

Comparison of Complications of Intravitreal Bevacizumab with Laser Photocoagulation for the Treatment of Retinopathy of Pre-maturity

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ABSTRACT

Aim: To compare the rate of complications of intra-vitreous bevacizumab (IVB) with laser photocoagulation (LP) for the treatment of retinopathy of pre-maturity (ROP).

Methods: This comparative study was conducted on 70 babies with diagnosis of ROP. These babies were recruited from January 2016 to July 2017. In 35 patients, IVB was given for treatment of ROP and in remaining babies LP was used to treat ROP. IVB was given using a 30 Gauge needle under local anesthesia. Laser beams at wavelength 810 nm were given for photocoagulation to the entire avascular retina. Relapse rate and high myopia formation was noted till six months after the principal procedure. Relapse rate and occurrence of high myopia was compared between the IVB and LP groups using Chi-square test.

Results: There were 80% babies who were having zone I ROP in IVB group and remaining 82.85% babies were having zone I ROP in LP group. Regarding study outcomes, relapse occurred in 2.85% babies in IVB group and in 11.42% babies in LP group (p-value 0.16). High myopia occurred in 5.7% babies in IVB group and in 17.1% babies in LP group (p-value 0.13). Very high myopia occurred in 2.85% babies and in 37.14% babies in LP group, with significant p-value <0.0001.

Conclusion: Intra-vitreous bevacizumab (IVB) is more safe as compared to laser photocoagulation (LP) for treatment of retinopathy of prematurity.

Keywords: Retinopathy of prematurity, bevacizumab, relapse rate.

INTRODUCTION

Retinopathy of prematurity (ROP) is a condition in which there is abnormal growth of retina vessels in pre-mature babies. ROP results in 20,000 cases of blindness in infants¹. Due to advancements in neonatal ICU care, death rate in very pre-mature infants is reduced but at the risk of ROP. Neonatal birth weight (NBW) and gestational age are two important factors of ROP. Incidence rate is 16% to 48% in very low NBW babies and 27% to 35% in babies having weight <1.5 kg^{2,3,4}. Good visual outcomes are reported in babies in whom early treatment is given⁵.

It is proved that abnormally high level of vascular endothelial growth factor (VEGF) are responsible for over growth of retinal vessels⁶. Out of many management options of ROP, bevacizumab (an anti-VEGF drug) and laser photocoagulation (LP) are commonly in use. LP is in use for ROP from more than 20 years and has several side effects like enduring damage of some portions of retina, high myopia and loss of visual field.^{7,8} Bevacizumab is in routine use for the treatment of age related macular degeneration and retinopathy due to diabetes, and from few years also being applied for ROP treatment⁹⁻¹².

Recent studies have reported that intra-vitreous bevacizumab (IVB) has good clinical outcomes as compared to LP. However very little data is available regarding safety of these drugs and very few comparisons have been made of these drugs regarding their complications. So we conducted this study for comparing the complications of IVB with LP in infant for the treatment of ROP.

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The objective of the study was to compare the rate of complications of Inj. bevacizumab with laser photocoagulation for the treatment of retinopathy of pre-maturity.

MATERIALS AND METHODS

This comparative study was conducted in National University hospital, Temple street, Dublin Ireland. A total number of 70 babies with diagnosis of ROP were selected for this. These babies were recruited from January 2016 to July 2017.

In 35 patients, IVB was given for treatment of ROP and in remaining babies LP was used to treat ROP. All patient's guardians signed an informed consent before taking their baby in study.

IVB was given using a 30 Gauge needle under local anesthesia. Before instillation eyes were cleaned using iodine solution and draped in a disposable sheet. After injection funduscopy was done to examine any retinal tear and flow in retinal artery.

In LP group, laser beams at wavelength 810 nm were given for photocoagulation to the entire avascular retina. LP was done in all patients in presence of a neonatologist.

Netilmicin eye drops were prescribed to all babies four times per day for 10 days. Fundoscopic examinations were performed on the first day, third day, first week, and first month after the treatment. Relapse rate and high myopia formation was noted till six months after the principal procedure.

For data collection, we entered data in SPSS v23 and analyzed it. Relapse rate and occurrence of high myopia was compared between the IVB and LP groups using Chi-square test. P-value ≤ 0.05 was considered significant difference.

RESULTS

There were 80% babies who were having zone I ROP in IVB group and remaining 82.85% babies were having zone I ROP in LP group (p-value 0.75). Mean gestational age at birth was 24.44±1.02 weeks in IVB group and 24.75±1.10 weeks in LP group (p-value 0.22). There were 68.57% male babies in IVB group and 74.28% male babies in LP group (p-value 0.59). Age at the day of treatment was 33.23±2.56 days in IVB group and 34.11±3.3 days in LP group (p-value 0.33) [Table 1].

Regarding study outcomes, relapse occurred in 2.85% babies in IVB group and in 11.42% babies in LP group (p-value 0.16). High myopia occurred in 5.7% babies in IVB group and in 17.1% babies in LP group (p-value 0.13). Very high myopia occurred in 2.85% babies and in 37.14% babies in LP group, with significant p-value <0.0001 (Table 2).

Table 1: Baseline data.

Variable	IVB	LP	P value
ROP			
Zone I	28(80%)	29(82.85%)	0.75
Zone II	7(20%)	6 (17.1%)	
Mean gestational age (weeks)	24.44 ± 1.02	24.75± 1.10	0.22
Male Babies	24 (68.57%)	26 (74.28%)	0.59
Age at treatment day (days)	33.23 ± 2.56	34.11 ± 3.3	0.33

Table 2: Study outcomes.

Variable	IVB	LP	P-value
Relapse rate	1 (2.85%)	4 (11.42%)	0.16
High myopia	2 (5.7%)	6 (17.1%)	0.13
Very high myopia	1 (2.85%)	13 (37.14%)	<0.0001

DISCUSSION

Presence of abnormally high levels of retinal VEGF is responsible for ROP¹³. So the principal aim of treatment is to reduce VEGF levels using different modalities. Huge data is available for safety of bevacizumab but little data is published regarding safety of bevacizumab and its comparison have been made with LP.

In present study we compared the complications rate of IVB with LP. Relapse occurred in 2.85% babies in IVB group and in 11.42% babies in LP group in our study. High myopia occurred in 5.7% babies in IVB group and in 17.1% babies in LP group and very high myopia occurred in 2.85% babies in IVB and in 37.14% babies in LP group.

Kabataş et al. compared IVB, with IVR with LP and reported re-occurrence rate of 0 to 14% after IVB therapy, 13% to 26% after LP therapy and 0 to 12.1% after IVR therapy. They reported that IB, IVR and LP are equally effective for ROP treatment and have similar complications¹⁴.

Geloneck et al. has concluded that bevacizumab is a more safetreatment than photocoagulation for the treatment of ROP, and is associated with less risk of severe myopia. In their study, very high myopia occurred in 36.4% infants treated with ranibizumab and only 3.8% in infants treated with laser photocoagulation¹⁵.

But in another study, the authors concluded that both of these drugs are equally effective for the treatment of ROP and have comparable rates of complications¹⁶.

On the other hand Hwang et al. found significantly less relapse rate of ROP in laser photocoagulation group, 3.0% versus 14% in bevacizumab group¹⁷. Sanghi et al. reported reoccurrence in 17.4% ROP patients after LP¹⁸. While some authors have reported 21%-78% reoccurrence rate after treatment with LP^{19,20,21}.

IVB has shown to be superior to LP and IVR but still no standard dose of IVB has been reported yet in guidelines and its long-term risks are not evaluated yet.²² Moreover, endocrine analysis have clearly reported a reduction in vitreal VEGF levels and some studies have reported that single injection can reduce in VEGF effect and this is helpful in reducing the severity and re-occurrence of ROP. However, it is also shown that IVB also reduces systemic VEGF for upto 2 weeks which can have severe adverse affects on somebody functions²³.

CONCLUSION

Intra-vitreous bevacizumab (IVB) is safer as compared to laser photocoagulation (LP) for treatment of retinopathy of prematurity.

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