

Changes in Intraocular Pressure and Ocular Pulse Amplitude After Intravitreal Bevacizumab Injection*

Intravitreal Bevacizumab Enjeksiyonu Sonrası Göz İçi Basıncı ve Oküler Pulse Amplitüdü Değişiminin İncelenmesi

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ABSTRACT

Purpose: Evaluating changes in intraocular pressure and ocular pulse amplitude in eyes with intravitreal bevacizumab injection.

Materials and Methods: 18 eyes of 17 patients with intravitreal bevacizumab injection were included in the study. Intraocular pressure (IOP) (by GAT and by PDCT) and ocular pulse amplitude (OPA) (by PDCT) were measured before and after the intravitreal injection.

Results: The IOP before injection was 15.25 ± 2.91 mmHg while 30 minutes and 1 week after the injection the IOP was 16.35 ± 3.32 mmHg and 14.65 ± 5.11 mmHg respectively by GAT. The IOP before injection was 18.17 ± 1.11 mmHg while 30 minutes and 1 week after the injection the IOP was 19.94 ± 1.26 mmHg and 17.25 ± 3.23 mmHg respectively by PDCT. The IOP values before the injection were not significantly different from the measurements both 30 minutes and 1 week after the injection by both of the methods (The p values for the measurements 30 minutes and one week after the injection by GAT were 0.180 and 0.550 respectively; and by PDCT they were 0.169 and 0.379 respectively). The OPA before the injection was 2.74 ± 1.01 mmHg whereas 30 minutes and 1 week after the injection the OPA values were 3.05 ± 1.20 mmHg and 2.58 ± 1.12 mmHg respectively. The OPA measurements 30 minutes after injection were significantly increased according to preinjection values ($p=0.035$).

Conclusion: Early changes in IOP after intravitreal bevacizumab injection were not noted by GAT and PDCT. The OPA by PDCT was significantly increased 30 minutes after the injection. This increase in OPA may be caused by early effects of bevacizumab on choroidal blood flow. However we think that we need future studies providing the nomograms of this new method for measurement of OPA to evaluate the clinical significance of measurements.

Keywords: Bevacizumab, IOP, GAT, Ocular Pulse Amplitude, Pascal Dynamic Contour Tonometer.

ÖZ

Amaç: İntravitreal bevacizumab enjeksiyonu sonrası oküler pulse amplitüdü ve göz içi basınç değişimlerini incelemek.

Gereç ve Yöntem: Ameliyathane şartlarında, steril ortamda intravitreal bevacizumab enjeksiyonu (1.25mg/0.05cc) yapılan 17 hastanın 18 gözü çalışmaya dahil edildi. Enjeksiyon öncesi ve sonrası dönemde göz içi basınç değerleri (GİB); Goldmann Aplanasyon Tonometresi (GAT) ve eşzamanlı olarak paskal dinamik kontür tonometresi (PDKT) ile ölçüldü ve oküler pulse amplitüdü (OPA) ölçümleri (PDKT ile) yapıldı.

Bulgular: Enjeksiyon öncesi GAT ile 15.25 ± 2.91 mmHg olan ortalama GİB'i, enjeksiyondan 30 dk sonra 16.35 ± 3.32 mmHg; enjeksiyondan 1 hafta sonra 14.65 ± 5.11 mmHg olarak bulundu. Enjeksiyon öncesi PDKT ile 18.11 ± 1.13 mmHg olan ortalama GİB, enjeksiyondan 30 dk sonra 19.94 ± 1.26 mmHg; enjeksiyondan 1 hafta sonra 17.25 ± 3.23 mmHg olarak saptandı. Her iki metod ile enjeksiyon öncesi göz içi basınç ölçümleri ile enjeksiyondan 30 dk sonra ve enjeksiyondan 1 hafta sonraki göz içi basınç ölçümleri arasında istatistiksel olarak anlamlı bir fark saptanmadı. (Sırasıyla 30. dakika ve 1. haftada GAT için $p=0.180$ $p=0.550$; PDKT için $p=0.169$ $p=0.379$). Enjeksiyon öncesi 2.74 ± 1.01 mmHg olan OPA; enjeksiyondan 30 dk sonra 3.05 ± 1.20 mmHg; enjeksiyondan 1 hafta sonra 2.58 ± 1.12 mmHg olarak tespit edildi. Enjeksiyondan 30 dk sonra ölçülen ortalama OPA değeri, enjeksiyon öncesi döneme göre artmış olarak saptandı. Bu fark istatistiksel olarak anlamlı bulundu ($p=0.035$).

Sonuç: Sonuç olarak, intravitreal bevacizumab enjeksiyonu sonrası erken dönemde GAT ve PDKT ile GİB da anlamlı değişiklikler izlenmemektedir. OPA ise enjeksiyondan 30 dk sonra sonra yapılan ölçümlerde anlamlı olarak yüksek bulunmuştur. Bu artış, bevacizumabın erken dönemde koroidal kan akımına etkilerinden kaynaklanabilir. Ancak PDKT ile OPA ölçümlerinin klinik olarak anlamlarını değerlendirebilmek için, bu ölçümlerin nomogramlarını belirleyen çalışmalara da ihtiyaç duyulduğunu düşünmekteyiz.

Anahtar Kelimeler: Bevacizumab, göz içi basınç, Goldmann Aplanasyon Tonometresi, Oküler Pulse Amplitüdü, Paskal Dinamik Kontür Tonometresi.

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INTRODUCTION

Goldmann applanation tonometry (GAT) is the most often utilized golden standart method for the indirect measurement of intraocular pressure (IOP) in ophthalmology practice.¹ However due to applanation of corneal surface, the measurements by this method can be influenced by corneal surface properties like thickness, curvature, rigidity and astigmatism.²

Pascal dynamic contour tonometry (PDCT) has been developed as an alternative to GAT to eliminate these drawbacks to measure the IOP by direct transcorneal contact.³ The PDCT measures the IOP directly and continuously providing values independent of the central corneal thickness (CCT) and corneal curvature.³⁻⁴ Also by ocular pulse amplitude (OPA) measurements provided by PDCT, the difference between systolic and diastolic pressure, which is an indirect measure of ocular blood flow and choroidal perfusion can be evaluated.⁵⁻⁶

Bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor, has been used frequently for ocular neovascular diseases in recent ophthalmology practice. Its application in wet type senile macular degeneration, cystoid macular edema, retinal vein occlusion, diabetic retinopathy, diabetic macular edema, pathological myopia and neovascular glaucoma have been observed.⁷⁻⁸ Several complications like anterior chamber inflammation, subconjunctival hemorrhage, vitritis, uveitis, posterior vitreous detachment and endophthalmitis after its intravitreal injection have been reported.⁷ We could not find a study evaluating the effects of bevacizumab on ocular blood flow in the literature.

We aimed to investigate the early IOP and OPA changes by intravitreal bevacizumab injections by this study.

MATERIALS AND METHODS

The study was approved by the appropriate institutional review board, and written consent was obtained from each patient after complete explanation of the procedure and possible side effects. 18 eyes of 17 patients with a mean age of 68 ± 8.90 (minimum 46, maximum 77) were included in the study. The diagnosis of retinal diseases included choroidal neovascular membranes (8 patients), proliferative diabetic retinopathy (6 patients), cystoid macular edema (2 patients) and retinal vein occlusion (2 patients). Patients with corneal surface prob-

lems, glaucoma, pseudoexfoliation and previous history of intravitreal injection were excluded. Intravitreal bevacizumab injection (1.25 mg/0.05 cc) was performed under sterile conditions in the operating room.

Before the procedure best corrected visual acuity was measured and complete ophthalmological examination, ultrasonic pachymetry (BV International, Clermont-Ferrand, France) and fundus fluorescein angiography were performed.

Before injection, 30 minutes and one week after injection the IOP (by GAT and PDCT) and OPA (by PDCT, Pascal Tonometer, Swiss Microtechnology AG, Port, Switzerland) were measured. During measurements 10 minutes interval was taken between GAT and DCT to minimize a tonographic effect. Applanation tonometry was measured by Goldmann tonometry. Two measurements were consecutively taken for each eye; only the second one was used in the study (original Goldmann method). During measurements with DCT quality scores (q values) less than three were included. All the measurements were done by the same person and the measurements of the eye without injection were also performed.

The results were evaluated by the SPSS 11.0 version. The comparison of same eye before and after injections was made by Wilcoxon signed rank test and the comparison of the eyes with and without injection of the same subject was done by Mann Whitney U test.

RESULTS

The mean central corneal thickness (CCT) of the eyes with injection was $509 \pm 27,9 \mu$ (minimum 459, maximum 560). The IOP and OPA values of eyes with Bevacizumab injection before, 30 minutes and one week after the injection are seen in Table.

The IOP values measured by GAT and PDCT before the injection were not significantly different than the values 30 minutes and one week after the injection (Table).

The mean OPA values measured 30 minutes after the injection were found to be increased according to pre-injection values and the difference was statistically significant ($p = 0.037$). However the OPA values measured one week after the injection had a decrement which was not statistically significant in comparison to the pre-injection values (Table).

The OPA values of eyes without injection (of the same subjects with intravitreal injection of the fellow eye)

Table: The IOP and OPA values of eyes with bevacizumab injection before, 30 minutes and one week after the injection of bevacizumab. (*: The p value for measurements at 30 minutes after injection, **: The p value for measurements 1 week after the injection).

| | Before injection (mmHg) | 30minutes after injection (mmHg) | p * | 1 week after injection (mmHg) | p** |
|-------------|----------------------------|-------------------------------------|-------|----------------------------------|-------|
| IOP by GAT | 15.25±2.91 | 16.35±3.32 | 0.180 | 14.65±5.11 | 0.550 |
| IOP by PDCT | 18.11±1.13 | 19.94±1.26 | 0.169 | 17.25±3.23 | 0.379 |
| OPA | 2.74±1.01 | 3.05±1.20 | 0.035 | 2.58±1.12 | 0.455 |

before the procedure (the injection of fellow eye) were not significantly different than the values 30 minutes and one week after the injection ($p>0.05$).

DISCUSSION

There have been several studies for observing early IOP changes after intravitreal vascular endothelial growth factor injections in recent years. A predictable assumed to be volume-related rise in IOP three minutes after intravitreal bevacizumab injection which spontaneously falls below 30 mmHg has been reported.⁹ Also increased IOP 30 minutes after the injection, which is again transient, has been mentioned.¹⁰ In another study with pegaptanib a mean rise of 8.74 ± 7.23 mmHg in the IOP from baseline at 30 minutes after injection has been shown to be normalized at 5-to 7- day follow up visit.¹¹

Hollands et al have reported the mean IOP values at baseline, 2, 5, and 30 minutes after injection as 14.0 mmHg (95% confidence interval [CI] 13.4-14.7), 36.1 (95% CI 33.5-38.6) mmHg, 25.7 (95% CI 23.8-27.5) mmHg, and 15.5 (95% CI 12.4-16.51) mmHg, respectively.¹⁰ Kernt M et al.: have reported 13.9 ± 2.6 mmHg as the highest mean immediate postinjection IOP.¹²

In our study the mean IOP at 30 minutes and one week after injection were 16.3 ± 3.3 mmHg (minimum-11.0 maximum-22.0) and 14.7 ± 5.1 mmHg (minimum-7.0 maksimum-22.0) respectively in accordance with the other studies,⁹⁻¹² decreasing more with time.

As observed in these studies done with GAT, the IOP recordings maybe variable in different studies due to the measurement method. In our study the IOP readings provided by GAT and PDCT are correlated, though the readings by PDCT are somewhat higher. Similarly some studies comparing the two methods show that the IOP readings by PDCT are about 2 mmHg more than those obtained by GAT.⁶

OPA is a method of measurement reflecting the changes in ocular blood flow.⁶ In our study there was a significant increase in OPA 30 minutes after injection ($p=0.037$). It has been shown that the OPA is affected by hemodynamic properties like systemic blood pressure (BP) and heart rate.⁶

Intensified monitoring of circadian BP and heart rate before and after intravitreal injection of bevacizumab has shown a general rise in mean BP, heart rate and pulse pressure and reduced nocturnal dipping assumed to be caused by pharmacodynamic effects on the vasal tone.¹³

We have evaluated the measurements of the eye without injection which may also be affected by the same systemic hemodynamic changes to have some proof about such a relation. Although the OPA is increased in the eye with injection, there was a decrease in OPA in the eye without injection.

Another factor that may affect the OPA is the intraocular volume and the IOP changes during injections observed in the early period. More controlled studies are needed to evaluate these relations.

We have to accept that PDCT may have some limitations in evaluating the OPA like other methods for evaluating ocular blood flow such as color doppler imaging and fundus fluorescein angiography.¹⁴ We think that different methods should be used together to better evaluate the ocular blood flow.

Finally, as a result of our study we may conclude that the changes of IOP measured by GAT and PDCT seem not to be significant in the early period. The OPA values 30 minutes after the injection were significantly increased, however the nomograms for these measurements for this new method should also be evaluated with future studies in order to have an idea about the clinical significance of the results obtained.

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