



ORIGINAL RESEARCH PAPER

Ophthalmology

EVALUATE THE EFFICACY OF DIFFERENT TREATMENT MODALITIES FOR RETINOPATHY OF PREMATURITY IN A TERTIARY CARE CENTRE OF CENTRAL INDIA

KEY WORDS:

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ABSTRACT

Purpose- The present study aims to evaluate various treatment modalities of retinopathy of prematurity focusing on Anti VEGF Therapy. **Materials and methods-** This study was conducted in A tertiary care eye centre of central India from March 2020 to March 2021. The Institutional Review Board approved the study, and informed consent was obtained from all the subjects' parents before participating. Some of the consents were taken in the local language to ensure validity. The patients' parents were free to withdraw from the study and were assured that their withdrawal would not affect the quality of the care provided to their child. Patients (infants) with a history of preterm birth coming to the outpatient. **Results-** The most common modality for treatment in the study group was conservative management. (59.1%). Laser Indirect Ophthalmoscopy was required in 22.7% of cases while Intravitreal Avastin and Vitreo-retinal surgery were needed in 12.5% and 5.7% of cases respectively. Spontaneous regression of ROP was noted in a total of 45.4% of cases, with the majority being from Stage I disease (35.2%). **Conclusions-** The efficacy of various treatment modalities utilized for ROP was assessed and Laser Therapy (LIO) was found to be an effective and preferable treatment option for severe cases. Intravitreal Avastin was also beneficial as stabilizing agent prior to Laser therapy and as a salvage treatment for progressive disease.

Introduction-

Retinopathy of prematurity is a multifactorial vasoproliferative disease whose incidence increases with a decrease in gestational age. It is characterized by the development of abnormal blood vessels in the premature infant's developing retina due to incomplete vascularization of the retinal tissue brought on by hyperoxia, which also causes endothelial cell death and VEGF (vascular endothelial growth factor) downregulation. Neovascularization is the outcome of this process, causing compensatory upregulation of VEGF. ¹ Growing evidence from developing countries points to ROP as a substantial contributor to childhood blindness and vision impairment. ² It was previously known by other names like Retrolental fibroplasia and Terry syndrome, as Terry first described it in 1942 based on his understanding that the initiating change involved a proliferation of the embryonic hyaloid system incorporating the retina. ³ The term used in current literature, 'Retinopathy of Prematurity' was given in 1951 by Heath.

Retinopathy of prematurity has been recognized as a leading cause of preventable childhood blindness in both developed and developing nations. To date, three blindness epidemics due to ROP have been documented worldwide. ^{4,5} In the Western world, the reported incidence of ROP varies from 21% to 65.8%. However, recent research in India has found that the incidence of ROP varies from 38% to 51.9% among low-birth-weight infants. The incidence of ROP is believed to be increasing in India because of better neonatal care and a higher neonatal survival rate. Out of the 26 million live births in India each year, almost 2 million newborns have birth weights under 2000 g and are at risk of developing ROP. It accounts for 0.25% of childhood blindness in India.

In contrast to after birth, the fetus is hypoxic while in utero. Even when oxygenation is at ambient levels, newborns born prematurely might have higher relative oxygen levels. High oxygen supplementation has a damaging effect on the capillaries. Premature birth and other conditions that alter normal retinal vascularization and the oxygen requirements of the developing retina are central to the causation of ROP.

The key risk factors associated with the causation of ROP are Low birth weight, young gestational age, fluctuations in

oxygen levels, or high unregulated oxygen supply at birth. Some studies have suggested that Intraventricular hemorrhage, sepsis, respiratory distress syndrome, white race, blood transfusion, multiple births, excessive mechanical ventilation, Apgar scores, and Necrotising enterocolitis be also associated with ROP.

It was demonstrated that controlling signaling through the VEGF receptor-2, specifically in retinal endothelial cells, restored the orientation of dividing endothelial cells to enable them to grow in an ordered manner toward the Ora Serrata in a representative model of ROP that recapitulated stresses to premature infants. This research demonstrated that inhibition of an overactive angiogenic pathway and subsequent regulation of the VEGFR2 pathway prevented peripheral retinal angiogenesis while inhibiting intravitreal or extraretinal neovascularization. This was different from many adult retinovascular disorders. ⁶ Clinical investigations used intravitreal neutralizing VEGF antibodies, administered by intravitreal injections, to control VEGFR2 signaling in endothelial cells. However, because VEGF receptors on glia and brain cells are also impacted, the intravitreal delivery of an antibody or fusion protein that binds the ligand, VEGF, does not allow for the targeted regulation of VEGFR2 in endothelial cells. In a typical model, additional research revealed that intravitreal neutralizing antibodies to VEGFA caused retinal capillary dropout in response to oxygen stressors, followed by the reactivation of neovascularization into the vitreous. ⁷ This is comparable to the development of an infant's eyes. ⁸ Additionally, in the experimental model, decreased expression of VEGFA thinned the retinal layers, while decreased expression of all forms of VEGF did not. ⁹ This study inspired the idea to do additional research to find an effective and secure intravitreal anti-VEGF dose. ^{10,11}

Materials and Methods

This study was conducted in a tertiary care eye centre of central India from March 2020 to March 2021. The Institutional Review Board approved the study, and informed consent was obtained from all the subjects' parents before participating. Some of the consents were taken in the local language to ensure validity. The patients' parents were free to withdraw from the study and were assured that their withdrawal would not affect the quality of the care provided to their child.

A cross sectional study as performed for a period of 12 months from march 2020 to March 2021 at a tertiary care eye hospital in central India Examination of infants was conducted in an ROP screening cubicle with all emergency drugs and resuscitation kits, under the observation of a neonatologist or an anaesthesiologist. A/C and fan were avoided to prevent hypothermia. Paracetamol drops were given, and a glucose swab was put in the Omouth during the procedure. Babies were wrapped adequately with a sterile cloth. Anterior segment was examined for any anomaly like tunica vasculosa lentis (remnants of a hyaloid artery), congenital cataract, and corneal opacity . Indirect ophthalmoscope with 20D lens was used for fundus examination under full mydriasis. Sterilized pediatric wire speculum was used for fundus examination. Antenatal and Perinatal history was obtained. Extreme care was taken not to disturb the external milieu of the baby in the ICU ventilator. Aseptic precautions were practiced-washing hands, wearing caps and masks during the examination. Associated systemic disease and risk factors for the development of ROP were enquired from parents. The data from the customized proforma was transferred to the MS Excel sheet for analysis. Online statistical software, was used for calculating the 'p- value'. Pearson Chi-square test and ROC were used wherever applicable to draw associations between variables. A p-value of <0.05 was taken as significant. The final data was presented in the form of tables, graphs, and pie charts.

Observations and Results
ANALYSIS OF EFFECT OF DIFFERENT TREATMENT MODALITIES FOR ROP IN PRE-TERM NEONATES

The following table shows the observed distribution of the effect of different treatment modalities of ROP in pre-term neonate cases.

Table 1: Effect of Treatment Modalities for ROP in Pre-Term Neonates

| TREATMENT MODALITY | PRE-TERM NEONATES UNDERGOING TREATMENT | PRE-TERM NEONATES SHOWED REGRESSION OF ROP |
|------------------------------------|--|--|
| LASER INDIRECT OPTHALMOSCOPY (LIO) | 20 | 20 |
| INTRAVITREAL AVASTIN | 11 | 11 |
| VITREOUS/RETINAL SURGERY | 5 | 1 |

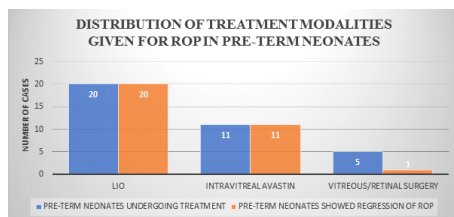


Figure 1 : Effect of Treatment Modalities for ROP in Pre-Term Neonates.

Inference: The above-displayed table and its graph show the distribution of different treatment modalities followed in treating Pre-Term Neonates with ROP. All those treated with Laser Indirect Ophthalmoscopy (LIO) and Intravitreal Avastin showed regression, and only one of the Vitreous/Retinal Surgery cases showed regression.

DISCUSSION
TREATMENT MODALITIES FOR ROP IN PRETERM NEONATES:

Most of the preterm neonates with ROP in our study were managed conservatively. (59.1%). 22.7% were treated with

Laser indirect Ophthalmoscopy, 12.5% received Intravitreal Avastin, and 5.7% required Vitreo-retinal surgery.

Table 2: Treatment modalities for ROP in various studies

| TREATMENT MODALITIES | STUDIES | | | |
|---|---------------|--------------------------------|------------------------------|---------------------------------|
| | Present Study | Anudeep K, et al ¹² | Hwang J, et al ¹⁴ | Vasavada D, et al ¹³ |
| Conservative management | 59.1% | 50% | 66% | 48% |
| Laser Indirect Ophthalmoscopy /Laser Photocoagulation | 22.7% | 50% | 15.2% | 46% |
| Intravitreal Avastin | 12.5% | - | 12.2% | 5% |
| Vitreo-retinal Surgery | 5.7% | - | 6.6% | 1% |

On comparing our observations regarding various modalities used for treating ROP with other studies, we noted that almost all the studies had the majority of the patients managed conservatively. Anudeep K, et al 12 and Vasavada D, et al¹³ reported a higher percentage of laser photocoagulation-treated patients than in our study, while Hwang J, et al 14 reported a lesser percentage of laser-treated patients than in our study but had comparable figures in Intravitreal Avastin treated patients. The percentages of patients undergoing vitreoretinal surgery for ROP were similar in most studies.

Conclusions

The incidence of ROP has been on the rise over the years due to the advancements and improvements in the management of preterm neonates in the NICU which have drastically improved the survival of these high-risk neonates which earlier often succumbed to various complications related to premature birth. This has presented as a challenging and uphill task to screen, diagnose and treat neonates who are at risk and develop Retinopathy of Prematurity so that ROP-related blindness can be prevented. This requires formulation and implementation of a proactive screening program that can identify such high-risk preterms based on their exposure to various risk factors associated with the development of ROP like prolonged oxygen exposure, presence of IUGR, RDS, neonatal sepsis, etc. The efficacy of various treatment modalities utilized for ROP was assessed and Laser Therapy (LIO) was found to be an effective and preferable treatment option for severe cases. Intravitreal Avastin was also beneficial as stabilizing agent prior to Laser therapy and as a salvage treatment for progressive disease.

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