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Intravitreal bevacizumab injection in the treatment of macular edema secondary to branch retinal vein occlusion

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玻璃体腔注射 bevacizumab 治疗视网膜分支静脉阻塞继发黄斑水肿

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摘要

目的:通过测量随访 12mo 后的中央黄斑厚度(CMT)和视力,评估玻璃体腔注射 bevacizumab 治疗视网膜分支静脉阻塞(BRVO)继发黄斑水肿(ME)的效果。

方法:被诊断为 BRVO 继发 ME 的患者行眼科检查、CMT 测量、荧光素血管造影。排除荧光素血管造影出现黄斑缺血患者,其他疾病继发的其他部位新生血管化患者,有眼内治疗史(激光治疗、玻璃体腔注射或眼科手术)患者。CMT >250μm 的 32 例患者给予 bevacizumab (Altuzan®, 0.125mg/0.05mL)注射治疗,并随访 12mo。分析最佳矫正视力(BCVA)logMAR 数据和 CMT 控制参数。使用 Minitab15.0 软件统计分析配对 t 检验,$P<0.05$ 有统计学意义。

结果:BCVA logMAR 数据和 CMT 控制参数的平均值较注射前有明显改变($P<0.01$)。平均最佳矫正视力增量为 0.477±0.235,平均 CMT 较注射前下降 257.906±88.865。10 例(31%)患者对单次注射有阳性反应,平均 12.6±0.66mo 未复发 ME。5 例(15.6%)患者接受两次注射,17 例(53%)3 次以上。单眼平均注射量 2.18±0.91 (1~4)。第一组 ME 复发时间为 2.45±0.63mo,第二组为 2.58±0.66mo,第三组为 3.17±0.48mo。5 例(15.6%)患者需要多次注射以减轻 ME,视力并未随 ME 的减轻而增加。

结论:玻璃体腔注射 bevacizumab 是常规治疗 BRVO 继发 ME 的方法,有效、快速、安全。为了使疗效持久,需加强后续处理,通过激光或长效药物保持无水肿状态。视网膜静脉循环和 ME 须通过荧光素血管造影观察,而不能采取频繁注射。是否需再次注射必须根据 ME 的临床表现和视力的预测来判断。

关键词:贝伐珠单抗;视网膜分支静脉阻塞;黄斑水肿

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Abstract

• AIM: To evaluate the 12mo results of intravitreal bevacizumab injection on central macular thickness (CMT) and visual acuity in the treatment of macular edema (ME) secondary to branch retinal vein occlusion (BRVO).

• METHODS: Thirty-two patients who underwent intravitreal bevacizumab (Altuzan®) 0.125mg/0.05mL injection for ME secondary to BRVO at least 12mo follow up period have been studied respectively. Patients with diagnosis of ME secondary to BRVO were applied an ophthalmic examination, CMT measurement, and fluorescein angiography, so patients whose CMT above 250μm were offered intravitreal bevacizumab treatment. Patients who had macular ischemia on fluorescein angiography, neovascularisation elsewhere secondary to other types of diseases, received any intraocular treatment before (such as laser treatment, intravitreal injection or eye surgery) have been out of trial. Data of logMAR best corrected visual acuity (BCVA) and CMT in control visits have been evaluated. For statistical analysis Student's paired t-test was used by Minitab15.0 software and a P-value < 0.05 was considered as statistically significant.

• RESULTS: Mean logMAR BCVA changes and mean CMT changes were statistically significant compared to pre-injection values at last visit ($P<0.01$). Mean BCVA increment was 0.477±0.235, mean CMT decline was 257.906±88.865 compared to pre-injection at last visit. Ten (31%) of the patients had a positive response with a single injection and no recurrence of ME for a mean of 12.6±0.66mo. Five (15.6%) patients received injection two times and 17 (53%) patients more than 3 injections. Mean injection per eye was 2.18±0.91 (1~4) respectively. Recurrence of ME was seen aproximately in 2.45±0.63mo at the first control, 2.58±0.66mo at the second control and 3.17±0.48mo at the third control respectively. Five (15.6%) of the patients needed multiple injections for reducing ME whereas visual acuity gain was not achieved as ME reduced in those patients.

• CONCLUSION: Treatment of ME secondary to BRVO with intravitreal bevacizumab seems effective, fast, safe, and commonly performed treatment. In order to achieve this lasting effect, we have to strengthen this post treatment non-edematous status by lasers or long lasting agents. Retinal venous circulation and ME must be observed on fluorescein angiography rather than making frequent injections. Reinjections must be done according to the clinical status of ME and the prediction of visual acuity gain.

• KEYWORDS: bevacizumab; branch retinal vein occlusion; macular edema
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INTRODUCTION

BRVO is the second most frequent retinal vascular disease after diabetic retinopathy[1]. ME is the major cause of visual impairment in BRVO. The macular grid laser photocoagulation is a proved treatment method for ME secondary to BRVO[2,3]. However, it may constrict peripheral visual field, complicate with paracentral scotomas, and is not applicable in early period of the disease. Surgical methods such as arteriovenous sheathotomy combined with removal of internal limiting membrane have risks, minimal benefits and experiences in surgery were insufficient[4]. These limitations, yet increased cataractous changes and induced ocular hypertension might occur[6,7]. The SCORE trial concluded that intravitreal triamcinolone injection in BRVO had no superiority to grid laser photocoagulation[8]. Because these side effects were commonly seen, clinicians preferred intravitreal bevacizumab treatment.

Bevacizumab is a full-length antibody for vascular endothelial growth factor (VEGF) and licensed for use in oncology but unlicensed in ophthalmology[9]. Cumulative data suggest that the risk for adverse events reported after intravitreal injection is low. These adverse events seen are endophthalmitis, retinal detachment, iritis/uveitis, intraocular hemorrhage, ocular hypertension, cataract and hypotony. Careful attention to injection technique and appropriate postinjection monitoring are essential for these impending side effects[10]. Intravitreal bevacizumab injection is commonly used off-labelly for ME secondary to BRVO in different treatment modalities[11,12]. We aimed to evaluate the longterm effect of intravitreal bevacizumab (Altuzan®, Roche) injection on BCVA and CMT in the treatment of ME secondary to BRVO retrospectively in this study.

SUBJECTS AND METHODS

Subjects In this retrospective study, we used the data of thirty-two patients who referred to Sakarya Training and Research Hospital with the diagnosis of BRVO between 18/12/2009 and 02/03/2012. This study has complied with the provisions of the Declaration of Helsinki. The ethics committee approval was obtained from Sakarya University Ethics Committee. Patients with contraindications against an intravitreal bevacizumab injection (acute ocular infection, recent history of stroke or myocardial infarction, unstable angina pectoris, uncontrolled hypertension, uncompensated renal insufficiency, allergy to bevacizumab, or pregnancy) were excluded from the treatment. All the patients were informed about the nature of off-label use and the experimental nature of the therapy before signing an informed consent prior to each injection. Also, they confirmed that they were aware of the potential side-effects of bevacizumab treatment. Patients who had any intravitreal injection or laser treatment before, neovascularization elsewhere or macular ischemia on angiography, glaucoma, age related macular degeneration, diabethic retinopathy were out of the trial. The study included 8 (25%) men and 24 (75%) woman. The mean age of the patients was 57.2±10.6 (34~78). 25 (78%) of the patients had hypertension, 3 (9%) of the patients had diabetes mellitus type 2, and 7 (22%) of the patients had no systemic diseases retrospectively. Diabetic patients had also systemic hypertension. 16 (50%) of the patients had vein occlusion in the right and 16 (50%) of the patients had vein occlusion in the left eye. 12 (37.5%) of the patients had superior temporal BRVO, 12 (37.5%) of the patients had inferior temporal BRVO and 8 (25%) of the patients had macular BRVO. Demographic properties of patients are seen in Table 1.

Methods All patients were applied an ophthalmic examination for determination of BCVA using Snellen charts, slit lamp examination of anterior and posterior segments, measurement of CMT by the Optovue, Ivue® spectral domain optic coherence tomography (OCT) and fundus fluorescein angiography by Kowa VX 10i fundus camera. The patients who had macular edema on fluorescein angiography and on OCT were evaluated as BRVO associated ME. The CMT over 250μm was accepted as BRVO related ME and checked with fundus fluorescein angiography, and then the patient was considered to be injected. The CMT was defined as the central circular area of the retina which is one milimetres in caliber and measured in micrometres (μm). BCVA was transformed into logMAR to facilitate statistical analysis.

Intravitreal injection was performed as follows: Eye lids were cleansed with 10% povidone iodine, conjonctiva was cleansed with 5% povidone iodine respectively. Bevacizumab was injected 1.25mg/0.05mL intravitreally via pars plana 3.5mm in phakic, 3mm in pseudophakic patients under sterile conditions in operation rooms. Patients were controlled for vision and intraocular pressure after the injection. Topical ofloxacin 3% (Exocin®) eye drops 4 times per day were reciped for 1wk after the injection. Primary outcomes were changes data in logMAR and CMT before and after the injection.

Table 1 Demographic properties of patients

Patient number	Systemic disease	Sex	Age (a)	Disease onset before treatment (mo)	Eye	Type of occlusion
1	H	F	56	13	L	S
2	H	F	53	0.5	R	I
3	H	F	50	5	L	I
4	H	F	78	10	L	S
5	H	M	57	9	R	Mc
6	H	F	49	6	R	S
9	H	F	74	12	L	I
10	H	F	65	3	L	I
13	N	F	47	1	L	S
14	H	M	59	1	R	Mc
15	H	F	50	2.5	L	S
17	H,D	F	71	11	L	Mc
24	H	F	50	8	R	I
27	H	F	68	0.5	R	I
28	N	F	47	10	R	I
29	H	F	72	9	R	Mc
32	H	M	52	2.5	R	I
7	N	F	47	1	L	Mc
8	H,D	F	56	1	R	Mc
11	H	F	68	2	R	S
12	N	M	42	2	L	S
16	N	F	34	1	R	S
18	N	F	47	3	L	Mc
19	H	F	65	0.25	L	S
20	H	M	56	1.5	R	Mc
21	H	F	52	2.5	L	I
22	H,D	F	54	2	R	S
23	N	M	47	1	L	S
25	H	M	58	1	R	S
26	H	F	66	13	R	I
30	H	F	73	11	L	I
31	H	M	67	1	L	I

H: Hypertension; D:Type 2 diabetus mellitus; N:None; F: Female; M:Male; R:Right; L:Left; I: Inferior; BRVO S:Superior BRVO; Mc: Macular BRVO.

All patients were visited on weekly basis after the injection and in one month during the month after the injection. Visual gain and possible complications were examined weekly after the injection. Decision of reinjection was made for steady visual acuity and dry macula with patient approval. Reinjections were offered in controls when OCT showed recurrent ME or cyst in macula on OCT and when ME is seen on angiography. First injections were all performed at initial examination. The second injections were performed before the first control when the patient accepted the second one. The third injection was performed before the second control and the fourth one was performed before the third control. Data were recorded at control sessions after the first months of the intravitreal injections. Patients were offered for recurrent injections when any cyst was detected on OCT, CMT was greater than expected and ME was seen on angiography. When the patient accepted, injection was performed. But in the situation when the patient rejected the re-injection, the patient was examined monthly and data were recorded at control points. Patient data are seen in Table 2. Some patients received one injection and some others received more injections. The results of injections were recorded at the first control, the second control, the third control and the last visit. Patients had no intravitreal injections during and among controls.

Statistical Analysis For statistical analysis Student's paired t-test was used by Minitab15.0 software and a P-value <0.05 was considered as statistically significant.

RESULTS

Mean follow up period was 12.37±0.73mo (12 ~ 15). Mean time interval between disease onset and the first injection was 4.60±4.30mo (0.25 ~ 13) respectively. The first, the second, the third and the last control visits were performed in 2.59±0.68; 2.78±0.72; 3.25±0.69 and 3.75±0.99mo

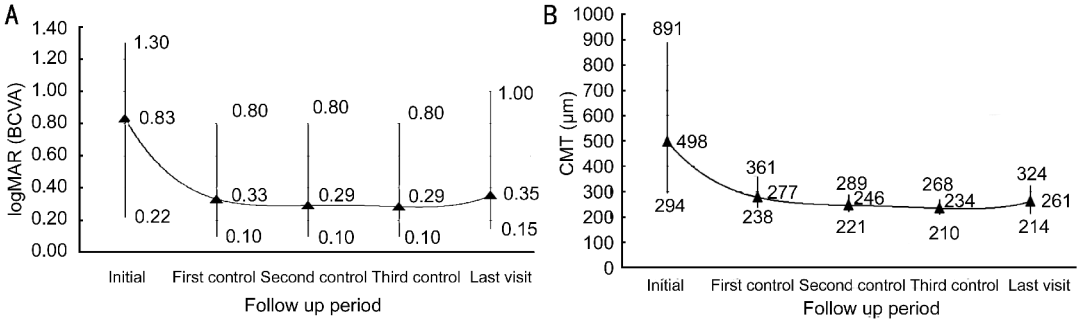
Table 2 Data of patients

Patient number	Initial logMAR	Initial CMT	1. Control logMAR	1. Control CMT	1. Control interval	2. Control logMAR	2. Control CMT	2. Control interval	3. Control logMAR	3. Control CMT	3. Control interval	Last Control logMAR	Last Control CMT	Last Control interval	Injection number
1	1.3	507	0.7	256	2	0.5	248	3	0.5	228	4	0.6	265	12	4
2	0.7	470	0.22	290	2.5	0.3	254	3.5	0.3	232	3	0.3	259	13	4
3	1	470	0.4	250	3	0.4	235	3	0.4	225	3	0.5	268	13	4
4	0.7	460	0.5	313	4	0.5	279	3	0.5	268	3	0.6	294	13	4
5	0.8	553	0.5	298	4	0,4	274	2	0,4	247	3	0,5	288	15	4
6	0.8	584	0.4	300	2	0.3	253	5	0.3	234	8	0.4	298	12	4
9	1.3	579	0.8	296	2	0.7	274	3	0.6	249	3	0.8	289	12	4
10	1.3	612	0.4	280	2	0.4	255	3	0.4	248	3	0.5	297	12	4
13	1.3	666	0.52	277	2	0.4	246	2	0.4	239	3	0.7	324	12	4
14	1.3	543	0.22	276	2	0.15	255	2	0.15	238	3.5	0.3	279	12	4
15	0.8	400	0.22	267	3	0.15	246	2	0.15	239	2	0.22	254	12	4
17	1.3	552	0.8	352	2.5	0.8	289	1.5	0.8	242	3.5	1	276	12	4
24	1.3	891	0.4	272	2	0.3	232	4	0.3	244	3	0.4	265	12	4
27	1	509	0.4	273	2	0.3	243	2	0.3	222	4	0.3	235	11	4
28	1.3	673	0.8	306	2	0.8	269	3	0.7	261	4	0.7	278	12	4
29	1	564	0.4	275	3	0.3	254	2	0.3	265	3	0.4	278	12	4
32	1.3	612	0.4	280	3	0.3	241	4	0.3	220	3	0.4	256	12	4
7	0.8	395	0.15	240	2	0.15	226	3	0.15	219	6	0.22	254	13	1
8	0.22	294	0.1	246	3	0.1	241	3	0.1	235	7	0.1	240	13	1
11	0.8	485	0.15	247	2	0.15	235	2	0.15	221	4	0.15	246	12	1
12	0.7	586	0.15	238	3	0.15	243	3	0.15	236	3	0.22	261	12	1
16	0.52	410	0.22	300	2	0.15	226	2	0.15	210	3	0.15	219	12	2
18	0.52	458	0.15	260	3	0.15	228	2	0.15	217	3	0.15	243	12	1
19	0.52	357	0.15	248	4	0.15	221	3	0.15	219	4	0.15	214	13	1
20	0.3	445	0.1	361	2	0.1	234	3	0.1	223	2	0.1	228	12	1
21	0.7	464	0.15	285	3	0.15	249	2	0.15	238	3	0.15	253	13	2
22	1	602	0.4	300	4	0.4	265	3	0.4	247	4	0.4	280	13	1
23	0.3	335	0.1	245	3	0.1	234	4	0.1	218	5	0.1	226	14	1
25	0.52	333	0.15	267	3	0.15	232	2	0.15	226	3	0.15	237	12	1
26	0.4	408	0.22	262	2	0.15	230	3	0.15	232	3	0.22	263	12	2
30	0.4	376	0.22	265	2	0.15	233	4	0.15	225	2	0.15	243	12	2
31	0.4	363	0.15	260	2	0.15	256	4	0.15	248	2	0.3	273	12	2

interval respectively. Mean injection per eye was 2.75±1.37 (1~4) respectively. Mean logMAR visual acuity was 0.831±0.575 before the injection and 0.354±0.224 at the last visit. The mean CMT was 498.625±122.157 before the injection and it was 277.656±28.735; 246.875±16.758; 234.844±14.252 and 261.969±24.979 at the first, the second, the third and the last visits respectively. The CMT decreases at control visits were statistically significant compared to initial CMT values ($P<0.01$). The mean logMAR visual acuity was 0.831±0.355 before the injection and it was 0.332±0.214; 0.292±0.193; 0.285±0.179 and 0.354±0.224 at the first, the second, the third and the last visits respectively. The decrease of logMAR values at control visits were statistically significant compared to initial logMAR values ($P<0.01$).

Initial treatment within the first 3mo group had a mean of 466.950±105.358μm initial CMT and a mean of 0.75±0.349 initial logMAR whereas this group had a mean of 253.9±25.266μm CMT and a mean of 0.253±0.151logMAR at last visit. Patients who had initial treatment after 3 months group had a mean of 551.417±129.223μm CMT and a mean of 0.966±0.332logMAR at initial visit whereas a mean of 275.416±14.969μm CMT and a mean of 0.522±0.228logMAR was detected at last visit. Mean CMT and mean logMAR were lower in the initial treatment within the 3mo group compared to initial treatment after 3mo group ($P<0.01$).

Ten (31%) patients received single injection, 2 (6.2%) patients received injection two times and 17 (53%) patients received multiple injections. Mean injection per eye was 2.18±0.91 (1~4) respectively. According to the post-injection responses, 10 (31%) of the patients had a positive response with a single injection and no recurrence of ME for a mean of 12.6±0.66mo. Seventeen (53%) of the patients had multiple injections. Recurrence of ME was seen aproximately in 2.45±0.63mo at the first control, 2.58±0.66mo at the second control and 3.17±0.48mo at the third control respectively. In our study, 5 (15.6%) of the patients needed multiple injections for reducing ME whereas visual acuity gain was not achieved even if ME reduced in those patients. Patients who had initial treatment in 3mo had a mean of 1.7±0.95 injection per eye whereas who had initial treatment after 3mo had a mean of 2.83±0.37 injection per eye.



Figures 1 The mean logMAR(A) and CMT (B) values at controls visits are seen.

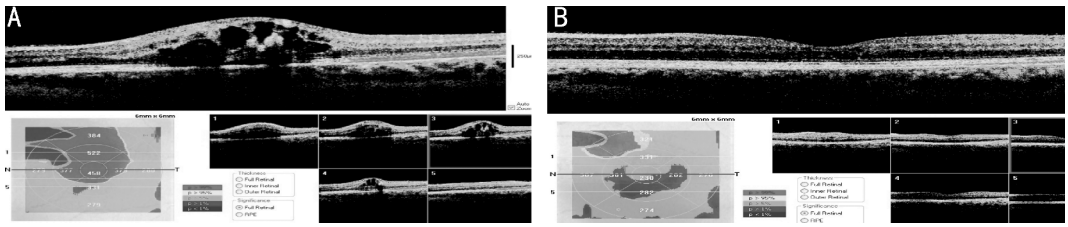


Figure 2 Below the OCT images of the patient 18 are seen before (A) and after (B) the treatment.

Patients who had initial injection in 3mo had a greater mean final visual acuity and a greater mean final CMT compared to patients who had initial injection after 3mo. (in 3mo logMAR 0.253±0.150 and CMT 253±26.27 compared to after 3mo logMAR 0.52±0.22 and CMT 275±14.96) None of the patients had any ocular or systemic side effects related to the intravitreal bevacizumab injection. The results of the first injection results were a guide for the final visual acuity in all the cases. CMT decreased in all patients with a mean of 236.656±109.281μm and logMAR visual acuity decreased in all patients with a mean of 0.477±0.235 at the final visit compared to the initial control (Figure 1). The OCT images of the patient 18 are seen before and after the treatment (Figure 2).

DISCUSSION

Our information about BRVO related ME currently comes from The Branch Vein Occlusion Study Group. According to the relevant study, the comparison of the treated patients with the control patients showedthe gain of at least two lines of visual acuity from baseline maintained for two consecutive visits and visual gain was significantly greater in the treated eyes[2]. So the study recommended us grid laser photocoagulation for ME secondary to BRVO. But laser treatment may complicate paracentral scotomas and it may not be applicable in the early period of the disease.

However, anti-VEGF agents result in a promising gain of visual acuity[13]. Intravitreal agents have replaced observation and grid laser photocoagulation in ME related to BRVO[13]. The ocular risk profile seems to be favorable for anti-VEGF agents in comparison with steroids. Authors indicate that intravitreal bevacizumab treatment is improving VA and CMT values in the long term in patients with BRVO associated ME[14]. They suggest bevacizumab as an evidence based treatment modality in the meta analyses of four trials, comparing it with the comparison groups. So this miraculous drug maintains its popularity.

Bevacizumab is a monoclonal humanized antibody against VEGF which has been licensed for usage in metastatic colon cancer by American Food and Drug Administration since 2006[15]. It is used off-labelly for age related macular degeneration and retinal vein occlusion. Intravitreal anti-VEGF treatment aims the molecular therapeutic level of the disease in BRVO associated ME. The drug has often been used intravitreally for BRVO associated ME off-labelly after Rosenfeld *et al*[16] published their article in 2005.

The outcome of the treatment is depended on initial visual acuity. Rehak *et al*[4] notified that macular oxygen status at the beginning of the disease indicates final visual acuity following the treatment. Irreversible structural changes occur in the macula at the beginning of the disease so important prognostic factor for final visual acuity appears to be the initial VA.

We compared final logMAR and CMT of the patients according to their initial logMAR visual acuities. Group 1 was those whose initial logMAR visual acuity was below 1, group 2 was those whose initial logMAR visual acuity was equal to 1 and above. Both groups had better final logMAR and CMT values compared to initial data internally which was statictically significant ($P<0.01$). The comparison between groups showed that group 1 ($P<0.05$) had a statistically better final logMAR and CMT compared to group 2. Our data confirmed that good initial visual acuity was associated with a better final visual outcome.

It seems that early treatment of BRVO associated ME results are better than the later ones. Thus it is considered as a progressive ischaemic capillaropathy during the first 6mo after the occlusion according to Silva*et al*[17]. Stahl *et al*[18] notified that treatment initiation within the first 3mo gained more visual acuity than the one between 4~6mo or more than 6mo. These findings confirm that treatment is essential within the first 3mo or during the first 6mo of the disease because of ME associated progressive ischemia.

In our study, patients who had initial injection in 3mo seemed

to have a lower injection numbers compared to patients who had initial injection after 3mo. Patients who received initial treatment in 3mo had a mean of 1.7±0.95 injection per eye but those received initial treatment after 3mo had a mean of 2.83±0.37 injection per eye. Our data confirms that early treatment resulted in early convalescence and prevented chronocity of ME, avoiding further injections. Patients who had initial treatment within the first 3mo have a lower mean CMT and mean logMAR compared to the patients who received initial treatment after 3mo.

There are a lot of unknown uncertainties and one of them is injection frequency. Visual prognosis is depended on recurrence of ME in BRVO. Repetetive injections are needed in order to maintain visual and anatomic responses according to Demir *et al*[19]. Rabena *et al*[11] reported an average of two injections per eye and mentioned that 6 patients (22%) developed recurrent ME which was cured with repetitive injections. Jaissle *et al*[20] mentioned that the number of re-injections necessary to maintain this effect declined in time. Hoeh *et al*[21] mentioned that the change of BCVA is correlated with the change of CMT in bevacizumab treatment, however, one third of the patients did not improve in continuous injection, so further injections might be discontinued in those patients. In bevacizumab treatment final CMT is correlated with the CMT after the first injection according to Ach *et al*[22]. Some authors advice that monthly injections to control ME may help limit disease severity in a large percentage of patients. In time, the treatment should be individualized based upon timing and severity of recurrent edema and/or progression of nonperfusion[23]. But we do not know whether a more frequent re-injection rate is beneficial or not. Because some patients are classified as non-responders, these patients do not have a better visual improvement as achieved with a slight CMT decline despite frequent injections[24]. It is mentioned that higher injection rates above a critical level do not result in a further increase in treatment effect. We suggest the patient being re-injected when needed and the benefits are presumed.

In our controls, we notified arecurrent ME aproximately in a mean of 2.45±0.63; 2.58±0.66; 3.17±0.48mo respectively. In our study, 5 (15%) of the patients needed multiple injections for reducing ME where as visual acuity gain was not achieved as ME reduced in those patients. We used a dose of 1.25mg/0.05mL bevacizumab intravitreally but intravitreal bevacizumab injection at doses up to 2.5mg appears to be effective in BRVO associated ME[25]. None of our patients gained better visual acuity than the first injection in the re-injections.

The reinjections may not always be safe. Some cases may response unexpectedly to progressive injection. Matsumoto *et al*[26] described rebound ME which was initially responded to intravitreal bevacizumab but subsequently recurred in excess of that observed before. This injection - related condition may be a result of retinal venous drainage capacity descent which may be secondary to the injection. Accumulated fluid in the retina is removed by drainage of retinal venous system, so clinicians should not think that much more injections bring about better results. Because repeated injections to prevent rebound effect have no clearly defined end point. We do not think that neither frequent injection interval nor repeated re-injection is beneficial in prevention of ME and in improvement of visual acuity. We suppose that the disorder is in the retinal venous drainage system.

We have not seen any rebound ME complication because we observed the retinal venous circulation before the decision of re-injections. Retinal venous circulation and ME must be observed on fluorescein angiography rather than making frequent injections. We do not say anything different from those stated in the previous articles but we argue that there is no any ideal regimen about intravitreal bevacizumab treatment in ME secondary to BRVO. The optimal time point for the initiation of the therapy remains unclear. There is still minimal knowledge concerning predictive factors for visual outcome. We preferred the pro re nata (p.r.n.) treatment which means injection when needed. We performed re-injections depending on the clinical status of ME, the prediction of visual acuity improvement and the patient's approval without being bound to a standard regimen. Monthly observation of BCVA and CMT gave us the chance to observe the clinical course of ME. Restriction of our study is the absence of a control group. Intravitreal bevacizumab treatment for BRVO associated ME is an off-label, safe, fast, effective and commonly performed treatment. Studies with control groups are needed for the approved usage of this product. BRVO is an interesting status that clinicians can not reverse occlusion because the disease occurs in seconds. So the occluded retina becomes swollen with blood and fluid which disturb photoreceptors. The bevacizumab prevents further swelling and edema by strengthening capillary wall. Intravitreal bevacizumab treatment is good enough to do this task quickly and effectively. In order to achieve this lasting effect we have to strengthen this post treatment nonedematous status by lasers or long lasting agents.

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