

Original Research Article

Therapeutic efficacy of intravitreal bevacizumab (Avastin)[®] in patients with parafoveal telangiectasia type II complicated by choroidal neovascular membrane and/or cystoid macular edema

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Abstract

AIM: To evaluate the therapeutic efficacy of intravitreal bevacizumab (Avastin)[®] on visual acuity and macular edema in patients with parafoveal telangiectasia type II complicated by choroidal neovascular membrane and/or cystoid macular edema.

METHODS: Study conducted over a period of **12 months**, at a tertiary eye care hospital including forty eyes of 25 patients (11 male, 14 female) suffering from type II parafoveal telangiectasia with choroidal neovascular membrane and/or cystoid macular edema who fulfilled the inclusion criteria. These were treated with intravitreal bevacizumab (Avastin). Each of the 40 eyes was enrolled into one of two groups, namely group 1: eyes with parafoveal telangiectasia type II with choroidal neovascular membrane and group 2: eyes with parafoveal telangiectasia type II with presence of cystoid macular edema but without choroidal neovascular membrane. All the patients underwent best corrected visual acuity slit lamp biomicroscopy, direct and indirect ophthalmoscopy, intra ocular pressure (IOP), clinical fundus photography, fundus fluorescein angiography (FFA) and optical coherence tomography (OCT). Follow up of patients was done at the first, third and sixth months after presentation.

RESULTS: 2 groups, in group 1-11 patients with equal male and female ratio, mean age 56.27±8.49 years, group 2-18 patients with female preponderance, mean age 53.5±7.18 years. In group 1, no significant improvement in mean BCVA before inj. Bevacizumab 0.121±0.06 and after injection 0.147±0.06 ($P=0.051$), while statistically significant improvement noticed in mean CFT, before inj. 469±89.67 and after injection 310.78±85.61 ($P=0.001$). similarly in group 2, no significant improvement in mean BCVA before inj. Bevacizumab 0.224±0.16 and after injection 0.254±0.09 ($P=0.453$), while statistically significant improvement noticed in mean CFT, before inj. 356.77±43.22 and after injection 253±42.59 ($P=0.001$). Transient hyperemia and subconjunctival hemorrhage were noticed in 2 patients in both group 1 and 2, while increase in blood pressure were observed in 2 patients in group 1 and 4 in group 2. None of the patients reported deterioration of vision following the injection.

CONCLUSION: In parafoveal telangiectasis type II complicated by choroidal neovascular membrane there is definite short-term improvement in the visual acuity (approaching statistical significance) and definite significant reduction of central foveal thickness following intravitreal injection of bevacizumab. In patients suffering from parafoveal telangiectasis type II complicated by cystoid macular oedema, there is definite significant reduction of central foveal thickness but no significant improvement in the visual acuity following intravitreal injection of bevacizumab. Bevacizumab is safe and well tolerated in eyes with parafoveal telangiectasis type II complicated by choroidal neovascular membrane and/or cystoid macular edema. No severe ocular or systemic adverse effects were encountered in this study.

KEYWORDS: parafoveal telangiectasia; choroid neovascular membrane; cystoids macular edema; bevacizumab; central foveal thickness

INTRODUCTION

Retinal telangiectasia refers to a developmental retinal vascular disorder characterized by an ectasia of capillaries of the retina, in which irregular capillary dilatation and incompetence occur in the retinal periphery or the macula^[1-3]. When only the capillaries of the foveal avascular zone are involved it is known as “parafoveal telangiectasia”. Idiopathic juxtafoveolar retinal telangiectasis is also known as parafoveal telangiectasia or idiopathic macular telangiectasia^[4,5].

The term “retinal telangiectasis” was first coined by Reese to describe the developmental vascular anomalies seen in patients with Coat’s disease and Leber’s military aneurysms. The term “parafoveal telangiectasis” was first used by Gass who observed that only the parafoveal retinal capillaries showed telangiectasia and fluorescein angiography (FA) was required to diagnose these cases.^[2] Gass and Oyakawa proposed the first classification of these entities into four groups based largely on their clinical and fluorescein angiographic (FA) features^[2,6,7,8].

In parafoveal telangiectasia type II, vascular endothelial growth factor has been implicated as the major angiogenic stimulus responsible for neovascularization. Several case series in the literature have investigated bevacizumab or ranibizumab for the treatment of parafoveal telangiectasia type II with choroidal neovascularization but with limited follow-up (12 months or less).^[3-7] However, only a few studies have been done thus far regarding the use of intravitreal bevacizumab (Avastin)® in parafoveal telangiectasia type II with or without choroidal neovascularization.^[7-11] Moreover, no prospective study has been performed thus far on Indian patients regarding use of intravitreal bevacizumab in parafoveal telangiectasia type II.

The purpose of the current study was to evaluate the anatomical and functional efficacy of intravitreal bevacizumab (Avastin)® in Indian patients suffering from parafoveal telangiectasia type II with or without choroidal neovascularisation in a prospective manner.

To evaluate the therapeutic efficacy of intravitreal bevacizumab (Avastin)® on visual acuity and macular edema in patients with parafoveal telangiectasia type II complicated by choroidal neovascular membrane and / or cystoid macular edema.

SUBJECTS AND METHODS

This Investigative, open label, prospective, interventional study was performed at the retina department of tertiary eye care institute over a **period of 12 months**.

Study Groups Group1: parafoveal telangiectasia (PFT) type II with choroidal neovascular membrane (CNVM);

Group 2: parafoveal telangiectasia (PFT) type II with cystoid macular edema (CME).

Interventional group 1 consisted of 11 patients (18 eyes) and interventional group 2 consisted of 14 patients (22 eyes).

Inclusion Criteria Patients were enrolled if they satisfied the inclusion criteria, namely: 1) Presented with type II parafoveal telangiectasia with choroidal neovascular membrane (CNVM) and / or cystoid macular edema (confirmed by fundus photography, fluorescein angiography, and optical coherence tomography); 2) Were males or females aged 40 years and above; 3) Were willing to provide signed written informed consent to participate in the study.

Exclusion Criteria Patients were not considered for enrolment in the study if they had any one of the following exclusion criteria: 1) Additional eye disease that could compromise visual acuity (VA); 2) Ocular inflammation; 3) Intraocular surgery had been performed ≤ 1 month before presentation; 4) Patient had received prior treatment with laser photocoagulation or other interventions for macular edema; 5) Media opacities that prevented clear visualization of the fundus and OCT examination; 6) Patient was pregnant; 7) Patients not willing to provide signed written informed consent to participate in the study.

Sample Size and Sample Technique Based on frequency of presentation of patients with parafoveal telangiectasis at the Study Place in previous years, it was estimated that, at the rate of five new patients per month, approximately 120 new patients (population size) would be seen during the study period of one year (August 2010 to July 2011). Expecting a response distribution of 20%, and taking into account a confidence level of 95% and margin of error of 5%, the recommended sample size in each arm of the study was calculated to be 49 patients (on-line sample size calculation, raosoft.com), using the formula $n = N \times [(N-1)E^2 + x]$, where ‘n’ refers to the calculated sample size, ‘N’ refers to the population size, ‘E’ refers to the margin of error and ‘x’ refers to the response

distribution(percentage).

Due to various constraints, in particular the reluctance of patients to receive an intraocular injection and to be enrolled in a formal study with regular follow-up, it was finally possible to enroll only a smaller number of patients.

Forty eyes of 25 patients (11 male, 14 female) suffering from type II parafoveal telangiectasia with choroidal neovascular membrane and/or cystoid macular edema who fulfilled the inclusion criteria and did not have any exclusion criteria, were enrolled. These were treated with intravitreal bevacizumab (Avastin)[®] 2.50mg (0.10mL volume of solvent). Each of the 40 eyes was enrolled into one of two groups, namely: 1) Group 1: eyes with parafoveal telangiectasia type II with choroidal neovascular membrane; 2) Group 2: eyes with parafoveal telangiectasia type II with presence of cystoid macular edema but without choroidal neovascular membrane

Efficacy Parameters Improvement of one line or more in best corrected visual acuity (BCVA) and reduction of central foveal thickness (CFT) by 50 microns or more at intervals of one month were taken to indicate acceptable criteria (value) of clinical efficacy of intravitreal bevacizumab in the present study. Due to the inherent time constraint of the current study, sustenance of the improved BCVA or reduced CFT over a longer time period was not possible.

Safety and Tolerability Safety and tolerability assessments (both ocular and systemic) of intravitreal bevacizumab administration were monitored by subjective evaluation of patients (complaints, detailed history and relevant examination), ocular examination and systemic evaluation (including relevant laboratory investigations). The greatest importance was given to all-cause mortality and serious adverse events, validated visual acuity measures, and effects on activities of daily living and quality of life. Severe ocular adverse events sought included retinal tear, endophthalmitis, lenticular opacity, vitreous hemorrhage, glaucoma, retinal detachment, and specific complications including anterior chamber reactions and fibrous proliferation retinal, pigment epithelial tear, submacular haemorrhage, progression of tractional retinal detachment and visual hallucinations. Systemic adverse events sought included increased blood pressure, myocardial infarction, stroke, transient ischemic attacks, deep vein thrombosis, angina, renal disorders, gastrointestinal bleeding, skin rash or redness and menstrual irregularities within 1 month of intravitreal bevacizumab injection.

Statistical Methods Data pertaining to age of patients are presented as proportions (percentage of patients in specific age ranges) as well as mean age (in years)±standard deviation. Data pertaining to BCVA (pre-treatment and post-treatment) in individual eyes are presented as decimal values and data pertaining to CFT (pre-treatment and post-treatment) in individual eyes are presented as μm (micrometers). Data pertaining to mean BCVA and mean CFT values are presented as mean±standard deviation.

The statistical significance of intergroup differences between mean age, mean BCVA (pre-treatment and post-treatment) and mean CFT (pre-treatment and post-treatment) in Group 1 eyes versus Group 2 eyes was calculated by the Student 't' test using SPSS software package for Windows (Version 16.0; SPSS Inc., Chicago, IL, USA). The statistical significance of intragroup differences between pre-treatment and post-treatment mean BCVA values and mean CFT values were also calculated by the Student 't' test. Values were considered statistically significant when $P < 0.05$.

Ethics The design and methodology of the study were reviewed and approved by the Institutional Review Board prior to the start of the investigation. In addition, written informed consent was obtained from each individual patient prior to enrolment in the study.

Methodology All eligible patients were followed for 12 months from baseline. The Primary end point in this study was to assess the efficacy of bevacizumab (Avastin)[®] 2.50mg (in a 0.10mL volume of solvent), by evaluating mean change from baseline in best-corrected visual acuity (BCVA) and central foveal thickness (CFT). Secondary endpoints in this study included the evaluation of tolerability and safety of bevacizumab (Avastin)[®] 2.50mg (0.10mL volume of solvent), and the Best Corrected Visual Acuity (BCVA) on Snellen's chart and intra-retinal thickness changes in Optical Coherence Tomography (OCT). Higher dose of avastin has been used to see whether more improvement in visual acuity and CFT, as it has already been mentioned in other studies where 2.5 mg dose used.

Visit Schedule At Visit 1 (baseline, week 0), the following information was collected to allow adequate characterization of the disease and the patient's medical history;

Workup Parameters (Baseline) 1) Best corrected visual acuity; 2) Slit lamp biomicroscopy; 3) Direct and indirect ophthalmoscopy; 4) Intra ocular pressure (IOP); 5) Clinical fundus photography; 6) Fundus

fluorescein angiography (FFA); 7) Optical coherence tomography (OCT)
Follow up of patients was done at the first, third and sixth months after presentation.

RESULTS

This investigative, open-label, prospective, interventional study was performed at the retina clinic of a tertiary eye care facility in southern India over a period of 12 months. Twenty five patients (40 eyes), comprising 11 males and 14 females (age range 40 to 70 years), who presented with parafoveal telangiectasia type II during the study period, who satisfied the inclusion criteria and who provided consent for participation, were included in the study. This study was approved by the Institutional Ethics Committee of the eye care facility. Upon presentation (baseline) and after ensuring that all investigational requirements were satisfied, patients were divided into two interventional groups:

Group 1: Parafoveal telangiectasia (PFT) type II with choroidal neovascular membrane (CNVM);

Group 2: Parafoveal telangiectasia (PFT) type II with cystoid macular edema (CME).

Interventional group 1 consisted of 11 patient (18 eyes) and interventional group 2 consisted of 14 patients (22 eyes). Patient demographics and baseline ocular characteristics are listed in Table 1-4.

Table 1 Gender of patients who presented with parafoveal telangiectasia type 2 with choroidal neovascular membrane (Group 1)

Gender	No. of patients
Male	6
Female	5
Total	11

Table 2 Age of patients who presented with parafoveal telangiectasia type 2 with choroidal neovascular membrane (Group 1)

Age group (Years)	No. of patients	Percentage (%)
40 – 50	3	27.27 %
51 – 60	3	27.27 %
61 – 70	5	45.45 %
Total	11	100

The mean age was 56.27±8.49 years (range=45 years to 70 years)

Table 3 Gender of patients who presented with parafoveal telangiectasia type 2 with cystoid macular edema (Group 2)

Gender	No. of patients
Male	5
Female	9
Total	14

Table 4 Age of patients who presented with parafoveal telangiectasia type 2 with cystoid macular edema (Group 2)

Age group (Years)	No. of patients	Percentage (%)
40 – 50	5	36 %
51 – 60	6	43 %
61 – 70	3	21 %
Total	14	100

The mean age of the patients was 53.5 ±7.18 years (range=40 years to 65 years)

Evaluation of Efficacy of Intravitreal Bevacizumab in Patients with Parafoveal Telangiectasia Type 2

a) Group 1 (PFT type II with CNVM) (figure-1) This group included 11 patients (18 eyes) with PFT type II with CNVM who were treated with an intravitreal injection of bevacizumab 2.50mg (0.1mL) under aseptic conditions. Of these 11 patients six were males (55%) and five were females (45%). The age distribution ranged between 45 to 70 years (mean age=56.27±8.5 years; median age=54 years); 45.45 % of the patients belonged to the 61-70 year age group. Two patients had both diabetes mellitus (DM) and hypertension (HTN), whereas one patient had both DM and ischemic heart disease (IHD).

Details about the pre-treatment and post-treatment best corrected visual acuity (BCVA in decimals) and central foveal thickness (in µm) values in each individual eye in this group are shown in Figure 1. The mean BCVA at presentation was 0.121 (approximately 6/60)±0.06 decimals, which was not significantly different ($P=0.051$) from the post-bevacizumab injection BCVA value of 0.147 (approximately 6/36)±0.06 decimals.

However, there was a significant difference ($P=0.001$) between the mean central foveal thickness at presentation ($469.17\pm89.67\mu\text{m}$) and the mean central foveal thickness ($310.78\pm85.61\mu\text{m}$) after the intravitreal injection of bevacizumab. One eye showed a decreased BCVA (from 6/60 to 3/60) following intravitreal bevacizumab; however, the same eye exhibited a reduction in central foveal thickness (from $417\mu\text{m}$ to $313\mu\text{m}$) following the injection. Ten eyes did not exhibit any change in BCVA, but showed a significant reduction in central foveal thickness.

b) Group 2 (PFT type II with CME) (figure-2) This group included 14 patients with PFT type II and CME who were treated with an intravitreal injection of bevacizumab 2.50mg (0.1mL) under aseptic conditions. Out of 14 patients, five were males (36%) and nine were females (64%). The age distribution ranged from 40 to 65 years (mean age 54.0 ± 7.18 years), six patients belonged to the 51-60 year age group. Four patients had DM and HTN as associated systemic illnesses, two patients had only HTN, two patients had only DM and one patient had bronchial asthma.

Details about the pre-treatment and post-treatment BCVA and central foveal thickness values in each individual eye in this group are shown in Figure 2

The mean BCVA at presentation was 0.224 (approximately 6/24) $\pm$ 0.16 decimals which was not significantly different ($P=0.453$) from the post-bevacizumab injection BCVA value of 0.2545 (approximately 6/24) $\pm$ 0.09decimals.

There was a significant difference ($P=0.001$) between the mean central foveal thickness at presentation ($356.77\pm43.22\mu$) and the mean central foveal thickness ($253\pm42.59\mu$) after the intravitreal injection of bevacizumab. One eye showed a decreased BCVA (from 6/36 to 3/60) following intravitreal bevacizumab; however, the same eye exhibited a reduction in central foveal thickness (from 410μ to 298μ) following the injection. Six eyes did not exhibit any change in BCVA, but showed a significant reduction in central foveal thickness.

c) Comparison between different parameters in Group 1 and Group 2 The mean age of the 11 patients in Group 1 (parafoveal telangiectasia type II [PFT] with choroidal neovascular membrane [CNVM]) was 56.27 ± 8.8 years and the mean age of the 14 patients in Group 2 (PFT with cystoid macular edema [CME]) was 53.5 ± 7.2 years (Table 5); this difference was not statistically significant (unpaired 't' test value=0.88 [degree of freedom {df}]=23; $P=0.39$).

Table 5 Comparison of mean age, pre-treatment and post-treatment best corrected visual acuity and pre-treatment and post-treatment central foveal thickness in patients and eyes with parafoveal telangiectasia type II.

Parameter	Group 1	Group 2
Age (years)	56.27 ± 8.50 (11 patients)	53.5 ± 7.18 (14 patients)
Pre- treatment Visual acuity (decimals)	0.121 ± 0.07 (18 eyes)	0.224 ± 0.16 (22 eyes)
Post- treatment Visual acuity (decimals)	0.147 ± 0.064 (18 eyes)	0.254 ± 0.098 (22 eyes)
Pre-treatment central foveal thickness (μ)	469.17 ± 89.67 (18 eyes)	360.73 ± 43.32 (22 eyes)
Post-treatment central foveal thickness (μ)	310.78 ± 85.61 (18 eyes)	253.45 ± 42.6 (22 eyes)

Group 1: 11 Patients (18 eyes) with parafoveal telangiectasis with choroidal neovascular membrane

Group 2: 14 Patients (22 eyes) with parafoveal telangiectasis with cystoid macular Edema

Males comprised six of 11 (55%) patients in Group 1 and five of 14 (36%) patients in Group 2; this difference was not statistically significant (χ^2 (d.f.=1)=0.6; $P>0.05$)

The pre-treatment mean best corrected visual acuity (BCVA) in Group 1 (18eyes) was 0.121 ± 0.06 decimals while that in 22 Group 2 eyes was 0.22 ± 0.16 decimals (Table 5; this difference was statistically significant (unpaired 't'test value=2.31[df=38]; 2-tailed $P=0.03$).

The post-treatment mean BCVA in Group 1 eyes (18 eyes) was 0.147 ± 0.06 decimals while the post-treatment mean BCVA in Group 2 eyes (22 eyes) was 0.254 ± 0.098 decimals (Table 5); this difference was highly statistically significant (unpaired 't'test value=4.51 [df=38]; 2-tailed $P<0.0001$).

The pre-treatment mean central foveal thickness (CFT) in 18 Group 1 eyes was $469.17\pm89.67\mu\text{m}$ while that in 22 Group 2 eyes was $360.73\pm 43.3\mu\text{m}$ (Table 5); this difference was highly statistically significant

(unpaired 't' test value=5.01 [df=38]; 2-tailed $P<0.0001$).

The post-treatment mean CFT in 18 Group 1 eyes was $310.78\pm 85.61\mu\text{m}$ while the post-treatment mean CFT in 22 Group 2 eyes was $253.0\pm 42.6\mu\text{m}$ (Table 5); this difference was statistically significant (unpaired 't' test value=2.78 [df=38]; 2-tailed $P=0.0084$).

Statistical Analysis a) Mean age of patients in Group 1 vs Group 2; Unpaired 't' test value=0.88 (degree of freedom [df]=23); $P=0.39$ (not significant);

b) Pre-treatment mean best corrected visual acuity (BCVA) in Group 1 vs Group 2 eyes; Unpaired 't' test value=2.31(df=38); 2-tailed $P=0.03$ (significant);

c) Post-treatment mean BCVA in Group 1 eyes vs Group 2 eyes; Unpaired 't' test value=4.51 (df=38); 2-tailed $P<0.0001$ (very significant);

d) Pre-treatment mean central foveal thickness (CFT) in Group 1 eyes vs Group 2 eyes; Unpaired 't' test value=5.01 (df=38); 2-tailed $P<0.0001$ (very significant);

e) Post-treatment mean CFT in Group 1 eyes vs Group 2 eyes; Unpaired 't' test value=2.78 (df=38); 2-tailed $P=0.0084$ (significant);

f) In Group 1 eyes, pretreatment mean BCVA vs post-treatment mean BCVA; Unpaired 't' test value=1.16 (df=34); 2-tailed $P=0.051$ (not significant);

g) In Group 2 eyes, pretreatment mean BCVA vs post-treatment mean BCVA; Unpaired 't' test value=0.75 (df=42); 2-tailed $P=0.46$ (not significant);

h) In Group 1 eyes, pretreatment mean CFT vs post-treatment mean CFT; Unpaired 't' test value=5.4 (df=34); 2-tailed $P=0.001$ (very significant);

i) In Group 2 eyes, pretreatment mean CFT vs post-treatment mean CFT; Unpaired 't' test value=8.28 (df=42); 2-tailed $P=0.001$ (very significant).

Evaluation of Safety and Tolerability of Intravitreal Bevacizumab When Used to Treat Parafoveal Telangiectasia Type 2 Safety and tolerability assessments (both ocular and systemic) of intravitreal bevacizumab administration were monitored by subjective evaluation of patients (complaints, detailed history and relevant examination), ocular examination and systemic evaluation (including relevant laboratory investigations).

In the current study, severe ocular adverse events were not noted in any of the enrolled patient eyes. Only transient hyperaemia and subconjunctival hemorrhage were noted in 2 eyes in group 1 and 2 eyes in group 2.

In the current study, increase in blood pressure were observed in few enrolled patients (in group 1- 2 patients and group 2-4 patients).

In the current study, none of the patients reported marked deterioration of vision following intravitreal bevacizumab administration.

In the current study, none of the patients reported persistent adverse effects on activities of daily living or quality of life after intravitreal bevacizumab administration. Interestingly, some of the patients reported beneficial effects on activities of daily living and quality of life due to improvement in the BCVA.

DISCUSSION

In the present investigation, 25 patients were enrolled; 11 (44%) were males and 14 (56 %) were females. The patients ranged in age from 40 to 70 years. Eight patients were between 40 to 50 years of age, nine patients were between 51 to 60 years of age and eight patients were between 61 to 70 years of age (Tables 1 and 3). In this study, 40 eyes of the 25 patients were studied.

Gass^[2] found that the long-term prognosis for patients with parafoveal telangiectasia II is poor, so that argon laser photocoagulation was not recommended by Gass for parafoveal telangiectasia type II. De Lahitte *et al*^[12] who evaluated the short-term effect of verteporfin photodynamic therapy in parafoveal telangiectasia Type II patients, found that there was no improvement in vision and no effect on permeability of vessels.

Allredge *et al*^[13] reported that intravitreal triamcinolone acetonide is not effective in patients with parafoveal telangiectasia type II, but provides only mild improvement of visual acuity^[15]. A study done by Wu *et al*^[14] also showed that intravitreal triamcinolone acetonide, in a dose of 4mg, does not improve visual acuity in most eyes with parafoveal telangiectasia type II.

The natural history of untreated choroidal neovascular membrane in parafoveal telangiectasia type II is generally poor, with 80% of eyes in a series of 26 eyes having a final visual acuity of 20/200 or worse.

^[15,16] Before the advent of VEGF antagonists, therapeutic options for subretinal neovascular membrane associated with parafoveal telangiectasia type II included laser photocoagulation, photodynamic therapy with

or without intravitreal triamcinolone acetonide, transpupillary thermotherapy and surgical removal of the membrane.^[16-24]

In the present investigation, in eyes with parafoveal telangiectasia type II with choroidal neovascular membrane, the mean best corrected visual acuity (BCVA) at presentation was 0.121 (approximately 6/60)±0.06 decimals, which did not differ significantly ($P=0.051$) from the post-bevacizumab injection mean BCVA value of 0.147 (approximately 6/36)±0.06 decimals. However, there was a significant difference ($P=0.001$) between the mean central foveal thickness at presentation ($469.17\pm89.67\mu\text{m}$) and the mean central foveal thickness ($310.78\pm85.61\mu\text{m}$) after intravitreal bevacizumab. In this group, one eye exhibited a decrease in BCVA (from 6/60 to 3/60) but also a reduction in central foveal thickness (from $417\mu\text{m}$ to $313\mu\text{m}$) following intravitreal bevacizumab. In addition, nine eyes did not exhibit any change in BCVA, but showed a significant reduction in central foveal thickness. These results suggest that in this group of eyes (parafoveal telangiectasia type II with choroidal neovascular membrane) that received intravitreal bevacizumab, visual acuity was improved (although not significantly) in some of the eyes whereas there was a significant reduction in mean central foveal thickness in many of the eyes.

In the present investigation, in eyes with parafoveal telangiectasia type II with cystoid macular edema, the mean BCVA at presentation (0.224 [approximately 6/24]±0.16 decimals) was not significantly different ($P=0.453$) from the post-bevacizumab injection mean BCVA value (0.2545 [approximately 6/24]±0.09 decimals). However there was a significant ($P=0.001$) reduction in the central foveal thickness from $356.77\pm43.22\mu\text{m}$ at presentation to $253\pm42.59\mu\text{m}$ after intravitreal administration of bevacizumab. In this group, one eye showed a decreased BCVA (from 6/36 to 3/60) but also a reduction in central foveal thickness (from $410\mu\text{m}$ to $298\mu\text{m}$) following intravitreal bevacizumab while six eyes did not exhibit any change in BCVA, but showed a significant reduction in central foveal thickness.

No significant ocular or systemic side-effects were observed in patients who received intravitreal injections of bevacizumab. The safety of anti VEGF agents has been documented in other studies also.^[27,29] However, any intravitreal injection follows a small but definite risk of complications such as retinal tears, endophthalmitis and cataract and it would seem wise to limit the number of intravitreal injections to the barest required. Thus in the present study, where 25 patients received anti-VEGF agents (11 patients in group 1 and 14 patients in group 2), the true rate of the adverse event in question in the population is about 3/25 or 12%. Hence, more detailed studies on larger number of patients is needed to confirm the safety of these anti-VEGF agents. However, the results of the present study are certainly promising, since the confidence in the efficacy of a treatment or management approach is enhanced if the results are based on a prospective randomized trial as in the case of the present study.^[26]

The results of the present investigation suggest that in eyes with parafoveal telangiectasia type 2 complicated by cystoid macular edema, the mean visual acuity and mean central foveal thickness values are significantly better than the same values in eyes with parafoveal telangiectasis type 2 complicated by choroidal neovascular membrane. In both groups of eyes, there is definite (although not statistically significant) short-term improvement in the best corrected visual acuity and statistically significant reduction in the central foveal thickness following intravitreal injection of bevacizumab.

In the present study, no complications occurred following intravitreal bevacizumab injection. Similarly, no apparent or serious ocular or systemic adverse events were observed in patients who had received intravitreal injections of bevacizumab. None of the patients died following injection of bevacizumab or during the course of the study.

In the current study, severe ocular adverse events were not noted in any of the enrolled patient eyes. (Only Hyperaemia and Subconjunctival hemorrhage were reported in a few patients).

In the current study high blood pressure was noted in 6 enrolled patients after injection. No other systemic adverse event was noted in any of the patients.

In the current study, none of the patients reported marked deterioration of vision following intravitreal bevacizumab administration.

In the current study, none of the patients reported persistent adverse effects on activities of daily living or quality of life after intravitreal bevacizumab administration. Interestingly, some of the patients reported beneficial effects on activities of daily living and quality of life due to improvement in the BCVA.

Micieli *et al*^[23] reviewed systemic adverse events associated with intravitreal bevacizumab in patients with ocular disease; 22 studies (12,902 eyes of 12,699 patients) were included in their review, which included prospective and

retrospective clinical studies and safety studies. The duration of follow-up ranged from one to 25 months. The most common side-effect reported was increased blood pressure (in 59 patients [0.46% of all patients]). Other reported adverse events included cerebrovascular accidents, myocardial infarction, transient ischemic attacks and angina, deep vein thrombosis, angina, renal disorders, gastrointestinal bleeding, skin rash or redness and menstrual irregularities. There were 23 deaths (0.18% of total). These authors concluded that the results of their review suggested that the systemic risk of bevacizumab was low; however, they opined that more active surveillance was needed to study the long-term safety of this drug in larger populations and to better evaluate the effects of bevacizumab on blood pressure. In another review, it was concluded that there was insufficient evidence to draw conclusions on the effects of intravitreal bevacizumab on mortality, serious morbidity, activities of daily living and quality of life.^[26]

An interesting aspect of the present investigation was the observation that while intravitreal bevacizumab may marginally improve BCVA in patients with parafoveal telangiectasis that is complicated by cystoid macular edema or choroidal neovascular membrane, it emphatically and significantly reduces central foveal thickness in eyes of parafoveal telangiectasia with these complications. Further studies of a longer duration and on a larger sample size of patients are required to confirm the initial results obtained in the present investigation.

One limitation of the present investigation was the short time-duration of the study; the results may have been different if the patients had been followed up for a longer duration of time. Another limitation of the present study was the limited sample size in each of the groups, with the number not reaching that required for unequivocal statistical analysis.

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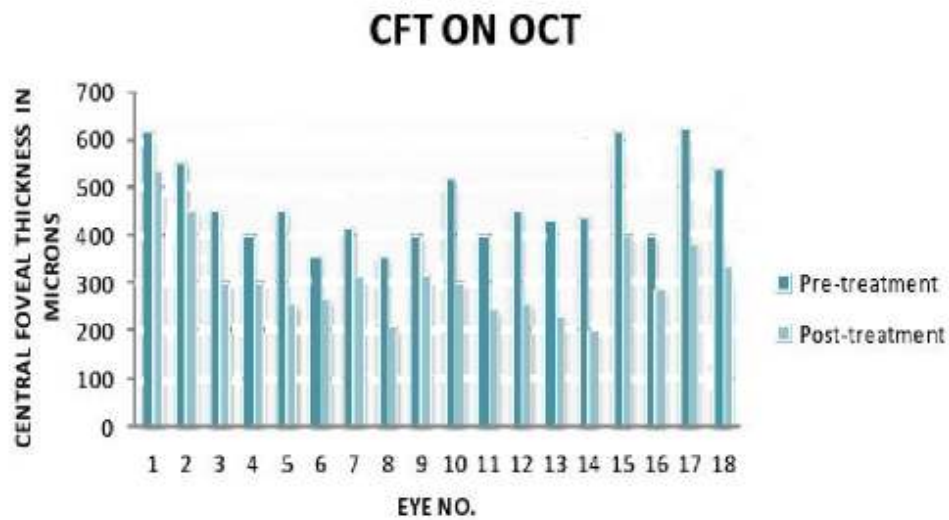
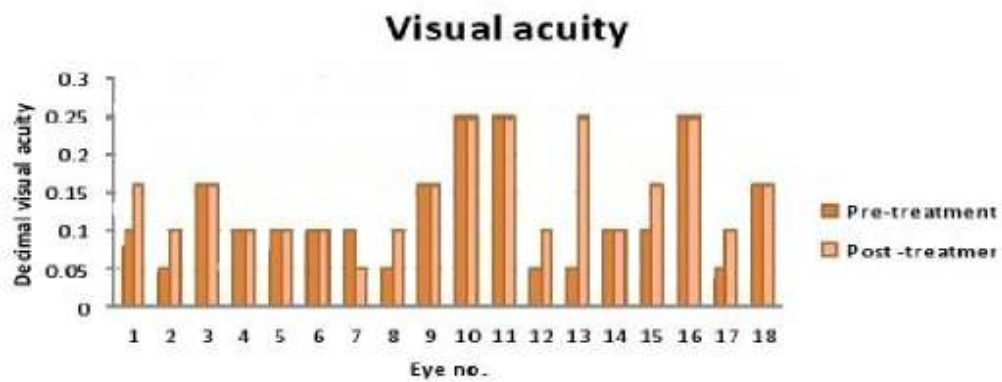


fig 1

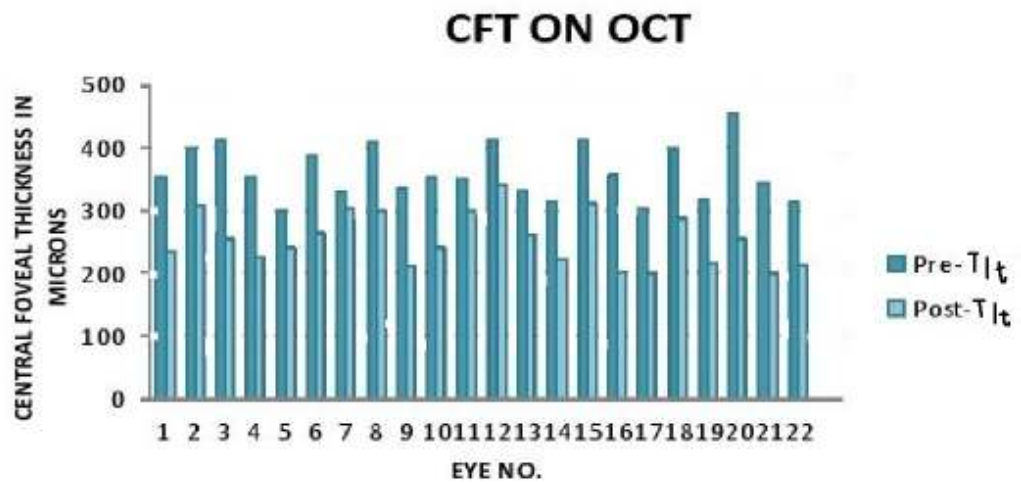
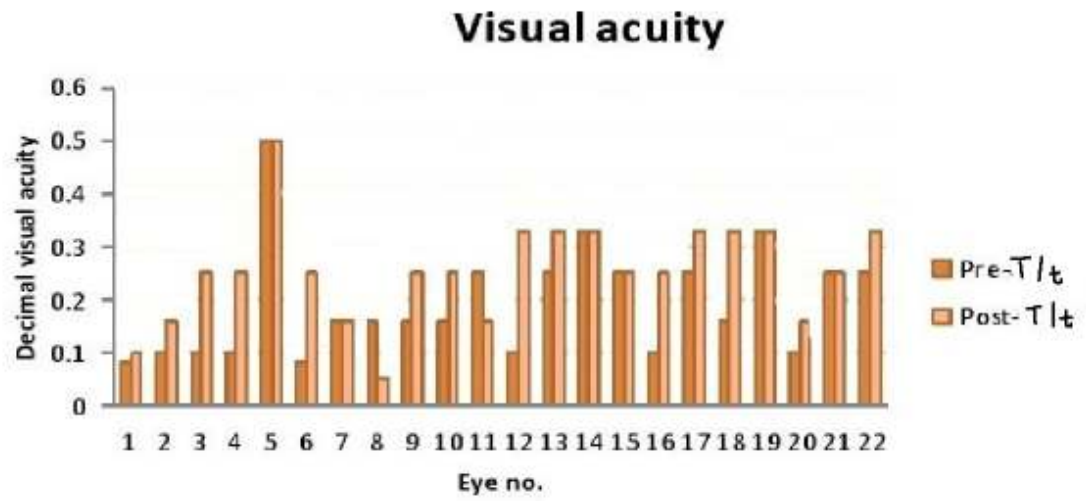


fig 2