand hygiene even touching the inanimate object or surface
  - Gloves don’t replace the hand hygiene need
  - Ensure Compliance
  - Regular Education, Monitoring
Potentially Best Practices – PBP’s

- **Gowning**
  - Daily washed dress
  - Routine gowning not required
  - Gowning for Procedures

- Prevent understaffing and Overcrowding

- Routine Disinfection Policy

- Decrease no of venipunctures and heel pricks
Potentially Best Practices – PBP’s

- **CVC Bundles**
  - Strict Asepsis during insertion
  - Topical antiseptic – Chlorhexidine/Povidone-Iodine
  - Sterile dressing – Transparent
  - Daily visual inspection
  - Minimum hub manipulation
  - Separate medication line for reducing repeated hub entry
  - Alcohol wipes rubbing of hub for 10 sec before entry
Potentially Best Practices – PBP’s

- CVC Bundles
  - Careful preparation of TPN and fluids
  - Change fluids and sets every 72 hours
  - Change lipids every 24 hours
  - Catheter removal at the earliest - 100 ml/kg feeds
  - Dedicated CVC team
Potentially Best Practices – PBP’s

- **VAP Policy**
  - Change position regularly – Lateral/Prone preferred
  - Sterile disposable circuits
  - Change circuits when visibly soiled
  - No routine suction
  - Strict asepsis during suction
  - Extubate at the earliest
  - Aggressive use of NIV - CPAP/HHHFNC
Potentially Best Practices – PBP’s

- Nutritional policy
  - Use Fresh Breast milk
  - Promote KMC
  - Promote enteral feeding
  - Probiotics can be used
  - NO H2 blockers
Potentially Best Practices – PBP’s

Antibiotic stewardship

- Make your own Antibiotic Policy
- Develop Clinical Guidelines for Sepsis
- Authorization for High end antibiotics
- Limit antibiotics where infection is likely
- Specific plans for Streamlining antibiotics – Broad spectrum to narrow spectrum
- Deescalating antibiotics
- Treat for appropriate duration
Potentially Best Practices – PBP’s

- Antibiotic stewardship
  - Discontinue empirical treatment when infection not identified
  - No routine prophylaxis
  - No prophylaxis in invasive devices
  - No Immunoprophylaxis
  - Know your NICU cultures

- Antifungal Policy
  - Consider Fluconazole prophylaxis only if incidence is high
Potentially Best Practices – PBP’s

- Participate in the surveillance program *NEOKISS 2007 Germany*
- Quality improvement Program

Thank You
Reducing neonatal nosocomial bloodstream infections through participation in a national surveillance system

- NEO-KISS 2000 in Germany
- 48 NICUs
- Incidence density of BSIs decreased significantly by 24% from 8.3 BSIs per 1000 patient-days in the first year to 6.4 in the third year
- Participation in ongoing surveillance of nosocomial infections in NICUs, requiring individual units to feedback data, may lead to a reduction in BSI rates
113 hospitals in 9 countries, 3493 infants receiving antibiotics for suspected or proven serious infection

Polyvalent IgG immunoglobulin-500 mg/kg 48 hours apart

No effect on the outcomes of suspected or proven neonatal sepsis