infant
for neonatal and paediatric healthcare professionals

BOOST-II UK: Benefits of oxygen saturation targeting

In the UK and Ireland around 3000 babies per year are born at less than 28 weeks' gestation. Two thirds of these very premature babies now survive to discharge, but most grow poorly in the first year after birth and many have respiratory problems requiring further hospital admission. A quarter have at least one major disability at two years of age, and many of these have cerebral palsy. Developmental progress, even in those with no physical disability, is a standard deviation below that of babies born at term.

The most common drug given to these vulnerable neonates is oxygen and yet there is not complete agreement as to the therapeutic range of this potent drug in this age group. Tin[1] has described the history of oxygen used in the care of very preterm babies. It has been more than 50 years since oxygen toxicity was identified as a cause of retinopathy of prematurity[1]. More recently, oxygen used in very preterm babies has been associated with poor lung outcomes[2] leading to reduced growth, impaired neurodevelopment and greater health costs[3]. It has also been associated with the development of periventricular leucomalacia[4] and is thought to contribute to the development of cerebral palsy[5]. In spite of all this, there is little evidence about the safety of its administration.

Blood oxygen levels are volatile and traditionally the only really reliable method of measuring them has been through analyses of arterial blood, with all the problems associated with arterial sampling. Over the last few decades oxygen saturation measurement (SpO_2), has become more accurate[6] and is now commonly used in the neonatal unit. In spite of recent observational studies[1] there is still a great deal of uncertainty about the optimal target range of SpO_2 for extremely premature babies.

There have been two recent randomised controlled trials. The STOP-ROP[7] study did not find evidence that targeting SpO_2 at more than 95% slowed the development of retinopathy in babies with prethreshold disease. The Australian BOOST[8] study did not find evidence that high SpO_2 levels improved growth of premature babies more than four weeks old. Both suggested that high saturations lead to worse respiratory outcomes.

BOOST-II UK, funded by the Medical Research Council, is a double blind randomised controlled trial to compare the effects of targeting SpO_2 levels in babies born at < 28 weeks' gestation. Its primary objective is to determine whether varying the concentration of inspired oxygen – low (85-89%) versus high (91-95%) SpO_2 – from the day of birth until the baby is breathing air (or until the baby has reached a post-menstrual age of at least 36 weeks) affects a number of outcomes, including death or severe neurosensory disability on assessment two years after the child was due to be born.

Recruitment should take place as soon after birth as possible. Blinding will be achieved with the help of offset oxygen saturation monitors which, within the range of 85-95% SpO_2, will read 3% above or below the true saturation. This means if the displayed saturations are maintained between 88-92%, the actual saturations will fall into either the high or the low range.

The aim is to recruit 1200 babies over the next four years from approximately 40 centres in the UK and Ireland. The interventional phase, during which the oxygen saturations will be targeted, will last for at least eight weeks, during which time babies may be transferred to many other neonatal units. Similar studies in America, Canada, Australia and New Zealand mean that data from around 5000 babies worldwide will be collected, and when combined in a prospective meta-analysis, should be able to detect small differences in outcome between the high and low saturation groups.

I have spent the last few months talking to professionals involved in the care of neonates about the study. Although it will involve more work at a time when resources, especially human resources, are already stretched, I believe that BOOST-II UK will succeed, because we all need this question answered. Recruitment will start early in 2007.

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References

1. **Tin W**. Optimal oxygen saturation for preterm babies Do we really know? *Biol Neonate* 2004; **85**: 319-25.
2. **Jobe A.H., Bancalari E.** Bronchopulmonary dysplasia. *Am J Respir Crit Care Med* 2001; **163**: 1723-29.
3. **Singer L., Yamashita T., Lilien L. et al.** A longitudinal study of developmental outcome of infants with bronchopulmonary dysplasia and very low birth weight. *Pediatrics* 1997; **100**: 987-93.
4. **Haynes R.L., Folkerth R.D., Keefe R.J. et al.** Nitrosative and oxidative injury to premyelinating oligodendrocytes in periventricular leukomalacia. *J Neuropathol Exp Neurol* 2003; **62**: 441-50.
5. **Collins M.P., Lorenz J.M., Jetton J.R. et al.** Hypocapnia and other ventilation-related risk factors for cerebral palsy in low birth weight infants. *Pediatr Res* 2001; **50**: 712-19.
6. **Hay W.W., Rodden D.J., Collins S.M. et al.** Reliability of conventional and new pulse oximetry in neonatal patients. *J Perinatol* 2002; **22**: 360-66.
7. **STOP-ROP Investigators.** Supplemental therapeutic oxygen for prethreshold retinopathy of prematurity (STOP-ROP), a randomized, controlled trial. I. Primary outcomes. *Pediatrics* 2000; **105**: 295-310.
8. **Askie L.M., Henderson-Smart D.J., Irwig L., Simpson J.M.** Oxygen-saturation targets and outcomes in extremely premature infants. *N Engl J Med* 2003; **349**: 959-67.