STOP-ROP
Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity
Abstract

Objective.

To determine the efficacy and safety of supplemental therapeutic oxygen for infants with prethreshold retinopathy of prematurity (ROP) to reduce the probability of progression to threshold ROP and the need for peripheral retinal ablation.

Methods.

Premature infants with confirmed prethreshold ROP in at least 1 eye and median pulse oximetry <94% saturation were randomized to a conventional oxygen arm with pulse oximetry targeted at 89% to 94% saturation or a supplemental arm with pulse oximetry targeted at 96% to 99% saturation, for at least 2 weeks, and until both eyes were at study endpoints. Certified examiners masked to treatment assignment conducted weekly eye examinations until each study eye reached ophthalmic endpoint. An adverse ophthalmic endpoint for an infant was defined as reaching threshold criteria for laser or cryotherapy in at least 1 study eye. A favorable ophthalmic endpoint was regression of the ROP into zone III for at least 2 consecutive weekly examinations or full retinal vascularization. At 3 months after the due date of the infant, ophthalmic findings, pulmonary status, growth, and interim illnesses were again recorded.

Results.

Six hundred forty-nine infants (325 conventional and 324 supplemental) were enrolled from 30 centers over 5 years. Five hundred ninety-seven (92.0%) infants attained known ophthalmic endpoints, and 600 (92%) completed the ophthalmic 3-month assessment. The rate of progression to threshold in at least 1 eye was 48% in the conventional arm and 41% in the supplemental arm. After adjustment for baseline ROP severity stratum, plus disease, race, and gestational age, the odds ratio (supplemental vs. conventional) for progression was .72 (95% confidence interval: .52, 1.01). Final structural status of all study eyes at 3 months of corrected age showed similar rates of severe sequelae in both treatment arms: retinal detachments or folds (4.4% conventional vs. 4.1% supplemental), and macular ectopia (3.9% conventional vs. 3.9% supplemental). Within the prespecified ROP severity strata, ROP progression rates were lower with supplemental oxygen than with conventional oxygen, but the differences were not statistically significant. A post hoc subgroup analysis of plus disease (dilated and tortuous vessels in at least 2 quadrants of the posterior pole) suggested that infants without plus disease may be more responsive to supplemental therapy (46% progression in the conventional arm vs. 32% in the supplemental arm) than infants with plus disease (52% progression in conventional vs. 57% in supplemental). Pneumonia and/or exacerbations of chronic lung disease occurred in more infants in the supplemental arm (8.5% conventional vs. 13.2% supplemental). Also, at 50 weeks of postmenstrual age, fewer conventional than supplemental infants remained hospitalized (6.8% vs. 12.7%), on oxygen (37.0% vs. 46.8%), and on diuretics (24.4% vs. 35.8%). Growth and developmental milestones did not differ between the 2 arms.

Conclusions.

Use of supplemental oxygen at pulse oximetry saturations of 96% to 99% did not cause additional progression of prethreshold ROP but also did not significantly reduce the number of infants requiring peripheral ablative surgery. A subgroup analysis suggested a benefit of supplemental oxygen among infants who have prethreshold ROP without plus disease, but this finding requires additional study. Supplemental oxygen increased the risk of adverse pulmonary events including pneumonia and/or exacerbations of chronic lung disease and the need for oxygen, diuretics, and hospitalization at 3 months of corrected age. Although the relative risk/benefit of supplemental oxygen for each infant must be individually considered, clinicians need no longer be concerned that supplemental oxygen, as used in this study, will exacerbate active prethreshold ROP.