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COMPARATIVE STUDY OF ANATOMICAL OUTCOMES BETWEEN INTRAVITREAL BEVACIZUMAB AND DOUBLE FREQUENCY Nd:YAG LASER IN RETINOPATHY OF PREMATURITY

Ophthalomology

Dr. Navdeep Dhunna — Junior resident, Government Medical College, Amritsar
Dr. Karamjit Singh* — Professor, Government Medical College, Amritsar*Corresponding Author
Dr. Saroj Bala — Professor, Government Medical College, Amritsar
Dr. Ashwani Kumar — Professor, Government Medical College, Amritsar

ABSTRACT

Background: Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness. Intravitreal anti-VEGF agents and laser photocoagulation are the mainstay treatments, each with distinct mechanisms and outcomes.**Aim:**To compare the anatomical outcomes of intravitreal bevacizumab injection and double-frequency Nd:YAG laser therapy in neonates with ROP.**Materials and Methods:**This prospective interventional study was conducted on 100 neonates (≤35 weeks gestation and/or ≤2000 g birth weight) screened for ROP. Infants were divided into two groups: Group 1 received intravitreal bevacizumab (n=50) and Group 2 received laser therapy (n=50). Baseline characteristics, disease profile, and risk factors were recorded. Patients were followed up to assess regression and anatomical outcomes. Statistical analysis was performed using chi-square and t-test.**Results:**The majority of infants belonged to the 28–32 weeks gestational age group in both cohorts. Type 1 ROP and Zone 2 posterior involvement were the most common findings. Early regression was observed in most cases, with 84% in the bevacizumab group and 90% in the laser group showing regression by day 3. Favourable anatomical outcomes were achieved in the majority of cases, with retinal detachment observed in only 2% in each group. Persistent avascular retina was more common with bevacizumab, while retinal haemorrhage was more frequent in the laser group.**Conclusion:**Both bevacizumab and laser therapy are effective in managing ROP with comparable anatomical outcomes. Laser provides faster regression, whereas bevacizumab allows continued vascular development but requires prolonged follow-up. Treatment should be individualized based on disease characteristics and follow-up feasibility.

KEYWORDS

Retinopathy Of Prematurity, Bevacizumab, Laser Photocoagulation, Anti-vegf, Anatomical Outcome

INTRODUCTION

Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness worldwide, primarily affecting premature infants with low birth weight and gestational age. The global burden of ROP has increased due to improved survival of preterm neonates, particularly in middle-income countries where neonatal care has advanced but screening programs remain inconsistent.[1] The disease is characterized by abnormal retinal vascular development resulting from an initial phase of hyperoxia-induced vascular arrest followed by hypoxia-driven pathological neovascularization mediated largely by vascular endothelial growth factor (VEGF).[2]

The management of ROP has evolved significantly over the years. Initially treated with cryotherapy, laser photocoagulation later became the gold standard following the Early Treatment for Retinopathy of Prematurity (ETROP) study, which demonstrated improved structural and visual outcomes with timely intervention.[3] Laser therapy works by ablating the avascular peripheral retina, thereby reducing angiogenic drive and halting disease progression.[4] However, laser treatment has certain limitations, including permanent destruction of peripheral retina, visual field constriction, high myopia, and technical difficulties in cases with poor pupillary dilation or media opacity.[5]

Advances in understanding the role of VEGF in ROP pathogenesis have led to the introduction of intravitreal anti-VEGF agents such as bevacizumab. These agents inhibit abnormal neovascularization while allowing continued physiological retinal vascularization, potentially preserving peripheral vision and reducing refractive complications.[2,6] The BEAT-ROP trial demonstrated that intravitreal bevacizumab was significantly more effective than conventional laser therapy in Zone I disease, with lower recurrence rates.[6]

Despite these advantages, anti-VEGF therapy raises concerns regarding late recurrence of disease, necessitating prolonged follow-up, as well as potential systemic side effects due to drug absorption in premature infants.[7,8] In contrast, laser photocoagulation provides more stable anatomical outcomes with fewer late recurrences, although at the cost of retinal tissue destruction and long-term refractive errors.[5]

Recent studies and meta-analyses comparing anti-VEGF therapy with laser photocoagulation have shown comparable efficacy in disease regression, though differences exist in recurrence patterns, refractive outcomes, and safety profiles.[9] Anti-VEGF therapy appears particularly beneficial in posterior (Zone I) ROP, whereas laser remains an effective and reliable treatment for Zone II disease.[1]

Given these considerations, the choice between intravitreal anti-VEGF injections and laser therapy remains a subject of ongoing debate. Evaluating anatomical outcomes following these treatment modalities is essential to guide clinical decision-making and improve visual prognosis in preterm infants. Therefore, the present study aims to compare the anatomical outcomes between intravitreal anti-VEGF bevacizumab injection and double frequency Nd:YAG laser in retinopathy of prematurity.

AIMS AND OBJECTIVES

1. To evaluate the anatomical outcomes following intravitreal anti-VEGF (bevacizumab) injection in neonates with retinopathy of prematurity (ROP).
2. To evaluate the anatomical outcomes following double frequency Nd:YAG laser therapy in neonates with ROP.
3. To compare the anatomical outcomes between intravitreal bevacizumab injection and double frequency Nd:YAG laser therapy in neonates with ROP.

MATERIALS AND METHODS

Study Design and Setting:

This prospective interventional study was conducted in the Neonatal Intensive Care Unit (NICU) and Department of Ophthalmology, Government Medical College, Amritsar.

Study Population:

Neonates with gestational age ≤35 weeks and/or birth weight ≤2000 g undergoing ROP screening were included.

Inclusion Criteria:

- Gestational age ≤35 weeks
- Birth weight ≤2000 g

Exclusion Criteria:
- Refusal of parental consent
- Incomplete documentation or follow-up
- Prior treatment elsewhere
- Advanced ROP (Stage ≥4 at presentation)
- Unknown gestational age

Sample Size:A total of 100 neonates diagnosed with ROP were enrolled and divided into two groups:
- Group 1: Intravitreal bevacizumab (n=50)
- Group 2: Laser therapy (n=50)

Study Procedure:
Baseline demographic and clinical details, including gestational age, birth weight, risk factors, and ROP stage, were recorded. Screening was performed at 4 weeks of birth and followed up as per standard guidelines. Detailed ocular examination was conducted after pupillary dilatation using indirect ophthalmoscopy, and findings were classified according to ICROP.

Treatment Protocol:
- Type 1 or high-risk ROP was treated with either intravitreal bevacizumab or laser photocoagulation.
- Type 2 ROP was kept under observation.
- Anti-VEGF was preferred in cases with poor pupillary dilatation, vitreous hemorrhage, aggressive posterior ROP, or unfit for laser.

Laser Therapy:
Laser photocoagulation was applied to the avascular retina using standard parameters to achieve near-confluent burns. Patients were monitored intra- and post-procedure, and followed up at regular intervals up to 3 months.

Intravitreal Bevacizumab Injection:
Under aseptic precautions and topical anesthesia, 0.625 mg (0.025 mL) bevacizumab was injected 0.75–1 mm posterior to the limbus. Follow-up was done within 48–72 hours and subsequently at regular intervals until complete retinal vascularization. Supplemental laser was considered if required.

RESULTS
The study included 100 neonates equally divided into two groups. The majority of infants in both groups belonged to the 28–32 weeks gestational age category (82.0% in the bevacizumab group vs 78.0% in the laser group). Mean gestational age, birth weight, and postmenstrual age at treatment were comparable between both groups, indicating homogeneity. Male predominance was observed in both groups (64.0% vs 70.0%). Most infants were delivered vaginally in both groups. These findings suggest that both treatment groups were comparable at baseline, minimizing selection bias.(Table 1)

Type 1 ROP was the most common presentation in both groups (86.0% in bevacizumab vs 92.0% in laser), while AROP was less frequent. Zone 2 posterior involvement was the predominant anatomical location (64.0% vs 56.0%), followed by Zone 2 anterior and Zone 1. Risk factors such as neonatal jaundice, RDS, and apnea were similarly distributed between groups. Statistical analysis showed no significant association between age, gender, and disease severity or zone distribution ($p > 0.05$), indicating comparable disease characteristics across both treatment modalities.(Table 2)

Early regression of ROP was observed in the majority of infants in both groups. In the bevacizumab group, 84.0% showed regression by the 3rd day, compared to 90.0% in the laser group. By the first week, additional regression was noted in 14.0% and 8.0% of infants respectively. Only 2.0% of cases in each group progressed to retinal detachment, indicating that both treatments are highly effective in inducing early regression, with slightly faster response observed in the laser group.(Table 3)

In the bevacizumab group, the most common unfavourable finding was persistent avascular retina, seen in all infants initially (100%) but progressively decreasing to complete resolution by 3 months. Retinal haemorrhage reduced steadily from 14.0% to 0%, and vitreous haemorrhage was rare (2.0%). Retinal detachment was observed in 2.0% of cases and persisted throughout follow-up. These findings indicate gradual vascular maturation but highlight delayed peripheral vascularization as a limitation of anti-VEGF therapy.(Table 4)

In the laser group, the most frequent complication was retinal haemorrhage, observed in 62.0% initially, which resolved completely by 3 months. Vitreous haemorrhage was seen in fewer cases and also resolved over time. Retinal detachment was noted in 2.0% of cases. Unlike bevacizumab, persistent avascular retina was not a major issue, suggesting that laser therapy ensures more complete retinal vascularization but is associated with higher early retinal tissue damage.(Table 5)

DISCUSSION
The present study compared anatomical outcomes of intravitreal bevacizumab and laser photocoagulation in retinopathy of prematurity (ROP), demonstrating that both modalities are highly effective with comparable baseline characteristics and favourable outcomes.

In the present study, the majority of infants belonged to the 28–32 weeks gestational age group, with comparable mean gestational age, birth weight, and postmenstrual age at treatment across both groups. Similar baseline comparability has been reported in the BEAT-ROP trial, which showed no significant differences between bevacizumab and laser groups [10]. This homogeneity strengthens the validity of comparison between the two treatment modalities.

Type 1 ROP was the predominant presentation in both groups, consistent with previous studies where it constitutes the majority of treatment-requiring ROP cases [11].Zone 2 posterior involvement was the most common anatomical location in this study, which is in agreement with findings reported by Lepore et al. [12].The distribution of neonatal risk factors such as respiratory distress syndrome, apnea, neonatal jaundice, and septicemia was similar in both groups, aligning with studies identifying these as key contributors to ROP development [13].

The present study demonstrated early regression of ROP in most infants, with 84% in the bevacizumab group and 90% in the laser group showing regression by the third day. Similar rapid regression following both anti-VEGF and laser therapy has been documented in previous studies [14].Although some literature suggests faster vascular response with anti-VEGF therapy, the present study observed slightly earlier regression in the laser group, possibly due to variation in disease severity and treatment timing [15].

Both treatment modalities showed high rates of favourable anatomical outcomes, with only 2% progressing to retinal detachment in each group. These findings are consistent with systematic reviews demonstrating comparable success rates between anti-VEGF and laser therapy [16].

The BEAT-ROP study also supports similar efficacy between the two modalities, especially in Zone II disease [10].

In the bevacizumab group, persistent avascular retina was the most common unfavourable outcome, gradually resolving over time. In contrast, the laser group showed a higher incidence of early retinal haemorrhage, which resolved during follow-up.These findings reflect known mechanisms of treatment, where anti-VEGF allows continued vascularization while laser causes retinal ablation [17].Previous studies have similarly reported delayed peripheral vascularization following anti-VEGF therapy [18].

Although recurrence was minimal in this study, literature suggests that anti-VEGF therapy may be associated with delayed recurrence and late reactivation compared to laser therapy . This highlights the need for prolonged follow-up in bevacizumab-treated cases.Both bevacizumab and laser therapy are effective modalities for ROP management. Laser provides immediate disease control, whereas bevacizumab allows continued vascular development but requires longer follow-up [18].Anti-VEGF therapy may be more beneficial in posterior disease, while laser remains effective in Zone II disease [12].

CONCLUSION
Both intravitreal bevacizumab and laser therapy are effective in treating ROP with comparable anatomical outcomes. Laser shows faster regression, while bevacizumab allows continued vascularization but requires longer follow-up. Treatment should be individualized based on disease severity and follow-up feasibility.

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Ethical Clerance: Taken from IEC

TABLES

Table 1: Baseline Characteristics of Study Population

Parameter	Group 1 (Bevacizumab) (n=50)	Group 2 (Laser) (n=50)
Gestational Age (weeks)	29.71 ± 1.86	29.32 ± 2.31
Birth Weight (grams)	1212 ± 302	1233 ± 223
PMA at Treatment (weeks)	37.82 ± 2.15	37.15 ± 2.13
Male	32 (64.0%)	35 (70.0%)
Female	18 (36.0%)	15 (30.0%)
Normal Delivery	39 (78.0%)	41 (82.0%)
LSCS	11 (22.0%)	9 (18.0%)

Table 2: Clinical Profile and Disease Characteristics

Parameter	Group 1 (Bevacizumab)	Group 2 (Laser)
Type 1 ROP	43 (86.0%)	46 (92.0%)
AROP	7 (14.0%)	4 (8.0%)
Zone 1	6 (12.0%)	7 (14.0%)
Zone 2 Anterior	12 (24.0%)	15 (30.0%)
Zone 2 Posterior	32 (64.0%)	28 (56.0%)
Neonatal Jaundice	18 (36.0%)	16 (32.0%)
RDS	11 (22.0%)	12 (24.0%)
Apnea	10 (20.0%)	11 (22.0%)
Septicaemia	5 (10.0%)	7 (14.0%)

Table 3: Early Anatomical Outcome (Regression of ROP)

Time of Regression	Group 1 (Bevacizumab)	Group 2 (Laser)
3rd Day	42 (84.0%)	45 (90.0%)
1st Week	7 (14.0%)	4 (8.0%)
No Regression (RD)	1 (2.0%)	1 (2.0%)

Table 4: Unfavourable Anatomical Outcomes – Bevacizumab Group

Outcome	3rd Day	1st Week	2nd Week	3rd Week	1st Month	3rd Month
Persistent Avascular Retina	50 (100%)	39 (78%)	28 (56%)	17 (34%)	3 (6%)	0
Retinal Haemorrhage	7 (14%)	7 (14%)	5 (10%)	4 (8%)	2 (4%)	0
Vitreous Haemorrhage	1 (2%)	0	0	0	0	0
Retinal Detachment	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)

Table 5: Unfavourable Anatomical Outcomes – Laser Group

Outcome	3rd Day	1st Week	2nd Week	3rd Week	1st Month	3rd Month
Retinal Haemorrhage	31 (62%)	26 (52%)	19 (38%)	8 (16%)	3 (6%)	0
Vitreous Haemorrhage	5 (10%)	5 (10%)	4 (8%)	2 (4%)	1 (2%)	0
Retinal Detachment	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)	1 (2%)

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