·Clinical Research·

Comparison of anti-vascular endothelial growth factors, laser treatments and a combination of the both for treatment of central retinal vein occlusion

Yoav Y. Pikkel[1], Adi Sharabi-Nov[2], Itzchak Beiran[3,4], Joseph Pikkel[5,6]

[1]Tzameret Medical Track, Hebrew University, Jerusalem 91120, Israel
[2]Research Wing, Ziv Medical Center, Safed, Israel and Tel-Hai Academic College, Kiryat Shmona 12208, Israel
[3]Department of Ophthalmology, Rambam Medical Center, Haifa 3525408, Israel
[4]The B. Rappaport Faculty of Medicine, Israel Institute of Technology, Haifa 3525427, Israel
[5]Department of Ophthalmology, Ziv Medical Center, Safed 13100, Israel
[6]Bar Ilan University, Faculty of Medicine, Safed 13101, Israel
Correspondence to: Joseph Pikkel. Department of Ophthalmology, Ziv Medical Center, Safed 13100, Israel. pikkel.86@gmail.com
Received: 2014-12-01 Accepted: 2015-05-27

Abstract

• AIM: To compare changes in visual acuity and macular edema in patients with central retinal vein occlusion (CRVO) treated with intravitreal injections of bevacizumab, macular grid photocoagulation combined with pan retinal photocoagulation (PRP), or both (bevacizumab+grid+PRP).

• METHODS: Our study is a retrospective cohort clinical study that examined patients that suffered from ischemic CRVO with macular edema. Study inclusion criteria were ischemic CRVO with macula edema and the availability of complete medical records for at least 12mo after treatment. Excluded were patients with diabetes or any other retinal disease. We reviewed the medical records of patients treated in one ophthalmology department - comparing changes in visual acuity and macular edema in patients treated with intravitreal injections of bevacizumab *vs* those that were treated with macular grid photocoagulation and PRP or both. The main outcome measures were the differences in best corrected visual acuity (BCVA) and in macular thickness, as assessed by optical coherence tomography, between the enrollment and the final follow up visits.

• RESULTS: Sixty-five patients met inclusion criteria. There were no statistically significant differences among the three groups in the mean changes in macular thickness as measured by ocular coherence tomography (131.5±41.2, 108.6±29.2, and 121.1±121.1, P=0.110), or in visual acuity (0.128±0.077, 0.088±0.057, and 0.095±0.065), for intravitreal injections, macular grid photocoagulation+ PRP and a combination of the treatments, respectively, P =0.111. The proportions of patients with macular edema after treatment were: 26.1%, 28.6%, and 14.3%, respectively, P=0.499.

• CONCLUSION: Similar benefit was observed for intravitreal injections, laser photocoagulation, or a combined regimen in the treatment of CRVO. A non-statistically significant trend for reduction in macular edema was observed following combined treatment.

• KEYWORDS: bevacizumab; grid laser photocoagulation; macular edema; optical coherence tomography; retinal vein occlusion

DOI:10.18240/ijo.2016.03.18

Pikkel YY, Sharabi-Nov A, Beiran I, Pikkel J. Comparison of anti-vascular endothelial growth factors, laser treatments and a combination of the both for treatment of central retinal vein occlusion. *Int J Ophthalmol* 2016;9(3):431-433

INTRODUCTION

Central retinal vein occlusion (CRVO) carries a potential risk for blindness. Decreased visual acuity (VA) in CRVO may result from macular edema (ME). CRVO associated ME has been reported to respond favorably to intravitreal injections of anti-vascular endothelial growth factors (VEGF) and pan retinal laser photocoagulation [1-4]. Though macular grid laser treatment is not indicated as a treatment for ME due to CRVO it was found as beneficial in cases of ME due to branch retinal vein occlusion and at least once was found as effective in ME due to CRVO [5]. Other medical and surgical therapies that have been investigated as treatments for CRVO associated ME failed to achieve ME absorption or caused undesirable side effects [6-13]. Thus, the currently accepted treatment for CRVO associated ME is anti-VEGF intravitreal injections. Subsequent application of macular grid photocoagulation and pan retinal photocoagulation (PRP) was suggested when such treatment fails[14]. Several studies[3-4,13,15] that compared the effectiveness of intravitreal anti-VEGF antibody injections to macular grid

Table 1 Comparison of outcomes among treatment groups $\bar{x} \pm s$

Variables	Anti-VEGF injections (n=23)	Laser grid+PRP (n=21)	Anti-VEGF injections+laser grid+PRP (n=21)	P
Age (a)	64.0±9.1	62.9±10.0	66.9±8.8	0.360
ΔOCT	131.5±41.2	108.6±29.2	121.1±34.5	0.110
ΔVA	0.128±0.077	0.088±0.057	0.095±0.065	0.111
No. of injections	3.5±1.2	-	3.2±1.1	0.365
ME no. (%)	6 (26.1)	6 (28.6)	3 (14.3)	0.499

SD: Standard deviation; OCT: Optical coherence tomography; VA: Visual acuity; ME: Macular edema; No.: Number.

photocoagulation demonstrated superiority of intravitreal anti-VEGF antibody injections as first line treatment. Nevertheless, widely excepted guidelines for optimal treatment do not yet exist. In the present study we compared changes in VA and in macular thickness, and in the proportions of patients with ME, following treatment by intravitreal anti-VEGF injections or by macular grid photocoagulation or by a combination of these two treatments.

SUBJECTS AND METHODS

The medical records of all patients treated for ischemic CRVO associated ME in the Ziv Medical Center Israel from January 1, 2010 to December 31, 2012 were reviewed. The study was approved by the local bio-ethical committee (0063-13 ZIV). Ischemic CRVO was defined as severe visual loss (6/60 or less), extensive retinal hemorrhages and cotton-wool spots, and poor perfusion to retina as observed in fleuroscein angiography. Data regarding age, gender, general health condition, primary VA, final VA and ME parameters were collected. Patients were divided into 3 groups for analysis, according to 3 treatment regimens that were administered during the study time: 1) patients treated with intravitreal bevacizumab injections only (one injection per month for the first 3mo), followed by injections according to clinical examination and optical coherence tomography (OCT) results; 2) patients treated with macular grid photocoagulation and PRP only; 3) patients treated with one intravitreal bevacizumab injection within one month of diagnosis, followed by macular grid photocoagulation and PRP and then followed by intravitreal bevacizumab injections according to clinical examination and OCT results.

Intravitreal injections of bevacizumab were preformed within one month from diagnosis in all groups. Intravitreal bevacizumab injections according to clinical examination and OCT results were continued until resolution of macular edema. In cases of persistent ME, intravitreal injections were stopped after 3 injections that did not cause any change in ME as shown in OCT.

The main outcome measures were the differences in best corrected visual acuity (BCVA) and in macular thickness, as assessed by OCT, between the enrollment and the final follow up visits. Inclusion criteria were ischemic CRVO with ME and the availability of complete follow up data for at least 12mo after the last injection or after macular grid photocoagulation.

Primary VA and final VA were measured using Snellen charts and recorded in decimal values. Patients' primary and final macular thickness were measured by OCT (OCT/SLO-OTI, Canada). Final ME was defined, as in other studies [13], as central retinal thickness greater than 270 μm and/or the presence of intraretinal cysts.

Exclusion criteria were diabetic retinopathy, patient that suffered from ME in the past due to any other reason and incomplete or unrecorded follow up of at least 12mo.

Statistical Analysis Differences among mean values of patients' age, Δ OCT and Δ VA among the 3 treatment groups were calculated by the ANOVA test. Differences in the numbers of injections were calculated by the independent sample t-test. The correlation between the proportion of patients with ME and the type of treatment was calculated by the Chi-square nonparametric test.

RESULTS

Of 79 patients who suffered from ME due to ischemic CRVO during the study period, 6 were excluded due to diabetic retinopathy. Of the rest 73 patients, complete medical records with at least 12mo follow-up were available for 65: 23 in the injected group, 21 in the macular grid photocoagulation + PRP group and 21 in the combined therapy group. At baseline, mean age, primary VA and macular thickness were similar among the groups (Table 1).

The mean number of intravitreal injections was similar in the two groups of patients who received injections (3.5 *vs* 3.2; Table 1). In all three groups there was an improvement in VA and reduction of macular thickness, with no statistically significant differences among the groups (Table 1). The rate of residual ME was lower in the combined treatment group comparing to the injection only, and grid+PRP groups: 14.3%, 26.1%, and 28.6%, respectively, P=0.499 (Table 1).

DISCUSSION

Treatment of ME secondary to CRVO is challenging and sometimes frustrating. Widely accepted guidelines for treatment are not currently available[7]. While both intravitreal bevacizumab injections and macular grid photocoagulation+ PRP, have demonstrated effectiveness, some ophthalmologists prefer one of the treatments over the other. Comparing outcomes of combined treatment in 19 patients who suffered

from ME due to branch retinal vein occlusion and 9 who suffered from ME due to CRVO, was done by Ogino *et al* [15] They concluded that grid photocoagulation combined with intravitreal bevacizumab has a substantial effect in reducing recurrent ME associated with retinal vein occlusion, but the effect on VA is limited. Shah and Shah [16] treated nine patients with ME secondary to CRVO with a single intravitreal injection of bevacizumab within 10d from diagnosis, followed 3wk later by pan retinal and macular grid photocoagulation. They concluded that early intravitreal bevacizumab therapy followed by pan retinal and macular grid laser may provide visually and anatomically favorable results for treatment of CRVO. They stated that the combined early treatment may also obviate the need for repeated injection [16-17]. These two studies did not compare treatment strategies. In the present study the number of injections needed was similar with or without grid laser; however, not all of the patients received an intravitreal injection within 10d from the CRVO event. All three treatment strategies resulted in improvement. Though there was no statistically significant difference in VA improvement or in macular thickness reduction among the three groups, better macular edema tended to resolve more often in the combined treatment compared to the other two groups. Though grid laser treatment is not recommended for treatment of CRVO related ME, in our retrospective study the combination of grid laser with PRP and/or bevacizumab injections did show some improvement in ME reabsorption and reducing macular thickness. A larger sample size is needed to confirm these findings.

Intravitreal bevacizumab injection, macular grid photocoagulation+PRP and a combination of these treatments are all effective in treating ME secondary to CRVO. In this study no statistically significant differences in VA improvement or in macular thickness reduction were found between the three groups. Large scale studies are needed to investigate if the tendency demonstrated herein for better results in the combination therapy group reaches statistical significance.

ACKNOWLEDGEMENTS

Conflicts of Interest: Pikkel YY, None; **Sharabi-Nov A,** None; **Beiran I,** None; **Pikkel J,** None.

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