Use of Anti Angiogenic Drug in the Treatment for Age Related Macular Degeneration

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ABSTRACT

Background: Age-related macular degeneration (AMD) is the leading cause of irreversible blindness. Currently 2.5-3 million people worldwide are blind due to AMD.

Objective: This study was to use of anti-angiogenic drug in the treatment for age related macular degeneration.

Methods: A cross sectional study was carried out among patients attending Eye OPD of a tertiary care eye center.

Results: 25 patients were included in this study. Among the 25 patients 15 were male & 10 were female. Mean visual acuity (VA) in this study improved from 5/60 to 6/36 during follow up. This was statistically significant (P <0.0001).

Conclusion: The results of this study suggest that IVB (1.25 mg) is well tolerated and associated with stabilization or improvement in visual acuity, decreased central macular thickness (CMT) by ocular coherence tomography (OCT), and reduction in angiographic leakage associated with neovascular AMD.

Key words: Angiogenic drug, Macular degeneration, Eye OPD, IVB, Bevacizumab

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness.²¹ Currently 2.5-3 million people worldwide are blind due to AMD.³ The disease adversely affects quality of life and activities of daily living causing many affected individuals to lose their independence in their retirement years. AMD is estimated to affect more than 8 million individuals in the USA; the advanced form affects more than 1.75 million. This number will increase to almost 3 million by 2020.²²³

The overall prevalence of neovascular AMD and/or geographic atrophy in the US population 40 years and older is estimated to be 1.47%. With the aging world population, it is bound to increase significantly, and could become a significant public health problem in next two decades, with serious socio-economic implications. The population over the age of 85 yrs is expected to increase by 107% by the year 2020, so the prevalence of this disease will continue to rise dramatically.²⁴

Two recent studies from Southern India suggest that AMD may be as commonly encountered as it is in Western countries.⁵⁶ The estimated prevalence of retinal diseases in India is 10.3%, of which AMD contributes 1.84% to 2.7%, the incidence increasing with age.⁶ The demographic profile of India is changing, with rapid increases in the older

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population. An approximately 2.5-fold increase in those aged 60 years and over is projected between 2001 (71 million at 2001 census) and 2031.[9] In a recent series, 32.5% of AMD patients were found to suffer from depressive disorders in addition to visual disability.[10]

**Aims & Objectives:** - The present study, has been planned to find the use of anti-angioenic drug in the treatment for age related macular degeneration

**METHODS**

**Study population:**- Twenty five patients each of best corrected visual acuity in age group 50-80 years were included as cases.

**Study Area:**- A cross sectional study was carried out among patients attending Eye OPD of a tertiary care eye centre. Consecutive patients attending the Eye OPD were screened for AMD on the basis of visual acuity

**Study duration:** - Duration of this study was three year.

**Sampling technique & Data collection:**- The screened patients were then subjected to following detailed ocular examination:

- a. best corrected visual acuity
- b. slit lamp biomicroscopic evaluation of the anterior segment
- c. dilated fundus examination with direct ophthalmoscopy, 90D and by indirect ophthalmoscopy
- d. applanation tonometry
- e. optical coherence tomography (OCT).

**PROCEDURE FOR INTRAVITREAL INJECTION**

The injection was given under sterile conditions in the operation theatre.

Individual dosing tuberculin syringes were prepared taking 1.25 mg bevacizumab in 0.05 cc.

The injections were given under topical anaesthesia consisting of 4% Xylocaine drops.

The eye was prepared with three applications of 10% povidone iodine. The eye was draped with sterile drapes. Wire speculum was placed in the eye to be injected.

The eye was held with a Lim's forceps and the intravitreal injection was given through pars plana route at three mm under sterile conditions in the operation theatre.

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**Exclusion Criteria:**

- a. Diabetes mellitus
- b. Renal disease
- c. Hypertension
- d. Coronary arterial disease
- e. Cerebro-vascular disease
- f. Systemic or ocular medications.

**Inclusion Criteria:**

- a. Diabetic retinopathy
- b. Retinal vascular occlusions
- c. Anterior ischemic optic neuropathy

**Systemic exclusion criteria:**

- a. Coronary artery disease
- b. Stroke
- c. Uncontrolled hypertension
- d. History of any other thromboembolic events
- e. Anticoagulant therapy
- f. Patients who have undergone laser/PDT/ other anti-VEGF

**Ocular exclusion criteria:**

- a. Persistent CNV seen on FFA
- b. Persistent fluid
- c. Increased central retinal thickness of ≥ 100 micrometers (mcm)
- d. New macular hemorrhage
- e. Persistent CNV seen on FFA

**RESULTS**

The study included 25 diagnosed patients of neovascular AMD.

**AGE DISTRIBUTION**

Mean age of patients was 65.2 yrs with a range of 51-82yrs.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>No of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>6</td>
<td>24%</td>
</tr>
<tr>
<td>60-69</td>
<td>9</td>
<td>36%</td>
</tr>
<tr>
<td>70-79</td>
<td>7</td>
<td>28%</td>
</tr>
<tr>
<td>&gt;80</td>
<td>3</td>
<td>12%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25</td>
<td>100%</td>
</tr>
</tbody>
</table>

15 patients were males (60%) and 10 were females (40%).

**BASELINE VISION**

The best corrected visual acuity before at baseline was as under. The mean visual acuity was 5/60 with a range of Hand movements close to face (HMCF) to 6/18.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>15 (60%)</td>
<td>10 (40%)</td>
</tr>
</tbody>
</table>

Table 1. Age distribution of the patients

Table 2. Sex distribution of patients
In this study, 15 patients were males (60%) and 10 were females (40%). This is in accordance with other studies which have also not found a significant difference in the sex distribution of AMD. Mean visual acuity (VA) in this study improved from 5/60 to 6/36 during follow up. This was statistically significant (P < 0.0001). The result is in accordance with the study of Ghazi et al that reported a reduction of BCVA from 20/203 at baseline to 20/113 at 12 weeks (P = 0.001). Mean visual acuity improved from 45.7 letters at baseline to 53.1 letters at 12 months (P = 0.004) in a study by Bashshur et al.

In this study, twenty eyes (62.5%) had a reduction of >10% of baseline retinal thickness on OCT after three injections. This was in accordance with a study by Avery et al who reported reduction of CRT in 55% eyes. Mean CRT decreased from 317.2 μm at baseline to 211.2 μm (P < 0.001) in our study. This was statistically significant. Mean CRT decreased from 327.4 μm at baseline to 227.8 μm at 12 months (P < .001) in the study of Bashshur et al.

In this study, the mean no of injections were 4.09 and no systemic side effects were noted. A mean of 3.4 injections were given over the course of the study by Bashshur et al, and no ocular or systemic side-effects were noted. Retinal hypoxia caused by any clinical condition results in the formation and release of VEGF. This can in turn result in formation of abnormal blood vessels. The strong supportive evidence from animal and human studies defined VEGF as an optimal therapeutic target for treatment of ocular diseases in which neovascularization leads to blindness. Recently anti-VEGF agents such as ranibizumab and pegaptanib sodium have been shown to be beneficial in the treatment of CNV secondary to AMD. However, both pegaptanib sodium and ranibizumab are not affordable to many patients. Prior to the commercial availability of ranibizumab, bevacizumab was administered as an off-label VEGF inhibitor to control exudative AMD. Bevacizumab is a humanized recombinant monoclonal IgG antibody that binds and inhibits all VEGF isoforms. This study has shown a promising result in favour of the use of intra-vitreal Bevacizumab in the treatment of neovascular AMD which appears to be safer and efficacious than conventional laser and PDT.

CONCLUSION
The results of this study suggest that IVB (1.25 mg) is well tolerated and associated with stabilization or improvement in visual acuity, decreased central macular thickness (CMT) by ocular coherence tomography (OCT), and reduction in angiographic leakage associated with neovascular AMD. Repeated intravitreal injections of 1.25 mg of Bevacizumab were safe and well tolerated during the course of this study with proper screening of patients for underlying risk factors.

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