

## A Comprehensive Review: Recent Advances in the Management of Retinopathy of Prematurity (ROP)

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### ABSTRACT

Retinopathy of prematurity (ROP) is a unique, proliferative vasculopathy in the retina of premature infants has set off the major cause of blindness in preterm infants throughout the world. In 1940s and 1950s it is also known as Retroental Fibrioplasia. Propranolol, a non selective beta adrenergic receptor inhibitor is used for ROP in various studies. Propranolol is used in infantile hemangioma due to blocking of VEGF (Vascular Endothelial Growth Factor) i.e it is tested for the RNV (Retinal Neo-Vascularization). Caffeine plays key role in the prevention of ROP progression. It is a frequently used drug in prematurity for the reduction of retinopathy in preterm infants. Adding supplementation of poly unsaturated fatty acids to the mother may mitigate the risk of ROP in premature infants. Vitamin A shows action by acting blocking of VEGF production. By providing vitamin A as a supplement during pregnancy it shows the reduction in ROP in premature infants. Exposure to the light may influence the ROP. Some studies had proven that light exposure may affect the progression of ROP. A red light exposure shows reduction in progression of ROP at 670 nm shows good results of development in ROP infants. NSAIDS such as ibuprofen and indomethacin are the widely used drugs in the treatment of ROP. Some studies have showed the effect of Insulin like growth factor - I (IGF-I) supplementation will give the potent outcomes in the management of ROP. A potential therapeutics strategy to treat ROP is with gene therapy using viral vectors. The most commonly used vector for humans can be adeno-associated virus because of its low immunogenicity. The first FDA approved adeno-associated virus gene therapy is the Voretigene neparovect to treat inherited retinal dystrophy caused by mutation of the RPE65 gene. It is very much essential to identify the novel therapeutics for ROP as the available therapies are causing unfavourable ocular outcome and also showing long term systemic effects on other organs. Gene therapy, cell therapy and non-coding RNAs have been shown a great impact in the management of ROP and further investigations are required to investigate the emerging treatment strategies.

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### Introduction

Retinopathy of prematurity (ROP) is a unique, proliferative vasculopathy in the retina of premature infants has set off the major cause of blindness in preterm infants throughout the world. In 1940s and 1950s it is also known as Retroental Fibrioplasia.

### New Strategies

#### Propranolol

Propranolol, a non selective beta adrenergic receptor inhibitor is used for ROP in various studies. Propranolol is used in infantile hemangioma due to blocking of VEGF (Vascular Endothelial Growth Factor) i.e it is tested for the RNV (Retinal Neo-Vascularization). The administration of Propranolol orally has given results of reduction in ROP development. Some adverse effects like bradycardia and hypertension has seen during the observation. Some of the other types of administration like eye drops 0.2% of Propranolol show excellent results in prevention of ROP development without any adverse reactions. Propranolol (oral administration) in infants had given reduction in ROP with the usage of anti VEGF drugs along with the laser therapy. By the

combination of laser therapy along with the Propranolol administration shows excellent results in prevention of advances ROP stages with optimal dosages of Propranolol in ROP treatment [1-4].

#### Caffeine

It plays key role in the prevention of ROP progression. It is a frequently used drug in prematurity for the reduction of retinopathy in preterm infants. By the combinational administration of caffeine along with VEGFS and MMPs (Matrix Metallo Proteins) shows good results in ROP progression without any serious adverse effects [5,6].

#### Poly unsaturated fatty acids

Supplementation of poly unsaturated fatty acids has ability to inhibit the oxygen driven retinopathy. Lack of poly unsaturated fatty acids may leads to retinal disorders. Poly unsaturated fatty acids contain docosahexaenoic acid and arachinoid acid which are the key components in brain and retina. Therefore, the premature infants are born with lack of poly unsaturated fatty acids is the major cause of ROP progression. By adding supplementation of poly

unsaturated fatty acids to the mother may mitigate the risk of ROP in premature infants [7-9].

### Vitamin-A

Vitamin-A is also known as retinol which play a key role in pregnancy and breastfeeding. It also promotes good eyesight by the chromogenesis in the retina of eye. The deficiency of vitamin-A may leads to xerophthalmia. Vitamin A shows action by acting blocking of VEGF production. By providing vitamin A as a supplement during pregnancy it shows the reduction in ROP in premature infants [10,11].

### Light

Exposure to the light may influence the ROP. Some studies had proven that light exposure may affect the progression of ROP. Randomized clinical trial conducted by the physicians had reported that light reduction of ROP did not give the sufficient effects in incidence of ROP. A red light exposure shows reduction in progression of ROP at 670 nm shows good results of development in ROP infants [12,13].

### NSAIDs

NSAIDs such as ibuprofen and indomethacin are the widely used drugs in the treatment of ROP. Ibuprofen had showed best results in RNV by blocking of VEGF signaling in mice OIR (Oxygen induced Retinopathy) model. Indomethacin had proved that improving the ROP without affecting the ordinary retinal development in OIR model. Administration of high dose of indomethacin showed good results with low adverse effects. Topical administration of ketorolac eye drops had given best results in the prevention and treatment [14,15].

### Serum Insulin Like Growth Factor-I

Insulin like growth factor - I (IGF-I) is a potent growth hormone produced by the mother in uterus. Premature infants does not has ability to produce the IGF-I by their own, but they show minimal amount of IGF-I. IGF-I minimal amount had greater risk in progression of ROP. By providing breast feeding to preterm infants can overcome the development of ROP. Some studies have showed the effect of IGF-I supplementation will give the potent outcomes in the management of ROP [16,17].

### Gene Therapy

A potential therapeutics strategy to treat ROP is with gene therapy using viral vectors. Viral vectors used to transfer the genes to retina can be lentiviruses,

adenoviruses and adeno associated viruses. The first FDA approved adeno-associated virus gene therapy is the Voretigene neparvovec to treat inherited retinal dystrophy caused by mutation of the RPE65 gene [18].

### Conclusion

It is very much essential to identify the novel therapeutics for ROP as the available therapies are causing unfavourable ocular outcome and also showing long term systemic effects on other organs. Gene therapy, cell therapy and non-coding RNAs have been shown a great impact in the management of ROP and further investigations are required to investigate the emerging treatment strategies.

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