Immediate versus Delayed Vitrectomy for the Management of Vitreous Hemorrhage due to Proliferative Diabetic Retinopathy

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ABSTRACT

Background: Vitreous hemorrhage secondary to proliferative diabetic retinopathy is a cause of severe vision loss in diabetic patients. Pars plana vitrectomy with endolaser panretinal photocoagulation remains the procedure of choice for non-clearing vitreous hemorrhage. With improvements in surgical techniques leading to better outcomes, fewer complications, less discomfort and a faster recovery time it is reasonable to operate on such patients, if there has been no significant spontaneous improvement.
Purpose: To compare the characteristics between groups of patient who underwent immediate and delayed vitrectomy for the management of vitreous hemorrhage (VH) due to proliferative diabetic retinopathy (PDR).
Methods: Retrospective review of 35 patients who underwent vitrectomy for VH secondary to PDR. Patients were excluded if they had prior vitrectomy, follow up < 1 month post-operatively, other retinal pathology, VH secondary to other causes, uveitis, or advanced glaucoma. Primary outcome was visual acuity in patients receiving immediate (< 30 days) versus delayed (> 30 days) vitrectomy. Secondary analyses included post-surgical complications.
Results: 35 eyes were included, 13 had immediate vitrectomy while 22 had delayed. There was no difference between the groups in terms of age, gender, diabetes control, or diabetes duration. Patients in the delayed group with severe vision loss also had significantly increased time with vision loss. Pre-op and final visual acuities were equivalent, including 7 days, 30-days or 3-months, in immediate versus delayed vitrectomy, respectively. Complications within 3 months were dominantly in the delayed vitrectomy Group compared to the immediate vitrectomy Group.
Conclusions: Immediate vitrectomy for VH due to PDR significantly decreases time spent with vision loss, and decreases post-surgical complications number. Modern vitrectomy surgery is safe and may be considered earlier in VH management.
Key word: Diabetic Retinopathy, Vitreous Hemorrhage, Pars Plana Vitrectomy

INTRODUCTION

Vitrectomy for vitreous hemorrhage (VH) in diabetes, although commonly performed, was last rigorously studied decades ago by the Diabetic Retinopathy Vitrectomy Study (DRVS) Research Group. Clearly, many changes have swept through the surgical retina field since that time, including intraoperative endolaser photocoagulation; minimally invasive vitrectomy techniques; improved surgical illumination; modern, higher-cut rate vitrectomy machines; and improvements in intraoperative ophthalmic imaging.[1]

Diabetic patient's ocular complications have become increasingly more frequent in the United States, as there has been a documented 133% increase in the incidence of diabetes mellitus from 1980 to 2011, with an overall cost of $245 billion to Medicare in 2012. Since 77.8% and 15.5% of patients with diabetes for more than 15 years will develop non-proliferative and proliferative diabetic retinopathy (PDR), respectively, it is imperative that standard treatment protocols are reviewed and revisited periodically.

Vitrectomy surgery for common complications of PDR, specifically, vitreous hemorrhage (VH) and traction retinal detachment (TRD), is safe and effective, as demonstrated by several retrospective reviews since the DRVS. Still, the most appropriate timing of

vitrectomy for the treatment of diabetic complications is yet to be defined. This is unnecessary that patients spend months with low vision awaiting a procedure that is known to safely and effectively improve their vision. Moreover, the frequent clinic visits and additional in-office procedures, such as completion of panretinal photocoagulation (PRP), can not improve outcomes beyond that of vitrectomy alone.

This retrospective case series compared two groups of patients with immediate and delayed vitrectomy for VH associated with PDR during the modern era of minimally invasive vitrectomy surgery. We hypothesized that patients undergoing immediate vitrectomy with endolaser (≤ 30 days after initial presentation) would spend less time with impaired vision than those undergoing delayed (> 30 days) vitrectomy with endolaser.[2,3,5-8]

MATERIAL AND METHOD

We retrospectively reviewed the medical records of patients affected by VH due to PDR who were subjected to PPV between February 2017-February 2018 at Vitreoretinal Unit Cicendo National Eye Hospital, Bandung, Indonesia. The diagnosis codes including PDR, VH, and vitrectomy. Patients were included if they underwent vitrectomy for non-clearing VH secondary to PDR.

Exclusion criteria included prior vitrectomy, retinal detachment (tractional, rhegmatogenous, or exudative), or other significant ophthalmic disease (including advanced glaucoma, age-related macular degeneration, vasculitis, uveitis or other inflammatory disorders, or significant corneal disease). Patients were also excluded if there was less than 30 days of documented follow-up.

The following preoperative variables were identified, patient age, gender, presenting and follow-up visual acuities, lens status, intraocular pressure (IOP), medical comorbidities, duration of diabetes, hemoglobin A1c (HbA1C) that was closest to date of surgery, and complication were recorded.

The intraoperative information recorded included PPV surgical time, spot amount of endolaser, and postoperative tamponade. We evaluate the time from the initial visit until the vitrectomy surgery was performed.

All patient were operated by five experienced posterior segment surgeons and postoperative follow-ups were made at the Vitreoretinal Unit Cicendo Eye Hospital, Bandung, Indonesia. Data in this study was documented and analyzed using Microsoft Excel 2016.

RESULT

After the application of inclusion and exclusion criteria, 35 patients were identified. A total 35 eyes of 35 subjects participated in the study. Table 1 shows the comparison of the characteristics of two groups that underwent immediate and delayed vitrectomy for non-clearing VH secondary to PDR. Other characteristics, including age, gender, diabetes duration, and diabetes control were similar between the groups.

The mean age was 54.03 ± 8.16 years, 15 (42.85%) patients were female and 20 (57.14%) patients were male. 13 eyes constitued immediate vitrectomy Group and 22 eyes constitued delayed vitrectomy Group. The mean preoperative IOP (intraocular pressure) was 15 ± 3 for Group 1 and 13.8 ± 4.7 for Group 2. The preoperative lens status showed statistically significant between phakic and pseudophakic, with 32 eyes (91.42%) are phakic.

TABLE 1			
Demographics and Patient Characteristics			
Characteristics		Immediate (13 patients)	Delayed (22 patients)
Mean age		53.84 ± 9.09	54.13 ± 7.77
Gender, n (%)			
	Male	6 (46.15)	14 (63.63)
	Female	7 (53.84)	8 (36.36)
Entrance VA, n (%)			
	< 1/60	7 (53.84)	13 (59.09)
	1/60 - 5/60	4 (30.76)	9 (40.90)
	> 0.08	2 (15.38)	0 (0)
Mean preop IOP, mmHg		15 ± 3	13.8 ± 4.7
Eye, n (%)			
	right eye	9 (69.23)	14 (63.63)
	left eye	4 (30.77)	8 (36.37)
Lens status, n (%)			
	Phakic	12 (92.30)	20 (90.90)
	Pseudophakic	1 (7.70)	2 (9.09)
DM years			
	<5 years	6	5
	>5 years	5	8
	Unknown	2	9
Co-Morbidity			
	Hypertension	8	17
	Kidney Disease	5	5
HbA1C, n (%)			
	<6.4%	2 (7.69)	6 (27.27)
	>6.4%	11 (84.61)	16 (72.72)

For duration of diabetes, we found that there were patients with newly diagnosis of diabetes or duration of diabetes less than 5 years in the two groups, and the amount was quite significant. The most common co-morbodity in both groups was hypertension with 25 patients (71.42%), followed by kidney failure with 10 patients (28.58%). The both groups were having the HbA1C more than 6.4% significantly.

Follow-up period was up to 3 months after vitrectomy. Table 2 shows the visual acuity at the initial visit, 1 week, 1 month, and 3 months after surgery. There were a significant differences in final visual acuity between the two Groups, when in the immediate vitrectomy Group shows good progression for the visual acuity between initial visit and 3 months postoperative.

TABLE 2			
Visual Acuity at the Initial Visit, 1 Week, 1 Month, and 3 Months Follow Up			
		Immediate (13 patients)	Delayed (22 patients)
Entrance VA, n (%)			
	< 1/60	7 (53.84)	13 (59.09)
	1/60 - 5/60	4 (30.76)	9 (40.90)
	> 0.08	2 (15.38)	0 (0)
1 week follow up, n (%)			
	< 1/60	6 (46.15)	13 (59.09)
	1/60 - 5/60	5 (38.46)	6 (27.27)
	> 0.08	2 (15.38)	3 (13.63)
1 month follow up, n (%)			
	< 1/60	3 (23.07)	7 (31.81)
	1/60 - 5/60	4 (30.76)	7 (31.81)
	> 0.08	5 (38.46)	8 (36.36)
3 months follow up, n (%)			
	< 1/60	1 (7.69)	5 (22.72)
	1/60 - 5/60	5 (38.46)	7 (31.81)
	> 0.08	7 (53.84)	10 (45.45)

We also recorded the intraoperative information, included the surgical time, endolaser spot, and postoperative tamponade, that shows in Table 3. The most frequent tamponade that have been used in immediate vitrectomy Group is fluid and sterile air with more than 40%, while the most popular tamponade in delayed vitrectomy Group is gas (40%).

TABLE 3

Intraoperative Information

Tamponade, n (%)			
	Fluid	6 (46.15)	7 (31.81)
	Sterile air	6 (46.15)	5 (22.72)
	Gas	1 (7.69)	9 (40.90)
	Silicone Oil	0 (0)	1 (4.54)
Mean surgical time, minutes		30.61 ± 11.19	28.63 ± 9.26
Endolaser spot		637.92 ± 268.53	564.54 ± 259.38

In Table 4, we summerize the complication that occurs postoperatively. Six patients experienced rebleeding in the delayed vitrectomy Group, whereas no patient had a complicated cataract in that Group. In other group, we found that there were 1 patient experienced rebleeding, and 1 patient experienced complicated cataract.

TABLE 4

Postoperative Complication

	Immediate (13 patients)	Delayed (22 patients)
Complicated Cataract, n (%)	1 (7.69)	0 (0)
Rebleeding, n (%)	1 (7.69)	6 (27.27)

DISCUSSION

VH has an incidence of about seven cases per 100.000 eyes which makes it one of the most common causes of acutely or subacutely decreased vision, with 32% secondary to PDR. About a third of these patients will undergo vitrectomy for non-clearing VH. Still, there is no defined timing of intervention in todays age of endolaser and minimally invasive vitrectomy techniques. We suggests that minimally invasive vitrectomy surgery with endolaser photocoagulation within 30 days of presentation yields visual results comparable to those of vitrectomy surgery that is delayed for additional PRP sessions or to await natural clearing of hemorrhage.[1]

Furthermore, the majority of eyes examined by several retrospective studies retained good vision in the operative eye by 3 months and even 10 years. Outcomes are gradually improving, which Gupta et al attribute to initiating surgical intervention on patients with better visual acuity. Even focusing on outcomes of surgical intervention within 6 months of presentation showed improvement in type 2 diabetics in the United Kingdom, a finding that was not substantiated in the DRVS. Our results add to the current literature by demonstrating that PDR-associated VH may be managed by vitrectomy even earlier than previously suggested, decreasing the time the patient spends with low vision, also decreasing the need for repeated office visits.[4,8-11]

Parikh et al. found that patients receiving PRP for PDR-associated VH were more likely than patients with PDR alone to undergo vitrectomy within 1 to 2 years of PRP treatment. Taking these results in context with the current study, immediate vitrectomy may alleviate the need for preoperative PRP, especially since endolaser will be performed concurrently intraoperatively. Current guidelines recommend taking patients to surgery by 3 months for non-clearing VH; however, this systematic review was based solely on data from DRVS. Many retina surgeons are taking these patients to surgery within 1

month; yet, this is the study to demonstrate that doing so is safe and effective.[1,8]

The DRVS did not just focus on vitrectomy for VH. Even for severe, active PDR, 44% of patients randomly assigned to immediate vitrectomy had visual acuity of 10/20 compared to only 28% in the conventional management group (including PRP, observation, or vitrectomy for complications). Moreover, a recent study demonstrated visual success (> 15-letter improvement) in tractional diabetic macular edema, epiretinal membrane, and PDR-associated TRD at 1 year following vitrectomy. Frequency of post-vitrectomy hemorrhage was low for patients without TRD (8.1%) and similar to our current study (7.69%). As the indications for diabetic vitrectomy expand, the appropriate timing for surgical intervention as well efficacy of adjunctive treatment will become increasingly important to understand.[9]

The study conducted by Zhang Rui et al (2016) found that, in the sample of the general Chinese population, the prevalence of retinopathy significantly increased in the tenth deciles of HbA1c, with optimal cutoffs of 6.4%, respectively. The current WHO guideline for diagnosing diabetes has high specificity but low sensitivity for detecting DR in this population. In our study, most sample shows that HbA1C that was closest to date of surgery is more than 6.4% (> 70%).[15]

There are limitations to to this retrospective reviews. In an effort to provide a more homogenous population, there were many exclusions, yielding low numbers of patients included for analysis. The accuracy of DM years is also still questionable. Most patients probably do not realize that they have diabetes melitus, until the appearance of visual complaints. Nevertheless, diabetic retinopathy is a heterogeneous disease and even with strict inclusion criteria one cannot guarantee that all patients would behave the same. Additionally, not all patients follow up for the same period of time, and follow-up appointments may be missed, which impacts the interpretation of final results. Importantly, this report includes only the results of the patients who underwent surgical intervention. Patients with natural clearing of PDR-associated VH were not included in this analysis in an effort to focus on the direct effect of surgery in this population. Treatment with anti-vascular endothelial growth factor agents was also not addressed in this study due to a broad range of treatment timing and indications. Most commonly, patients in this population were injected for diabetic macular edema. Although there is evidence that injection of bevacizumab (Avastin; Genentech, South San Francisco, CA) 1 to 2 weeks prior to vitrectomy may facilitate neovascular membrane removal, there is significant concern that rapid contracture of such membranes may cause TRD.[12-14]

Regardless of how complications of diabetic retinopathy are treated, prevention and immediate detection are clearly the goals of the savvy retina practioner. In addition to the literature presented, the results provide further support for the utility and efficacy of immediate vitrectomy for VH secondary to PDR. We believe that immediate vitrectomy for PDR-associated VH will improve not only quality of life for these individuals but also decrease economic burden by facilitating their return to work and increased productivity. A prospective study with randomization into immediate vitrectomy or delayed vitrectomy with or without adjunctive therapy (PRP or intravitreal injection)

would most prociently assess these questions.

CONCLUSION

Immediate vitrectomy for VH due to PDR significantly decreases time spent with vision loss, and also decreases post-surgical complications number. Modern vitrectomy surgery is safe and may be considered earlier in VH management.

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