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Original Article

Effect of intravitreal conbercept vs triamcinolone acetonide at the end of surgery on macular structure and function in patients with severe proliferative diabetic retinopathy

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Abstract: *Objective:* This study is to compare the efficacy of vitrectomy combined with intravitreal injection of triamcinolone acetonide (IVTA) versus intravitreal injection of conbercept (IVC) at the end of surgery in patients with severe proliferative diabetic retinopathy (S-PDR). *Methods:* A retrospective study of the medical records of 44 eyes diagnosed as S-PDR between November 2014 and December 2015 was performed. The patients underwent 23G vitrectomy combined with retinal laser photocoagulation and drug intravitreal injection at the end of surgery. They were divided into 2 groups: 22 eyes undergone IVC while 20 eyes undergone IVTA. Best-corrected visual acuity (BCVA), foveal thickness (FT), and macular volume (MV) were compared at baseline and 1, 3, and 6 months after surgery were recorded and compared. *Results:* The values of BCVA, FT and MV at 1, 3, and 6 months were significantly improved from baseline in both groups ($p < 0.05$). The extent of FT and MV reduction during the first month after surgery was greater in IVC groupthan in IVTA group ($p = 0.024$). The values of FT and MV in IVTA group werebetter than that in IVC group at the last follow-up examination. An increase in IOP was noted in 0/22 eyes in IVC group and 3/20 eyes in IVTA group at different follow-up, and the IOP of all three eyes was controlled using topical medication. *Conclusions:* Vitrectomy combined with IVC and IVTA at the end of surgery both were beneficial to S-PDR. The effects of IVC were more obvious in the early period after surgery, however, the effect of IVTA was more stable in the long period follow-up.

Keywords: Diabetic retinopathy, vitrectomy, intravitreal injection, conbercept, triamcinolone acetonide

Introduction

Diabetic retinopathy (DR) is a significant source of visual morbidity among the older adults in the developed world and is one of the three major causes of blindness in the developing countries [1]. Complications of DR include ischemic maculopathy, macular edema, neovascular glaucoma, and sequelae of fibrovascular proliferation [2, 3]. The sequelae of fibrovascular proliferation includes vitreous hemorrhage (VH), severe proliferative diabetic retinopathy (S-PDR), and tractional retinal detachment (TRD).

In china, many patients with S-PDR need surgery therapy, and pars plana vitrectomy (PPV) combined with panretinal photocoagulation (PRP) is traditionally performed for non-clearing VH, significant fibrovascular proliferation, refractive macular edema, and/or TRD, particularly if macula-involving exists. PRP itself is a destructive therapy. Previous studies have shown that 25-43% of eyes with PDR treated with PRP will develop into macular edema (ME) or experience an exacerbation in ME, resulting in visual disturbances [4-6]. Although retinal thickness and macular edema can be reduced obviously and photo sensitive and conductive function of the retina can be improved effectively after vitrectomy [7, 8], persistent and recurrent ME sometimes occurs in eyes after vitrectomy of PDR and DME [9]. For many patients, the vitrectomized chronic and recurrent nature of retinal

Table 1. Preoperative characteristics of baseline in patients

	IVC group	IVTA group	*P* value
No. of eyes	22	20	
Age (year)	58.1 ± 12.5	62.8 ± 6.4	0.094
Male/Femal	12/10	9/11	
Types of diabetes (type 1/type 2)	2/20	1/19	
Duration of diabetes (year)	13.4 ± 6.68	14.8 ± 5.82	0.373
TRD	13 (59.1%)	10 (50%)	0.582
IOP (mmHg)	11.9 ± 3.5	13.7± 2.3	0.14
BCVA logMAR	1.57 ± 1.1	1.66 ± 0.8	0.363
FT (um)	479.9 ± 100.5	463.3 ± 79.6	0.061
MV (mm^3)	16.83 ± 7.5	17.91 ± 9.2	0.477

diseases require continued drug therapy after surgery [10-12].

It is documented that intravitreal injection of triamcinolone acetonide (IVTA) could significantly decrease central retinal thickness, and for patients with continuous DME after vitrorectomy, IVTA is still an effective treatment method [13, 14]. Another study argues that intravitreal bevacizumab injection for persistent DME after vitrectomy could temporarily improve central retinal thickness and visual function [15]. There are some studies about the roles of using anti-VEGF drugs or TA at the end of vitrectomy for preventing postoperative recurrent VH [16, 17].

Recently, conbercept (Chengdu Kanghong Biotech Co., Ltd., Sichuan, China), a kind of anti-VEGF drugs, has been developed and available for clinical application. It is widely used for curing patients with age-related macular degeneration (AMD) and macular edema due to various causes. In China, a large proportion of the DR patients are not aware of their retinal conditions until the development of VH. Conbercept is effective for VH, but some patients give up choice to take it because of economical questions.

IVTA and conbercept are both applied in clinic, however, to our knowledge, there are no reports about macular structure and function evaluation after vitrectomy combined with IVTA and conbercept at the end of surgery. Therefore, in the present study macular structural and the function after conbercept or triamcinolone acetonide injection at the conclusion of surgery in S-PDR were investigated so as to compare the effectiveness and difference of the two drugs, and further support the guidance for clinical application.

Patients and methods

Participants

We retrospectively reviewed the medical records of 44 patients with 44 eyes (15 were male and 29 were female) diagnosed as S-PDR with VH or TRD. These patients had undergone 23G vitrectomy combined with retinal laser photocoagulation and intravitreal injection at the end of surgery between November 2014 and December 2015. We divided the patients into 2 groups: eyes with vitrectomy plus conberceptintravitreal injection (IVC group), and eyes had undergone vitrectomy plus triamcinolone acetonide intravitreal injection (IVTA group). The IVC groupreceived injection of conbercept (0.5 mg in 0.05 ml) at the end of vitrectomy, whereas the IVTA group received injection of triamcinolone acetonide (4 mg in 0.1 ml). Baseline characteristics of study eyes are listed in **Table 1**.

The exclusion criteria is listed as follows: patients that were with prior history of vitreoretinal surgery; patients that were with prior history of intravitreal drugs injections; patients with uncontrolled systemic disease, glaucoma, elevated intraocular pressure; patients that were with evidence of any retinal disease that might affect visual acuity or macular microstructure; patients who had undergone cataract extraction with vitrectomy; and patients who had recurrent vitreous hemorrhage after surgery. Prior written and informed consent were obtained from the patients and the study was approved by the ethics review board of Chengdu Second People's Hospital.

Preoperative examinations

Preoperative ocular examinations included best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, intraocular pressure measurement, funduscopic, ocular B ultrasonic, and Optical coherence tomography (OCT). BCVA was examined using Snellen visual acuity charts. OCT examinations were completed with

Table 2. Comparison of BCVA, FT and MV in the two groups at different follow-up time

	BCVA (logMAR)			FT (um)			MV (mm^3)		
	IVC Group	IVTA Group	*P* value	IVC Group	IVTA Group	*P* value	IVC Group	IVTA Group	*P* value
1 mo	0.64 ± 0.11	0.70 ± 0.18	0.58	238.3 ± 94.6	240.2 ± 98.3	0.124	8.64 ± 2.05	9.23 ± 1.88	0.022*
3 mo	0.78 ± 0.19	0.73 ± 0.33	0.66	287.5 ± 102.4	256.4 ± 90.5	0.095	10.01 ± 2.17	10.30 ± 2.65	0.08
6 mo	0.94 ± 0.30	0.84 ± 0.53	0.74	320.1 ± 86.3	283.4 ± 77.9	0.037*	13.7 ± 4.73	10.64 ± 3.19	0.015*

Note: *Statistically significant difference between the two groups.

dilated pupils using the Zeiss Stratus OCT system (Carl Zeiss Meditec, USA). OCT measurements of the macula were generated from 6-mm linear scans in a spoke-like radial configuration with each line centred in the fovea and angled 30° apart. Automatic delineation of the inner and outer boundaries of the neurosensory retina generated by built-in OCT software was verified for each of the 6 scans using the retinal thickness (single eye) analysis protocol. All OCT evaluations were performed in the afternoon (between 13:00 and 18:00). For this study, FT was defined as the average thickness of the macular area with a diameter of 1000 μm centred on the patient's foveola. The outcomes of FT and MV were obtained from OCT reports. Fuorescein angiograms and fundus photographs before surgery were not obtained clearly because VH had not been cleared.

Therapeutic regimen

In all 44 patients, a 3-port 23-G PPV was performed by a single surgeon. Vitrectomy, retinal laser photocoagulation and IVC or IVTA were sequentially performed. Vitrectomy with removal of the fiber proliferative membrane was conducted in all of the patients. Retinal endolaser photocoagulation was performed intraoperation in cases with apparent high risk characteristics. All patients received fluorescein angiography within four weeks after operation and supplementary of retinal photocoagulation was performed when there was extensive retinal capillary dropout. At the conclusion of the operation, patients in the IVC group received an intravitreal injection of conbercept (10 mg/mL, 0.5 mg in 0.05 ml), and the control group received an intravitreal injection of TA (40 mg/mL, 4 mg in 0.1 ml). Patients of IVTA were instructed to maintain a sitting position for approximately six hours in the immediate postoperative period to facilitate inferior sedimentation of the injected triamcinolone acetonide.

Postoperative examination

All patients were followed up for 6 months with return visits in the first, third and sixth month. Postoperative examination including BCVA, slit-lampbiomicroscopy, intraocular pressure measurement and fundus examinations, was conducted at two days, one week, and one month after vitrectomy. Fluorescein angiography was performed within four weeks after operation and subsequent examinations were generally scheduled every one to three months.

As outcome measures, BCVA, FT and MV were recorded at one, three, and six months after the administration of surgical therapy. BCVA was then transformed to a logarithmic scale for statistical analysis. Additionally, we compared the differences in BCVA, FT and MV after surgery between the two groups at different follow up time.

Main outcome measures

BCVA was analyzed on a logarithm of minimal angle of resolution (logMAR) scale. Counting fingers vision was defined as 0.01 (2.0 logMAR) and hand movement was defined as 0.001 (3.0 logMAR). As for primary outcome measurement, changes in BCVA, FT and MV were compared between patients of the two groups at 1, 3, and 6 months after surgery. And as for secondary outcome measurement, BCVA, FT and MV were compared within each group before surgery and at each follow-up time.

Statistical analysis

Statistical analyses were performed using the software program SPSS19.0 (SPSS Inc, Chicago, IL, USA). Data were expressed as mean ± SD for continuous variables. Mean changes in BCVA from baseline at months 1, 3 and 6 were assessed using the paired t test or rank-sum test with 95% confidence intervals. Changes in BCVA, FT and MV measurements between

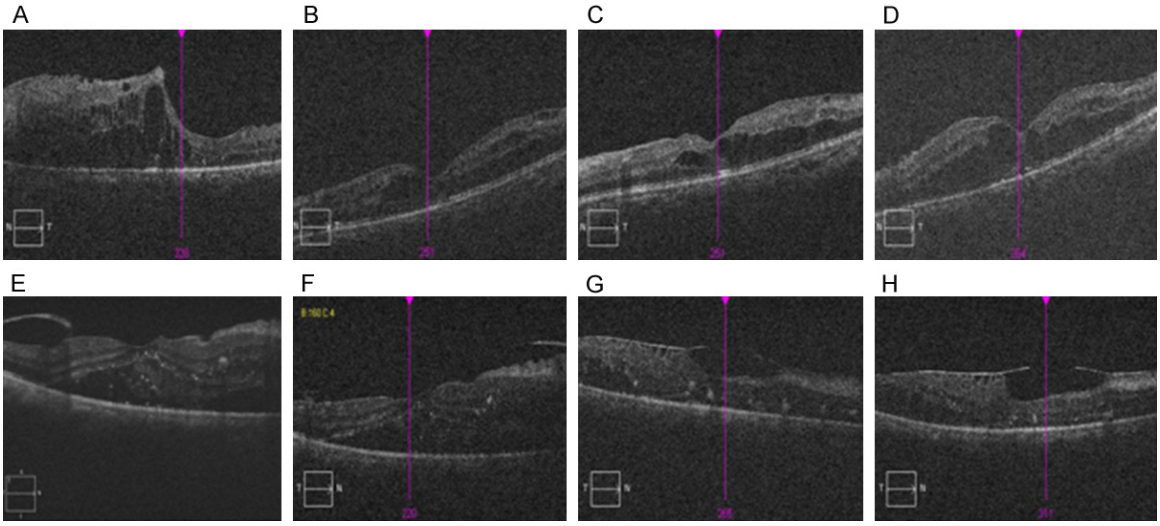

Figure 1. Macular structures of in patients with severe proliferative diabetic retinopathy (S-PDR) preoperation and postoperation with intravitreal injection of acetonide and conbercept at the end of surgery. (A-D, IVC group): (A) OCT preoperation; (B-D) 1, 3, and 6 months postoperation. (E-H, IVTA group): (E) OCT preoperation; (F-H) 1, 3, and 6 months postoperation.

groups were assessed using χ^2 test. BCVA, FT and MV measurements within each group were assessed using Paired Student's t-test. A *p* value of less than 0.05 was considered to be statistically significant.

Results

General situation of the eyes included in the study

In order to make sure that there were no differences in eyes between the two groups before the study, comparison was performed at the beginning of the experiment. During the inclusion period of the study, S-PDR that had undergone vitrectomy, retinal laser photocoagulation and IVC or IVTA were identified in 44 patients. Of these patients, 42 patients with 42 eyes were finally enrolled in the study. Two eyes were excluded because they have recurrent vitreous hemorrhage after vitrectomy. As detailed in **Table 1**, baseline characteristics of the study eyes, such as patients' age, sex, types of diabetes, years of diabetes, IOP, TRD, BCVA, FT and MV were compared. The comparison result argued that there was no difference between the two groups pre-examination.

Primary outcome measurement

To compare the effect of IVC and IVTA at the end of surgery to macular, BCVA, FT, and MV were investigated. The values of BCVA, FT, and and MV in the two groups before and after operation were shown in **Table 2**. The macular OCT images of the two groups before and after the operation were illustrated in **Figure 1**. Comparison of IVC group and IVTA group showed no statistically significant differences in BCVA at any time during the study. FT (μm) measurements showed a statistically significant difference between the two groups at the 6-month follow-up. And the mean ± SD was 479.9 ± 100.5 in IVC group and 463.3 ± 79.6 in IVTA group at baseline (p = 0.061). During the following time, the mean FT of IVC group versus IVTA group were 238.3 ± 94.6 versus 240.2 ± 98.3 at 1 month (p = 0.124), 287.5 ± 102.4 versus 256.8 ± 90.5 at 3 months (p = 0.09), and 320.1 ± 86.3 versus 283.4 ± 77.9 at 6 months (p = 0.037), respectively.

At the 1-month and 6-months follow-up, MV (mm^3) showed a statistically significant difference between the two groups from 1 month to 6 month follow up. IVTA group showed more stable effect at the 6 months follow up. The mean ± SD was 16.83 ± 7.5 in IVC group and 17.91 ± 9.2 in IVTA group at baseline (p = 0.477) and IVC group versus IVTA group were 8.64 ± 2.05 versus 9.23 ± 1.88 at 1 month (p = 0.022), 10.01 ± 2.17 versus 10.30 ± 2.65 at 3 months (p = 0.08), and 13.70 ± 4.73 versus 10.64 ± 3.19 at 6 months (p = 0.015). To sum

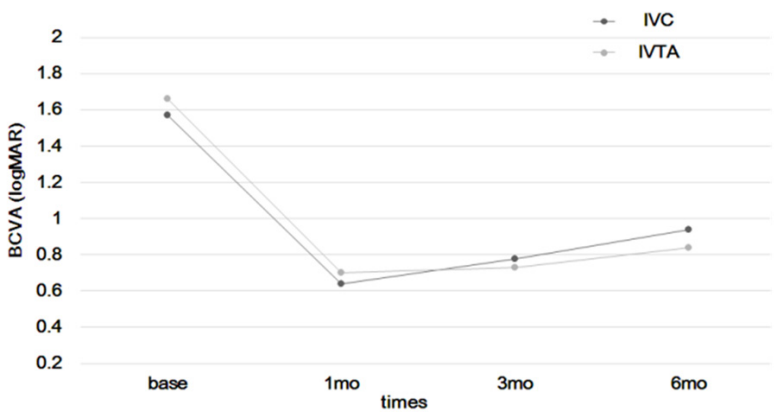

Figure 2. Comparison of BCVA (logMAR) at each follow-up with the baseline in each group. BCVA was significantly improved in both groups from baseline, and there were significant differences between the baseline and every follow-up measurement.

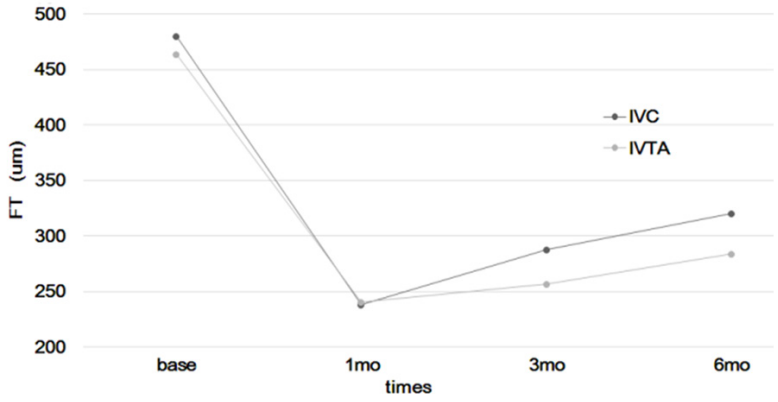

Figure 3. Comparison of FT at each follow-up with the baseline in each group. There were significant differences between baseline values and each follow-up measurement in both groups.

up, the results indicated that the effects of IVC were more obvious in the early period after surgery, however, the effects of IVTA were more stable in the long period follow-up.

Secondary outcome measurement

In order to learn the change of macular function of preoperation and postoperation suffer from vitroectomy versus TA or conbercept, BCVA, the preoperation and postoperation FT and MV were compared. In IVC group, as illustrated in **Figure 2**, BCVA (logMAR) increased significantly from 1.57 ± 1.1 at baseline to 0.64 ± 0.11 at 1 month ($p = 0.001$), 0.78 ± 0.19 at 3 months ($p = 0.013$), and 0.94 ± 0.30 at 6 months ($p = 0.028$). In IVTA group, BCVA increased significantly from 1.66 ± 0.8 at baseline to 0.70 ± 0.18 at 1 month ($p = 0.011$), 0.73 ± 0.33 at 3 months ($p = 0.03$), and 0.84 ± 0.23 at 6 months ($p = 0.041$). The result demonstrated that there were statistically significant differences between the baseline and every follow-up in both groups.

FT reduced significantly in IVC group with a mean ± SD value (um) of 479.9 ± 100.5 at the baseline to 238.3 ± 94.6 at 1 month ($p < 0.001$), 287.5 ± 102.4 at 3 months ($p = 0.017$) and 320.1 ± 86.3 at 6 months ($p = 0.042$). In IVTA group, FT reduced from baseline of 463.3 ± 79.6 to 240.2 ± 98.3 at 1 month ($p < 0.001$), 256.8 ± 90.5 at 3 months ($p = 0.011$) and 283.4 ± 77.9 at 6 months ($p = 0.035$) (**Figure 3**). Together, the results suggested statistically significant differences in both groups when baseline values were compared to the data at each follow-up period.

MV reduced significantly in IVC group from a baseline of 16.83 ± 7.5 to 8.64 ± 2.05 at 1 month ($p = 0.029$), 10.01 ± 2.17 at 3 months ($p = 0.03$), and 13.70 ± 4.73 at 6 months ($p = 0.066$). And in IVTA group, MV reduced from baseline of 17.91 ± 9.2 to 9.23 ± 1.88 at 1 month ($p = 0.032$), 10.30 ± 2.65 at 3 months ($p = 0.040$), and 10.64 ± 3.19 at 6 months ($p = 0.048$) (**Figure 4**). Statistically significant difference was observed when baseline values were compared to measurements at 1- and 3-month follow-up in both groups; however, no significant difference was observed in the IVC group at 6 months follow-up examination.

Three eyes (15%) IOP increased transitorily in the IVTA group after surgery, and all reduced to normal by dropping anti-glaucoma drugs; however, no such situation occurred in the IVC group. Together, the results indicated that IVC

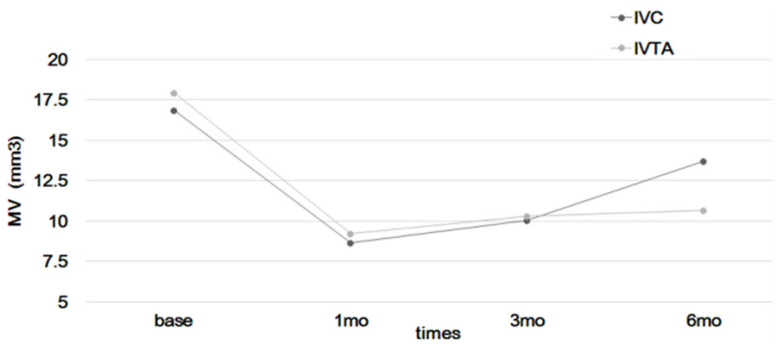

Figure 4. Comparison of MV at each follow-up with the baseline in each group. Statistically significant differences were observed when baseline values were compared with measurements at 1 and 3 months follow-up in both groups, however, no significant difference was observed in the IVC Group at 6 months follow-up examination.

(0.5 mg) and IVTA (0.4 mg) at the end of vitrectomy all had benefits for patients with PDR.The effect of TA is more persistent, and conbercept was more safety.

Discussion

In china, vitrectomy is the most common surgery therapy for PDR patients, especially for patients with VH and TRD. Many researchers have paid close attention to the complication of intraoperative bleeding and postoperative recurrent VH. With the improvement of surgery technology and the increasing application of anti-VEGF drugs, the incidence of intraoperative bleeding and postoperative recurrent VH have reduced significantly [18-20]. A randomized clinical study reported that intravitreal injection of anti-VEGF drug one week prior to vitrectomy was effective in reducing intraoperative bleeding and early postoperative vitreous hemorrhage in PDR patients [18, 21]. However, for many smoothly vitrectomized eyes, macular edema (ME) sometimes persists or recurs in eyes with PDR and DME after vitrectomy.

Conbercept, as a kind of anti-VEGF drugs, is a recombinant and soluble protein composed of VEGF receptorand the Fc portion of immunoglobulin G [22, 23]. Once binding to VEGF, conbercept could competitively inhibit the binding VEGF to VEGF receptors and thereby blocking the activation of VEGF receptors. A Phase I study demonstrated that conbercept can lead to improvements in BCVA, reduction in central retinal thickness, and decrease in the area of choroidal neovascularization (CNV) in patients with neovascular age-related macular degeneration [23]. Recently, conbercept had been used widely in China.

It is well established by clinical studies that treatment of both anti-VEGF drugs and TA could decrease macular thickness for DME, and even for DME after vitrectomy [24, 25]. However, the use of the drugs is either preoperative or postoperative while refractory DME occurs, and there is no joint application of Conbercept or TA at the end of PPV and no analysis of the comparison of the structure and function of the macular. To address this issue, in this study, the effects of IVC and IVTA at the end of vitrectomy were compared, and as for the consolidation of PPV, reduction in FT and MV was observed in both groups. Both the IVC group and the IVTA group caused a significant reduction in FT and MV at different follow-up period while compared to the base line. Two groups both decreased FT appeared at 1 month, and a rising trend at 3 months and 6 months was found. The FT of IVTA group was more stable than IVC group with a small rising trend during our follow up period. In the periodof 6-months follow-up visit, a different increase in FT was noted, and there was significant difference between the two groups studied at the last examination. The FT of IVTA group was lower obviously than the one of IVC group. By comparing the effects of both drugs, triamcinolone showed a greater reduction power. The data were similar to that of Fernando Marcondes Penha [26]. They found that triamcinolone seems to be more effective to reduce CMT up to 6 months when compared with bevacizumab in DME. However, the subjects of previous studies were patients with DME but without PPV, and MV wasn't observed. These observations suggested that both drugs had limited effect on reducing macular edema after surgery, and both had an upward trend in FT and MV in periods longer than 6 months.

Regarding BCVA, both medications resulted in significant visual improvement at different follow up time comparing with the base line. Jirawison C *et al*. [27] have conducted a retro-

spective, comparative, nonrandomized study to investigate patients with diabetic eye disease receiving a 1.25 mg bevacizumab injection at the end of vitrectomy. They found that bevacizumab injection had significant recovery on BCVA at the end of six months. In this study, when the outcomes were compared between the two groups, although BCVA showed no statistically significant differences, the IVTA group seemed to have more prolong and stable BCVA especially at 3 month and 6 month. While for IVC group, a best improvement was noted in 1 month, with a visual decreasing in subsequent visits. Maybe the cataract occurs after vitrectomy is the reason of vision decreasing, however, we didn't record the incidence rate and severity of cataract, and as a result more detailed examinations are needed.

A frequent adverse effect described for the intraocular use of triamcinolone is corticosteroid glaucoma. In our study, three eyes (15%) of IVTA group showed an increased IOP, and fortunately all could be controlled by dropping antiglaucoma drugs and the IOP finally decreased to normal.

Vitrectomy combined with IVC and IVTA at the end of surgery both had a beneficial effect on anatomical and functional outcomes in eyes with S-PDR. Conbercepthad the better effect at the aspect of FT and MV reduction in the short period after vitrectomy than triamcinolone acetonide. The effect of IVTA was more stable in the long period follow-up. Conbercept was safer than triamcinolone acetonideat the aspect of IOP after surgery. The limitation of our current study was that it was a retrospective study only examined a small number of patients. In addition, there was only a fairly short follow-up period for this study. Thus, further randomized control studies with longer follow-up periods will be performed to confirm the consequences of our study.

Disclosure of conflict of interest

None.

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References

[1] Bressler NM, Bressler SB, Congdon NG, Ferris FL 3rd, Friedman DS, Klein R, Lindblad AS, Milton RC, Seddon JM; Age-Related Eye Disease Study Research Group. Potential public health impact of age-related eye disease study results: AREDS report no. 11. Arch Ophthalmol 2003; 121: 1621-4.

[2] Moss SE, Klein R, Klein BE. The 14-year incidence of visual loss in a diabetic population. Ophthalmology 1998; 105: 998-1003.

[3] Fong DS, Ferris FL 3rd, Davis MD, Chew EY. Causes of severe visual loss in the early treatment diabetic retinopathy study: ETDRS report no. 24. Early treatment diabetic retinopathy study research group. Am J Ophthalmol 1999; 127: 137-141.

[4] McDonald HR, Schatz H. Visual loss following panretinal photocoagulation for proliferative diabetic retinopathy. Ophthalmology 1985; 92: 388-393.

[5] McDonald HR, Schatz H. Macular edema following panretinal photocoagulation. Retina 1985; 5: 5-10.

[6] Higgins KE, Meyers SM, Jaffe MJ, Roy MS, de Monasterio FM. Temporary loss of foveal contrast sensitivity associated with panretinal photocoagulation. Arch Ophthalmol 1986; 104: 997-1003.

[7] Chen XL, Zhang YN. Effect of vitrectomy on macular structure and function for proliferative diabetic retinopathy. International Eye Science 2012.

[8] Murakami T, Uji A, Ogino K, Unoki N, Yoshitake S, Dodo Y, Horii T, Nishijima K, Yoshimura N. Macular morphologic findings on optical coherence tomography after microincision vitrectomy for proliferative diabetic retinopathy. Jpn J Ophthalmol 2015, 59: 236-43.

[9] Romano V, Angi M, Scotti F, del Grosso R, Romano D, Semeraro F, Vinciguerra P, Costagliola C, Romano MR. Inflammation and macular oedema after pars plana vitrectomy. Mediators Inflamm 2013; 2013: 971758.

[10] Laidlaw DA. Vitrectomy for diabetic macular oedema. Eye (Lond) 2008; 22: 1337-1341,.

[11] Androudi S, Ahmed M, Fiore T, Brazitikos P, Foster CS. Combined pars plana vitrectomy and phacoemulsification to restore visual acuity in patients with chronic uveitis. J Cataract Refract Surg 2005; 31: 472-8

[12] Arrigg PG, Cavallerano J. The role of vitrectomy for diabetic retinopathy. J Am Optom Assoc 1998; 69: 733-740.

[13] Watanabe A, Tsuzuki A, Arai K, Gekka T, Kohzaki K, Tsuneoka H. Efficacy of intravitreal triamcinolone acetonide for diabetic macular

edema after vitrectomy. J Ocul Pharmacol Ther 2016; 32: 38-43.
[14] Costa JF, Sousa K, Marques JP, Marques M, Cachulo ML, Silva R, Gomes N, Figueira J. Efficacy and safety of postvitrectomy intravitreal triamcinolone therapy for diabetic macular edema. Eur J Ophthalmol 2016; 26: 485-90.
[15] Okamoto Y, Okamoto F, Hiraoka T, Oshika T. Vision-related quality of life and visual function following intravitreal bevacizumab injection for persistent diabetic macular edema after vitrectomy. Jpn J Ophthalmol 2014; 58: 369-374.
[16] Cheema RA, Mushtaq J, Al-Khars W, Al-Askar E, Cheema MA. Role of intravitreal bevacizumab (Avastin) injected at the end of diabetic vitrectomy in preventing postoperative recurrent vitreous hemorrhage. Retina 2010; 30: 1646-1650.
[17] Park DH, Shin JP, Kim SY. Intravitreal injection of bevacizumab and triamcinolone acetonide at the end of vitrectomy for diabetic vitreous hemorrhage: a comparative study. Graefes Arch Clin Exp Ophthalmol 2010; 248: 641-50.
[18] Su L, Ren X, Wei H, Zhao L, Zhang X, Liu J, Su C, Tan L, Li X. Intravitreal conbercept (KH902) for surgical treatment of severe proliferative diabetic retinopathy. Retina 2016; 36: 938-43.
[19] Romano MR, Gibran SK, Marticorena J, Wong D, Heimann H. Can a preoperative bevacizumab injection prevent recurrent postvitrectomy diabetic vitreous haemorrhage? Eye (Lond) 2009; 23: 1698-1701.
[20] Smith JM, Steel DH. Anti-vascular endothelial growth factor for prevention of postoperative vitreous cavity haemorrhage after vitrectomy for proliferative diabetic retinopathy. Cochrane Database Syst Rev 2015; CD008214.
[21] Ahmadieh H, Shoeibi N, Entezari M, Monshizadeh R. Intravitreal bevacizumab for prevention of early postvitrectomy hemorrhage in diabetic patients: a randomized clinical trial. Ophthalmology 2009; 116: 1943-8.
[22] Shinkai A, Ito M, Anazawa H, Yamaguchi S, Shitara K, Shibuya M. Mapping of the sites involved in ligand association and dissociation at the extracellular domain of the kinase insert domain-containing receptor for vascular endothelial growth factor. J Biol Chem 1998; 273: 31283-31288.
[23] Zhang M, Zhang J, Yan M, Luo D, Zhu W, Kaiser PK, Yu DC; KH902 Phase 1 Study Group. A phase 1 study of KH902, a vascular endothelial growth factor receptor decoy, for exudative age-related macular degeneration. Ophthalmology 2011; 118: 672-678.
[24] Watanabe A, Tsuzuki A, Arai K, Gekka T, Kohzaki K, Tsuneoka H. Efficacy of intravitreal triamcinolone acetonide for diabetic macular edema after vitrectomy. J Ocul Pharmacol Ther 2016; 32: 38-43.
[25] Okamoto Y, Okamoto F, Hiraoka T, Oshika T. Vision-related quality of life and visual function following intravitreal bevacizumab injection for persistent diabetic macular edema after vitrectomy. Jpn J Ophthalmol 2014, 58: 369-374.
[26] Penha FM, Maia M, Cardillo JA, Arevalo JF, Wu L, Rodriguez FJ, Berrocal MH, Farah ME; Pan-American Collaborative Retina Study. Comparison of a single intravitreal injection of bevacizumab versus triamcinolone acetonide as primary treatment for diffuse diabetic macular oedema. Acta Ophthalmol 2012; 90: e160-1.
[27] Jirawison C, Ittipunkul N. Intravitreal bevacizumab at the end of diabetic vitrectomy for prevention of postoperative vitreous hemorrhage: a comparative study. J Med Assoc Thai 2012; 95 Suppl 4: S136-42.