A STUDY TO ASSESS CHANGE IN CONTRAST SENSITIVITY AND VISUAL ACUITY IN PROLIFERATIVE DIABETIC RETINOPATHY PATIENTS UNDERGOING ANTI-VEGF TREATMENT AND ROLE OF LOW VISION AID IN SUCH PATIENTS

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ABSTRACT

Objective: The aim of this study was to study the effect of intravitreal anti-vascular endothelial growth factor (VEGF) on the visual acuity (VA) using logMAR charts and the contrast sensitivity (CS) using the pelli-robson chart in patients of advanced diabetic retinopathy.

Methods: The study was done at our institution where 40 patients of DR were included in the study, 20 cases (20 eyes) and 20 controls (20 eyes). Moreover, it comes under the criteria of low vision and above 18 years of age and VA >6/60. VA and CS were compared before injection and after injection at 14 days, 30 days, and 90 days, respectively.

Results: On comparing the mean of CS change before injections and after injections at 14 days (p=0.036), 30 days (p=0.012), and 90 days (p=0.012), respectively, showed a significant association between change in CS change within group but on comparing with control group at 14 days (p=0.195), 30 days (p=0.247), 90 days (p=0.247), respectively, showed no significant association. Another comparison of mean VA before injection and after injection in the case group at 14 days, 30 days, and 90 days, respectively (p=0.329) remains the same. Which is insignificant but on comparison with the control group (p=0.02) showed a significant association.

Conclusion: Whatever VA and CS are achieved with anti-VEGF was completed at 14 days of injection.

Keywords: Diabetic retinopathy, Visual acuity, Contrast sensitivity, Anti-vascular endothelial growth factor injections.

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of blindness in developed countries. Increased blood glucose levels and the metabolic pathways directly related to hyperglycemia, along with inflammation, alteration of retinal blood flow autoregulation, and hemorheological factors play an important role in the pathogenesis of DR [1] India is emerging as the diabetic capital of the world. According to the WHO, 31.7 million people were affected by diabetic mellitus in India in the year 2000. This figure is estimated to rise to 79.4 million by 2030. Almost two-third of all Type 2 and all Type 1 diabetics are expected to develop DR over a period of time [2-4]. Although there are significant advancements being made in the early diagnosis and treatment of patients, unfortunately, the number of patients at risk for the development of blindness due to DR is still thought to be increasing since the worldwide incidence of diabetes is on an increasing trend. This increasing incidence of diabetes mellitus is mainly the result of changing dietary habits in developing countries as well as increasing obesity in developed country. In the coming year 2050, there will be 50 million or more diagnosed and undiagnosed diabetic patients in the United States, of whom as many as half or 25 million may have DR unless major changes in nutritional status and disease prevalence occur [5,6]. The prevalence of adult diabetes worldwide is expected to rise from 4.0% in 1995 to 5.4% by 2025 [7]. Due to this increasing prevalence, it is expected that DR and diabetic macular edema are an important cause of visual impairment. DR is the leading cause of legal and functional blindness in the working population [8].

The most commonly used psychophysical test is visual acuity (VA) but it has many drawbacks as it evaluates only optotypes with high degrees of contrast while in the reality objects have different degrees of variability in contrast and spatial frequency [9]. Contrast sensitivity (CS) testing allows measurement of the patient’s ability to see low contrast patterns and provides more information on visual function than VA [10]. As a result, CS testing in clinical trial protocols may provide a more complete picture of the effect of treatment on visual function. All retinal layers are characteristically involved in DR and consequently affect both VA and CS [11]. CS is a very useful tool, along with VA in patients with DR as it correlates with the subjective visual disability better than high contrast VA in Snellen’s charts. Therefore, the literature recommends measurement of CS in all patients of DR. Hence, we have undertaken the study with the aim to assess the change in VA and CS in patients of advanced DR receiving intravitreal anti-vascular endothelial growth factor (VEGF).

Aims and objectives

The aim of this study was to study the effect of intravitreal anti-VEGF on the VA using logMAR charts and the CS using the pelli-robson chart in patients of advanced DR.

METHODS

The study was done in the regional institute of Ophthalmology, Banaras Hindu University. Forty patients of DR were included in the study, and all were on medication for glycemic control and their blood glucose level was in the normal range. Out of 40 patients 20 cases (20 eyes) and 20 controls (20 eyes). All patients underwent a complete ophthalmic check-up including a VA on Snellen and logMAR chart, a detailed fundus
evaluation with direct and indirect ophthalmoscope after which all were evaluated with 78D slit lamp biomicroscopy and IOP measure with applation tonometry.

This study included both male and female having DR with and without Proliferative diabetic retinopathy (PDR) and came under the criteria of low vision and above 18 yrs of age and VA >6/60. Furthermore, it excluded patients receiving multiple anti-VEGF, pre-treatment for DR along with any other associated ocular disease (uveitis, systemic disease (stroke, HTN), and any other major surgery within the last month of recruitment. All the patients were evaluated for 3 months.

Data were collected and statistically analyzed using a Student’s t-test paired for comparison within the study group and a Student’s t-test two samples assuming equal variance for comparison between the study group and control group.

**Inclusion criteria**

The following criteria were included in the study:

- Patients consent.
- Both male and female having DR and falling in criteria of low vision and above 18 years of age and VA >6/60 were included in the study.
- Patients have been recruited from eye and endocrinology OPD BHU.
- Subjects are 40 consecutive Type 2 DM patients with or without PDR.
- Patients selected for anti-VEGF intravitreal injection bevacizumab were included in the study.

**Exclusion criteria**

The following criteria were excluded from the study:

- Patients with multiple injections of anti-VEGF were excluded from the study.
- Patients with any other associated ocular disease, for example, uveitis, corneal disorder, congenital anomalies, active external eye infection, etc.
- Patients with any other associated systemic disease, for example, connective tissue disorder, thyroid disease, MI, stroke, hypertensive, etc.
- Pre-treatment for DR, pre-retinal hemorrhage presence of change in the vitreous-retinal interface such as epiretinal membrane, macular hole, vitreoretinal traction syndrome, previous systemic anti-VEGF, chronic renal failure, and any other major surgery within past months of recruitment.

**OBSERVATION AND RESULTS**

Majority patients in the case group were in the age group of 50–65 years whereas in the control group, patients were in the age group of 40–60 years. However, in the present study, first of all, CS change within the case group was compared and the mean of CS in the case group before receiving anti-VEGF were 0.64 (Standard Deviation [SD] 0.0487) and after receiving anti-VEGF, mean of CS in the case group were 0.79 (SD±0.519) on day 14 follow-up. Showing significantly change in CS (aired Student’s t-test, p=0.036) and after follow-up at 30 days mean of CS was 0.822 (SD±0.491) showing an increase in CS (p=0.012). Above analysis showed that there is an association between changes in CS within the case group (Table 1).

However, on comparing the mean of change in CS on 14 days (=0.79 [SD±0.519]) to the mean of change in CS on 30 days (=0.822 [SD±0.491]) p-value was found to be 0.258 which is non-significant, showing no association with each other. Similarly, when the mean of change in CS on 30 days (=0.822 [SD±0.491]) were compared with a mean of change in CS on 90 days (=0.822 [SD±0.491]), no p-value was found as both the data were same.

Another comparison was made in this study between case groups receiving anti-VEGF versus control group not receiving anti-VEGF. When the case group was compared with the control group, the mean of CS in the case group was 0.64 (SD±0.487), and the mean of CS in the control group was 1.0075 (SD±0.599) and showed significantly higher CS in the case group. Similarly, mean of CS of the case group was 0.7925 (SD±0.519) as compared to the control group-mean 1.0225(SD±0.58) on 14 days showed no statistical association. Similarly, in the case group mean of 0.8225 (SD±0.49) and the control group mean of 1.0225 (SD±0.58) on day 30 and the study group mean of 0.822 (SD±0.491) and the control group mean of 1.022 (SD±0.58) on day 90 reflected no statistical association (Table 2).

Another comparison was made between mean VA in logMAR in DR patients receiving anti-VEGF in the case group and not receiving in the control group: Moreover, comparison was made before injection and 14 days after injection, 30 days after injection and then 90 days after injection. This showed that after giving intravitreal anti-VEGF in DR patients there was a significant improvement in logMAR VA after 14 days of follow-up and thereafter, it remained stable or deteriorated (Table 3).

Comparison of mean of logMAR VA within the case group before injection and after injection is 0.66 (SD 0.25) and 0.64 (SD 0.25), respectively, with p=0.329 which is insignificant. Moreover, again on compare the mean of logMAR VA on day 14 to the mean of logMAR VA on day 30 remain insignificant because there was no p-value and again there was no p-value when compare 30 days mean logMAR VA to 60 days mean logMAR VA (Table 4).

Only a few patients benefited by low vision aid in the case group after 90 days of follow-up by handheld magnifier and telescope.

**DISCUSSION**

In this study, cases with or without DR having low vision and CS with pre-defined inclusion and exclusion criteria were included in the case group. Remaining cases who visited the outpatient department having normal or altered CS were included in the study as a control group. The discussion of analysis on observed data on various parameters is presented here as under.

**Comparison of CS**

On comparison of CS in our study, first of all CS changes within the case group were compared. Moreover, found that there is a constant

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean±SD</th>
<th>p-value</th>
<th>0 day versus 14 days</th>
<th>0 day versus 30 days</th>
<th>0 day versus 90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injection Contrast Sensitivity</td>
<td>0.64±0.487</td>
<td>0.036 (Significant)</td>
<td>0.012 (Significant)</td>
<td>0.012 (Significant)</td>
<td></td>
</tr>
<tr>
<td>Post-injection Contrast Sensitivity at 14 days</td>
<td>0.79±0.519</td>
<td>0.258 (Non-significant)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-injection Contrast Sensitivity at 30 days</td>
<td>0.822±0.491</td>
<td>0.012 (Significant)</td>
<td>0.012 (Significant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-injection Contrast Sensitivity at 90 days</td>
<td>0.822±0.491</td>
<td>0.012 (Significant)</td>
<td>0.012 (Significant)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Comparison of mean contrast sensitivity between study group versus control group before injection and after injection

<table>
<thead>
<tr>
<th>Day</th>
<th>Case Group Mean±SD</th>
<th>Control Group Mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injection</td>
<td>0.64±0.487</td>
<td>1.007±0.599</td>
<td>0.03 Significant</td>
</tr>
<tr>
<td>14</td>
<td>0.792±0.519</td>
<td>1.02.25±0.581</td>
<td>0.195 Not Significant</td>
</tr>
<tr>
<td>30</td>
<td>0.822±0.491</td>
<td>1.02.28±0.581</td>
<td>0.247 Not Significant</td>
</tr>
<tr>
<td>90</td>
<td>0.822±0.491</td>
<td>1.02.25±0.581</td>
<td>0.247 Not Significant</td>
</tr>
</tbody>
</table>

Table 3: Comparison of mean VA in logMAR between case group versus control group before injection and after injection

<table>
<thead>
<tr>
<th>Day</th>
<th>Case Mean±SD</th>
<th>Control Mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injection</td>
<td>0.6625 Mean±SD</td>
<td>0.6425 Mean±SD</td>
<td>0.06 Not significant</td>
</tr>
<tr>
<td>14</td>
<td>0.6425 Mean±SD</td>
<td>0.3248 Mean±SD</td>
<td>0.02 Not significant</td>
</tr>
<tr>
<td>30</td>
<td>0.6425 Mean±SD</td>
<td>0.3286 Mean±SD</td>
<td>0.02 Significant</td>
</tr>
<tr>
<td>90</td>
<td>0.6425 Mean±SD</td>
<td>0.3286 Mean±SD</td>
<td>0.02 Significant</td>
</tr>
</tbody>
</table>

Table 4: Comparison of mean visual acuity in logMAR within the case group before injection and after injection

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-injection</td>
<td>0.6625 Mean±SD</td>
<td>Pre-injection versus 14 days=0.32, pre-injection versus 30 days=0.32, pre-injection versus 90 days=0.32</td>
</tr>
<tr>
<td>14</td>
<td>0.6425 Mean±SD</td>
<td>14 days versus 30 days=0.32, 14 days versus 90 days=0.32</td>
</tr>
<tr>
<td>30</td>
<td>0.6425 Mean±SD</td>
<td>30 days versus 90 days=0.32</td>
</tr>
<tr>
<td>90</td>
<td>0.6425 Mean±SD</td>
<td>0.326</td>
</tr>
</tbody>
</table>

association between changes in CS in the case group when CS was compared with pre-injection versus days 14, 30, and 90.

However, on comparing the mean of change in CS on day 14 (0.79 [SD ±0.519]) to the mean of change in CS on day 30 (0.822 [SD ±0.491]) p-value was found to be 0.258 (non-significant). This means CS was not improved. Similarly, when the mean of change in CS on day 30 (0.822 SD ±0.491) was compared with the mean of change in CS on day 90 (0.822 [SD ±0.491]), no p-value was found as both the data were same. This means that there was no significant change in the case group. This clearly shows that there is a significant improvement in the change in CS in diabetic patients post-anti-VEGF up to day 14. However, in day 30 there was no statistical significance with p-value 0.02. This showed significant improvement in logMAR VA because the p-value (0.02) was significant. This indicates there was a definitive improvement in VA post-injection. Further, on comparing post-injection logMAR VA between the case and control group on days 14 with either days 30 p-value (0.02) or days 60 p-value (0.02) there was no significant difference this clearly indicates that whatever improvement in VA was noted post-injection on day 14 remains constant throughout follow-up.

Another comparison of the mean of logMAR VA within the case group before injection and after injection is 0.66 (SD 0.25) and 0.64 (SD 0.25), respectively, had a p-value of 0.32 which is insignificant and again on comparing the mean of logMAR VA on day 14 to mean of logMAR VA on day 30 remained insignificant because there was no p-value. There was no p-value on comparing 30 days mean logMAR VA to 60 days mean logMAR VA. This indicates that with passage of time, there was no significant improvement of VA within the case group.

In 1982, Sharon et al. in their study “CS in diabetic with retinopathy and cataract” found a systematic decrease in CS with increase in retinopathy grading with frequency attenuation almost parallel over all frequencies [12,13]. In our study on the use of anti-VEGF in DR patients, CS improved and became sustained.

On comparing our study with that of Preti et al. study, the mean logMAR VA in our study was 0.64 in the case group and 0.42 in the control group whereas in preti et al study mean LogMAR VA 0.28 in the case group and 0.24 in the control group. This showed that clearly, our patients were having slightly good vision as compared to their study.

Similar to Preti et al., the CS p-value of our study was not statistically significant, just as the p-value of Preti et al study which was also not statistically significant. However, when results were compared within the case group, our study showed a significant association whereas Preti et al. showed that injection bevacizumab does not deteriorate the CS rather maintains the CS in the study group.

Our study showed significant improvement in CS in the case group after giving anti-VEGF on day 14 and then remaining constant till follow-up. Similarly, Preti et al. study also showed significant improvement in CS on day 30 at spatial frequency three cpd. As in our study, it was shown on day 14.

In comparison with Preti et al. study, we can see that there is not much difference in terms of improvement in VA and CS in patients of DR receiving anti-VEGF treatment alone in our study, as compared to patients receiving anti-VEGF with PRP in their study. Our study gives the benefit to our understanding that whatever VA and CS are achieved patients receiving anti-VEGF with PRP in their study. Our study gives the benefit to our understanding that whatever VA and CS are achieved with anti-VEGF was completed at 14 days of injection. Both the studies showed no significant difference between groups.

**Limitations of the study**

Main limitation of our study is the sample size, which is relatively small, single-centered and most of the patients enrolled in our study are dilated.

**CONCLUSION**

Our study gives the benefit to our understanding that whatever VA and CS are achieved with anti-VEGF was completed at 14 days of injection. Moreover, the assessment of the status of low vision and the use of various low vision aids elevates the low vision in these patients.

**CONFLICTS OF INTEREST**

There are no conflicts of interest.

**REFERENCES**


