

CENTRES SUPPORT BID FOR MAIN TRIAL

Already 30 centres have confirmed their willingness to contribute to a main INNOVO trial and these statements have been appended to the application which was sent to the MRC at the end of January. We hope very much that the Health Services Research Board will be convinced by our case when they meet in April. However, we have to wait until July until we know whether funding is forthcoming.

RECRUITMENT

74 BABIES HAVE NOW BEEN RECRUITED from 15 centres. 'On-line' centres have estimated their likely recruitment rate. We expect to recruit 50-60 babies in the <34 week category and 25-30 babies in the ≥34 week category for each twelve month period. As the number of participating centres grows we anticipate that this rate will be exceeded. We expect to complete recruitment for the <34 category within three years.

NEW CENTRES

Kuopio and Oulu in Finland, Royal Gwent in S. Wales and Guy's Hospital, London are now 'on-line'. Norfolk and Norwich, and Ayrshire Central now have LREC approval.

COCHRANE LIBRARY UPDATES

Preterm babies

The Cochrane review on inhaled nitric oxide in preterm infants has now been published¹. The conclusions are based on a single study from Liverpool with a very small sample size. There has been no demonstration of improvement in a clinically relevant outcome.

In view of the risk of increased bleeding time and depression of platelet function, the reviewers conclude that premature infants should not receive inhaled nitric oxide outside of RCTs.

‘Mature’ babies

The corresponding review² for babies born at or near term has been updated. All 8 trials provided data on short term effects on improvement in oxygenation. The review found (based on 5 trials) that INO

- reduced the requirement for ECMO (Relative Risk (RR) 0.69; 95% Confidence Interval (CI) 0.56 to 0.85),
- reduced the risk of death or ECMO (RR 0.72 (95% CI 0.60 to 0.87)),
- but did not suggest any benefit of INO on mortality alone (RR 1.03; 95% CI 0.62 to 1.72), although this CI is wide.

No long term follow up information is available from any of the trials. Neither did the review report data about side-effects and toxicity.

Nevertheless, the reviewers conclude: “*On the evidence presently available it appears reasonable to use inhaled nitric oxide...for term and near term infants with hypoxic respiratory failure who do not have a diaphragmatic hernia*”.

Criticisms

Diana Elbourne and David Field have commented on this to the Criticisms section of the Cochrane Library, making three main points: there is a need for further information about longer term neurodevelopmental outcomes;

¹ Finer NN, Barrington KJ. Nitric oxide for respiratory failure in infants born at or near term (Cochrane Review). In: The Cochrane Library, Issue 1, 1999. Oxford: Update Software

² Barrington KJ, Finer NN. Inhaled nitric oxide in preterm newborn infants with respiratory failure (Cochrane Review). In: The Cochrane Library, Issue 1, 1999. Oxford: Update Software

- reducing the need for ECMO may not represent an adverse outcome as, appropriately used, it has benefits both for mortality and for respiratory function, without leading to greater risk of neuro-developmental problems;
- the effect of INO in reducing the use of ECMO may be an over-estimate as several of the trials were stopped early on the advice of data monitoring committees.

Indeed, Finer and Barrington do temper their conclusions by suggesting the need for further research to assess “*what are the long term effects, if any, of INO on the developing lung and on the infant’s neurodevelopment outcomes*” – exactly what we are all aiming to do in INNOVO.

TREATMENT OR TRIAL

In response to a survey of ‘on-line’ centres (20 responded), most centres had not used INO at all or only once for *preterm* babies outside the trial. Seven centres used it more frequently, and one centre had used it a great deal.

For *mature* babies, 8 centres used INO for 2 or more babies and 2 used it for more than 20 babies.

As there is currently no evidence to suggest that treatment is beneficial in the long term, we would hope you will treat only in the context of the trial. Centres are now being asked to keep a log of all babies treated with INO outside the trial, as this helps to assess the generalizability of the trial results.

PARTICIPATION IN TRIALS

The research study led by Claire Snowdon, on the views of parents, neonatologists and neonatal nurses about trial participation is being piloted in Leicester, Liverpool and Cambridge. She is keen to continue interviewing (and where possible tape recording when consent is requested). Claire is shortly expecting her first baby, and we wish her well. Other study researchers will continue her work until she returns from maternity leave. If you have asked a parent to participate in INNOVO and wish to be interviewed, please contact the trial office.

DATA MONITORING COMMITTEE

An interim analysis is underway and the report will be considered by the members of the Data Monitoring Committee; Adrian Grant, Edmund Hey and Stephen Evans. The DMC report to the Steering Committee which meets on 22 April and will be sent to the MRC.

TECHNICAL SUPPORT

Roger Smith, respiratory technician from Leicester will continue to offer support to 'on-line' centres for the remaining phase of the pilot.

WEB-SITE

Information has been posted on our fledgling web-site aimed at potential centres. This will be updated regularly and will come into its own if and when the main trial is funded.

See <http://eps.lshtm.ac.uk/msu>



INNOVO TRIAL PROJECT MANAGEMENT GROUP

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