International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 05|Issue 06 (November-December)|2022 Page: 1069-1073

Original Research Paper

COMPARISON OF INTRAVITREAL BEVACIZUMAB AND LASER PHOTOCOAGULATION FOR THE TREATMENT OF TYPE 1 RETINOPATHY OF PREMATURITY

Authors:

Arul Prasath S.V[#], Babitha Rexlin G[#], Rini Evangeline J*, Ramesh Kumar T[#]

#Professor, Department of Paediatrics, Kanyakumari Government Medical College Hospital, Asaripallam, Tamilnadu, India.

Corresponding Author: *Resident, Ramesh Kumar T, Department of Paediatrics, Kanyakumari Government Medical College Hospital, Asaripallam, Tamilnadu, India. Email: drrameshkumarmuhilai@gmail.com

Article Received: 04-10-2022 Revised: 24-10-2022 Accepted: 14-11-2022

ABSTRACT:

Background: ROP is a Vaso proliferative retinal condition that affects preterm babies. Early identification and treatment of ROP is highly beneficial in protecting a newborn's vision. ROP was initially treated with cryotherapy. Laser photocoagulation later became the conventional therapy for ROP over time. Bevacizumab, a recombinant monoclonal antibody against VEGFR, is currently used to treat ROP. In this study, we investigated the effectiveness of bevacizumab against laser photocoagulation for treating type 1 ROP **Method:** This retrospective study was conducted in the department of neonatology, Kanyakumari government medical college. Thirty-six neonates who met the criteria for Type 1 ROP and were treated with either PRP or bevacizumab were followed up till 90 weeks postmenstrual age. The primary outcome markers such as ROP recurrences needing re-treatment and significant complications were documented for each treatment group. **Result:** A total of 72 eyes from 36 premature newborns with type 1 ROP were treated. Laser photocoagulation was performed in 30 eyes in 15 cases (41.7%), while IVB injection was performed in 42 eyes in 21 cases (41.7%). (58.3%). A total of 6 eyes had a recurrence, and the recurrence rate was 6.7% for PRP and 9.5 % for IVB. All cases with recurrence had Zone 2 ROP. **Conclusion:** Both PRP and IVB are effective treatment options for treating type 1 ROP in both zones 1 and 2. Future RCT studies including larger sample numbers and longer follow-up periods are recommended.

Keywords: ROP-Retinopathy of prematurity, PRP-pan retinal photocoagulation, IVB-intravitreal bevacizumab.

INTRODUCTION:

ROP is a Vaso proliferative retinal condition that affects preterm new born babies. ROP is responsible for 3% to 10% of childhood blindness globally.[1] In India and other Countries with low and moderate incomes, ROP is becoming the primary reason for avoidable childhood blindness.[2] The actual cause of ROP is multifactorial, but oxygen, as well as vascular endothelial growth factor (VEGF) levels, have been found to perform critical roles in the first and second phases of ROP: relative hyperoxia and decreased levels of VEGF in phase 1 with delayed physiologic retinal vascular development, followed by relative hypoxia and increased levels of VEGF in phase 2.[3,4] Owing to the increased survival of preterm neonates, there has been an increase in the incidence of ROP.[5] Early identification and treatment of ROP is highly beneficial in protecting a new born's vision. The ETROP research indicated that when type-1 retinopathy of prematurity is evident, ROP should be treated.[6] Eyes with type 2 ROP must be monitored for the advancement of type 1 ROP. ROP was initially treated with cryotherapy. Laser photocoagulation ultimately replaced cryotherapy as the primary therapy in most hospitals. However, it is possible that parts of the peripheral retina would be destroyed in laser therapy. Vascular endothelial growth factors (VEGF) are the major cause of retinal neovascularization, anti-VEGF medication delivered intravitreally may be beneficial in treating ROP.[7] Bevacizumab, a recombinant monoclonal antibody against VEGF would be used for treating ROP. The clinical trial Bevacizumab Excludes the Angiogenic Threat of Retinopathy of Prematurity (BEAT-ROP), which contrasted intravitreal anti-VEGF antibody-bevacizumab treatment with laser therapy, found that bevacizumab helped babies with zone I/posterior zone II, stage 3+ ROP. Furthermore, the effect of anti-VEGF medication on VEGF suppression may be transitory.[8] For type 1 ROP, Following a single anti-VEGF drug therapy, either ranibizumab or bevacizumab, recurrence of extraretinal fibrovascular proliferation (EFP) was documented.[9] In investigations of new borns given intravitreal bevacizumab, and monitored for 60 weeks after birth, problems such as chronic peripheral avascular retina, new intravitreal

neovascularization, retinal detachment, and macular dragging were documented.[10] In our study ,We examined the efficacy of bevacizumab in combination with laser photocoagulation for treating type 1 ROP.

METHODS:

A retrospective study of babies treated for Type 1 ROP was carried out after obtaining approval from the institutional ethical committee to compare the efficacy of IVB versus laser therapy. Using a convenient sampling method, all consecutive infants with Type 1 ROP between January 2019 to December 2020 at Kanyakumari govt medical college who received either IVB or PRP were included in the study. Infants with type 1 ROP but with associated ocular anomalies like congenital cataracts, glaucoma, and other ocular infections were excluded from the study. Infants who fulfilled the Type 1 ROP criterion were treated with either PRP or bevacizumab. Following IVB or PRP therapy, each new born was initially checked for 1 to 2 weeks till the ROP was reversed. Subsequently, each infant was followed up till 90 weeks postmenstrual age, birth weight, age at diagnosis of ROP, Gestational age at birth, recurrence, and complications were recorded. ROP regression refers to disease involution and also resolution. Reduced plus illness, vascularization of the avascular peripheral retina, improved pupillary dilatation, increased medium clarity, involution of the tunica vasculosa lentis, and clearance of intraretinal hemorrhages are all signs of vascular regression. ROP regression is characterized by neovascular tissue thinning and whitening. An Arrest of anterior progression of the retinal vasculature along with a new demarcation line/ridge, or extraretinal fibrovascular proliferation (EFP) or leakage on fluorescein angiography, with or without recurrence of plus disease was used to define recurrence of ROP[11] Recurrence did not need extraretinal fibrovascular growth. Recurrence signifies reactivation following a time of regression but ROP persistence was defined as the absence of neovascularization and disease regression one week following treatment.[12] Major problems included lens opacity necessitating cataract surgery, corneal opacity necessitating corneal transplantation, and pre-retinal or intravitreal haemorrhage necessitating vitrectomy. ROP has necessitated re-treatment and retinal detachment progression, as well as severe problems linked with each therapy group, which were the primary end measures. If a chronic or recurring disease was found, it was treated again. IBM SPSS Statistics was used for statistical analysis.

RESULT:

In our study, 72 eyes representing 36 Preterm infants with type 1 ROP were treated, and the follow-up time was ultimately completed. Among type 1 ROP, zone 1 was affected in 26 eyes in 13 cases, and zone 2 was affected in 46 eyes in 23 cases. In 15 cases, laser photocoagulation was performed on 30 eyes (41.7%), and IVB injection was done on 42 eyes in 21 cases (58.3%). ROP regression and full or near total retinal vascularization were noted in 28 of the 30 eyes in Group 1. (93.3%). Two eyes developed retinal folds and traction (6.6%). In Group 2, the administration of IVB resulted in ROP regression in 38 (90.5%) of the eyes. ROP recurrence occurred in four eyes (9.5%) (table 2). Finally, at 90 weeks of PMA, ROP regression was accomplished in all instances in this group, and vascularization seemed complete on clinical inspection. Overall, the recurrence rate for PRP was 6.7% and 9.5% for IVB. The rate of ROP recurrence did not differ substantially between the two groups (p= 0.760). Recurrence occurred in six eyes, all of which had Zone 2 ROP. There was no reappearance in eyes treated for zone 1 ROP (table 3). ROP appeared in 4/22 (18.2%) of Zone 2 ROP eyes treated with IVB as well as in 2/24 (8.3%) of Zone 2 ROP eyes treated with PRP (table 4). However, it was statistically insignificant (P=0.484). No serious problems were observed in both PRP and IVB groups except in one case of PRP, which developed retinal traction in those implanted with the circumferential band.

Table 1: Patients with retinopathy of prematurity who received IVB or pan-retinal photocoagulation (PRP).

		IVB	PRP	P value
No of eyes (Patients)		42 (58.3%)	30 (41.7%)	n/a
ROP Zone	Zone 1	20(76.9%)	6 (23.1%)	0.089
	Zone 2	22 (47.8%)	24 (52.2%)	
Sex	Male	10 (50%)	10 (50%)	0.257
	Female	11 (31.3%)	5 (68.8%)	
Mean gestational age at birth (weeks)		30.4	29.4	0.167
Mean gestational age at birth (weeks) in ROP zone	Zone 1	29.8	31.6	0.014
	Zone 2	31	28.9	0.213
Birth weight (kg)	<1 KG	5	2	0.599
	1-1.5 KG	12	11	
	1.5 -2 KG	4	2	
Mean post-natal age at diagnosis (days)		56.67	54.13	0.911

Table 2: Comparison of Recurrence of ROP in intravitreal bevacizumab (IVB) and pan-retinal photocoagulation groups (PRP).

Group	Recurrence	No recurrence	P value
PRP	2 (6.7%)	28 (93.3%)	0.760
IVB	4 (9.5%)	38 (90.5%)	
Total	6 (8.3%)	66 (91.7%)	

Table 3: Comparison of Recurrence of ROP in zones 1 and zone 2 of both IVB and PRP groups.

Group		Recurrence	No recurrence	P value
PRP	Zone 1	0 (0%)	6 (100%)	0.605
	Zone 2	2 (8.3%)	22 (91.7%)	
IVB	Zone 1	0 (0%)	20 (100%)	0.156
	Zone 2	4 (18.2%)	18 (81.8%)	

Table 4: Comparison of recurrence of ROP in zone 2 in PRP and IVB groups.

	Recurrence	No recurrence	P value
PRP	2 (8.3%)	22 (91.7%)	0.484
IVB	4 (18.2%)	18 (81.8%)	
Total	6 (13%)	40 (87%)	

DISCUSSION:

In this study, we observed that recurrence rate and complications following treatment of type 1 ROP with either IVB injection or laser photocoagulation are almost similar. However, the re-treatment rate in patients with zone II illness treated with IVB was much higher (18.2%) than in those treated with PRP [8.3%]. But it was statistically insignificant (P-value =0.484). In study by Rohipoor et al. re-treatment occurred in 14.4% of IVB-treated eyes and 8.8% of RLP-treated eyes (P=0.065), and for patients with zone I illness, re-treatment did not show a significant difference between the two groups. However, the re-treatment range in patients with zone II disease who received IVB was much higher [12.3%] than in those treated with RLP [7.9%]. They concluded that both IVB as well as RLP are helpful therapies for type 1 ROP (P= 0.017).13 Kabatas et al., in retrospective research comparing three distinct treatment approaches, including IVB, Intravitreal ranibizumab (IVR), and laser photocoagulation, discovered that all three were similarly successful on ROP remission with minimal recurrence rates and no anterior region problems.14 WC. Wu et al. studied that Previously, laser photocoagulation was the primary therapeutic method. However, laser photocoagulation destroys the peripheral retina, making normal retinal vascularization impossible.15 Walker K et al. performed another therapy option for ROP: intravitreal anti-VEGF injection. Anti-VEGF intravitreal injection requires less equipment and expertise than laser photocoagulation and could be conducted without general anaesthesia.16 Mintz-Hittner HA et al. in the BEAT-ROP research, PRP had a greater recurrence rate than IVB (22% against 4% overall; 35% against 3.2% for Zone-I ROP). There was a substantial therapeutic benefit for zone I retinopathy of prematurity, not zone II disease. Based on the results development of peripheral retinal vessels remained following treatment with intravitreal bevacizumab, while conventional laser therapy resulted in irreversible retinal damage.17 Christopher et al. retinopathy of prematurity recurrence was observed in 14% of 22 IVB-treated eyes and 3% of 32 PRP-treated eyes. IVB and PRP are two successful therapies for type 1 ROP with minimal risk of complications. According to their findings, IVB was related to less myopia than PRP, even though PRP had an extended duration of follow-up.18 Also, as per NNF guidelines for screening and treatment of ROP 2021, Intra-vitreal Bevacizumab is not recommended for treatment of zone 2 ROP due to a higher incidence of the need for re-treatment and lack of evidence on possible harmful effects.19 In our study, there were no significant changes in total recurrence of type 1 ROP (zone 1 and 2) in PRP and IVBp-value-0.760. Though a difference in the recurrence rate of about 10% is confirmed between the type 1 zone 2 ROP treated with IVB and PRP, it is statistically insignificant (p=0.484). Our study didn't discover any serious issues with either PRP or IVB. Only one case treated with PRP developed retinal traction in which the encircling band was implanted. The limitation of our study is: Because this was a retrospective investigation, adequate controls might not be included in the study methodology. The sample size was small, which might have hampered our results' precision and generalizability. Furthermore, the PRP and IVB groups

had different distributions of Zone I and Zone II illnesses. Future RCT studies and of larger sample size are recommended to overcome such limitations.

CONCLUSION:

These findings revealed that laser photocoagulation and IVB are better therapies for type 1 ROP, with minimal complication and incidence rates. However, routine monitoring and close supervision are required until complete retinal vascularization. Additional studies with more follow-up may be needed to validate the existing results. Our study adds that IVB is a successful therapeutic option for type 1 ROP with zone 2 illness that has not been studied previously.

LIMITATIONS:

Funding: No funding sources.
Conflict of interest: None declared.
Ethical approval: The study was approved by the Institutional Ethics Committee.

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