Evidence-Based Neonatology: Session III

EBM Exercises – Discussion & Review

Wednesday, March 3, 2010
UCIMC

Presented by:
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UCI Science Library

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By the end of the three sessions, you will be able to:

- Have a basic knowledge of EBM
  - Practice the skills involved in EBM including clinical question formation and acquisition of medical evidence from the literature.
  - Identify EBM resources from the UCI Grunigen Medical Library website
  - Distinguish between the evidence from primary vs. secondary sources.
  - Review and develop critical appraisal skills and application of available evidence to patient care and medical education.

- Access the UCI Libraries’ restricted online resources locally and remotely
Ref:
All-Purpose 2x2 Table Analyser

or The CATmaker's Scratching Post.

1. Type the appropriate numbers in the white boxes (you can TAB between boxes to save using the mouse).
2. Click (or un-click) the sets of calculations you want to do (Rx for therapy, Dx for diagnosis and H for harm/etiology).
3. Click CALC.
4. Click CLEAR to, er, clear the values and start again.

Please note that you will need the Shockwave plug-in to view this interactive image. If you do not have Shockwave installed, you will be presented with the opportunity to download it. We recommend you do so, as this adds functionality to your browser.

Page last edited: 08 January 2009
Your clinical question?

Does probiotic administration in Very Low Birth Weight (VLBW) infants reduce the incidence of Necrotizing Enterocolitis (NEC) when compared to placebo?

Type of question being asked?

Therapy

PICO (Patient, Intervention, Comparison, and Outcome)

P = Very Low Birth Weight infants
I = Probiotic
C = Placebo
O = reduce the incidence of Necrotizing Enterocolitis

Type of Study you need?

RCT
Your search concepts and searchable keywords?  
Probiotics, “infant, very low birth weight”, Necrotizing Enterocolitis

Database you searched and the search strategy?  
PubMed Clinical Queries Therapy/Narrow Search

Search (Probiotics AND infant, very low birth weight AND Necrotizing Enterocolitis) AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months 23:37:29

No. of citations found and type of research evidence?  
7; RCTs + meta-analyses

CONCLUSIONS: Enteral supplementation of probiotics reduced the risk of severe NEC and mortality in preterm infants. This analysis supports a change in practice in premature infants > 1000 g at birth. Data regarding outcome of ELBW infants could not be extracted from the available studies; therefore, a reliable estimate of the safety and efficacy of administration of probiotic supplements cannot be made in this high risk group. A large randomized controlled trial is required to investigate the potential benefits and safety profile of probiotics supplementation in ELBW infants.
Your clinical question?

Do preterm infants with necrotizing enterocolitis have improved survival to discharge from NICU when using percutaneous peritoneal drain compared to exploratory laparotomy?

Type of question being asked?

Therapy

PICO (patient, Intervention, Comparison, and Outcome)

P = Preterm infants with necrotizing enterocolitis
I = percutaneous peritoneal drain
C = exploratory laparotomy
O = improved survival to discharge from NICU
Type of Study you need?  
**RCT**

Your search concepts and searchable keywords?  
(Necrotizing Enterocolitis, OR intestinal perforation)  
(drain OR drainage), laparotomy

Which database did you search and the search strategy?  
PubMed Clinical Queries Therapy/Narrow Search  
Search ((necrotizing enterocolitis OR intestinal perforation) AND (drain OR drainage) AND laparotomy) AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months 23:59:29 3

No. of citations found and type of research evidence?  
3 RCTs
CONCLUSIONS: Seventy-four percent of neonates treated with primary peritoneal drainage required delayed laparotomy. There were no significant differences in outcomes between the 2 randomization groups. Primary peritoneal drainage is ineffective as either a temporising measure or definitive treatment. If a drain is inserted, a timely "rescue" laparotomy should be considered. Trial registration number ISRCTN18282954; http://isrctn.org/

CONCLUSIONS: The type of operation performed for perforated necrotizing enterocolitis does not influence survival or other clinically important early outcomes in preterm infants. (ClinicalTrials.gov number, NCT00252681.). Copyright 2006 Massachusetts Medical Society.
Your clinical question?

What is the efficacy of epinephrine compared to other inotropes in reducing mortality and morbidity in preterm infants with cardiovascular compromise?

Type of question being asked?

Therapy

PICO (Patient, Intervention, Comparison, and Outcome)

P = Preterm infants with cardiovascular compromise
I = Epinephrine
C = Inotropic agents
O = reducing mortality and morbidity

Type of Study you need?

RCT
Your search concepts and searchable keywords?
Epinephrine, (Cardiotonic Agents OR inotropic agents), (preterm OR prematurity)

Database you searched and the search strategy?
PubMed Clinical Queries Therapy/Narrow Search

Search (Epinephrine AND (Cardiotonic Agents OR inotropic agents) AND (preterm OR prematurity))) AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months 00:10:18 4

No. of citations found and type of research evidence?
4; RCTs
Your selected study and the main outcome?


CONCLUSIONS: Low/moderate-dose epinephrine is as effective as low/moderate-dose dopamine for the treatment of hypotension in low birth weight infants, although it is associated with more transitory adverse effects.

CONCLUSIONS: Among hypotensive LBW infants, cardiovascular support with low/moderate-dose DP or low-dose EP increased cerebral perfusion, as indicated by the increase in both CBV and HbD. Low-dose EP was as effective as low/moderate-dose DP in increasing MBP among LBW infants.
Your clinical question?

What is the efficacy of concomitant therapy with dopamine and indomethacin in reducing the incidence of renal dysfunction in preterm infants without increasing cerebral injury, mortality, or the rate of failure to close the PDA?

Type of question being asked?

Therapy or (Etiology ??)

PICO (patient, Intervention, Comparison, and Outcome)

P = Preterm infants
I = dopamine and indomethacin
C = Placebo
O = reduce incidence of renal dysfunction without increasing cerebral injury, mortality, or the rate of failure to close the PDA
Question #8: Search Strategy

Type of Study you need?

**RCTs and a Meta-analysis**

Your search concepts and searchable keywords?

**dopamine AND indomethacin AND kidney**

Which database did you search and the search strategy?

PubMed Clinical Queries Therapy/Narrow Search

Search (dopamine AND indomethacin AND kidney) AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months

2

PubMed Clinical Queries Etiology/Narrow Search

Search ( (dopamine AND indomethacin AND kidney) ) AND (Etiology/Narrow[filter]) Limits: Humans, English, All Infant: birth-23 months

No. of citations found and type of research evidence?

2 RCTs Therapy search; 1 Meta-analysis Etiology search
Clinical Queries Filters

Clinical Queries using Research Methodology Filters

<table>
<thead>
<tr>
<th>Category</th>
<th>Optimized For</th>
<th>Sensitive/Specific</th>
<th>PubMed Equivalent</th>
</tr>
</thead>
<tbody>
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<td>therapy</td>
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<td>(((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR randomized*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading]))</td>
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<td></td>
<td>specific/narrow 93%/37%</td>
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<td>(randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]))</td>
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<tr>
<td></td>
<td>specific/narrow 54%/98%</td>
<td></td>
<td>(specificity[Title/Abstract])</td>
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<tr>
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<td>((relative[Title/Abstract] AND risk*[Title/Abstract]) OR (relative risk[Text Word]) OR risks[Text Word] OR cohort studies[MeSH:noexp] OR (cohort[Title/Abstract] AND study*[Title/Abstract]))</td>
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<tr>
<td></td>
<td>specific/narrow 51%/33%</td>
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<td></td>
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</tr>
<tr>
<td>prediction</td>
<td>specific/narrow 54%/29%</td>
<td></td>
<td>(validation*[tiab] OR validate*[tiab])</td>
</tr>
</tbody>
</table>

The Clinical Queries search filters are based on the work of Haynes RB et al.

CONCLUSION: The additional use of dopamine does not reduce the renal side effects of indomethacin.

Effect of dopamine on failure of indomethacin to close the patent ductus arteriosus. Fajardo CA, Whyte RK, Steele BT. J Pediatr. 1992 Nov;121(5 Pt 1):771-5. PMID: 1432432

Conclusion: The proportion of failures of medical treatment was not statistically different among the three groups. We conclude that concomitant dopamine therapy neither decreases the failure rate in indomethacin-treated infants nor reduces the magnitude of the indomethacin-induced oliguria.

CONCLUSIONS: There is no evidence from randomized trials to support the use of dopamine to prevent renal dysfunction in indomethacin-treated preterm infants.
Your clinical question?

What is the efficacy of hypothermia for improving neurodevelopmental outcome after hypoxic ischemic encephalopathy?

Type of question being asked?

Therapy or (Etiology ??)

PICO (patient, Intervention, Comparison, and Outcome)

P = Newborn with hypoxic-ischemic encephalopathy
I = hypothermia
C = no treatment
O = improving neurodevelopmental outcome

Type of Study you need?

RCTs and a Meta-analysis
Your search concepts and searchable keywords?
(Brain Hypoxia-Ischemias OR hypoxia ischemic encephalopathy),
(Hypothermia OR cooling), (Brain Damage, brain OR neurodevelopment)

Which database did you search and the search strategy?
PubMed Clinical Queries Therapy/Narrow Search
Search hypothermia AND (brain hypoxia ischemia OR hypoxic ischemic encephalopathy) AND (brain damage OR brain OR neurodevelopment) AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months

PubMed Clinical Queries Etiology/Narrow Search
Search (Search hypothermia AND (brain hypoxia ischemia OR hypoxic ischemic encephalopathy) AND (brain damage OR brain OR neurodevelopment)) AND (Etiology/Narrow[filter]) Limits: English, All Infant: birth-23 months
No. of citations found and type of research evidence?
26 in Therapy search; 12 in Etiology search

Your selected study and the main outcome?

INTERPRETATION: Therapeutic hypothermia decreases brain tissue injury in infants with hypoxic-ischaemic encephalopathy. The predictive value of MRI for subsequent neurological impairment is not affected by therapeutic hypothermia.
Meta-analysis findings from a etiology search

CONCLUSIONS: Although two small randomised controlled trials demonstrated neither evidence of benefit or harm, current evidence is inadequate to assess either safety or efficacy of therapeutic hypothermia in newborn infants with hypoxic ischaemic encephalopathy. Therapeutic hypothermia for encephalopathic asphyxiated newborn infants should be further evaluated in well designed randomised controlled trials.
CONCLUSIONS: There is evidence from the eight randomised controlled trials included in this systematic review (n = 638) that therapeutic hypothermia is beneficial to term newborns with hypoxic ischaemic encephalopathy. Cooling reduces mortality without increasing major disability in survivors. The benefits of cooling on survival and neurodevelopment outweigh the short-term adverse effects. However, this review comprises an analysis based on less than half of all infants currently known to be randomised into eligible trials of cooling. Incorporation of data from ongoing and completed randomised trials (n = 829) will be important to clarify the effectiveness of cooling and to provide more information on the safety of therapeutic hypothermia, but could also alter these conclusions. Further trials to determine the appropriate method of providing therapeutic hypothermia, including comparison of whole body with selective head cooling with mild systemic hypothermia, are required.
Your clinical question?

What is the efficacy of insulin therapy for hyperglycemia in VLBW infants?

Type of question being asked?

Therapy

PICO (patient, Intervention, Comparison, and Outcome)

P = Very Low Birth Weigh Infants
I = Insulin Therapy
C = Placebo or no treatment
O = decrease morbidity or mortality?

Type of Study you need?

RCTs
Your search concepts and searchable keywords? 

**Very Low Birth Weigh Infants; Insulin; hyperglycemia**

Which database did you search and the search strategy? 

**PubMed Clinical Queries Therapy/Narrow Search**

Search Insulin AND very low birth weight AND hyperglycemia AND (Therapy/Narrow[filter]) Limits: English, All Infant: birth-23 months 17:51:30

**No. of citations found and type of research evidence?**

13 in Therapy search; 14 in Etiology search

CONCLUSIONS: Early insulin therapy offers little clinical benefit in very-low-birth-weight infants. It reduces hyperglycemia but may increase hypoglycemia (Current Controlled Trials number, ISRCTN78428828.) 2008 Massachusetts Medical Society

CONCLUSIONS: Glucose infusion rate: There is insufficient evidence from trials comparing lower with higher glucose infusion rates to inform clinical practice. Large randomized trials are needed, powered on clinical outcomes including death, major morbidities and adverse neurodevelopment. Insulin infusion: The evidence reviewed does not support the routine use of insulin infusions to prevent hyperglycemia in VLBW neonates. Further randomized trials of insulin infusion may be justified. They should enrol extremely low birth weight neonates at very high risk for hyperglycemia and neonatal death. They might use real time glucose monitors if these are validated for clinical use. Refinement of algorithms to guide insulin infusion is needed to enable tight control of glucose concentrations within the target range.

AUTHORS' CONCLUSIONS: Evidence from randomized trials in hyperglycemic VLBW neonates is insufficient to determine the effects of treatment on death or major morbidities. It remains uncertain whether the hyperglycemia per se is a cause of adverse clinical outcomes or how the hyperglycemia should be treated. Much larger randomized trials in hyperglycemic VLBW neonates that are powered on clinical outcomes are needed in order to determine whether, and how, the hyperglycemia should be treated.
Feel free to contact your medical librarians anytime!

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Thank you!!