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Intravitreal bevacizumab versus intravitreal triamcinolone in the prevention of intraoperative bleeding in diabetic vitrectomy; a randomized clinical trial

Behzad Safarpour Lima[1], Shima Sayanjali[1], Morteza Entezari[2], Homayoun Nikkhah[2], Ali Rastegarpour[3], Mehdi Yaseri[4], Alireza Asary Yazdi[5], Hamid Fateh Moghaddam[1], Alireza Ramezani [2*].

[1]Department of Ophthalmology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Ophthalmology, Ophthalmic Epidemiology Research Center, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Radiology, University of California Los Angeles, CA, United States
[4]Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran
[5]Quantitative Health Department, Cleveland Clinic, OH, United States

Abstract

Diabetic retinopathy is a diabetes complication that affects eyes. It's caused by damage to the blood vessels of the light-sensitive tissue at the back of the eye. So, the aim of this study was to compare the effects of intravitreal injection of TA and bevacizumabon intraoperative bleeding in eyes candidate for diabetic vitrectomy. Consecutive patients undergoing primary pars plana vitrectomy for complications of active PDR were recruited for this prospective study. The indications for vitrectomy included non-clearing vitreous hemorrhage, tractional retinal detachment, or active fibrovascular proliferation with or without TRD. Patients undergoing vitrectomy due to diabetic macular edema were not included. Patients were divided into two groups using a randomizing table; the first group received an intravitreal injection of bevacizumab 1.25 mg, and the second group received an intravitreal injection of triamcinolone 2 mg before surgery. After the operations, the attending surgeon completed a study questionnaire. All statistical analyses were performed by SPSS version 21. The P-value less than 0.05 was considered statistically significant. In this study, 141 eyes of 141 diabetic patients with an average age of 54 ± 10 were included. Of them, 74 and 67 were allocated to the IVB and IVT groups, respectively. There was no statistical difference between the groups regarding demographic and preoperative characteristics. We also did not notice any difference in the intraoperative data between the groups except for the uses of PFCL and internal tamponade that were significantly higher in the IVB group. Intraoperative bleeding occurs in 53 (71.6%) and 46 (68.7%) of the eyes in the IVB and IVT groups, respectively. The ATE based on the results of the AIPW model for the two groups in terms of intraoperative bleeding was 1.3% which failed to show a statistically significant difference. Our study demonstrated that preoperative IVT injection could at least be as effective as preoperative IVB injection as far as intraoperative bleeding in diabetic vitrectomy is concerned.

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. **Contact**: Alireza Ramezani,, Department of Ophthalmology, Ophthalmic Epidemiology Research Center, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran arramezani@gmail.com Tel: +98 21 22585952 Fax: +98 21 22562138

INTRODUCTION

Diabetic retinopathy (DR) is the most common cause of blindness in adults (1-5). Retinal angiogenesis has been identified as an important factor in the development of this complication (2, 3). Similar to all ischemic inflammatory responses, DR is associated with an increased immune and inflammatory response (6).

Retinal hypoxia following microvascular occlusion, as well as hyperglycemia are associated with the expression of a number of pathogenic angiogenesis factors including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), and basic fibroblast growth factor (bFGF) (3, 7). Of these factors, VEGF is the strongest angiogenic mediator and can cause the development of new blood vessels in the retina after long lasting hypoxia (2, 3, 5, 7-9). In addition to hypoxia and genetic factors, the expression of VEGF can also be increased by a number of other factors. TGF-β_1 triggers VEGF expression in the human retinal pigment epithelium (RPE). Interleukin 6 (IL_6) also plays a role in vascular permeability and angiogenesis (6).

Vitrectomy for advanced proliferative diabetic retinopathy (PDR) is usually complicated by fibrovascular vessel hemorrhage (10, 11). Intraoperative hemorrhage before adequate traction release is one of the main causes of vitrectomy failure (10). Even with using the appropriate maneuvers, recurrent hemorrhage from multiple sites may result in prolonged operative time and fatigue (10). Thus, many researchers have been working on controlling angiogenesis and preventing intraoperative and postoperative hemorrhage. Ever since VEGF has been found to be a key factor, it has been the focus of numerous studies (11).

Bevacizumab is a humanized recombinant monoclonal antibody which can attach to all isomers of VEGF and inhibit their action (7). IVB helps induce the regression of angiogenesis in PDR and the amount of leakage has been shown to significantly decrease 24 hours after IVB injection (8). It also induces changes in new vessels and immature cells which result in apoptotic vascular endothelial cells in the fibrovascular membrane (FVM). The injection of IVB preoperatively, reduces the need for delamination and segmentation intraoperatively, (12) and decreases the number of intraoperative coagulation spots (13). However, bevacizumab can increase the risk of fibrotic complications (4, 5) and the progression and development of tractional retinal detachment (TRD) has been reported shortly after IVB injection (5).

Triamcinolone acetonide (TA) is a corticosteroid suspension which has been used for quite a while now as a periocular medication for controlling inflammatory ophthalmic diseases. Recently, it has been used for a wider array of diseases including macular edema in diabetic retinopathy (DR), retinal venous occlusion, and age-related macular degeneration (AMD) (7). Intravitreal triamcinolone (IVT) injections also decrease the risk of DR progression (14).

Studies show that TA significantly reduces neovascularization (2, 6, 7, 11) and vascular leakage (15). The concentration of VEGF after IVT injection decreases significantly. (6, 16-18) While TA reduces the effects of VEGF on neovascularization, it also decreases the number of VEGF and IL_6 receptors (6). In addition, TA decreases VEGF mRNA expression (7, 19) and reduces its stability (6). Triamcinolone blocks hypoxia-response pro-inflammatory genes before VEGF production (15).

With regards to the fact that triamcinolone is relatively low-cost and more accessible, and tractional retinal complications are less common with TA than anti-VEGFs, we decided to compare the effects of intravitreal injection of TA and bevacizumabon intraoperative bleeding in eyes candidate for diabetic vitrectomy.

Material and Methods

Consecutive patients from 2012 to 2014 undergoing primary pars plana vitrectomy for complications of active PDR were recruited for this prospective study. The indications for vitrectomy included non-clearing vitreous hemorrhage, tractional retinal detachment, or active fibrovascular proliferation with or without TRD. Patients undergoing vitrectomy due to diabetic macular edema were not included. Patients with the following characteristics were also excluded: (1) patients with a history of systemic thrombotic events (acute myocardial infarctions or cerebrovascular accidents); (2) patients who required hemodialysis, had a known bleeding disorder, or were receiving anticoagulants other than aspirin; (3) patients with an abnormal prothrombin time (PT), activated partial thromboplastin time (PTT), or platelet count; (4) patients with a history of untreated glaucoma; and (5) patients with a history of intraocular surgical procedures except cataract surgery.

Study protocol was approved by Institutional Review Board at Shahid Beheshti University of Medical Sciences. Written consent was obtained from all patients after explaining the study. All patients underwent a basic examination including BCVA (best corrected visual acuity) with a standard refraction method using a Snellen chart and converting it to

LogMAR for statistical analysis, applanation tonometry, biomicroscopy of the anterior segment, and biomicroscopic examination of the fundus with a dilated pupil and indirect ophthalmoscopy.

Patients were divided into two groups using a randomizing table; the first group received an intravitreal injection of bevacizumab 1.25 mg, and the second group received an intravitreal injection of triamcinolone 2 mg before surgery. We planned to inject around one week prior to the surgery; however, this time might have changed according to various patient- or surgeon-dependent situations such as the time needed for preoperative clarification. All patients underwent a standard 3-port 23-gauge pars plana vitrectomy by one of three attending physicians who were retina and vitreous subspecialists. After the operations, the attending surgeon completed a study questionnaire.

Demographic information, intraoperative findings, and surgical techniques were recorded as the following variables: age, sex, preoperative BCVA, the severity of preoperative vitreous hemorrhage, the presence or absence of fresh vitreous hemorrhage on preoperative examination, the time interval from injection to surgery, the duration of surgery, the number of tool exchanges through the sclerotomy into the eye, the vitreoretinal status based on the surgeon's intraoperative observations (vitreous hemorrhage only, localized TRD, and active fibrovascular proliferation with or without TRD), the extent of fibrovascular proliferation based on the modified grading system by Elliott (grade 0, none or focal adhesion ≤ 3 sites; grade 1, broad adhesion ≥ 1 site(s) or vitreous-retinal adhesion at the disc, macula, and arcade; or grade 2, vitreous-retinal attachment extending to the periphery or no posterior vitreous detachment) (20, 21), surgery complexity score developed by Grigorian and colleagues (ranged between 0 to 8 based on the number of quadrants with fibrovascular proliferation, being anterior or posterior to the equator, presence of TRD, and absence of posterior vitreous detachment) (22), the performing of segmentation or delamination, the use of intraocular scissors, the use of perfluorocarbon liquid (PFCL), the use of endodiatermy and number of cauters, the use of endolasers and number of lasers, intraoperative hemorrhage and its severity (defined as either mild or significant, signifying a new blood clot smaller or larger than half the area of posterior pole, respectively), (20) the number of each type of hemorrhage, the incidence and number of intraoperative breaks, and the use of tamponade and its type. The severity of preoperative vitreous hemorrhage was graded from 0 to 3 signifying in the incremental order the absence of hemorrhage, mild hemorrhage, moderate hemorrhage with visible red reflex but fundus details not visible, and severe hemorrhage with both red reflex and fundus details not visible. The occurrence of intraoperative bleeding and its severity, which is categorized as mild and significant, were compared between the two groups as the main outcome measures. Whether endodiathermy was applied for the patient, and its number of applications were considered as the secondary outcome measures.

Normal distribution of quantitative data was evaluated by Kolmogorov-Smirnov test and Q-Q plot. To present data we used mean ± standard deviation, median, range, and frequency. To evaluate the difference between two groups we used Mann-Whitney, student t-test, and Chi-square tests, and presented the results with 95% confidence interval. We used augmented inverse probability weighting (AIPW) to estimate the average treatment effect (ATE) which uses observational data to estimate the effect caused by receiving one treatment instead of another. AIPW estimators use inverse-probability weights to correct for the missing-data problem arising from the fact that each subject is observed in only one of the potential outcomes. Multiple logistic regression test was used to determine the simultaneous effect of variables. All statistical analyses were performed by SPSS (version 21.0, IBM CO., Chicago, IL). The P-value less than 0.05 was considered statistically significant.

Results

In this study, 141 eyes of 141 diabetic patients (83 females and 58 males) with average age of 54 ± 10 were included. Of them, 74 and 67 were allocated to the IVB and IVT groups, respectively. There was no statistical difference between the groups regarding demographic and preoperative characteristics (Table 1). We also did not notice any difference in the intraoperative data between the groups except for the uses of PFCL and internal tamponade that were significantly higher in the IVB group (P=0.041 and P=0.036, respectively).

Intraoperative bleeding occurs in 53 (71.6%) and 46 (68.7%) of the eyes in the IVB and IVT groups, respectively. This difference was not statistically significant (P=0.701). The rates of mild (56.6% vs. 58.7%), significant (22.6% vs. 10.9%), and both kinds of bleedings (20.8% vs. 30.4%) as well as the mean number of bleedings (totally and in each category) for each eye did not differ significantly between the groups either (Table 3). Endodiatermy was applied in 25 (34.2%) and 27 (40.3%) of the eyes in the IVB and IVT groups, respectively (P=0.408). The mean

number of applying endodiatermy for each eye did not also differ significantly (Table 3).

The ATE based on the results of AIPW model for the two groups in terms of intraoperative bleeding was 1.3% which failed to show a statistically significant difference (95% CI: -20.5% to 17.9%, P-value=0.893). However, the 24% difference ATE in terms of endocautherization between the two groups was statistically significant (95% CI: 1.2% to 47.6%, P-value=0.039).

Table 1. Demographic and preoperative characteristics of patients.

			Total	IVB	IVT	P
Age	Mean ± SD		54 ± 10	52 ± 10	55 ± 9	0.063†
	Median (Range)		53 (23-75)	51 (23-75)	55 (32-75)	
Gender	Mean (SD)	Male	58 (41.1%)	30 (40.5%)	28 (41.8%)	0.880*
		Female	83 (58.9%)	44 (59.5%)	39 (58.2%)	
BCVA (logMAR)	Mean ± SD		2.15 ± 0.84	2.15 ± 0.84	2.15 ± 0.85	0.982†
	Median (Range)		1.8 (1-3.3)	1.8 (1-3.3)	2.1 (1-3.3)	
Injection-to-surgery interval (days)	Mean ± SD		8.8 ± 4.2	8.8 ± 4.8	8.8 ± 3.2	0.430‡
	Median (Range)		8 (1-29)	8 (1-29)	8.5 (1-17)	
Preoperative vitreous hemorrhage severity	Mean (SD)	.0	17 (12.1%)	7 (9.5%)	10 (15.2%)	0.381‡
		1.0	53 (37.9%)	30 (40.5%)	23 (34.8%)	
		2.0	43 (30.7%)	19 (25.7%)	24 (36.4%)	
		3.0	27 (19.3%)	18 (24.3%)	9 (13.6%)	
	Mean ± SD		1.6 ± 0.9	1.6 ± 1	1.5 ± 0.9	
	Median (Range)		1.5 (0-3)	1.5 (0-3)	1.5 (0-3)	
Preoperative fresh vitreous hemorrhage	Mean (SD)	No	53 (37.6%)	24 (32.4%)	29 (43.3%)	0.184*
		Yes	88 (62.4%)	50 (67.6%)	38 (56.7%)	
Preoperative Diagnosis	Mean (SD)	VH only	34 (24.8%)	17 (23.6%)	17 (26.2%)	0.925*
		Localized TRD	31 (22.6%)	17 (23.6%)	14 (21.5%)	
		Active FP	72 (52.6%)	38 (52.8%)	34 (52.3%)	
Lens status	Mean (SD)	Phakic	105 (83.3%)	58 (87.9%)	47 (78.3%)	0.151*
		Pseudophakic	21 (16.7%)	8 (12.1%)	13 (21.7%)	

† Based on t-test.
‡ Based on Mann-Whitney test
* Based on Chi-Square test

BCVA: best corrected visual acuity; TRD: tractional retinal detachment; FP: fibrovascular proliferation

Table 2. Intraoperative data in each group.

	Total	IVB	IVT	P

Preoperative VH severity	Mean (SD)	Null	18 (12.8%)	6 (8.1%)	12 (17.9%)	0.129‡
		Mild	66 (46.8%)	35 (47.3%)	31 (46.3%)	
		Dense	57 (40.4%)	33 (44.6%)	24 (35.8%)	
TRD	Mean (SD)	No	38 (27.0%)	18 (24.3%)	20 (29.9%)	0.460*
		Yes	103 (73.0%)	56 (75.7%)	47 (70.1%)	
Location of TRD	Mean (SD)	Extramacular	41 (39.8%)	21 (37.5%)	20 (42.6%)	0.602*
		Macular	62 (60.2%)	35 (62.5%)	27 (57.4%)	
Macular edema	Mean (SD)	No	38 (27.0%)	19 (25.7%)	19 (28.4%)	0.720*
		Yes	103 (73.0%)	55 (74.3%)	48 (71.6%)	
Fibrovascular proliferation extent	Mean (SD)	0	47 (33.6%)	24 (32.9%)	23 (34.3%)	0.737‡
		1	68 (48.6%)	35 (47.9%)	33 (49.3%)	
		2	25 (17.9%)	14 (19.2%)	11 (16.4%)	
Surgery complexity score	Mean ± SD Median (Range)		3.4 ± 2.2 4 (0-8)	3.5 ± 2.2 4 (0-8)	3.2 ± 2.3 4 (0-8)	0.478‡
Performing segmentation Mean (SD)	Mean (SD)	No	31 (22.5%)	16 (22.2%)	15 (22.7%)	0.943*
		Yes	107 (77.5%)	56 (77.8%)	51 (77.3%)	
Use of intraocular scissor Mean (SD)	Mean (SD)	No	41 (29.3%)	19 (26.0%)	22 (32.8%)	0.377*
		Yes	99 (70.7%)	54 (74.0%)	45 (67.2%)	
Use of perfluorocarbon liquid Mean (SD)	Mean (SD)	No	78 (59.1%)	35 (50.7%)	43 (68.3%)	0.041*
		Yes	54 (40.9%)	34 (49.3%)	20 (31.7%)	
Use of internal tamponade	Mean (SD)	No	77 (55.0%)	34 (46.6%)	43 (64.2%)	0.036*
		Yes	63 (45.0%)	39 (53.4%)	24 (35.8%)	
Intraoperative break formation	Mean (SD)	No	99 (70.7%)	47 (63.5%)	52 (78.8%)	0.047*
		Yes	41 (29.3%)	27 (36.5%)	14 (21.2%)	
Number of break(s)	Mean ± SD Median (Range)		1.4 ± 0.7 1 (1-4)	1.4 ± 0.6 1 (1-3)	1.4 ± 0.9 1 (1-4)	0.709‡
Durationof Vitrectomy (min)	Mean ± SD Median (Range)		51 ± 24 45 (4-150)	53 ± 23 53 (20-135)	50 ± 26 45 (4-150)	0.216‡

‡ Based on Mann-Whitney test.* Based on Chi-Square test.
TRD: tractional retinal detachment; VH: vitreous hemorrhage

Table 3. Outcomes based on intraoperative data

				Total	**IVB**	**IVT**	**Diff 95% CI**	**P**
Intraoperative bleeding(s) Mean (SD)		No		42 (29.8%)	21 (28.4%)	21 (31.3%)		
		Yes		99 (70.2%)	53 (71.6%)	46 (68.7%)	3.0% (-12.4%-18.3%)	0.701*
			Mild	57 (57.6%)	30 (56.6%)	27 (58.7%)		
			Significant	17 (17.2%)	12 (22.6%)	5 (10.9%)		
			Both	25 (25.3%)	11 (20.8%)	14 (30.4%)		
Number of mild bleeding(s)	Mean ± SD Median (Range)			1.7 ± 0.8 2 (1-4)	1.9 ± 0.9 2 (1-4)	1.6 ± 0.5 2 (1-3)	0.268 (-0.067-0.604)	0.291‡
Number of significant bleeding(s)	Mean ± SD Median (Range)			0.7 ± 1.1 0 (0-4)	0.8 ± 1.1 0 (0-4)	0.7 ± 1 0 (0-4)	0.119 (-0.309-0.546)	0.720‡
Number of bleeding(s) (per paitents)	Mean ± SD Median (Range)			1.6 ± 1.4 1 (0-7)	1.6 ± 1.4 1 (0-5)	1.7 ± 1.5 2 (0-7)	-0.107 (-0.619-0.405)	0.596‡
Endocauterization	Mean (SD)	No		88 (62.9%)	48 (65.8%)	40 (59.7%)	-6.1% (-22.3%-10.2%)	0.408*
		Yes		52 (37.1%)	25 (34.2%)	27 (40.3%)		
Number of applying cauterization	Mean ± SD Median (Range)			4 ± 2.4 3 (1-10)	4.3 ± 2.4 4 (1-10)	3.7 ± 2.4 3 (1-10)	0.547 (-0.748-1.841)	0.194‡

‡ Based on Mann-Whitney test.
* Based on Chi-Square test.

Table 4. Occurrence of intraoperative bleeding and their severity

		Mean ± SD Median (Range)	P
Intraoperative bleeding	No	8.79 ± 3.51 9 (1-14)	0.114‡
	Yes	7.43 ± 2.90 7 (1-14)	
Intraoperative bleeding severity	Mild	8.14 ± 3.21 9 (1-14)	0.335§
	Significant	6.40 ± 2.17 6.5 (2-10)	
	Both	7.00 ± 2.68 7 (3-11)	

‡ Based on Mann-Whitney test.
§ Based on Kruskall-Wallis test.

DISCUSSION

This clinical trial demonstrated that preoperative injection of IVB or IVT did not differ significantly on the severity of intraoperative bleeding during vitrectomy for advanced diabetic retinopathy.

Research studies have shown that after IVB injection, VEGF level decreases in both vitreous body and aqueous humor (8, 13, 23, 24). Additionally, as angiogenesis decreases, the risk of bleeding decreases both during and after surgery, (4-6, 8, 10, 13, 25-27) hence the facilitation of surgery (10, 12, 13, 28-31).

Corticosteroids are known anti-angiogenics and anti-inflammatory agents. (2) IVT lowers the risk of DR progression. Previous research studies suggest that not only does TA effectively decrease new vessel formation, (6, 7, 18, 23, 31-34) but it also decreases vascular permeability (15) and lowers blood-brain barrier dysfunction. (31) TA causes both VEGF and IL-6 receptors to down-regulate. It also decreases VEGF effect on neovascularization (6).

Physiopathologic evidence suggests antiangiogenic properties for triamcinolone, and the effect of triamcinolone on decreasing postoperative bleeding has also been shown previously. To our knowledge however, the effect of preoperative injection of IVT on intraoperative bleeding has not been investigated. Park et al. compared the effect of IVT versus IVB injection at the end of vitrectomy with a control group in diabetic vitrectomy. In this retrospective study they demonstrated that the rate of early postoperative vitreous hemorrhage was significantly lower in the IVB and IVT group than the controls (35). We observed no significant difference in injection-to-surgery interval between IVT and IVB groups in our study (P=0.430). Jorge et al. have shown that in up to 70% of patients there was small amount of perfusion in active permeating new vessels up to one week after IVB injection (36). Therefore, it is likely that early injection of bevacizumab within one week before surgery would reduce its anti-bleeding effects and compromise its comparability with triamcinolone. On the other hand, Sami et al. have pointed out that IVB injection earlier than 7 days before surgery would cause progressive fibrosis of fibrovascular membrane with its severe adhesion to retina (4). Despite the absence of any significant difference between two groups regarding various demographic, preoperative, and intraoperative factors that could have changed the outcomes, two factors of using PFCL and internal tamponade were significantly higher in the IVB group. On the other hand, the mean time of injection-to-surgery interval was 8.8 ± 4.8 days in the IVB group which was more than the recommended safe time by some authors (4). Therefore, one might conclude that prolongation of this time caused progressive fibrosis of fibrovascular membrane and hence more complicated TRDs that necessitated a higher use of PFCL and internal tamponade. In the multivariate analysis however, the increase in the injection-to-surgery time was not correlated with the frequency of factors reflecting the complexity of the surgery.

In another controlled trial, Modarres et al. concluded that IVB injection before vitrectomy for PDR facilitates the surgery. They used the duration of surgery as the outcome of interest in their study and showed that despite the similarity of the complexity score between the groups, the surgical time was significantly shorter in the IVB group than in the controls (62 ± 57.3 minutes vs. 95.5 ± 36 minutes, respectively) (37). We believe that the duration of surgery would reflect not only the severity of intraoperative bleeding but also the advancement of diabetic proliferations. Therefore, we did not use this

factor as an outcome of interest in our study; however, the groups did not differ in this regard either.

In a comparative case-control study on 41 eyes, Yeh et al. demonstrated that the severity of intraoperative and postoperative bleeding was significantly lower in the eyes with IVB pretreatment compared to the controls. Their findings also indicate that all patients of both groups experienced some forms of intraoperative bleeding. The reported rate of Grade I, II, and III bleeding by Yeh and colleagues in IVB group was 90%, 10%, and 0%, respectively, while the same rate in no-injection group was 23.8%, 71.4%, and 4.8%, respectively (P<0.01) (27). Similarly, in an interventional randomized prospective trial of 22 eyes, Rizzo et al. reported seemingly lower numbers for the instances of any form of bleeding among IVB group compared to the no-injection control (5 vs. 16 in 11 eyes in each group). The 70.2% rate of bleeding in our study among patients of both groups showed a lower bleeding rate than that of Yeh and colleagues.

In the current study, we also used the *need to perform intraocular endodiathermy* as well as the number of endodiathermy applications to compare the effect of drugs on intraoperative bleeding. Two groups did not show any difference in these regards. Hattori et al. used intraoperative endodiathermy as their main outcome and showed that the number of endodiathermy applications during diabetic vitrectomy in IVB group was significantly lower than the no-injection group (13).

While Modarres et al. have used 2.5 mg IVB in their study, more recent findings suggest chorioretinal changes as well as mitochondrial damage may occur with higher IVB doses. By using the number of endodiathermy applications, Hattori et al. demonstrated that when IVB is administered as an ancillary medicine before surgery in PDR patients, even lower-than-standard doses of IVB (lowest examined 0.16 mg) was as effective as the standard dose (1.25 mg) in lowering the intravitreal concentration of VEGF as well as controlling intraoperative bleeding (13, 37). We used the standard dose of 1.25 mg IVB in our study.

We did not use control group in our study because preoperative IVB injection in diabetic vitrectomy has been shown to be superior to no-injection controls in previous studies. Nonetheless, absence of control group could be counted as a limitation. Another limitation was the absence of an objective outcome to measure the rate and severity of bleeding. Although we know of no superior alternative method, the comparison between the two groups was made based on the surgeon's judgment of the amount and severity of the bleeding. In order to evaluate the effect of IVB on intraoperative bleeding in diabetic patients with macular involving TRD, Lucena et al. used erythrocyte counts in vitrectomy cassette (38). Nevertheless, erythrocyte count is not a reliable method as it could be affected by the duration of the surgical operation as well as the amount of fluid used.

Conclusion

In conclusion, our study demonstrated that preoperative IVT injection could at least be as effective as preoperative IVB injection as far as intraoperative bleeding in diabetic vitrectomy is concerned. Therefore, it could be construed that preoperative IVT injection could be a substitute for IVB injection in certain cases especially in patients prone to retinal traction following IVB injection, since retinal traction has not been a reported complication of IVT injection. Nevertheless, further studies with larger sample sizes and controlled groups are recommended to confirm the effect of IVT on lowering the amount and severity of intra- andeven postoperative bleeding.

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