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CHANGES IN INTRAOCULAR PRESSURE AFTER INTRAVITREAL INJECTION OF BEVACIZUMAB IN PATIENTS OF DIABETIC MACULAR OEDEMA

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Abstract

Objective: *To determine the mean change in intraocular pressure after Bevacizumab injection in patients of diabetic macular oedema (DME).*

Methods: *This quasi-experimental study involving 100 patients of DME was conducted in the department of ophthalmology, King Edward Medical University/Mayo Hospital, Lahore from November 2024 to April 2025. The intravitreal injections were carried out in a sterile environment within the operating theater using topical anesthesia. A dose of Avastin (1.25 mg, or 0.05 ml) was injected into the vitreous at specific distances from the limbus. Post-injection, patients were positioned seated, and IOP measurements were taken immediately after the injection, as well as at intervals of 5 minutes and 30 minutes thereafter.*

Results: *The average age of the participants was 53.1±5.9 years. The gender distribution was noted, showing that 47% participants were male, while 53% participants were female. The duration of diabetic macular oedema (DME) was 8.5±3.2 months. The mean IOP prior to injection was 12.8±2.3 mmHg. After the injection, the mean IOP increased significantly to 22.4±3.7 mmHg, the statistical analysis yielded a p-value of less than 0.0001.*

Conclusion: *There is a significant increase in IOP after intravitreal bevacizumab injection for the treatment of diabetic macular oedema.*

INTRODUCTION

Diabetes mellitus is a long-term metabolic disorder marked by persistent high blood sugar levels. The global incidence of diabetes continues to rise, posing substantial health risks worldwide. According to the

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10th edition of the IDF Diabetes Atlas, in 2021, approximately 537 million adults aged 20 to 79 were living with the condition. Projections indicate this number will increase to around 643 million by 2030 and reach approximately 783 million by 2045.[1, 2] The disease can inflict severe damage on various organs, including the heart, blood vessels, eyes, and kidneys, leading to major health issues such as heart attacks, strokes, blindness, and renal failure.[3, 4]

Diabetic retinopathy (DR) is a common complication associated with diabetes and is a leading cause of visual impairment and blindness among adults of working age. Among the various retinal complications, diabetic macular oedema (DME) stands out as the primary contributor to vision loss in diabetic individuals, with its prevalence increasing on a global scale. The occurrence of DME varies significantly, affecting approximately 4.2% to 14.3% of those with type 1 diabetes (T1DM) and about 1.4% to 5.57% of individuals with type 2 diabetes (T2DM).[5, 6]

Anti-VEGF therapies are widely recognized as the primary treatment for various choroidal and retinal vascular conditions. Bevacizumab (Avastin, manufactured by Genentech), a humanized monoclonal antibody targeting vascular endothelial growth factor, received approval for treating colorectal cancer. Since 2005, it has been employed off-label for intravitreal injections and has gained popularity due to its affordability and effectiveness compared to other anti-VEGF options.[7, 8] Intravitreal injections are known to cause both temporary and prolonged increases in intraocular pressure (IOP), largely due to the increased volume of the vitreous body and potential toxicity of the drug on the trabecular meshwork. Elevated IOP can adversely affect the optic disc, particularly in patients with glaucoma who may already have optic nerve compromise.[9] This study aims to assess the mean change in intraocular pressure after Bevacizumab injection in patients of diabetic macular oedema (DME).

METHODS:

This quasi-experimental study involving 100 patients of DME was conducted in the department of ophthalmology, King Edward Medical University/Mayo Hospital, Lahore from November 2024 to April 2025. We included patients aged over 18 years, with a Best Corrected Visual Acuity (BCVA) of 20/40 or worse, and no previous intervention for DME. Patients with IOP > 21 mmHg, macular oedema secondary to any other cause, macular ischemia, or uveitis were excluded.

Following the acquisition of informed consent, all participants in the study underwent a thorough ocular assessment. This included evaluating best-corrected visual acuity, conducting a slit-lamp examination of the anterior segment, measuring intraocular pressure (IOP) using Perkins' Applanation Tonometer, and performing a dilated fundus examination with an indirect ophthalmoscope. Each patient also received optical coherence tomography. Demographic details such as age, gender, and the duration of diabetes mellitus (DM) and hypertension (HTN) were recorded. To ensure safety, all patients were given prophylactic treatment with topical ofloxacin (3 mg/mL), to be applied four times daily for three days prior to the procedure. The intravitreal injections were carried out in a sterile environment within the operating theater using topical anesthesia. A dose of Avastin (1.25 mg, or 0.05 ml) was injected into the vitreous at specific distances from the limbus: 3.5 mm for pseudophakic and aphakic patients, and 4 mm for phakic patients, utilizing a half-inch long 29-gauge needle in the superior-temporal quadrant. To minimize reflux of the medication following the injection, a sterile cotton swab was applied to the injection site. Povidone-iodine solution (5%) was used for antisepsis before and after the procedure. Post-injection, patients were positioned seated, and IOP measurements were taken immediately after the injection, as well as at intervals of 5 minutes and 30 minutes thereafter. These measurements were consistently recorded by the same observer throughout the study. After IOP assessment, visual acuity was evaluated by checking hand motion vision at a distance of 50 cm with the non-injected eye covered. Lastly, topical ofloxacin was continued for all patients, administered four times daily for five days following the intravitreal injection.

Data was analyzed using SPSS v25. Paired sample test was applied to compare pre-injection and post-injection IOP values, taking p-value ≤0.05 as a significant change.

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RESULTS:

The average age of the participants was 53.1 years, with a standard deviation of 5.9 years. The gender distribution was noted, showing that 47 participants, accounting for 47.0%, were male, while 53 participants, making up 53.0%, were female. Additionally, the duration of diabetic macular oedema (DME) among the participants was measured, revealing an average duration of 8.5 months, with a standard deviation of 3.2 months (Table 1).

Table 2 presents a comparison of pre-injection and post-injection IOP values. The mean IOP prior to injection was 12.8 mmHg with a standard deviation of 2.3. After the injection, the mean IOP increased significantly to 22.4 mmHg, with a standard deviation of 3.7. The statistical analysis yielded a p-value of less than 0.0001 (Table 2).

Table 1. Baseline Study Characteristics.

Age	53.1±5.9
Gender (%)	
Male	47 (47.0%)
Female	53 (53.0%)
Duration of DME (months)	8.5 ± 3.2

Table 2. Comparison of Pre-Injection and Post-Injection IOP.

	Pre-Injection IOP	Post-Injection IOP	P-value
Mean	12.8	22.4	<0.0001
S.D.	2.3	3.7	

DISCUSSION:

Diabetic macular oedema (DME) is a serious complication associated with diabetic retinopathy (DR), posing a significant threat to vision and being a leading cause of blindness globally. The likelihood of developing DME tends to rise with the length of time a person has diabetes, with nearly 40% of diabetics experiencing this condition within three decades of their diagnosis.[10, 11] Those with type 1 diabetes are particularly vulnerable compared to individuals with type 2 diabetes. Several factors increase the risk of DME, including poor blood sugar management, cardiovascular issues, kidney dysfunction, and the use of diuretic medications. Although the detailed mechanisms behind DME are not fully understood, research indicates that factors such as sustained high blood sugar levels, abnormal lipid metabolism, and inflammatory processes play roles in its development.[12, 13] Recent studies highlight that retinal tissue hypoxia—insufficient oxygen supply—may also be central to the disease's progression. Hypoxia stimulates the production of vascular endothelial growth factor (VEGF), a molecule that increases blood vessel permeability and promotes leakage from retinal vessels, contributing to oedema.[14]

Hollands and colleagues documented the average intraocular pressure (IOP) at several time points following an injection: initially at 14.0 mmHg (with a 95% confidence interval (CI) ranging from 13.4 to 14.7), then rising sharply to 36.1 mmHg (95% CI, 33.5-38.6) at 2 minutes, decreasing to 25.7 mmHg (95% CI, 23.8-27.5) at 5 minutes, and finally returning close to baseline at 15.5 mmHg (95% CI, 12.4-16.5) after 30 minutes.[15]

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A 2014 study by Lemos-Reis and colleagues investigated the short-term increase in intraocular pressure (IOP) following an injection. The researchers observed that when there was no sub-conjunctival reflux, the IOP rose on average by 28.6 mmHg, with a standard deviation of 13.8 mmHg. Conversely, when reflux was present, the average IOP increase was significantly lower, at 7.7 mmHg, with a standard deviation of 10.3 mmHg.[16]

Additionally, Kernt M and colleagues reported that the highest average immediate post-injection IOP was 13.9±2.6 mmHg.[17]

A research conducted by El Chehab and colleagues observed an increase in intraocular pressure, with the average rising by 46.5 mmHg within the first minute following the injection.[18]

According to one RCT, group A (intravitreal bevacizumab) and group B (intravitreal bevacizumab along with Anterior chamber paracentesis) were compared, showing baseline mean pre-IOP values of 15 ± 3 and 16 ± 3 mmHg in Group A and Group B, respectively and mean change in IOP immediate post-IOP, 5 min IOP, and 20 min IOP were (22 ± 5), (16 ± 6) and (9 ± 4) mmHg.. The values of all postinjection measurements were significantly lower in Group B ($P < 0.001$ for all measurements).[19]

Following injections, an increase in intraocular pressure (IOP) is typically temporary, with pressures usually returning to baseline within a few hours. A comprehensive review analyzing 46 studies, conducted by De Varies and colleagues, found that the average IOP elevation was 23.4 mmHg, which normalized after approximately one hour.[20]

Intravitreal injections of anti-VEGF agents continue to be a standard approach in retinal therapy, pending the development of alternative drug delivery methods. One common side effect observed post-injection is a significant increase in intraocular pressure (IOP), which can be quite pronounced and, in some cases, alarming. This phenomenon has been documented in multiple studies, including ours. Patients with a history of glaucoma are particularly vulnerable to these IOP spikes; abrupt elevations in eye pressure pose a risk of damaging the optic nerve and compromising vision.

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