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RESEARCH ARTICLE

ROLE OF INTRAVITREAL BEVACIZUMAB TREATMENT FOR EXUDATIVE ARMD WITH GOOD VISUAL ACUITY.

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ABSTRACT:

To investigate the visual outcome of intravitreal Bevacizumab on visual outcomes of patients with exudative age related macular degenerations with good visual acuity. A cohort study of 30 eyes of 30 newly diagnosed patients of exudative age related macular degenerations was conducted in tertiary care centre in period of 1 Under all aseptic precaution intravitreal injection of Bevacizumab was given to 30 eyes of 30 patients at the dose of 1.25 mg in 0.05 ml. Intraocular tension was monitored in each patient and those raised were managed accordingly. Visual acuity was taken on day 1, day 7, 1 month and 3 month and 6 month of procedure.Year from July 2011 to June 2012.Thirty eyes of 30 patients were included. Of the 30 eyes, 10 (33.34%) had stable BCVA, 19(63.43%) had improved BCVA and only 1(3.33%) had detoriated BCVA. No significant ocular or systemic side effects were observed. Prompt intravitreal Bevacizumab treatment for newly diagnosed exudative age related macular degenerations in patients with good initial best corrected visual acuity is associated withsustained or improved visual acuity.

Keywords: Bevacizumab, visual acuity

INTRODUCTION

Antivascular endothelial growth factor (VEGF) therapy has been recently established as an effective treatment for subfoveal neovascular age-related macular degeneration(AMD). Two anti-VEGF agents, pegaptanib [1] and ranibizumab have been demonstrated to be effective in treating neovascular AMD. Bevacizumab a humanized monoclonal VEGF antibody derived from the same murine monoclonal antibody as ranibizumab, is approved for intravenous use in the management of colorectal cancer.[2] Bevacizumab was initially used via intravenous injection in the management of AMD-related choroidal neovascularization (CNV)[3]. Given the potential systemic thromboembolic side effects associated with the intravenous use of bevacizumab, ophthalmologists have more recently been administering the medication via intravitreal injection in neovascular AMD[4]. Several laboratory [5-8] andclinical studies [9-14] have supported the short-term safety and efficacy of intravitreal bevacizumab. However, the long term effects, the optimal dose, and the best treatmentregimen have not been clarified. We report our short-term experience with intravitreal bevacizumab in the treatment ofAMD-related

subfoveal CNV, and based on these findings,suggest that a treatment in patients with good initial best corrected visual acuity is associated withsustained or improved visual acuity.

METHODS:

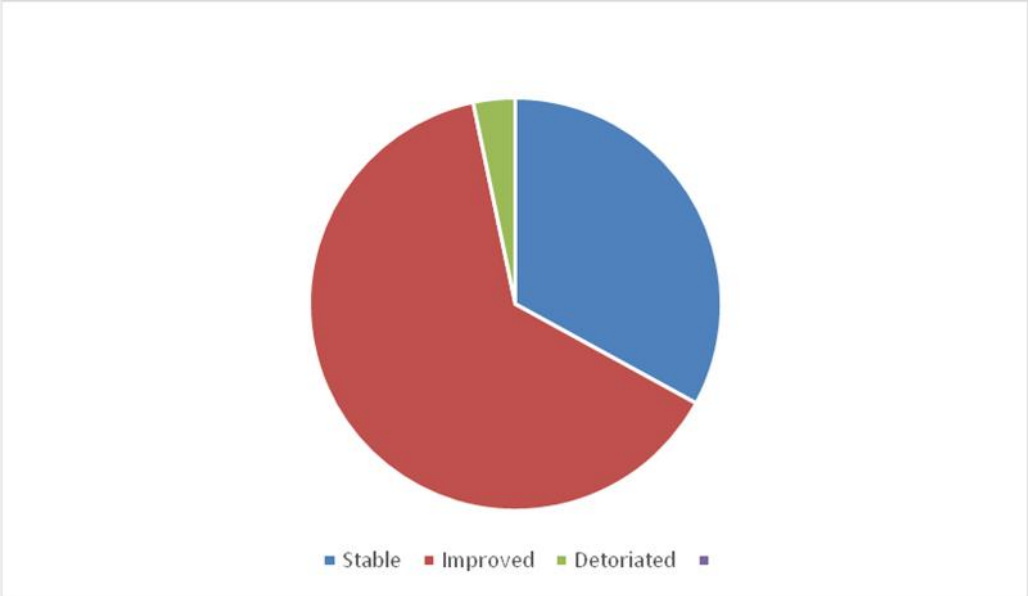
Thirty patients who completed six month follow-up were included in this study. Newly diagnosed patients with visual acuity ≥ 6/24 were included in this study and Patients with prior treatment for wet ARMD, Patients with atrophic ARMD,Patients with diminution of vision due to other retinal disorders and media opacities were excluded from study.All included patients received 1.25 mg of intravitreal bevacizumab (0.05 ml of commercial solution of Avastin) following complete ocular examination, which included best corrected Snellen's visual acuity. Visual acuity was taken on day 1, day 7, 1 month and 3 month and 6 month of procedure. Intra ocular tension was monitored in each patient and those raised were managed accordingly.Moreover, ocular imaging with FA and OCT was not routinely performed at each follow up visit; however, OCT imaging was done for all included patients at presentation and at 12 weeks following initiation of treatment. Best-corrected Snellen acuity was converted into logarithm of the minimum angle of resolution (log MAR) for statistical analysis. Mean visual acuity and OCT central macular thickness at baseline and each follow up visit were compared using a Student's *t*-test to determine statistical significance with 95% confidence intervals ($P < 0.05$).

RESULTS

Out of the 30 patients included in the study, 21 were females. The age ranged from 62 to 89 years (mean, 77.7 years). All treated eyes completed 12 weeks of follow up. Visual acuity and OCT data were available for all eyes at baseline and at 12 weeks follow up. The two-, four-, and eight-week data were available for 65.5%, 55.2%, and 55.2% of eyes, respectively. Twenty-nine eyes (97.77%) had stable or improved BCVA (Table 1) and nineteen eyes (64.43%) ended up with improved vision. Nineteen (64.43%) and 10 (33.34%) eyes experienced at least one and two lines of vision improvement, respectively. Only one eyes had worse BCVA at 6 month compared to baseline. Improvement in average visual acuity occurred over the first four weeks of follow up after which a trend towards stabilization was observed (figure 1).The majority of the change in average central macular thickness was observed over the first two weeks following treatment and improvement was maintained through the 6 month follow up visit . Worsening in average central macular thickness was observed at the four-week visit compared to the two-week visit but this was not associated with worsening in average BCVA.Average mean central macular thickness measured by OCT improved from 306 μm at baseline to 197 μmat 12 weeks ($P = 0.003$).

During the three months follow up, fewer than a fiveof the eyes (five eyes, 16.66%) required repeat injections,(Figure 2)with only three eyes (10.00%) requiring retreatment at eight weeks and none at four weeks. No ocular or systemic side effects were observed, although patients were not specifically monitored for variations in their blood pressure during follow up.

Status of visual acuity after procedure	Number of eye(30)	Percentage (%)
Stable	10	33.34
Improved	19	64.43
Detorioted	01	3.33



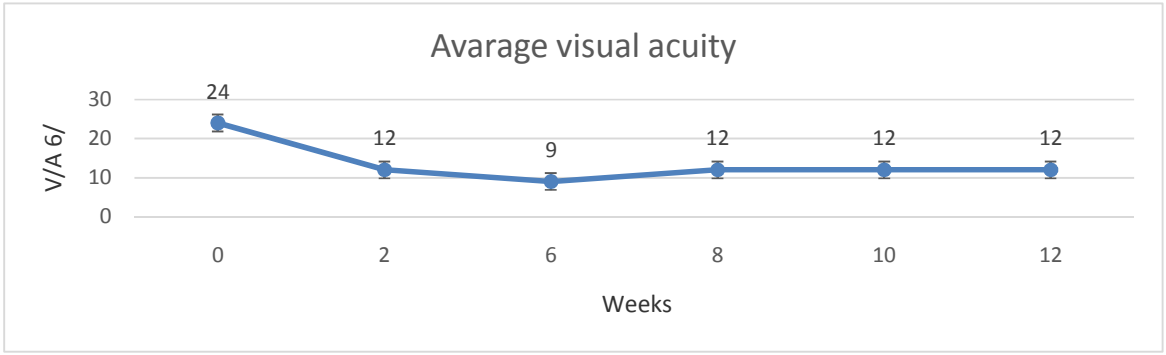


Figure 1

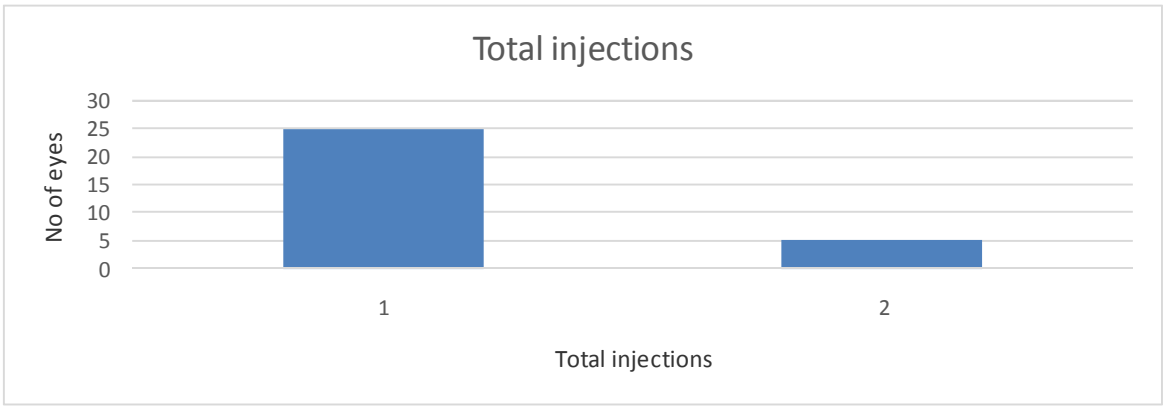


Figure 2

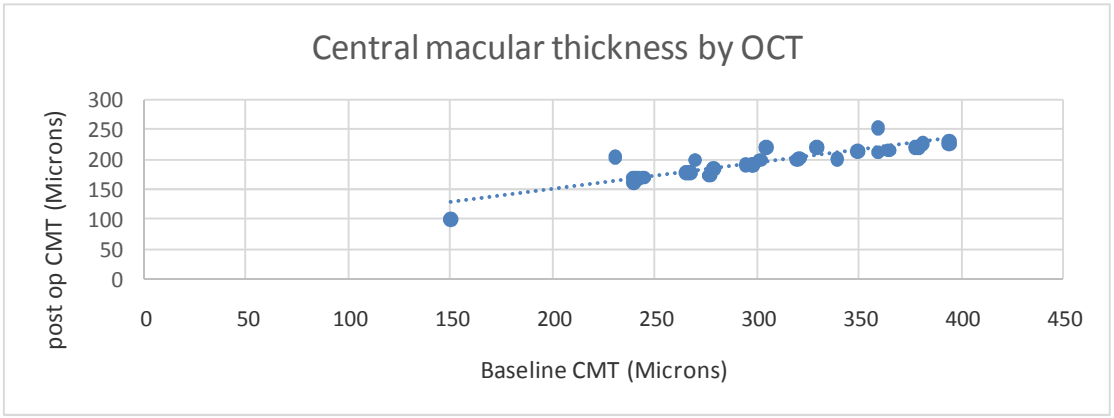
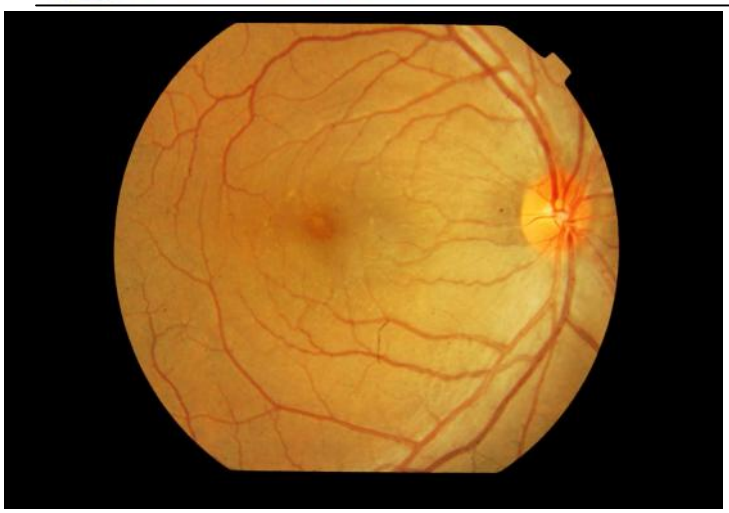
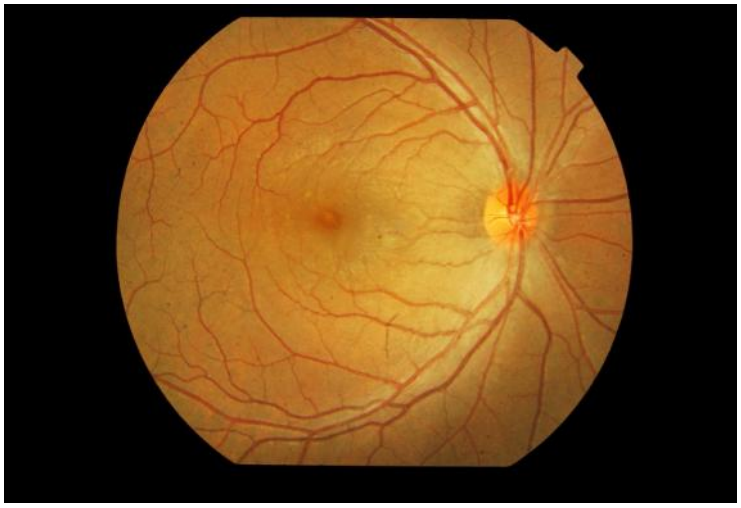


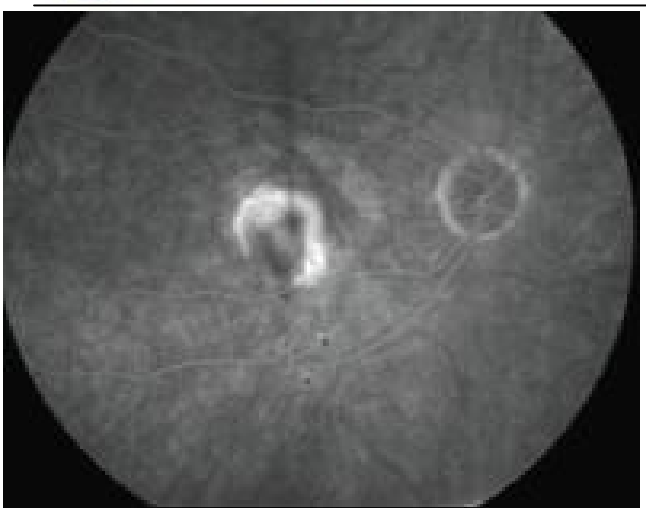
Figure 3



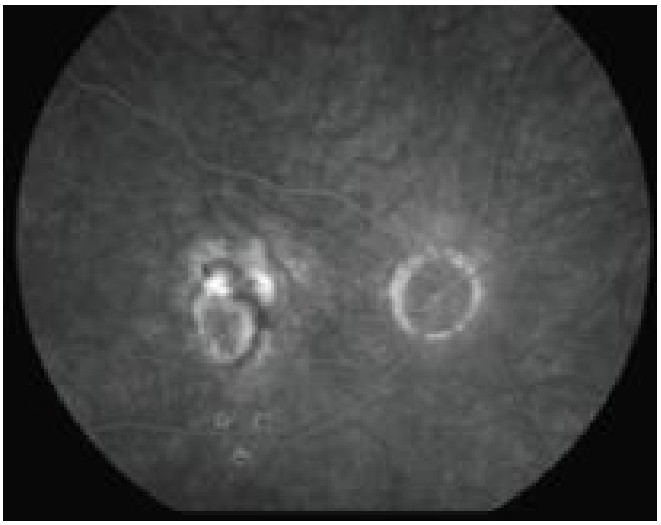
Pre treatment



Post treatment



Pre treatment



Post treatment

CONCLUSION:

Most eyes treated with bevacizumab in this study had a favourable anatomical and functional response, and 63.43% had improved BCVA by at least one line. Most of the change in BCVA and central OCT thickness was observed in the first month and first two weeks following initial treatment respectively. However, the treatment regimen used in this study differs from previous studies in that patients were not routinely treated on a monthly basis for the first three months in a manner similar to the ranibizumab studies. In the series reported by Bashshur and colleagues [13] and Avery and colleagues, [9] all eyes received monthly bevacizumab for the

first three months. Moreover, Spaide and colleagues [11] reported that "patients were treated with the thought that they would be given three injections separated by one month and then followed until leakage reoccurred." But no further details regarding the number of eyes reinjected as a function of time were reported. On the other hand, Rich and colleagues [12] reported that "while reinjections were at the discretion of the treating physician, most patients were treated until the OCT revealed no evidence of macular fluid and then retreated when the fluid recurred." In this study, because we wished to minimize the 'off-label' use of an unproven agent, injections were repeated only if we felt that the effects of the injection were 'wearing off ', as indicated by no further improvement or worsening later during follow up after an initial favourable functional and/or anatomical response. While it remains unknown how best to treat patients with intravitreal anti-VEGF therapy, particularly bevacizumab, webelieve that fixed interval regimens used in previous studiesmay interfere with the ability to understand the pharmacokineticproperties of this drug. This also does not allow forestablishing the optimal frequency of reinjection. Treating on a monthly basis for the first three months[9,][13]or until the OCTreveals no evidence of macular fluid[12]obscures the durationof effect of each injection and result in excessive number ofinjections that may be unnecessary.Only eyes that experienced no further improvement or worsening after an initial favourable response were retreated.

The half-life of intravitreal bevacizumab is thought to be about twice that of ranibizumab [16]. Thus, less frequent bevacizumab administration may theoretically be required over a certain period of time compared to ranibizumab. During the three months follow up in this study, less than a fifth of the eyes (five eyes, 17.2%) required repeat injections, with only three eyes (10.3%) requiring retreatment at eight weeks and none at four weeks. This suggests that monthly injections may not be necessary and that treatment effect appears to be maintained for at least eight weeks in the majority of cases. While it is possible that we inadvertently selected a group of 30 eyes that happened to be exceptional responders to bevacizumab, the fact that our findings are comparable to those reported by other investigators suggests that a less frequent dosing regimen may be as effective as monthly injections. [9, 12, 13]

While the results of this study are encouraging, several shortcomings are worth mentioning. These include the retrospective design with varying baseline characteristics of included eyes, short-term follow up, small number of patients, lack of a control group, nonstandardized visual acuity testing in the study. Yet this short term data suggests that intravitreal bevacizumab is a safe and effective treatment for neovascular AMD. It also suggests that an injection frequency less than once per month may be sufficient since initial treatment effect was maintained for at least eight weeks in the majority of cases. We believe that an injection interval of eight weeks is not only as effective as four weeks, but also safer and less expensive.

Disclosure:

The authors have no financial interest in the study.

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