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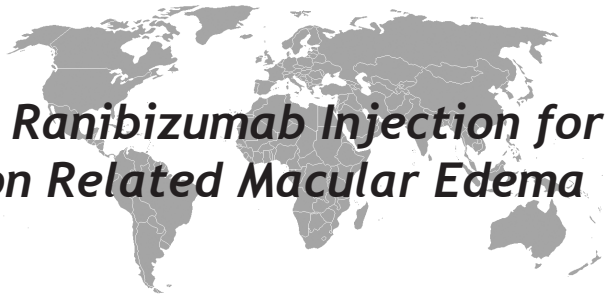
Original Article



The Outcome of Intravitreal Ranibizumab Injection for Branch Retinal Vein Occlusion Related Macular Edema

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ABSTRACT

Branch retinal vein occlusion related macular edema (BRVO-ME) is the leading cause of visual loss in patients with Branch retinal vein occlusion (BRVO). In the current study, our aim was to investigate the outcome of intravitreal ranibizumab injection for BRVO-ME. The medical records of randomised thirteen eyes of thirteen patients (7 women and 6 men) with BRVO-ME were reviewed retrospectively. Three and 10 eyes had inferior temporal and superior temporal branch retinal vein occlusion-related macular edema, respectively. At the enrollment visit, all patients received a complete ophthalmic examination, including central subfield (CSF) thickness and average cube thickness measurements using spectral-domain optical coherence tomography (SD-OCT), best corrected visual acuity (BCVA) and intraocular pressure (IOP) measurements. The median patient age was 53 years (range, 38-74). Of the patients, median CSF thickness was 453 µ (range, 221-907), median average cube thickness was 293 µ (range, 237-433), median BCVA was 0.30 logMAR unit (range, 0.05-1.00 logMAR unit), and median IOP scores was 18 mmHg (range, 15-25) at baseline. Compared with baseline, a statistical significance in median CSF thickness scores at week 1 (p=0.015), months 1 (p=0.015), 2 (p=0.030), and 3 (p=0.045) was noted. Compared with baseline, a statistical significance in median BCVA scores at months 2 (p=0.045), 3 (p=0.030), and 6 (p=0.045) was noted. Compared with baseline, no statistical significance in median IOP scores and median average cube thickness scores at week 1, months 1, 2, 3, and 6 was noted (p>0.05, for all). No statistical significance in median CSF thickness scores, median BCVA scores, median IOP scores, or median average cube thickness scores was noted between the other follow-up periods. No complication related to ranibizumab injections was detected during the follow-up period. The treatment method does not cause any increase in IOP score. Besides ranibizumab injection can cause a dramatic decrease in CSF thickness scores and a dramatic increase in BCVA scores as early as at week 1 postoperatively.

Key words: *Branch retinal vein occlusion, macular edema, ranibizumab.*

Retina Ven Tıkanıklığına Bağlı Makula Ödeminde İntravitreal Ranibizumab Enjeksiyonun Sonuçları

ÖZET

Retinal ven dal tıkanıklığına bağlı maküler ödem (RVDTMÖ) Retinal ven dal tıkanıklığı (RVDT) hastalarında görme kaybının en sık nedenidir. Bu çalışmadaki amacımız, RVDTMÖ için intravitreal ranibizumab enjeksiyonu sonuçlarını araştırmaktı. Rastgele 13 (7 bayan ve 6 erkek) hastanın 13 RVDTMÖ olan gözü geriye dönük olarak gözden geçirildi. Üç hastanın alt temporal RVDTMÖ, 10 hastanın üst temporal RVDTMÖ bulunan gözü çalışmaya alındı. Çalışmanın ilk gününde tüm hastalara, spectral domain OKT kullanılarak merkezi altalan kalınlığı (MAK), ortalama küp kalınlığı, düzeltilmiş en iyi görme keskinliği (EİDGK) ve göziçi basıncı (GİB) ölçümü dahil, tam bir göz muayenesi yapıldı. Ortanca hasta yaşı 53 (aralık, 38-74) idi. Başlangıçta hastaların ortanca MAK değeri 453 µ (aralık, 221-907), ortanca ortalama küp kalınlığı 293 µ (aralık, 237-433), ortanca EİDGK 0.30 logMAR ünitesi (aralık, 0.05-1.00 logMAR ünitesi), ve ortanca GİB değeri 18 mmHg (aralık, 15-25) idi. Başlangıç değerleri ile karşılaştırıldığında, birinci hafta (p=0.015), 1. ay (p=0.015), 2. ay (p=0.030), ve 3. ay (p=0.045) takiplerinde ortanca MAK değerlerinde istatistiksel olarak anlamlı fark saptandı. Başlangıç değerleri ile karşılaştırıldığında, 2. ay (p=0.045), 3. ay (p=0.030) ve 6. ay (p=0.045) takiplerinde ortanca EİDGK değerlerinde istatistiksel olarak anlamlı fark saptandı. Başlangıç değerleri ile karşılaştırıldığında, birinci hafta, 1, 2, 3 ve 6. ay takiplerinde ortanca GİB değerleri ve ortanca küp kalınlığı değerlerinde istatistiksel olarak anlamlı fark saptanmadı (p>0.05, hepsi için). Diğer takip periyotlarında elde edilen ortanca MAK değeri, ortanca ortalama küp kalınlığı, ortanca EİDGK, ya da ortanca GİB değeri arasında istatistiksel olarak anlamlı fark saptanmadı. Takip süresince ranibizumab enjeksiyonuna bağlı komplikasyon saptanmadı. RVDTMÖ hastalarında intravitreal ranibizumab enjeksiyonunun etkinlik ve uzun dönemde güvenilirliğini ortaya koymuştur. Tedavi yöntemi GİB artışına yol açmamıştır. Ayrıca, intravitreal ranibizumab enjeksiyonu, enjeksiyon sonrası 1. haftada dahi MAK değerinde çarpıcı bir düşüşe, ve EİDGK değerinde çarpıcı bir yükselişe sebep olmuştur.

Anahtar kelimeler: *Maküler ödem, ranibizumab, retinal ven dal tıkanıklığı.*

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INTRODUCTION

Retinal vein occlusions are estimated as great as 180.000 cases per year in USA. Branch retinal vein occlusion (BRVO) cases account for nearly 80% of retinal vein occlusion cases (1,2). BRVO related macular edema (BRVO-ME) is the leading cause of visual loss in patients with BRVO. Besides the classical grid laser treatment, several new treatments for BRVO-ME, including intravitreal triamcinolone injections, intravitreal dexamethasone implants, and inhibitors of vascular endothelial growth factor (VEGF) agents, have been evaluated in randomized clinical trials (3-5). Of these, the most effective treatment modality has been anti-VEGF agents. Prospective studies showed the effectiveness of intravitreal injection of ranibizumab (IVR), a humanised VEGF antibody fragment that neutralises all isoforms of VEGF-A and their biologically active degradation products, in BRVO-ME (6). The rationale to employ IVR for management of BRVO is that elevated levels of VEGF resulting in increased vascular permeability and subsequent BRVO-ME have been reported in BRVO patients (7-9).

In the current study, our aim was to investigate the outcome of IVR for BRVO-ME.

MATERIALS AND METHODS

Retrospective, interventional, noncomparative case series. The current study was a single-arm, single-center study conducted in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice. All patients provided written informed consent. The medical records of randomized thirteen eyes of thirteen patients (7 women and 6 men) with BRVO-ME were reviewed retrospectively. Three and 10 eyes had inferior temporal and superior temporal branch retinal vein occlusion-related macular edema, respectively. Patients with macular edema (ME) due to causes other than BRVO or patients receiving treatments other than IVR were excluded. At the enrollment visit, all patients received a complete ophthalmic examination, including central subfield (CSF) thickness and average cube thickness measurements using spectral-domain optical coherence tomography (SD-OCT), best corrected visual acuity (BCVA) and intraocular pressure (IOP) measurements. Each patient received 0.5 mg IVR at baseline. The mean duration between the diagnosis of BRVO-ME and the first intravitreal injection of ranibizumab was 1.92 months. On the follow-up period the patients received additional IVR on PRN basis. Therefore; 2, 2, and 5 patients received 4, 3 and 2 additional injections, respectively. The average duration between re-injections was 2.29 months. Only 1 eye with BRVO-ME underwent argon laser photocoagulation after intravitreal injection of ranibizumab. Patients with CSF thickness more than 277 µ, or those with persistent or recurrent ME affecting BCVA based on the investigator's evaluation received additional IVR. At the study follow-up visits scheduled on week 1 and months 1, 2, 3, and 6 after injection, slit-lamp examination, CSF thickness, average cube thickness, BCVA and IOP measurements were performed. IVR was administered under sterile conditions at the theatre. The BCVA was measured using a 4-meter ETDRS backlit light-house. IOP measurements were done using Goldmann applanation tonometer. OCT was obtained using Cirrus HD 4000 OCT (Carl Zeiss Meditec, Inc, Dublin, California, USA).

Friedmann test and Bonferroni adjusted Wilcoxon signed-ranks tests were employed for statistical analyses. p value < .05 was considered as statistically significant.

RESULTS

The median patient age was 53 years (range, 38-74). Of the patients, median CSF thickness was 453 µ (range, 221-907), median average cube thickness was 293 µ (range, 237-433), median BCVA was 0.30 logMAR unit (range, 0.05-1.00 logMAR unit), and median IOP score was 18 mmHg (range, 15-25) at baseline (Table). Compared with baseline, a statistical significance in median CSF thickness scores at week 1 (p=0.015), months 1 (p=0.015), 2 (p=0.030), and 3 (p=0.045) was noted. Compared with baseline, a statistical significance in median BCVA scores at months 2 (p=0.045), 3 (p=0.030), and 6 (p=0.045) was noted. Compared with baseline, no statistical significance in median IOP scores and median average cube thickness scores at week 1, months 1, 2, 3, and 6 was noted (p>0.05, for all). No statistical significance in median CSF thickness scores, median BCVA scores, median IOP scores, or median average cube thickness scores was noted between the other follow-up periods. No complication related to IVR was detected during the follow-up period.

***Table**. Best corrected visual acuity, intraocular pressure, central subfield thickness, and average cube thickness scores of the eyes of the patients with branch retinal vein occlusion related macular edema that underwent intravitreal injection of ranibizumab*

	BCVA	IOP (mmHg)	CSF (μ)	TAC (μ)
Baseline	0,2 (0-0,9)	18	453[a]	293
Week 1	0,5 (0,1-1,0)[a]	18	289[a]	303
Month 1	0,6 (0,1-1,0)[a]	19[b]	256[a]	292
Month 2	0,6 (0,1-1,0)[a]	20[b]	278[a]	306
Month 3	0,9 (0-1,0)[a,b]	17[c,d]	263[a]	291
Month 6	1,0 (0-1,0)[a,b,c,d]	18[d]	260[a]	297

Scores are presented as median.
BCVA: Best corrected visual acuity, IOP: Intraocular pressure, CSF: Central subfield thickness, TAC: Average cube thickness.
a p<0.05, different from baseline score, b p<0.05, different from Week 1 score, C p<0.05, different from Month 1 score, d p<0.05, different from Month 2 score.

DISCUSSION

The BRAVO study was the first randomized controlled masked clinical trial that proved the efficacy of IVR in patients with BRVO-ME (10). In another trial, that was a prospective randomized controlled one, and was conducted by Tan MH et al, the greater efficacy of IVR in center-involving BRVO-ME has been shown, when compared with laser grid treatment (11). Tan MH (11) observed improvement in BCVA and reduction in central foveal thickness that is in line with the BRAVO study, as did we. Brown DM et al (12) conducted a study in order to assess the efficacy and safety of 0.3 mg IVR and 0.5 mg IVR in patients with BRVO-ME and concluded that both treatment modalities were effective. In another study, (10) reported that monthly 0.3 mg or 0.5 mg IVR for 6 months in patients with BRVO eliminated BRVO-ME in most patients.

IVR helps visual gain in patients with BRVO-ME. The retinal pigment epithelium pump keeps the cones and rods deturgesced during the BRVO-ME, thereby contributing to visual gain.

Grid laser treatment cannot be immediately given to most patients with BRVO because of their retinal hemorrhages. Conversely, safe and well-tolerated IVR can be immediately administered to the patients with BRVO-ME. In the current trial, compared with baseline, statistical significance in median CSF thickness scores and median BCVA scores noted at week 1 demonstrated that IVR achieves an immediate improvement, which is a particular advantage of IVR on grid laser therapy (p<0.05, for all). In the current study any potential side affects of IVR, such as endophthalmitis, thromboembolic events, retinal tear or retinal detachment were not observed.

The inferiorities of our trial are the lack of the control group and that the follow-up period consisted of the first 6 months following BRVO-ME, a time period during which the improvement could occur spontaneously. Further studies with longer follow-up periods, and control groups, such as BRAVO study, are needed. Whether monthly dosing or as needed IVR therapy is more effective, goes on being the subject of debate. In the current study our aim was to perform the least number of IVR in order to prevent its potential side affects, such as endophthalmitis, thromboembolic events, retinal tear or retinal detachment. In the current study 2, 2, and 5 patients received 4, 3 and 2 additional injections, respectively. In other words, only 9 additional IVR totally were performed to 13 eyes.

In conclusion, IVR is an efficient treatment modality in patients with BRVO-ME. How to decrease the number of IVR will probably go on being the target of the study groups in the near future.

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