High or low oxygen saturation for the preterm baby

The observational study by Tin et al\(^1\) of outcome related to oxygen saturation in infants of less than 28 weeks gestation from a number of disparate units in the Northern Region shows results that are interesting, but only from the point of hypothesis generation.

Monitoring of oxygen saturation is simple but not without problems.\(^2\) Setting aside whether preterm infants requiring additional oxygen should be managed by monitoring oxygen saturation or oxygen partial pressure, does this study have any implications for management of such infants in the future? Is there any other corroborative evidence that the outcome of infants managed at lower saturations do better in terms of neurodevelopmental, respiratory, growth, or visual outcome?

The STOP-ROP study was designed to test the hypothesis that supplemental oxygen would reduce progression of retinopathy of prematurity (ROP). Infants with prethreshold ROP were randomised to either high (96–99%) or low (89–94%) saturation groups. There were no significant differences in the visual outcomes. Supplemental oxygen, however, increased the risk of adverse respiratory events including pneumonia and chronic lung disease with significant need for extra oxygen, diuretic therapy, and hospitalisation at 3 months corrected age. There was no difference in growth or neuromotor development.\(^3\) The respiratory morbidity in this study was not the primary study outcome and we must await the “Benefits of Oxygen Saturation Targeting Trial” from Australia to confirm or refute these findings (D Henderson-Smart, personal communication).

More pertinent may be work in an animal model of ROP indicating that management in lower oxygen (reducing the mean partial pressure of oxygen by 2 kPa to the lower end of the “safe” range) reduces the incidence and severity of ROP.\(^4\) Preliminary data from this model also show that apopotic proteins (compared with antiapoptotic proteins) in the brain are increased with higher oxygen.\(^5\)

Preterm babies must be given adequate oxygen, but possibly our reference to well term infants is inappropriate—infants with relatively low saturations because of cyanotic heart disease are not automatically compromised with regard to either growth or neurodevelopment.\(^6\) The use of oxygen has been estimated to have caused 16 children to die or survive with severe disability for every child whose sight was saved.\(^7\)

Memories are short, and over the last two decades the introduction of simple non-invasive monitoring of oxygen saturation has saved many infants from repeated arterial puncture, transfusion, and the complications of both techniques, but with little attention to the well known and very poor correlation between \(S\text{ao}_2\) and \(P\text{a}O_2\). In vivo correlation studies would indicate that to keep \(P\text{a}O_2\) between 7 and 10 kPa (50–70 mm Hg), oxygen saturation levels between 85 and 94% need to be accepted, but that at 94% saturation \(P\text{a}O_2\) may vary from 6 to 17 kPa.\(^8\)

The paper by Tin and colleagues forces us to look again at what we are doing in terms of oxygen monitoring; it would appear that using lower settings for alarms (\(S\text{ao}_2\) 70–90%) may have significant benefits for children in terms of less respiratory support, less weight loss, and, most notably, lower rates of serious retinopathy. These differences are so striking that the authors suggest that a randomised trial may be necessary— is this so?

There are difficulties with these data, in that in essence they are comparing the whole spectrum of care in different centres (with one exception) categorised by saturation monitoring policy. There are no direct observations nor do the authors attempt to define correlations between the monitors and blood gases. Furthermore, the actual levels measured are essentially conjecture on the part of the interviewed staff, and it is acknowledged that a different style of care persisted in the units practising monitoring in the lowest range. The authors claim that the higher saturation range is an attempt to keep saturation at a normal “physiological” level, something impossible to determine in an extremely preterm infant.

The rates of retinopathy in the high level monitoring group also seem rather high for UK units. In the Trent study, before the availability of treatment, 17.7% of infants of 27 weeks or less had grade 3 or worse.\(^9\) In the EPI Cure study (a cohort of babies of 25 completed weeks or less born in 1995 in the United Kingdom and Ireland, who have the very highest risk of retinopathy), the rate of treated ROP was only 14.5%, almost half the rate in the highest risk group in Tin’s study without the inclusion of 26 and 27 week infants. This value is inside the 95% confidence interval of the three lower level monitoring groups. Does some other factor account for these differences, or are the rest of us getting it “more right”?

What about a randomised trial? It should be easy enough with only around 125 infants required per arm (95% power). In vivo correlation studies indicate that allowing saturation levels to climb to 98% is likely to result in \(P\text{a}O_2\) levels that are much too high, as judged by recommendations based around \(P\text{a}O_2\) measures (50–80 mm Hg).\(^7\) Surely this should not be considered good practice? If I was asked to review such a project I would be critical of the high saturation arm; after all we do not simply wish to rediscover the issues dealt with in the 1950s. Five hundred infants per group would be needed to show a reduction from 15% to 6%; seeing a trial such as this through to completion would be very challenging.

New technology is coming to our assistance, at least in the first few days after birth, with new indwelling continuously reading probes giving us access to direct \(P\text{a}O_2\) levels.\(^{10}\) Many of
us have not stopped using the umbilical oxygen sensors that were the mainstay of care 20 years ago and the reliability of which seems to be now much improved. Transcutaneous monitoring is effective and at least offers detection of rapid swings in CO₂ tensions which may be of harm to the developing brain. Closer monitoring of PaO₂ is therefore possible.

Back to basics: thinking about correlations between arterial and saturation measures and what one is trying to achieve may be better approaches than a randomised trial which places one arm at potentially great risk.

NEIL MARLOW
Academic Division of Child Health, Level E, East Block
Queen’s Medical Centre, Nottingham NG7 2UH, UK
Neil.Marlow@Nottingham.ac.uk

References