Oxygen therapy in Preterm: Savior or Threat ?

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Retinopathy of prematurity (ROP) refers to the developmental disorder of the retina in premature infants and is one of the most serious vision threatening disease among premature infants.Earlier ROP was thought to be associated with oxygen therapy. Later it was also reported in cases without oxygen therapy. Therewere some premature infants who received oxygen therapy but didn't develop ROP. Finally, it was concluded that etiology of ROP is multifactorial occurring most frequently in the small and sick infants, but following three factors were found to be significantly associated with ROP: low gestational age (LGA), low birth weight (LBW) and prolong supplementary oxygen therapy after delivery.

Retinal vascularization starts at optic nerve head at 16 weeks of gestation then progresses to the periphery. Vascularization is almost completed by term.Inside the uterus, the fetus is in a hypoxic state in contrast to after birth. In premature infants, the growth of retinal vessels is stimulated by vascular endothelial growth factor (VEGF). The pathogenesis of ROP includes 2 phases. In the first phase, the immature retina is usually exposed to hyperoxia, which inhibits vascular endothelial growth factor (VEGF) and thus vessels stop growing. The second phase, precipitated by the increasing metabolic demand of the developing retina with a compromised vascular supply which is characterized by relative hypoxia, this stimulates VEGF and uncontrolled neovascularization occurs that extends into the vitreous and further causes sequelae of disease. Both duration and saturation of oxygen is very crucial in prevention of ROP.

The optimal oxygen saturation targets for preterm newborns are still controversial. In many studies oxygen is established as an important risk factor causing ROP. Oxygen is a drug and it should be administered in a quantity that is absolutely necessary. If a preterm neonate born at < 32 weeks gestation needs resuscitation at birth, inhaled oxygen concentration (FiO2) should be titrated to prevent hyperoxia and achieve gradual increase in oxygen saturation. Oxygen level in blood should be continuously monitored using pulse oximeter. It has been observed that if oxygen saturation in a baby on oxygen therapy is kept between 85% and 93%, in about 90% samples partial pressure of oxygen is in desirable range (40 to 80 mm Hg) and helps in preventing occurrence and progression of ROP.Due to inadequate antioxidant defense system, premature infants are not evolved to live in an oxygen-rich ectopic environment. During recovery phase of respiratory illness in preterm neonates, targeting higher oxygen saturations results in exposure of various organs to free radicals, which can lead to the progression of many pathology such as ROP, necrotizing enterocolitis, bronchopulmonary dysplasia, and periventricular leukomalacia.

Two landmark studies- Surfactant, Positive Airway Pressure, Pulse Oximetry Randomized Trial (SUPPORT) and Benefits of Oxygen Saturation Targeting Study II (BOOST-II) compared 85-89% SaO2 vs. 91-95% SaO2 and found that lower oxygen levels were associated with increased mortality, but lower rates of ROP.

Recently certain studies have reported that earlylow oxygen saturation (70%–96%) in the first few postnatal weeks (till 32 weeks PMA) and late high oxygen saturation (94%–99%) (after32 weeks PMA) decreasesthe risk of progression to severe ROP. The beneficial effect of early low and late high oxygen can be explained by the 2 sequential phases of ROP pathogenesis. During first phase, ROP is triggered by hyperoxia between birth and 30 to 32 weeks' gestational age. Early low oxygensupplementationis used to avoid this hyperoxia.The second proliferative phase begins around 32 to 34 weeks' gestational age and is associated with an increased VEGF expression in the retina in response to relative hypoxia, which results in pathologic neovascularization. Supplemental oxygen can be used therapeutically to downregulate VEGF expression and to limit the neovascular complications of ROP. It was concluded thatif oxygen saturations were controlled in both phases of ROP, it may reduce the occurrence and severity of ROP. But large randomized clinical trials along with long-term developmental follow-up are warranted to confirm these findings.

It isalso found that variability in oxygen saturation contributes to the severity and high incidence of ROP. So it is advised to reduce the variation of oxygen saturation with the help of proper monitoring and good neonatal care. We should also try to limit the duration of supplemental oxygen whenever possible, as duration of oxygen supplementation is also a very important factor leading to ROP.

Use of oxygen in preterm infants is a two edge sword. It's a struggle to save the life of baby at cost of risking his vision. Optimal oxygen saturations level for such babies is still not been established. Larger randomized control trials and much more research work are needed in this field to solve this dilemma.