

# Incidence of Endophthalmitis after Bevacizumab (Avastin)

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**Purpose:** To assess the rate of infectious endophthalmitis after an intravitreal injection of Bevacizumab (Avastin).

**Material and Methods:** The patients undergoing intravitreal injections of anti-vascular endothelial growth factor Bevacizumab (Avastin) from June 1<sup>st</sup>, 2006, through to June 30, 2011 were followed up for one month after injection at Unit 3, Department Of Ophthalmology, Lahore General Hospital, Lahore to determine rate of infectious endophthalmitis after an intravitreal injections of anti-vascular endothelial growth factor Bevacizumab (Avastin).

**Results:** 7 (0.134%) cases of clinically suspected endophthalmitis were identified after a total of 5189 intravitreal injections of anti-vascular endothelial growth factor (Avastin). The mean interval between intravitreal anti VEGF injections and onset of symptoms was 2.55 days. The interval between onset of symptoms and examination was average 4 days.

**Conclusion:** Endophthalmitis remains an infrequent but severe complication of intravitreal injections of Bevacizumab (Avastin). Using a strict injection protocol may help in reducing the incidence of infection.

The use of intravitreal anti-vascular endothelial growth factor (anti VEGF) agents such as Bevacizumab and Ranibizumab has increased dramatically during the past few years following reports of successful treatment of neo-vascular age related macular degeneration<sup>1-6</sup> diabetic macular oedema,<sup>7-9</sup> macular oedema secondary to retinal vein occlusion<sup>10-11</sup> and others. A serious complication associated with treatment is infectious endophthalmitis with a reported incidence ranging between 0.03% and 0.16% per injection,<sup>1,12-15</sup> which may cause permanent loss of vision despite prompt and appropriate antibiotic therapy. Various protocols have been proposed to minimize the infection rate<sup>16,17</sup>.

We wished to enquire into the infection rate within our own environment.

## MATERIAL AND METHODS

This prospective study was conducted at unit 3, Department of Ophthalmology, Lahore General

Hospital, Lahore from June 1, 2006, through June 30, 2011.

All patients who received intravitreal injections of Bevacizumab (Avastin) were included in the study. Patients receiving other intravitreal injections (including corticosteroids, antibiotics, antivirals and other medications) were excluded.

All intravitreal injections in the current study were performed with nursing assistance and procedure was recorded in doctor and nursing logbook.

The protocol of intravitreal injections at our department does not include pre injection antibiotics. The LGH (Lahore General Hospital) protocol of sterilization was as follow: A registered pharmacist formulated the injection preparation at Shokat Khanum Memorial Hospital. The injection protocol included insertion of pledget soaked in 5% povidone iodine and proparacaine 0.5% in conjunctival sac five minutes before injection. After five minutes lashes, eyelid skin were swabbed and conjunctival sac was irrigated with 5% povidone iodine and after another

five minutes lashes and lids were cleaned with alcohol swab and pledget was removed. The eyelids were draped with sterile drape and a sterile speculum was used to open the lids. The injection was performed in the infero-temporal quadrant with the injecting physician wearing sterile gloves, followed by one drop of a topical antibiotic (Moxifloxacin). All the patients were instructed to use antibiotic drops four times a day for one week. Sterilization protocol was same for all the patients of our study.

Clinical diagnosis of Endophthalmitis was made on the basis of the presence of anterior chamber reaction, keratic precipitates, hypopyon, fibrin and / or posterior synechie.

**Data Analysis:** The data were entered into computer and analyzed using SPSS 16 (statistical package for social sciences). The data were described in terms of mean  $\pm$  SD (standard deviation) for quantitative variables. Frequencies and percentages were given for qualitative variables. Independent sample t-test was used to observe groups mean differences. One-way ANOVA (Analysis of Variance) was applied to observe mean differences among groups. Pearson Chi-Square was used to observe associations between qualitative variables. A p-value of  $<0.05$  was considered statistically significant.

## RESULTS

A total of 5189 intravitreal injections of Bevacizumab (Avastin) were performed at our department over a period of five years (June 1<sup>st</sup>, 2006, through to June 30<sup>th</sup>, 2011). There were 7 (0.134%) cases of clinically suspected endophthalmitis. Patients presented with symptoms of pain, red eye and decreased vision. The mean interval between intravitreal injection and onset of symptoms was 2.55 days. The interval between onset of symptoms and examination was average 4 days.

## DISCUSSION

We report 7 cases of clinically suspected endophthalmitis after intravitreal anti-vascular endothelial growth factor Avastin (incidence 0.134%). A clinical diagnosis of Endophthalmitis of anterior chamber reaction with keratic precipitates, hypopyon, fibrin and / or posterior synechie.

The institutional injection protocol remained unchanged during the duration of study. This protocol is different from published suggested protocols<sup>14,18</sup>.

The current study is one of the largest series reported to date in case of endophthalmitis after intravitreal injections of anti-vascular endothelial growth factor Avastin. The strength of this study is that the study was conducted at one unit of Ophthalmology department of a hospital rather than at different hospitals and protocol of disinfection and injection remained the same.

**Table 1:** Incidence of endophthalmitis after intravitreal injection: Selected prospective clinical trials.

Study	Medication	Number/ Incidence (per eye), n (%)	Number/ incidence (Per Injection), n (%)
MARINA <sup>19</sup>	Ranibizumab	5/477(1.0)	5/10,443(0.05)
ANCHOR <sup>20</sup>	Ranibizumab	2/227(0.7)	-

**Table 2:** Incidence of endophthalmitis after intravitreal injection: Selected large retrospective case series.

Study	Medication	Rate of Infection (Per Injection),n(%)
Mason et al <sup>21</sup>	Bevacizumab	1/5,233(0.02)
Fung et al <sup>22</sup>	Bevacizumab	1/7,113(0.014)
Wu et al <sup>23</sup>	Bevacizumab	7/4,303(0.16)
Artunay et al <sup>24</sup>	Bevacizumab	2/3,022(0.066)

The low incidence of endophthalmitis after intravitreal injection of Avastin is probably due to strict adherence to this protocol. Most prospective clinical trials involving intravitreal anti-VEGF injections reported rates of endophthalmitis per study and per injection on the order of 1% and 0.1% respectively<sup>19,20</sup>. Most retrospective case series reported cases of endophthalmitis in populations of patients receiving variable number on injections and were typically reported as rates per injection, rather than rates per eye<sup>21-24</sup>.

Our case series found the rate of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor Avastin to be 0.134%. The diagnostic clues of endophthalmitis were the main outcome measure. There was anterior chamber reaction in all patients with keratic precipitates, hypopyon.

## CONCLUSION

Endophthalmitis remains an infrequent but severe complication of Bevacizumab (Avastin). Using a strict injection protocol may help in reducing the incidence of infection.

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