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The Effect of Topical Anti-Glaucomatous Drops on Intraocular Pressure Changes in Patients Treated with Intravitreal Aflibercept

İntravitreal Aflibersept Uygulanan Hastalarda Topikal Antiglokomatöz Damlanın Göziçi Basıncı Değişimine Etkisi

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ABSTRACT

Aim: The aim is to investigate the effect of using topical dorzolamide-timolol (DT) drops before intravitreal aflibercept (IVA) administration on intraocularpressure (IOP) changes.

Materials and Methods: Forty-five eyes of 45 patients with diabetic retinopathy and macular edema who received DT drops 1 hour before IVA were considered as group 1, and 45 eyes of 45 patients without DT drops were considered as group 2. Patients who had previously undergone intravitreal injection, intraocular surgery, and who used any eye drops were excluded from the study. IOP values were measured with Tonopen contact handheld tonometer before blepharostatinsertion (BBIOP), after blepharostat insertion (ABIOP) and at 1 minute after injection (AIIOP).

Results: There were 23 males and 22 females in group 1 and 22 males and 23 females in group 2 (p=0.96). The mean age was 55.23 ±7.53 years in group 1 and 55.70 ±9.78 years in group 2.(p=0. 97) In group 1, BBIOP was 18.12 ±4.18 mmHg, ABIOP 20.98 ±4.42 mmHg, AIIOP 43.20 ±15.80 mmHg, while in group 2, BBIOP 18.65 ±3.52 mmHg, ABIOP 22.80 ±3.90 mmHg, AIIOP 39.08 ±13.18 mmHg. The difference between AIIOP and BBIOP was 25.04 ±16.30 mmHg in group 1 and 20.36 ±13.82 mmHg in group 2, the difference was not statistically significant.(p=0.21) The difference between AIIOP and ABIOP was 22.32 ±16.48 mmHg in group 1 and 16.18 ±13.05 mmHg in group 2, the difference was statistically significant.(p=0.03)

Conclusion: In the group using topical DT drops before IVA administration, BBIOP and ABIOP values were lower, while AIIOP values were higher.

Key Words: Aflibercept, antiglaucomatous drop, intraocular pressure

ÖZ

Amaç: İntravitreal aflibersept(IVA) uygulaması öncesi topikal dorzolamid-timolol(DT) damla kullanımının göziçi basıncı(GİB) değişimine etkisinin incelenmesidir.

Gereç ve Yöntem: Diyabetik retinopati ve makula ödemi nedeniyle IVA uygulamasından 1 saat önce DT damlatılan 45 hastanın 45 gözü grup 1, DT damlatılmayan 45 hastanın 45 gözü grup 2 olarak kabul edildi.Daha önceden intravitreal enjeksiyon yapılan,göziçi cerrahisi geçiren ve herhangi bir göz damlası kullanan hastalar çalışmaya alınmadı. Enjeksiyon öncesi blefarosta takılmadan önce (ÖGİB), blefarosta takıldıktan sonra (BGİB), enjeksiyon sonrası 1. dakikada(EGİB) Tonopen kontakt el tonometresi ile GİB değerleri ölçüldü.

Bulgular: Grup 1 de 23 erkek, 22 kadın, grup 2 de 22 erkek, 23 kadın mevcut olup (p=0.96) yaş ortalaması grup 1 de 55.23 ±7.53 yıl, grup 2 de 55.70 ±9.78 yıldı.(p=0.97) Grup 1 de ÖGİB 18.12 ±4.18 mmHg, BGİB 20.98 ±4.42 mmHg, EGİB 43.20 ±15.80 mmHg iken grup 2 de ÖGİB 18.65 ±3.52 mmHg, BGİB 22.80 ±3.90 mmHg, EGİB 39.08 ±13.18 mmHg bulundu. Grup 1 de EGİB-ÖGİB farkı 25.04 ±16.30 mmHg, grup 2 de EGİB-ÖGİB farkı 20.36 ±13.82 mmHg bulunurken aradaki fark istatistiksel olarak anlamlı değildi.(p=0.21) Grup 1 de EGİB-BGİB farkı 22.32 ±16.48 mmHg, grup 2 de EGİB-BGİB farkı 16.18 ±13.05 mmHg bulundu, aradaki fark istatistiksel anlamlıydı.(p=0.03)

Sonuç: IVA uygulaması öncesi topikal DT damla kullanılan grupta ÖGİB ve BGİB değerleri daha düşükken,EGİB değerleri daha yüksek bulunmuştur.

Anahtar Kelimeler: Aflibersept, antiglokomatöz damla, göz içi basıncı

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Introduction

Intravitreal injection is the most widely used ophthalmic intervention in the world. Although its safety has been demonstrated, it may cause various ocular side effects. One of these side effects is sudden increase in intraocular pressure (IOP).[1,2] In diabetic retinopathy and age-related macular degeneration, the two diseases in which intravitreal antiVEGFs are most commonly used, the commonly used treatment protocol is three injections one month apart and then repeated injections.[1] Repetition of IOP elevations that may occur during injections may have important clinical consequences in patients with poor visual nerve reserve such as glaucoma and some retinal diseases[3]

The aim of our study was to investigate the effect of topical antiglaucomatous drops before intravitreal injection on intraocular pressure changes during injection.

Materials and Methods

Ninety eyes of 90 patients who underwent intravitreal aflibercept (IVA) for diabetic retinopathy and macular edema in the ophthalmology department of Karabük University Medical Faculty Training and Research Hospital were retrospectively evaluated with the approval of the ethics committee. Forty-five eyes of 45 patients who received topical DT drops 1 hour before intravitreal injection were considered as group 1 and 45 eyes of 45 patients who did not receive topical DT drops were considered as group 2. Patients who were on ocular medication or who underwent surgery were excluded from the study.

All injections were performed under operating room conditions following the same protocol. All injections were performed by the same surgeon and the same type of blepharostat was used. Intraocular pressures were measured with a contact handheld tonometer Tonopen (Tono-pen XL tonometer, Mentor O&O Inc. Norwell, MA, USA) before blepharostat insertion (BBIOP), after blepharostat insertion (ABIOP) and 1 minute after injection (AIIOP) with the patient lying supine on the operating table. All patients underwent ocular surface cleaning with 10% povidone iodine following topical anesthesia. Following sterile drape and blepharostat application, IVA 2 mg/0.05 ml was injected using a 30 G syringe tip, marking 3.5 mm from the limbus. Following the injection, the entry site was massaged with ear cotton. BBIOP, ABIOP, AIIOP values and both BBIOP-AIIOP differences and ABIOP-AIIOP differences were compared between the two groups.

We aimed to evaluate the effect of topical DT drops on intraocular pressure changes in patients treated with intravitreal aflibercept.

Statistical analyses were performed using SPSS version 16.0 (SPSS Inc, Chicago, Illinois, USA) and a p value below 0.05 was considered statistically significant. Before the analysis, it was shown that the variables were suitable for normal distribution by Kolmogorov Smirnov test.Mean and standard deviation values of the groups were calculated. Independent t test was used to compare the numerical variables of the two groups. The chi-square test was used to evaluate whether there was a difference between the groups in terms of gender.

Results

There were 23 male and 22 female patients in group 1 and 22 male and 23 female patients in group 2, there was no statistically significant difference between the groups in terms of gender (p=0.96). The mean age was 55.23 ±7.53 years in group 1, 55.70 ±9.78 years in group 2, there was no statistically significant difference between the groups. (p=0.97) In group 1, BBIOP was 18.12 ±4.18 mmHg, ABIOP 20.98 ±4.42 mmHg, AIIOP 43.20 ±15.80 mmHg, while in group 2, BBIOP 18.65 ±3.52 mmHg, ABIOP 22.80 ±3.90 mmHg, AIIOP 39.08 ±13.18 mmHg. The difference between AIIOP and BBIOP was 25.04 ±16.30 mmHg in group 1 and 20.36 ±13.82 mmHg in group 2, the difference was not statistically significant.(p=0.21) The difference between AIIOP and ABIOP was 22.32 ±16.48 mmHg in group 1 and 16.18 ±13.05 mmHg in group 2, the difference was statistically significant.(p=0.03) (Table 1)

Discussion

The sudden increase in IOP observed during intravitreal injection is expected immediately after injection due to the increase in vitreous volume and studies have reported that it may be transient or permanent.[3-6] It is thought that intravitreal antiVEGFs leave the vitreous cavity via choroidal circulation or aqueous drainage after retinal penetration.[7] One or both of these routes are effective in normalization of elevated IOP.

Goldmann applanation tonometry (GAT) is a widely used and accepted gold standard method for the measurement of IOP, which is still the only treatable risk factor in glaucoma. The Tonopen electronic tonometer, which has become widely used in ophthalmology practice in the last decade, is recommended as an alternative to Goldmann applanation tonometry for IOP measurement.[8] It is a handheld applanation tonometer that is easy to calibrate and use and allows IOP measurement in patients with corneal pathology. In comparative studies of Tonopen and Goldmann applanation tonometry, it was reported that Tonopen gave accurate results both in the normal population and in eyes with glaucoma.[9,10] We also used Tonopen in our study.

Five hundred and thirty retina specialists participated in the study in which clinicians were questioned about intra-

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Table 1. Comparison of age, gender and IOP values in groups

	Group 1	Group 2	P value
Age	55.23 ±7.53	55.70 ±9.78	0,97
Gender	23 M, 22 F	22 M, 23 F	0,96
BBIOP	18.12±4.18 mmHg	18.65 ±3.52 mmHg	
ABIOP	20.98 ±4.42 mmHg	22.80 ±3.90 mmHg	
AIIOP	43.20±15.80mmHg	39.08±13.18mmHg	
AIIOP-BBIOP	25.04±16.30mmHg	20.36±13.82mmHg	0,21
AIIOP-ABIOP	22.32±16.48mmHg	16.18±13.05mmHg	0,03

vitreal antiVEGF injection protocol, drug preference, needle diameter, injection volume, injection technique and long-term IOP elevation observations. 292 retina specialists said that they believed that intravitreal antiVEGF injection caused long-term IOP elevation, but drug preference was not related to IOP elevation. It was stated that rapid injection technique and the use of high volume may cause persistent IOP elevation in antiVEGF injection. Rapid IOP elevation may cause trabeculum damage and lead to this complication.[11]

In our study, we evaluated the change in IOP before and after injection in patients who received intravitreal aflibercept with the use of topical DT drops 1 hour before the procedure. The AIIOP-ABIOP difference was significantly higher in the group with topical DT drops. The reason for this may be that the IOP decreased more in the group that received drops before injection and the difference between the IOP after injection was found to be higher. All patients were treated by the same surgeon, using the same method, using the same diameter needle tip.

According to the Kim et al. study, intravitreal injection is well tolerated by patients in the short post-injection period. In their series, IOP values in all patients decreased to normal values within 30 minutes without any intervention. Repeated or prolonged IOP follow-up after intravitreal injection was not considered necessary. However, it has been reported that post-injection IOP monitoring may be necessary in patients who received more than 0.05 ml injection with a fine needle such as 27 gauge, which does not allow vitreous reflux, or in patients who did not have vitreous reflux after injection despite injection with a larger needle, or in patients with a history of glaucoma.[12] The tolerance of the patients in our study was also good, patients with a previous diagnosis of glaucoma were not included in our study and IOP values were normal in all patients after 1 day, but we think that careful evaluation is needed in patients with low optic nerve reserve such as glaucoma.

Frenkel et al. recommended discontinuation of topical drops or systemic medication for intravitreal injections and paracentesis only in patients with known optic nerve damage with previous episodes of sudden IOP elevation and loss of light perception within minutes after injection.[13] In our study, no patient had loss of light perception and anterior chamber paracentesis was not required. In a prospective, double-blind, placebo-controlled study by Theoulakis et al., placebo (artificial tears) or Combigan (brimonidine-timololol) was instilled in one eye of 88 patients with normotensive age-related macular degeneration who received intravitreal ranibizumab the day before and twice daily on the day of injection, and IOP was measured before and 5, 10, 15 minutes and 1 hour after injection.[14] As a result, IOP was found to be normal in all patients at 1 hour after injection.

Limitation: Although IOP returned to normal in all patients on post-procedure day 1, the limitation of our study is that we did not evaluate the interval period.

Conclusion: In our study, we aimed to evaluate the effect of topical DT drops on IOP changes induced by the injection procedure in patients receiving intravitreal aflibercept and we observed that IOP changes were greater in patients receiving DT drops.

Conflict of Interest: The authors declare no conflict of interest related to this article.

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Ethics Committee Approval: In this study,national and international ethical rules are observed.

Ethic Board: KBÜ Etik Kurul 2023/1580

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