



# ESPEN Congress Prague 2007

Key papers in the field of nutrition  
Physician

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# A physician's choice 2007

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# Parenteral nutrition-related liver disease. Lessons from paediatrics

- A problem in adults but much more in children
  - eg transplantation needs
- Usually in adults with very short intestine
  - <40cm
- Aetiological elements
  - portal support of liver, growth/trophic factors
  - not considered now
- Lessons for adults from recent paediatric observations and an adult ICU study

# The highest risk babies

Christensen R. Utah. J Perinatol 2007

- Often unclear which neonates are most at risk
- Important to plan intervention and assessment
- Evaluation of NICU patients on PN for >14 days

# The highest risk babies

Christensen R. J Perinatol 2007

- analysis of all neonates receiving PN for 14 days or more (2002-06)
- 9861 neonates
- 6543 (68.5%) received PN
- 1366 (21%) for  $\geq$  14 days
- PNALD defined from direct (conjugated) bilirubin  $> 34\mu\text{mol/l}$  (2.0 mg/dl)      n = 357

# The highest risk babies

Christensen R. J Perinatol 2007

- Duration-related risk

– Number of days	Incidence
– 14-28	14%
– 29-56	43%
– 57-100	72%
– >100	85%

- Mortality

- Deaths (at >28 days) much more common if PNALD (p<0.0001)

# The highest risk babies

Christensen R. J Perinatol 2007

## Prior status and risk

- birth weight <500 g (OR 30.7)  
500-749 g (OR 13.1)
- gastroschisis (OR 20.3)
- jejunal atresia (OR 24.0)

# The highest risk babies

Christensen R. J Perinatol 2007

## Conclusion

- very high risk for PNALD if
  - <750 g birth weight
  - gastroschisis or jejunal atresia
- valuable in neonatology but little help in adults

# The highest risk adults in ICU

Grau T. Madrid. Crit Care 2007

Prospective cohort study in 40 intensive care units

## Definitions

- cholestasis: ALP >280 IU/l, GGT >50 IU/l, or bilirubin >21
- liver necrosis: AST >40 IU/l or ALT >42 IU/l, plus bilirubin >21 or INR >1.4
- mixed pattern: ALP >280 IU/l or GGT >50 IU/l, plus AST >40 IU/l or ALT >42 IU/l

# The highest risk adults in ICU

Grau T. Crit Care 2007

- 725 of 3,409 patients received artificial nutrition
- 303 received IVN
- 30% developed abnormal liver function

# The highest risk adults in ICU

Grau T. Crit Care 2007

## Univariate analysis

Abnormal liver function associated with

- IVN ( $p < 0.001$ )
- multiple Organ Dysfunction Score on admission ( $p < 0.001$ )
- sepsis ( $p < 0.001$ )
- delayed use of artificial nutrition ( $p < 0.03$ )
- malnutrition on admission ( $p < 0.01$ )

# The highest risk adults in ICU

Grau T. Crit Care 2007

Multivariate analysis

Liver dysfunction was associated with

- IVN ( $p < 0.001$ )
- sepsis ( $p < 0.02$ )
- delayed use of artificial nutrition ( $p < 0.03$ )
- energy provision  $> 25$  kcal/kg per day ( $p < 0.05$ )

# The highest risk adults in ICU

Grau T. Crit Care 2007

## Conclusions

- Septic, critically ill patients should not be over-fed particularly when IVN is employed
- Artificial nutrition in the first 24 hours after admission seems to have protective effects

# Are lipids the cause ?

Shin J. Korea. Eur J Pediatr 2007

- 22 neonates with cholestasis (29.8w, 1298g)
- 22 without cholestasis (29.5w, 1286g)
- mean peak direct bilirubin 78 vs 20

# Are lipids the cause ?

Shin J. Eur J Pediatr 2007

Univariate analysis - PNAC was significantly related to

- duration of fasting
- parenteral nutrition
- days of antibiotics use
- C-reactive protein
- +ve gastric culture
- enteral feeding intolerance
- higher total amino acid amount given
- higher total lipid given
- higher average daily lipid
- absence of prenatal dexamethasone

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- duration of fasting
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- **higher total lipid given**
- **higher average daily lipid**
- absence of prenatal dexamethasone

# Are lipids the cause ?

Shin J. Eur J Pediatr 2007

Logistic regression analysis (multivariate)

- cumulative lipid = independent risk factor
  - $p = 0.041$ ; OR 1.174

Recommendation

- decrease cumulative iv lipid

Suggestions

- reduce iv amino acids
- prompt control of infection
- prenatal administration of dexamethasone

# Or is it catheter infection ?

Hermans D. Brussels. J Pediatr Gastroent Nutr 2007

- Bacterial infection in infants = risk for PNAC
- Not known if a risk factor for hepatic fibrosis
- Retrospective study of sepsis incidence in children with and without severe liver fibrosis  
n=30; 1985-2000

# Or is it catheter infection ?

Hermans D. J Pediatr Gastroenterol Nutr 2007

- PN duration 65 months (range, 8-150 months)
- group A (n = 16) developed severe liver fibrosis
- group B (n = 14) had normal or near normal architecture at time of biopsy

# Or is it catheter infection ?

Hermans D. J Pediatr Gastroenterol Nutr 2007

Duration of PN was shorter in group A

- 30.5 months vs 105 months;  $p < 0.001$

Incidence of sepsis was significantly higher

- 3.2 episodes/year vs 1.5/year

First infection occurred earlier

- 1 month vs 4 months (NS)

Groups otherwise similar

# Or is it catheter infection ?

Hermans D. J Pediatr Gastroenterol Nutr 2007

## CONCLUSIONS

- Early onset of infections may be causally relevant to subsequent development of liver fibrosis in long-term PN
- New strategies required to minimise early infection in children on PN

# Does erythromycin prevent it ?

Ng P. Hong Kong. Gastroenterology 2007

Double-blind, randomized, placebo-controlled study of "high-dose" oral erythromycin as a prokinetic anti-microbial agent

End points

- Frequency of PNAC
- Time to achieve full enteral feeding
- Duration of parenteral nutrition required

# Does erythromycin prevent it ?

Ng P. Gastroenterology 2007

- Consecutive very low birth weight infants randomized to erythromycin (12.5 mg/kg every 6 hours for 14 days) or placebo
- If less than half intended milk feeds by day 14 of life
- Mechanical obstruction excluded
- 182 VLBW infants (91+91)

# Does erythromycin prevent it ?

Ng P. Gastroenterology 2007

Incidence of PNAC significantly lower in treated infants

18/91 vs 37/91 ( $p = 0.003$ )

Treated infants achieved full enteral nutrition 10 days earlier ( $p < 0.001$ )

Duration of parenteral nutrition decreased by 10 days ( $p < 0.001$ )

Recurrent septicaemia less common

4/91 vs 13/91 ( $p = 0.003$ )

No apparent adverse events

# Does erythromycin prevent it ?

Ng P. Gastroenterology 2007

## CONCLUSIONS

- High-dose oral erythromycin valuable
- Application to adult practice ?

# Parenteral nutrition-related liver disease. Lessons from paediatrics

Aetiology and anatomy are important

Identifiable risks

- sepsis & delayed treatment of sepsis
- delayed introduction of artificial nutrition
- excess energy provision
- lipids
- perhaps also excess amino acids
- catheter infections especially early ones

Postulated intervention

- erythromycin probably helpful