Blood oxygen levels in preterm infants

**Overview:** High blood oxygen level in preterm infants is associated with retinopathy of prematurity, but insufficient oxygen increases the risk of cerebral palsy and early neonatal death. However, the optimum oxygen range in preterm infants is not known. In the **BOOST** trial (2003), preterm infants with a blood oxygen level of 91–94% did not have better growth and development outcomes at 12 months than infants with blood oxygen of 95–98%. In the 2010 **SUPPORT** trial, infants with a blood oxygen target of 85–89% had lower rates of retinopathy of prematurity but higher mortality rates than infants with a target of 91–95%.

**Current advice:** No UK guidance exists on optimum blood oxygen in preterm infants. The **American Academy of Pediatrics** suggests blood oxygen levels of 85–95%. The **World Health Organization** recommends that infants with blood oxygen of less than 90% should be given oxygen. The oxygen flow should be regulated to a level of 92–95%. Oxygen can be stopped once the child maintains a blood oxygen level of above 90% in room air.

The UK Resuscitation Council’s guidance on newborn life support *(NICE accredited)* recommends that when using supplemental oxygen in preterm infants, blood oxygen should not increase more than in term infants (that is, from about 60% soon after birth to more than 90% at 10 min). It warns that blood oxygen above 95% can result in damaging hyperoxaemia.

**New evidence:** The **BOOST II group (2013)** reported a pooled analysis from 3 trials in Australia, New Zealand and the UK that looked at outcomes at hospital discharge in 2448 infants born before 28 weeks’ gestation without major congenital abnormalities. In all trials, infants were randomly assigned to a low blood oxygen target (85–89%) or a high blood oxygen target (91–95%). The primary outcome was death or severe neurosensory disability at 18 months to 2 years. During the studies, the pulse oximeters used were noted to be reporting fewer values of 87–90% than expected; subsequent investigation showed that the oximeters were displaying values 1–2% higher than they should. A software update was then applied to correct the calibration. The studies were stopped early because mortality at 36 weeks was significantly higher in infants with a low saturation target than in infants with a high target (21.8% versus 13.3%, relative risk [RR]=1.45, 95% confidence interval [CI] 1.15 to 1.84, p<0.001). The revised oximeter software was used in 1187 infants. Among this group, more infants died before hospital discharge in the low target group than in the high target group (23.1% versus 15.9%, relative risk [RR]=1.45, 95% confidence interval [CI] 1.15 to 1.84, p=0.002). The original oximeter software was used in 1261 infants, with no significant difference in deaths between infants in the low and high blood oxygen groups. Pooled analysis of all infants showed no significant difference in deaths but identified a lower rate retinopathy of prematurity in the low target group than in the high target group (10.6% versus 13.5%, RR=0.79, 95% CI 0.63 to 1.00, p=0.045).
Schmidt et al. for the COT Group (2013) conducted a similar international study in which preterm infants aged 23 weeks 0 days to 27 weeks 6 days were randomly allocated to low (85–89%) or high (91–95%) blood oxygen targets. The primary outcome was a composite of death or survival with disability at 18 months. After the safety concerns in the BOOST trial became known, the data and safety monitoring board for the COT trial analysed mortality and oximeter data but found no safety concerns.

In 1147 infants with adequate outcome data (95.5% of those enrolled), no significant difference was observed in the rate of death or disability at 18 months between the low target group and the high target group (odds ratio [OR]=1.08, 95% CI 0.85 to 1.37, p=0.52). In addition, no difference was reported in any component of the composite primary outcome – gross motor disability, cognitive or language delay, severe hearing loss and bilateral blindness – or in any secondary outcome, including retinopathy of prematurity. The oximeter software was also corrected in this study, but a subgroup analysis by oximeter software version showed no significant interaction for either the composite primary outcome or mortality at 18 months.

Commentary: “Oxygen is a commonly used therapy, but little evidence is available to guide its rational use in very preterm babies. Most neonatal units aim for a blood oxygen level of 85–95%, although some units use higher and some lower values. High blood oxygen levels are associated with the eye disease retinopathy of prematurity, but the tipping point where mortality increases through low oxygen had not been defined.

“The BOOST trials were designed to allow the first prospective meta-analysis of trials in this area. Overall, 5 studies with common interventions, methods and long-term outcome measures were conducted. All studies have reported mortality and short-term outcomes for babies of less than 28 weeks’ gestation, and 2 trials have reported 18–24 month outcomes.

“The BOOST and COT studies have rather different short-term outcomes. The BOOST II studies reported a large number of deaths in the low target group with the new oximeter software, but similar mortality between groups using the old software. By contrast, the COT study found no difference in mortality between the low target group and the high target group. Neither COT, nor the earlier SUPPORT trial, found differences in other 18–24 month outcomes.

“On the basis of these diverse results, many neonatal units have opted to use a blood oxygen target of 90–95% and to maintain levels of less than 95% if possible. The long-term outcome evaluations for the BOOST II studies are awaited, after which the prospective meta-analysis may shed further light on this continuing dilemma.” – Professor Neil Marlow, Professor of Neonatal Medicine, University College London

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