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Should lower target ranges for oxygen saturation be favoured, in order to minimise the risk of retinopathy of prematurity (ROP)?

Manja et al. (2015) systematically reviewed the evidence evaluating the effect of restricted vs liberal oxygen exposure on morbidity and mortality in extremely preterm infants. They found that there was no significant differences in retinopathy of prematurity at 24 months. However, an earlier systematic review and meta-analysis of 10 trials (Saugstad, 2011) concluded that “A low oxygen saturation approach reduces severe retinopathy of prematurity by 50%, i.e., from 20.9 to 9.5%, and bronchopulmonary dysplasia/lung problems by 25%, i.e., from 40.8 to 29.7%.”

A retrospective chart review (Tlucek, 2010) compared babies screened for ROP during the 2 years immediately before (Group 1, n=387) and the 2 years after (Group 2, n=386) the initiation of a new oxygen protocol. In the new protocol, target oxygen saturation was adjusted from 90%-99% to 85%-93%. Mean birth weights (BWs) and gestational ages were 1,194 g and 29.2 weeks (ranges, 525-2,085 g; 23 2/7-39 6/7 weeks) for Group 1 and 1,139 g and 28.9 weeks (ranges, 520-2,500 g; 22 6/7-35 3/7 weeks) for Group 2 (p= 0.02/0.10). ROP developed in 32.7% of infants in Group 1 and 27.8% in Group 2 (p =0.17). The incidence of ROP requiring treatment was 19.9% in Group 1 and 20.5% in

Group 2 (p = 0.91). Subanalysis of infants with BW <= 1,000g (Group 1, n = 119; Group 2, n = 141) revealed ROP incidence of 75.1% versus 57.1%, respectively (p < 0.01); treatable disease occurred in 37.5% and 21.9% of affected infants (p = 0.19). The authors concluded that lowering target oxygen saturation for inborn premature infants was associated with decreased incidence of ROP only in infants with BW <= 1,000 g. Severity of disease, including need for treatment, was similar in both groups.
A meta-analysis of 10 studies (Chen, 2010) found that low oxygen saturation (70%-96%) in the first several postnatal weeks was associated with a reduced risk of severe ROP (RR 0.48 [95% CI 0.31-0.75]). High oxygen saturation (94%-99%) at > or = 32 weeks' PMA was associated with a decreased risk for progression to severe ROP (RR: 0.54 [95% CI: 0.35-0.82]).
A randomised trial comparing target ranges of oxygen saturation of 85 to 89% or 91 to 95% among 1316 infants who were born between 24 weeks 0 days and 27 weeks 6 days of gestation (Carlo, 2010) found that the rates of severe retinopathy or death did not differ significantly between the lower-oxygen-saturation group and the higher-oxygen-saturation group (28.3% and 32.1%, respectively; RR with lower oxygen saturation, 0.90; 95% CI 0.76 to 1.06; P=0.21). Death before discharge occurred more frequently in the lower-oxygen-saturation group (in 19.9% of infants vs. 16.2%; RR 1.27; 95% CI, 1.01 to 1.60; P=0.04), whereas severe retinopathy among survivors occurred less often in this group (8.6% vs. 17.9%; RR 0.52; 95% CI, 0.37 to 0.73; P<0.001). There were no significant differences in the rates of other adverse events.
Three large international randomised controlled trials also reported an increased risk in death when targeting oxygen saturation below 90%. The trials evaluated the effects of targeting an oxygen saturation level of 85 to 89% compared to a range of 91 to 95% on disability free survival for 2 years in 2488 infants born < 28 weeks.(Stenson 2013) Recruitment had to be stopped early when an analysis showed an increased rate of death in the low oxygen group at 36 weeks. (23.1% vs. 15.9%; relative risk in the lower-target group, 1.45; 95% confidence interval [CI], 1.15 to 1.84; P=0.002). Those in the lower-target group for oxygen saturation did have a reduced rate of retinopathy of prematurity (10.6% vs. 13.5%; relative risk, 0.79; 95% CI, 0.63 to 1.00; P=0.045). However, they also had an increased rate of necrotizing enterocolitis (10.4% vs. 8.0%; relative risk, 1.31; 95% CI, 1.02 to 1.68; P=0.04).

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