

Feedback from ESPR, Porto, Portugal, October 2013

Please give details of the best lecture/learning from the meeting:

1.

Professor John Wyatt presented a lecture on the ethics of mortality statistics. In this thought provoking lecture he points out that our ethical attitude influences survival, which influences the survival statistics, which in turn affects our ethical attitude towards extremely preterm infants. I'm sure we can all relate to this within the neonatal community.

He also highlighted the NICHD birth outcome data website (http://www.nichd.nih.gov/about/org/der/branches/ppb/programs/epbo/Pages/epbo_case.aspx) which gives a prediction of outcomes at extreme preterm gestations in conjunction with other factors e.g. antenatal steroids and birth weight. The website shows that we shouldn't be over focusing on gestational age. Mortality and morbidity predictions are multifactorial and we should be using objective and individualised information and be open with parents.

He suggests that we should read the following: Proactive management promotes outcomes in extreme preterms (Hakansson et al 2004) and Death or Disability?: The 'Carmentis Machine' and decision-making for critically ill children.

2.

HFOV: is this still necessary?

Now there are reduced ventilation days because of CPAP, but BPD still a problem.

Need to improved ventilation strategies to prevent lung injury.

HFOV in term babies may be useful if conventional fails. It can optimise the use of iNO by reducing the functional residual capacity.

In preterm: use HFOV early on may be in first hour, in baby with surfactant deficiency not responding to conventional ventilation as expected. Early use of HFOV in severe RDS can reduce BPD.

In term neonate: it is only used if conventional fails.

3.

I particularly enjoyed the 'keynote lecture' on Thursday 10th by Professor Adele Diamond (Vancouver) on Development of Executive Functions. This includes functions such as reasoning, selection, inhibition and perseverance – all of which are crucial to achieving success in life, but which are often difficult for young children to establish. She illustrated with a simple test of EFs in which different hand-signals have to be made when 'hearts' or 'flowers' were shown in different places on a screen – one could see some members of the audience struggling!

Although the lecture focussed on issues for children with ADHD, the topic is very relevant to ex-preterm infants, who often have longer term difficulties in learning and behaviour. AD said that EFs are more important than IQ in achieving success. EFs rely on the dopamine neuro-transmitter system which is important in the pre-frontal cortex. Polymorphisms in the DR4 (dopamine receptor) gene affect function. Methylphenidate (a drug used in ADHD) blocks the dopamine receptor, and care needs to be taken with drug dosing to minimise adverse effects on EF. Stress has a negative effect on EFs, and again this may affect individuals differently as a manifestation of differences in genetic polymorphisms, for example, the gene for COMT (catecholamine methyl transferase). In preterm infants nutrition may be one of the factors which modulates genetic expression, so this could open up areas for future research in the area of nutrition and outcome. In relation to stress, AD finished her lecture by emphasising the importance of making children happy – allowing them to explore and learn in the medium which suits each individual best, be it music, dance, nature or animals. Altogether this was an inspiring, informative and beautifully delivered lecture to open the conference.

4.

My research interest is nutrition and one particularly interesting lecture was one by S Moltu from Norway, on the risks of aggressive nutrition in preterm infants. A RCT carried out by her group looking at providing enhanced early nutrition improved first week nutrient intakes and better postnatal growth, but also cause increased rates of septicaemia causing the trial to be discontinued after 50 patients. (Moltu et al, Clin Nutr. 2013 Apr;32(2):207-12 and Moltu et al JPGN 2013 online). In addition, the infants in the intervention group had significant electrolyte deviations during the first week of life with hypophosphatemia, hypokalaemia and hyperkalaemia. Dr Moltu went on to talk about the the risks of aggressive nutrition, describing a clinical picture similar to that of refeeding syndrome may occur. In particular, when giving enhanced protein, additional phosphate is required for tissue accretion (10mg phosphate per gram of protein). This may explain the hypophosphatemia seen in the intervention group, as their demand for phosphate would be higher due to additional protein delivery. A similar clinical picture had been observed in a study by another groups (Bonsante et al Plos One 2013, DOI: 10.1371/journal.pone.0072880). with increased early amino acid intake associated with high risk of hypophosphatemia. They also saw increased septicaemia.

This evidence all suggests an emerging picture of a neonatal refeeding syndrome, characterised by hypophosphatemia. In addition to the mechanism surrounding protein intake and phosphate requirement, there is also likely to be an effects of switching from early catabolism to anabolism. This suggests a need to ensure adequate potassium and phosphate provision in parenteral nutrition, particularly when providing early and enhanced amino acid delivery.

Another excellent session was a keynote lecture by Prof Shoo Lee from Toronto on 'Changing the Paradigm of Neonatal Care'. In this lecture Prof Lee emphasised the importance of the need to move away from the traditional RCT model of trials to a more pragmatic quality improvement approach, with multifaceted interventions consisting of collections of best practice gleaned from the experience of successful centres and units, rather than trials of single interventions, as in many cases it is a collection of practices that improve outcomes rather than a single thing in isolation (and in reality interventions are rarely used in isolation. He gave examples of success his groups has had in

reducing NEC by implementing a collection of best practices taken from units in Japan, including the exclusive use of mothers milk and rapid increases in feed volumes. He also called for a need to focus on implementation science in order to effectively introduce such interventions.

5.

Among the conference sessions I attended was a poster symposium on Diagnostic Methodology chaired by Professor Gorm Greisen. This was a multi-disciplinary session with topics that spanned a wide range of paediatric specialities. Two of the presentations were of particular interest to my field of research and were concerned with the development of screening measures for identifying developmental and behavioural problems in the early years. These were relevant to neonatal follow-up practices given their focus on the assessment of socio-emotional and cognitive development in young children. In addition to the presentations themselves, the ensuing group discussion that was facilitated by Professor Greisen was particularly interesting and thought-provoking. This addressed fundamental issues surrounding development assessment in general and specifically around the selection of what might be a 'Gold Standard' measure. Questions were raised about whether parents may be better assessors of their child's development than a formally trained examiner. Engaging in these discussions resonated with my research and practice and allowed me to meet a colleague with similar interests and thus a potential future collaborator. Overall, given the importance of the discussion, attending the conference afforded greater opportunities for learning than would be possible from reading these study results in journal publications.

6.

Pulmonology symposium: Alternative methods of administering surfactant:

Interesting findings from different studies: Use of NG tube to deliver surfactant : Tracheal instillation during spontaneous breathing: small group, of very selected babies: decreased need for needing mechanical ventilation.

Use of Aerosolised surfactant:

Research Ethics: different countries have different rules in conducting research and reviewing a study ethically. Sometimes more of a hindrance in conducting a study, than facilitating multicentre research trails. Important to standardize as this will help conducting large multicentre randomised studies. Also the lecture of how can we define minimal risk when conduction research was interesting.

7.

INTERNATIONAL GUIDELINES ON RDS MANAGEMENT – 2013 EDITION

D. Sweet, Belfast United Kingdom (12th October 2013)

PERMISSIVE HYPERCAPNIA FOR EXTREMELY LOW BIRTHWEIGHT INFANTS – A RANDOMISED CONTROLLED MULTICENTRE TRIAL

T. Ulrich et al. (11th October 2013)

HIGH-FLOW NASAL CANNULAE VS. NASAL CPAP FOR POST-EXTUBATION RESPIRATORY SUPPORT OF VERY PRETERM INFANTS: A MULTICENTRE, RANDOMISED, NONINFERIORITY TRIAL.

B. Manley et al. (11th October 2013)

Please list 3 key points from the meeting to be shared with the neonatal community:

1) ESPR although “Paediatric” has mostly neonatal research presented, the neonatal community should be encouraged to attend this valuable meeting.

2) There are current trends to study neonatal circulation and its management. The most noteworthy ones are research into methods to assess circulation rather than blood pressure (Cardiac output and SVC flow) and there is a current trial involving dobutamine v placebo to assess improvement in SVC flow (NEOcirc003).

3) Porto is a fantastic cultural city well worth visiting.

1) A low energy intake during the first 4 weeks of life is a significant and independent risk factor for severe ROP in extremely preterm infants. Based on the odds ratio, an increase of the energy intake by 10% would reduce the incidence of severe ROP with 26%.

2) After discharge each g/kg/d in protein intake and each 10 kcal/kg/d in energy intake were associated with 6.43 point increase and 3 point increase in the locomotor subscale scores, respectively.

3) HIGH-FLOW NASAL CANNULAE VS. NASAL CPAP FOR POST-EXTUBATION RESPIRATORY SUPPORT OF VERY PRETERM INFANTS: A MULTICENTRE, RANDOMISED, NON-INFERIORITY TRIAL. HFNC therapy was non-inferior to NCPAP as post-extubation support in very preterm infants. HFNC use resulted in no increase in mortality or morbidity, and caused less nasal trauma than NCPAP.

1) Early nutrition can improve brain growth in VLBW infants: Corviello, C., et al (Young Investigators, Plenary Saturday am) showed significant positive correlations between energy and fat intake and brain volume on quantitative MRI; Morgan, C., et al (Friday 0900 Parallel Session) showed increased head circumference at 28 days in those infants randomised to receive a concentrated PN with higher protein intake.

2) PN should be started as early as possible in very preterm infants in order to avoid nutrient deficits, however, the metabolism of PN must be understood. Babies randomised to high initial protein but with relatively low phosphate and potassium content developed severe metabolic disturbance in a Norwegian RCT – amino acid infusion stimulates insulin secretion which promotes intracellular transfer of these nutrients resulting in low circulating levels (Moltu, S., et al, Keynote Lecture, Parallel Session, Sunday, 1430)

3) Quality improvement techniques and systematic monitoring are both important and effective in reducing nosocomial infection rates in high risk neonates. All NICUs should have systems in place to regularly review infection rates, for example: Vermont Oxford (USA and international), NEO-KISS (Germany), EPIC (Canada), and a rolling programme of education for all staff on techniques, care-bundles etc to minimise infection risk – excellent key-note lecture by Prof Shoo Lee (Friday 1130) and symposium on Nosocomial Infection (Sat 1100).

1) Early enhanced nutrition does improve growth in preterm infants

2) Possibility of a refeeding type syndrome in neonates receiving enhanced early nutrition and need to monitor phosphate levels

3) Need for more pragmatic interventions and study methods addressing more complex neonatal issues (eg NEC) using multifaceted interventions, implementation science and quality improvement techniques.

1) Developmental screening tests should have adequate psychometric properties and should be carefully selected to provide appropriate follow-up measures. When appraising the results of diagnostic accuracy studies one should be mindful of the 'Gold Standard' measure selected.

2) A presentation by Dr Julia Jaekel provided new evidence to suggest that the origins of "specific mathematics learning difficulties" may differ from mathematics difficulties diagnosed using low attainment scores, and may be neurodevelopmental in nature. This has implications for how mathematics difficulties should be identified in children born preterm and how interventions may be developed for these children.

3) A qualitative study presented in a session on parents' involvement in neonatal care highlighted issues related to the disappointment that research participants may feel when recruited to a control arm of a study and to their lack of understanding of their importance to the research. This has practical implications for researchers for enhancing the knowledge and experience of participants who are recruited to RCTs.

1) DOES PASSIVE COOLING WORK?-A RETROSPECTIVE COHORT STUDY OF NEONATES COOLED DURING

NEONATAL TRANSPORT FOR NEONATAL ENCEPHALOPATHY: Early referral to a cooling centre after identification of baby for cooling, helps achieves cooling to the target temperature quickly. One caveat: in their study longer stabilising times was associated with achieving therapeutic temperature: this needs to be looked into, as the quicker you stabilise and transfer the more effective it should be, so confounding factors need to be kept in mind.

2) PREVENTING EARLY POSTNATAL HEAD GROWTH FAILURE IN VERY PRETERM INFANTS: THE RANDOMISED CONTROLLED SCAMP NUTRITION STUDY: Interesting to see that concentrated PN (12% glucose and 3.8g/k protein/lipid) can be used from the very beginning and has had a positive impact on head growth.

3) TIME OF BIRTH AND RISK OF RESPIRATORY ILLNESS IN PRETERM INFANTS <30 WEEKS GESTATION (GA): A RETROSPECTIVE MATCHED-PAIR COHORT STUDY: Interesting study : : After adjusting for the most important risk factors for respiratory illness preterm infants born at night seem to be at higher risk for intubation and surfactant than during daytime with an increased risk for developing BPD subsequently. This could suggest potentially modifiable factors, such as staffing levels and experience as well as education and training in current best practice delivery room management that could be addressed with the goal of improving outcomes.

- 1) New guidelines on management of RDS
- 2) Minimally invasive surfactant techniques
- 3) SPIN & SCAMP studies