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Investigation of the recurrent vitreous hemorrhage risk factors after early 25G vitrectomy in diabetic vitreous hemorrhage

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Abstract

Vitreous hemorrhage (VH) is one of the main causes of vision loss in diabetic retinopathy (DRP). Early surgery increases the visibility of the retina, allowing early recognition of DRP complications and additional treatments. One of the most important reasons affecting success after surgery is recurrent vitreous hemorrhage (RVH). We aimed to investigate the risk factors for RVH after early 25G vitrectomy in diabetic VH. Eighty eyes of eighty patients who underwent early 25G PPV surgery with a diagnosis of VH due to proliferative diabetic retinopathy (PDR) were included in this retrospective study. Vision acuity changes and intraocular pressure (IOP) changes were compared. The effect of arterial hypertension (HT), coronary artery disease (CAD), preoperative antiglaucomatous usage, and anticoagulant usage on RVH was investigated. A value of $P < .05$ was accepted as statistically significant. Postoperative RVH was observed in 18 (22.5%) patients. There was no correlation between the age of the patients and the development of postoperative RVH ($r = -0.197$, $P = .08$). The rate of HT and the mean HbA1C levels were found to be higher in the patients who developed RVH than in those who did not ($P = .04$ and < 0.001, respectively). The presence of CAD, preoperative glaucoma disease, and the use of anticoagulants did not have any effect on RVH ($P = .229$, 0.843, 0.932, respectively). HT and increased HbA1c were found to be risk factors for RVH in VH patients who underwent 25G vitrectomy in the early period in our study.

Abbreviations: ALP = argon laser photocoagulation, CAD = coronary artery disease, DRP = diabetic retinopathy, HT = hypertension, IOP = intraocular pressure, PDR = proliferative diabetic retinopathy, RVH = recurrent vitreous hemorrhage, VH = vitreous hemorrhage.

Keywords: pars plana vitrectomy, risk factors, vitreous hemorrhage

1. Introduction

VH is one of the main causes of vision loss in DRP. The conservative approach to treatment aims to increase the absorption of the hemorrhage by giving the patient an upright position and restricting his or her movement.[1] Argon laser photocoagulation (ALP) is another treatment option in diabetic VH. However, if the retina cannot be seen clearly due to hemorrhage, adequate ALP cannot be performed, and the effect of ALP treatment is limited. Intravitreal anti-VEGF (vascular endothelial growth factor) therapy is another treatment option.[2,3]

The aim of early surgery is to plan the treatment of the patient as quickly as possible before vision-threatening complications such as hemosiderosis bulbi, pigmentary-ghost cell glaucoma, and proliferative retinopathy develop in VH. In one study, it is found that spontaneous resolution was not possible in the vast majority of patients with VH results below 5/200, even after waiting for a year.[4] In another study, it was reported that better visual results were obtained with early vitrectomy in advanced proliferative DRP, especially in type 1 DM.[5] As long as additional vision-threatening complications such as macular edema and tractional retinal detachment do not develop, dramatic improvement is observed in these patients with pars plana vitrectomy (PPV) surgical treatment with the current technology. Early surgery increases the visibility of the retina, allowing early recognition of DRP complications and additional treatments. It has also been reported by the Diabetic Retinopathy Vitrectomy Study Group that early vitrectomy is beneficial in VH due to PDR.[6]

One of the most important reasons affecting success after surgery is RVH. The frequency of recurrent hemorrhage after VH surgery has been reported to be between 13% and 38% in the literature.[6,7] Postoperative hypotonia, fibrovascular proliferation, lower extremity amputation, and antihypertensive

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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use are important causes of RVH after VH surgery.[8,9] In our study, we aimed to investigate the rate and causes of RVH in patients who underwent 25G PPV in the early period due to VH and compare the results with those of studies in the literature.

2. Methods

In this retrospective study, 80 eyes of eighty patients who underwent early 25G PPV surgery with a diagnosis of VH related to PDR, with <6 months duration, reducing the visual aquity to <5/200 at 2 measurements 1 month apart between 2016 and 2021 were included in the study, consecutively. The severity of VH was graded according to Diabetic Retinopathy Vitrectomy Study (Table 1).[10] Early vitrectomy and panretinal photocoagulation performed in patients whose visual aquity was <5/200 at 2 measurements 1 month apart. RVH was defined as VH that recurred within the first 6 months after vitreous cleaning with initial PPV surgery.[11] All eyes with RVH were followed-up for 2 months and, the eyes with VH that did not regress underwent PPV surgery and laser photocoagulation if needed. After the first vitreous cleaning, rehemorrhage from the 1st postoperative day to the end of the 1st month was defined as early rehemorrhage, and between the 1st and 6th month late rehemorrhage.[12] Information about the medical history of the patients was obtained from the patients' medical records. Patients with VH other than DRP, tractional retinal detachment, trauma, high myopia, senile macular degeneration, and uveitis were excluded from the study. All surgeries were performed by a single surgeon at Pamukkale University Training and Research Hospital (M.A.A.). Retrobulbar or general anesthesia was used for anesthesia depending on the patient condition. All phakic patients(28 patients) underwent cataract surgery with phacoemulsification and intraocular lens implantation before starting vitrectomy. An infusion cannula with a 25G trocar and other 2 ports were placed, and the VH was cleaned with a 25G ocutoma and an endoilluminator. The vitreous base was cleared with the shaving mode. Tractional bands, if any, were released and excised with a vitrectomy probe. The surgeon peeled the epiretinal membrane at his discretion. At the end of the operation, an intravitreal injection of 2 mg (0.05 mL) aflibercept was administered. A retinal ALP laser was applied to the patients who needed ALP treatment. ALP was performed with 500 microns spot size, 0.1 second exposure, in mild white intensity hue, by protecting the vascular structures from 1 disc diameters away from the peripapillary area and 2 disc diameters away from the vascular arcades to the ora serrata in 4 quadrants. Dexamethasone and moxifloxacin eye drops 6 × 1 were started in the postoperative period. The medication was discontinued under the control of the patient. The visual acuity and IOP changes preoperatively, 1 day postoperatively, 1 month postoperatively and 6 months postoperatively were compared. Presence and the number of NVE and, the ratio of ischemic retina without retina to total retina were investigated. The relationship between phacoemulsification with vitrectomy, DM duration, preoperative VH level and RVH was investigated. The effect of HT, CAD, preoperative glaucoma disease, and anticoagulant use on RVH was investigated. This study was conducted in accordance with the Helsinki Declaration and was approved by the Institutional Review Board of Pamukkale University, School of Medicine.

Table 1

VH grading.

	Description
Grade 0	No vitreous hemorrhage
Grade 1	Mild VH with visible fundus details
Grade 2	Moderate VH with no visible fundus details. There is an orange funus reflex
Grade 3	Severe VH without fundus details and orange reflex

VH = vitreous hemorrhage.

2.1. Statistical analysis

All statistical analyses were performed using SPSS 21 software (IBM Corporation, Armonk, NY, USA). The Pearson correlation was used for the relationship between age and RVH ratio. Spearman correlation was used for the relationship between the time from surgery to the development of RVH and HbA1c levels. Repeated measures ANOVA was used to compare the changes in IOP and visual acuity. Pearson chi-square test was used to investigate the effect of the presence of HT, CAD, preoperative antiglaucomatous use and the use of anticoagulants on RVH. The Mann–Whitney *U* test was used to compare the groups for HbA1C levels, ALP spot counts and total ALP power, the number of NVE and, the ratio of ischemic retina without retina to total retina. A value of $P < .05$ was accepted as statistically significant.

3. Results

The mean age of the patients was 61.88 ± 10.79 years. Thirty-seven (46.3%) patients were male, and forty-three (53.7%) patients were female. The mean follow-up period of the patients was 15.15 ± 10.28 months. Postoperative RVH was observed in 18 (22.5%) patients. RVH developed in 9 (11.3) patients within the first month and in 9 (11.3) patients after the first month. Thirty-six patients had grade 2, forty-four grade 3. There was no statistically significant difference between VH severity and RVH($P = .86$). There was no significant correlation between the age of the patients and the development of postoperative RVH (r = -0.197, $P = .08$). There was a significant difference between the patients' mean postoperative 1st-day visual acuity and their preoperative visual acuity ($P < .001$). There was no significant difference between the postoperative 1 month and postoperative 1st day visual acuity ($P = 776$). There was a significant difference between the postoperative 6th month and 1st-month visual acuity ($P = .045$) (Table 2). There was no statistically significant IOP change between all preoperative and postoperative visits. ($P = .204$). In 28 phakic patients, vitrectomy combined with cataract surgery. No statistically significant difference was observed between combined surgery and RVH ($P = .34$) (Table 3). There was no significant relationship between diabetes mellitus duration and RVH ($P = .98$). The rate of HT and the mean HbA1C levels were found to be higher in the patients who developed RVH than in those who did not ($P = .04$ and < 0.001, respectively). NVE was found in 9 (50%) of 18 patients in RVH

Table 2

Changes in vision and IOP.

	Preoperative	Postoperative 1st day	Postoperative 1st mo	Postoperative 6th mo	*P* value
Vision (log-MAR)	2.37	0.97	0.94	0.83	<.001
IOP (mm-hg)	14.31 ± 3.02	14.31 ± 3.64	14.27 ± 3.01	14.97 ± 1.99	.204

IOP = intraocular pressure.

group and 27 (44%) of the other group. Mean NVE counts were 2.1 ± 1.2 in the RVH group and 1.8 ± 1.2 in the other group. There was no statistically significant difference between the 2 groups (P = .363). The ratio of ischemic retina without laser to total retina was 56 ± 20.7% in the RVH group and, 51.8 ± 20.7% in the other group. The presence of CAD, preoperative glaucoma disease, and the use of anticoagulants did not have any effect on RVH (P = .229, 0.843, 0.932, respectively) (Table 3). The mean number of laser spots and the mean total laser power were higher in the patients who developed RVH (P = .02 and 0.02, respectively) (Table 4).

4. Discussion

The most common postoperative complication in patients undergoing PPV due to PDR is bleeding. It may affect vision in the postoperative period and cause the need for resurgery.[13] Therefore, postoperative vitreous bleeding is an important problem for VH patients undergoing PPV.[14] It can develop immediately in the postoperative period, or it can develop weeks later. Studies have been carried out to determine the cause of bleeding. In their study, Soto-Pedre et al commented that persistent VH had 2 peaks, of which the first peak was due to possible lysis of red blood cells remaining at the vitreous base or active neovascularization at the end of the first week.[8] The second peak developed between the 2nd and 3rd months due to the fibrovascular tissue that developed on the side of the sclerotomy. In their study, Bhende et al reported that fibrovascular tissue developed between 6 and 8 weeks after vitrectomy in the areas where the port entrances were made.[15] In a study by Krieger, it is reported that as the incision width increases, the amount of fibrovascular tissue developing in the port region increases.[16] Since our study used small-width 25G ports in patients who underwent vitrectomy, we did not think that a port origin was present in patients who developed late hemorrhage in the study group. In our study, we found the rate of RVH to be 22.5% in VH patients who underwent early vitrectomy. We found the early RVH rate to be 11.3% and the late RVH rate to be 11.3%. Lee et al found an early RVH rate of 45.1% and a late RVH rate of 11.9%.[11] Sato et al found the incidence of early and late PVH to be 18.9% and 17.9%, respectively.[12] Mahalingam et al found the postoperative RVH rate to be 21.6% in patients who underwent sutureless PPV for diabetic VH. Of these, 9.5% were detected as immediate RVH and 12.1% as late RVH.[9] The recurrence rate in our study is consistent with the literature. According to our results, early vitrectomy in VH does not constitute an extra risk factor for recurrent hemorrhage.

There was a significant increase in the visual acuity of the patients after vitrectomy. This increase was at maximum at 6 months. Patients are rehabilitated faster with vitrectomy treatment. This result may increase the patients' compliance with treatment. In addition, with the increased visibility of the retina, ALP treatment can be made more effective and reliable.

Ostri et al reported that elevated systolic and diastolic blood pressure and poor glycemic control aggravate DRP and increase the need for vitrectomy.[17] Mahalingan et al found poor glycemic control and uncontrolled HT as risk factors for RVH in patients with late hemorrhage.[9] In our study, we did not find any statistically significant relationship between DM duration and VH severity and RVH but arterial HT and increased HbA1C levels were found to be risk factors for RVH. In addition, in our study, we found that with more severe impaired blood sugar regulation, the earlier the development of RVH. Arterial HT may increase the amount of recurrent hemorrhage by increasing the underlying diabetes-related vascular endothelial damage. Poor glycemic control may increase the risk of RVH by increasing vascular damage on the one hand and increasing ischemia-related neovascularization on the other hand. In the postoperative period, it is necessary to strictly monitor arterial blood pressure, control blood sugar levels in patients to prevent RVH.

Mean NVE counts and the ratio of ischemic retina without laser to total retina were higher in the RVH group but the difference was not statistically significant. The mean count of laser spots and total laser power were found to be higher in the patients who developed RVH. This result may be related to the amount of neovascularization in the preoperative period. The presence of uncontrolled HT, which causes vascular damage independent of diabetes, may also be the cause of RVH despite adequate ALP treatment. In addition, ALP treatment reduces the risk of VH by preventing neovascularization. While the vascular component of abnormal fibrovascular structures regresses rapidly with ALP treatment, the fibrous component may not regress as quickly. Traction of the vascular structure of the retina by this fibrous component may be the cause of early RVH.

Postoperative hypotonia was found to be the most important cause of early RVH, and dense fibrovascular tissue for which tamponade was needed in late recurrent hemorrhages was found to be the most important reason. Lee et al reported that postoperative hypotonia increased the risk of postoperative RVH by 11.2 times in their study.[16] We prevented postoperative hypotonia by suturing the ports with 8.0 Vicryl sutures in patients with leakage from the incision after the scleral ports were removed. IOP changes were not observed in the controls of the patients. This result indicates that postoperative hypotonia did not develop. We thought that

Table 3

Risk Factors for RVH.

		Presence of RVH		*P* values
		Non-exist	Exist	
Fakoemulsification and Vitrectomy		20 (%71.4)	8 (%28.6)	P = .34
Vitrectomy		42 (%80.8)	10 (%19.2)	
DM Duration (yr ± SD)		14.6 ± 5.0	16.7 ± 5.2	P = .98
Anticoagulant use	Not-using	42 (67.7%)	12 (66.7%)	P = .93
	Using	20 (32.3%)	6 (33.3%)	
Mean HbA1C levels		7.5 ± 1.4	9.6 ± 1.8	P = .001
Presence of HT	Non-exist	4 (22.2%)	30 (48.4%)	P = .04
	Exist	14 (77.8%)	32 (51.6%)	
Presence of CAD	Non-exist	35 (56.5%)	13 (72.2%)	P = .22
	Exist	27 (43.5%)	5 (27.8%)	
Antiglaucomatous use	Not-using	52 (85.2%)	15 (83.3%)	P = .84
	Using	9 (14.8%)	3 (16.7%)	

CAD = coronary artery disease, DM = diabetes mellitus, HT = hypertension, RVH = recurrent vitreous hemorrhage.

Table 4

The relationship of ALP with the development of RVH.

	Presence of RVH		
	Non-exist N = 62(%77.5)	Exist N = 18(%22.5)	*P*
Mean total laser count	1669 ± 893	2119 ± 646	.02
Mean total laser power (mW)	462 ± 255	593 ± 180	.02

ALP = argon laser photocoagulation, RVH = recurrent vitreous hemorrhage.

the lower rate of early RVH in our patients, as compared to other studies, may be related to our control of hypotonia. We think that RVH originates from the vitreous base in patients who develop early hemorrhage. In addition, in a study, Sato et al found that bleeding from the optic disc was the cause of early hemorrhage, and a high HbA1c level was the cause of late hemorrhage.[12] We did not observe any bleeding from the disc in any of the patients. This may be because we take care not to apply traction to the vessels while removing the vitreous around the optic disc.

In previous studies, no significant correlation was found between the use of anticoagulants or antiplatelets and postoperative RVH hemorrhage.[11,18,19] In contrast, Fabinyi et al reported that preoperative use of anticoagulants or antiplatelets increases the risk of RVH and the need for additional surgery.[20] In our study, no significant relationship was found between the use of anticoagulants and recurrent hemorrhage. The relationship between the use of anticoagulants and recurrent hemorrhage after PPV has not been fully determined. Preoperative discontinuation of anticoagulant agents may cause additional systemic problems by increasing the tendency to thrombosis in patients. However, the coagulation parameters should be checked in the preoperative period, and if there is a change in the blood values that may cause bleeding intraoperatively, It is necessary to decide together with the physician following the anticoagulant treatment.

Khuthaila et al found that the rate of postoperative RVH was higher in younger patients. No statistically significant correlation was found between age and the development of RVH, in our study.[18]

4.1. Conclusion

The rate of RVH was found to be low in VH patients who underwent early vitrectomy. Providing rapid visual rehabilitation of patients may also increase patient compliance. Arterial HT and poor glycemic control were found to be risk factors for RVH in VH patients who underwent 25G vitrectomy in the early period in our study. In addition, RVH was observed earlier in patients with poor glycemic control. Our results suggest that patients should be followed closely during the postoperative period, especially with monitoring of the blood sugar and hemodynamic parameters.

4.2. Limitations

If the number of our patients was slightly higher, perhaps different parameters affecting the result could have been found. A larger patient group could not be used for this study because the patients had their postoperative follow-up in different centers and did not comply sufficiently with the follow-up. We could not evaluate the duration of the surgeries.

Author contributions

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