Comparing Treatment Strategies for Uncomplicated Diabetic Vitreous Hemorrhage: Medical Therapy versus Early Pars Plana Vitrectomy

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ABSTRACT

Purpose: Pars plana vitrectomy (PPV) is typically reserved for refractory and complicated cases of diabetic vitreous hemorrhage (VH). However, no consensus guidelines are available for uncomplicated VH treatment. This study aimed to compare outcomes of medical versus surgical treatments for uncomplicated diabetic VH.

Methods: We conducted a retrospective review of medical records for patients with diabetic VH, focusing on uncomplicated cases. Patients were assigned to medical and surgical groups (early and rescue PPV). The medical group treatments included observation only, intravitreal anti-VEGF injection, and panretinal photocoagulation (PRP), with PRP completed after VH resorption in all cases. The surgical groups underwent PPV or a preoperative single intravitreal anti-VEGF before PPV.

Results: There were 34 patients in the medical group and 35 in the surgical groups (24 early PPV, 11 rescue PPV). Patients in the surgical group had longer VH duration, higher VH grade, and poorer baseline CDVA compared to medical group ($p<0.01$ each). CDVA significantly improved in all groups post-treatment. VH clearance rates were higher in the surgical group (90%±18 for early PPV, 88%±25 for rescue PPV) compared to the medical group (70%±22, $p=0.001$). Final CDVA did not significantly differ between medical and surgical subgroups ($p=0.549$). Recurrent VH was the predominant complication in both groups. Eight surgical patients had elevated IOP, with three developing glaucoma. Rescue PPV was required in 24.4% of initially medically treated patients.

Conclusion: Medical management should be the initial approach for uncomplicated diabetic VH, while PPV should be considered for cases of persistent or severe VH.

Keywords: Diabetic vitreous hemorrhage, intravitreal anti-VEGF injection, panretinal photocoagulation, pars plana vitrectomy

INTRODUCTION

Vitreous hemorrhage (VH) is a severe complication of proliferative diabetic retinopathy (PDR) that can significantly impair visual acuity. Panretinal photocoagulation (PRP) is the standard treatment for PDR[1]. PRP inhibits VEGF release from ischemic areas in the retina, and its use alone achieves regression of retinal neovascularization in approximately 60% of patients[2,3]. Uncomplicated diabetic VH cases can be managed by monitoring for applying PRP until spontaneous resolution occurs [4]; however, only 20% of diabetic VH cases resolve spontaneously[5]. In the remaining 80% of cases, PRP may be infeasible due to the obstruction of retinal details by the vitreous hemorrhage[6]. Therefore, pars plana vitrectomy (PPV) is reserved for the treatment of VH in PDR cases[7].

PPV is also performed to clear non-self-absorbed VH and to allow the surgeon to conduct PRP in a single session[8]. Surgical treatment additionally provides a rapid improvement in visual acuity. Nevertheless, despite advances in microincisional sutureless vitrectomy, surgery carries the risk of serious complications, such as retinal detachment, suprachoroidal hemorrhage and endophthalmitis [9]. Furthermore, recurrent VH may be observed following surgery in 20–40% of PDR patients [10].

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Most of these cases usually require additional laser therapy and adjunctive treatment.

One alternative treatment for PDR could be the intravitreal injection of anti-VEGF agents, which is known to provide transient regression of retinal neovascularization [11]. Although more evidence is required to determine the role of these agents in diabetic VH, some clinical studies have shown that anti-VEGF injection can shorten VH clearance time and reduce the need for surgery by 30% [12]. Injection of anti-VEFG agents before PPV also helps to reduce both intraoperative and postoperative bleeding [13,14]. The aims of the present study were to compare the efficacy of medical and surgical approaches as treatments for uncomplicated diabetic VH and to determine how patients can obtain the best benefits from each treatment strategy.

MATERIAL AND METHODS

The medical records of 101 patients with diabetic VH who were treated at the Istanbul Medeniyet University Department of Ophthalmology in recent years were retrospectively reviewed. Patients with non-diabetic VH, chronic VH (>3 months), ocular pathologies such as tractional retinal detachment (based on ultrasonography) and glaucoma, history of vitrectomy, and intravitreal injection were excluded (as shown in Figure 1). In bilateral cases, the first treated eye was included in the study. The study protocol was approved by the local human research ethics committee (document no=2022/0258), and informed consent was obtained from all patients before the procedures. The study protocol adhered to the tenets of the Declaration of Helsinki.

Patients were categorized into three groups based on the treatment received: medical, early surgical, and rescue surgery. The medical group included observation-only, monthly intravitreal anti-VEGF injection, and PRP treatments. In all cases, PRP was completed following the resorption of the VH. Both the early and rescue surgery groups underwent pars plana vitrectomy (PPV), with some patients receiving a single preoperative intravitreal anti-VEGF injection before PPV. The rescue surgery group was scheduled for PPV if the hemorrhage did not reduce after a two-month observation period after the initial medical treatment. PRP was completed in a single session for patients who underwent PPV. Patients that underwent surgery had a temporary discontiuation of oral anticoagulants. They were followed under supervision of a cardiologist with low molecular wieght heparin durig perioperative period. Oral anticoagulants were restarted after the sugery. All patients underwent a detailed ophthalmological examination before treatment and during follow-up visits.

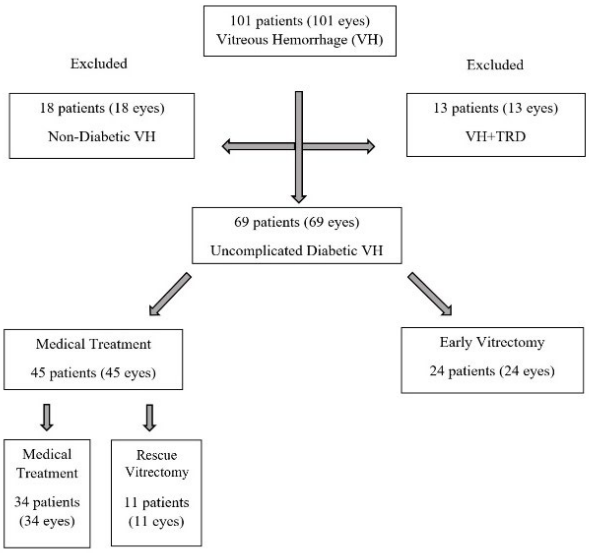

Figure 1. *The flow chart describing patient inclusion criteria to the study groups.*

Patients with a history of vitreous hemorrhage were restrospectively studied. Patients with uncomplicated diabetic vitreous hemorrhage were divided in to medical and surgical treatment groups based on the primary management approach. Some of the patients in the medical management group required further surgical treatment and we named this group as rescue vitrectomy group. VH; vitreous hemorrhge, TRD; tractional retinal detachment.

Demographic and clinical characteristics, including age, gender, best-corrected distance visual acuity (CDVA) with a Snellen chart, time to reach CDVA, amount of VH, VH clearance rate, need for PPV at any point during follow-ups, history of PRP before onset, use of anticoagulants, and ocular and systemic disease history, were recorded. Additionally, complications following treatment, such as recurrent hemorrhage, development of cataracts, transient or persistent increased intraocular pressure (IOP), corneal epithelial defect, retinal breaks, retinal detachment, and endophthalmitis, were specifically noted. The amount of VH was graded based on the visibility of retinal details, as follows [15]:

Grade 1 (mild VH): hazy vitreous with a discernible optic disc and retinal vessels.

Grade 2 (moderate VH): blurred view of the optic disc and retinal vessels.

Grade 3 (severe VH): non-visualization of both the optic disc and retinal vessels.

The VH clearance rate was considered complete (100%) if the posterior pole and peripheral retina were clearly visible,

allowing for the application of PRP. Partial VH clearance was defined relative to the optic disc level, where a 50% VH clearance corresponded to a clear fundus above the optic disc level. The VH clearance rate was recorded as 25% if the superior quadrant of the retina was partially visible. In cases where residual hemorrhage partly obscured the inferior quadrant of the retina, the VH clearance rate was defined as 75%.

Statistical analyses were performed using SPSS 21 software (IBM Corp., Chicago, IL, USA). The distribution of the data was determined using the Kolmogorov–Smirnov test. The data were presented as mean ± SD for normal distribution and median (minimum–maximum) for non-normal distribution. The Student t-test and Mann–Whitney U test were used for intergroup comparisons. The Kruskal–Wallis test compared three or more groups. The chi-square test was used for categorical values. P values below 0.05 were considered statistically significant.

RESULTS

In total, 34 patients (23 males, 11 females; mean age 59.3 ± 9.5 years) were included in the medical group. The surgical group was divided into early PPV (12 males, 12 females; mean age 63.7 ± 7.3 years) and rescue PPV (6 males, 5 females; mean age 61.3 ± 11.3 years) subgroups. There were no significant differences in gender (p=0.378) or age (p=0.196) between the groups. The mean follow-up time was similar across the groups: 11.6 ± 3.6 weeks for the medical group, 13.7 ± 7.2 weeks for the early PPV group, and 13.2 ± 12.7 weeks for the rescue PPV group (p=0.283). The grade of VH was higher in the surgical group (p=0.017). Patients in the medical group presented with mild, moderate, and severe VH, while those in the surgical groups had moderate or severe VH, as illustraed in Figure 2. No statistically significant correlation was observed between the degree of VH and patients' clinical and demographic characteristics, such as age, gender, type of diabetes, nephropathy, hypertension, PRP history, use of oral anticoagulants, and HbA1c levels (p>0.05). PPV was required for 24.4% of patients (11 out of 45) who initially received medical treatment. The clinical and demographic characteristics of the patients are shown in Table 1.

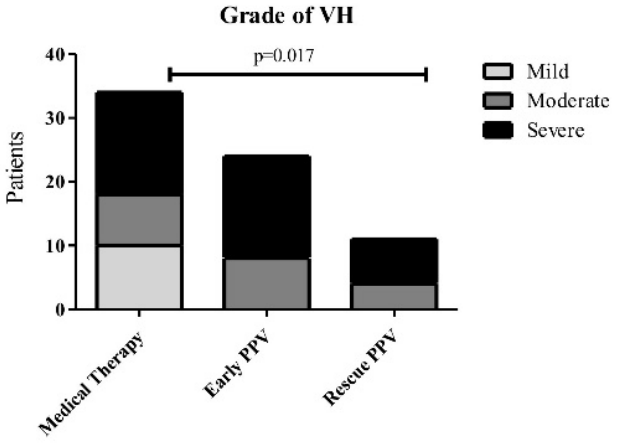

Figure 2. *Distribution of vitreous hemorrhage severity among the groups.*

Patients in the medical group presented with varying severities of vitreous hemorrhage (VH), including mild, moderate, and severe. In contrast, patients in the surgical groups predominantly exhibited moderate or severe VH. VH; vitreous hemorrhge, PPV; pars plana vitrectomy.

Table 1. Demographic and clinical characteristics of the patients.

	Medical Therapy (n:34)	Early PPV (n:24)	Rescue PPV (n:11)	(p) value
Age (mean±SD)	59.3±9.5	63.7±7.3	61.3±11.3	0.196*
Sex (M/F)	23/11	12/12	6/5	0.378***
VH onset (mean±SD week)	5.1±3.6	17.2±31.5	12.2±14.4	**0.003****
Follow-up (mean±SD week)	11.6±3.6	13.7±7.2	13.2±12.7	0.283**
Grade of VH (n, mild/moderate/severe)	10/8/16	0/8/16	0/4/7	**0.017*****
PDR (type 1/2 DM)	4/30	0/24	1/10	0.227***
Lens status (P/PP)	24/10	13/11	8/3	0.368***
HA1C (mean±SD)	9.7±2.6	9.9±2.2	9.4±1.8	0.832*
HT, n (%)	16 (47%)	17 (70%)	9 (81%)	0.056***
Nephropathy, n (%)	6 (17%)	9 (37%)	5 (45%)	0.110***
PRP history, n (%)	23 (67%)	12 (50%)	8 (72%)	0.291***
OAC, n (%)	12 (35%)	10 (41%)	3 (27%)	0.704***

n, patient number; SD, standard deviation; VH, vitreous hemorrhage; M, male; F, female; PDR, proliferative diabetic retinopathy; DM, diabetes mellitus; P, phakic; PP, pseudophakic; HA1c, hemoglobin A1c; HT, hypertension; PRP, panretinal photocoagulation; OAC, oral anticoagulants; *One Way Anova; **Kruskal-Wallis test, ***Pearson chi-square test

The initial corrected distance visual acuity (CDVA) was worse in the surgical group (median 2.2 logMAR; range 0.20 to 3.10 logMAR for early PPV and median 2.1 logMAR; range 0.70 to 3.10 logMAR for rescue PPV) compared to the medical group (median 1.0 logMAR; range 0.26 to 3.1 logMAR, p=0.002). However, CDVA significantly improved in both the medical and surgical subgroups over the course of treatment. There was no statistically significant difference in the final CDVA among the medical group and both surgical groups (p=0.549), as illustrated in Figure 3.

VH clearance was more effective in the surgical groups compared to the medical group (90 ± 14% for early PPV and 88 ± 25% for rescue PPV vs. 70 ± 22% respectively, p=0.001). The total number of intravitreal injections administered during follow-up was significantly lower in the early PPV group (p=0.010). There was no significant difference between the medical and surgical groups in the time taken to achieve CDVA improvement (median 7 weeks; range 2 to 24 weeks for early PPV, median 5 weeks; range 0 to 24 weeks for rescue PPV vs. median 6 weeks; range 2 to 16 weeks for medical, p=0.622). Recurrent hemorrhage was the most common complication observed in both medical and surgical groups. Eight patients in the surgical group (6 early PPV, 2 rescue PPV) experienced elevated IOP, with three developing glaucoma; one of these patients had a previous history of glaucoma. Additionally, cataract development was noted in one patient from the early PPV group. No cases of endophthalmitis were reported (see Table 2).

Subgroup analyses within the medical group showed no significant differences in initial and final CDVA or VH clearance rates among the observation-only, intravitreal anti-VEGF injection, and PRP treatment subgroups (p=0.366, p=0.509, p=0.970, respectively). Similarly, in the early and rescue PPV groups, which underwent pars plana vitrectomy (PPV) or received a preoperative single intravitreal anti-VEGF injection, initial and final CDVA values and VH clearance rates were comparable across the subgroups (Table 3).

DISCUSSION

Vitreous hemorrhage is a serious complication of PDR and causes severe visual impairment. PPV is performed in cases of refractory VH and complicated VH with tractional retinal detachment [16]. However, there is currently no consensus guideline for managing uncomplicated diabetic VH management. Some retinal specialists choose an aggressive approach, some others a softer one. In the present study, we aimed to compare the clinical outcomes of medical versus surgical approaches for uncomplicated diabetic VH to determine the optimal treatment method for patients.

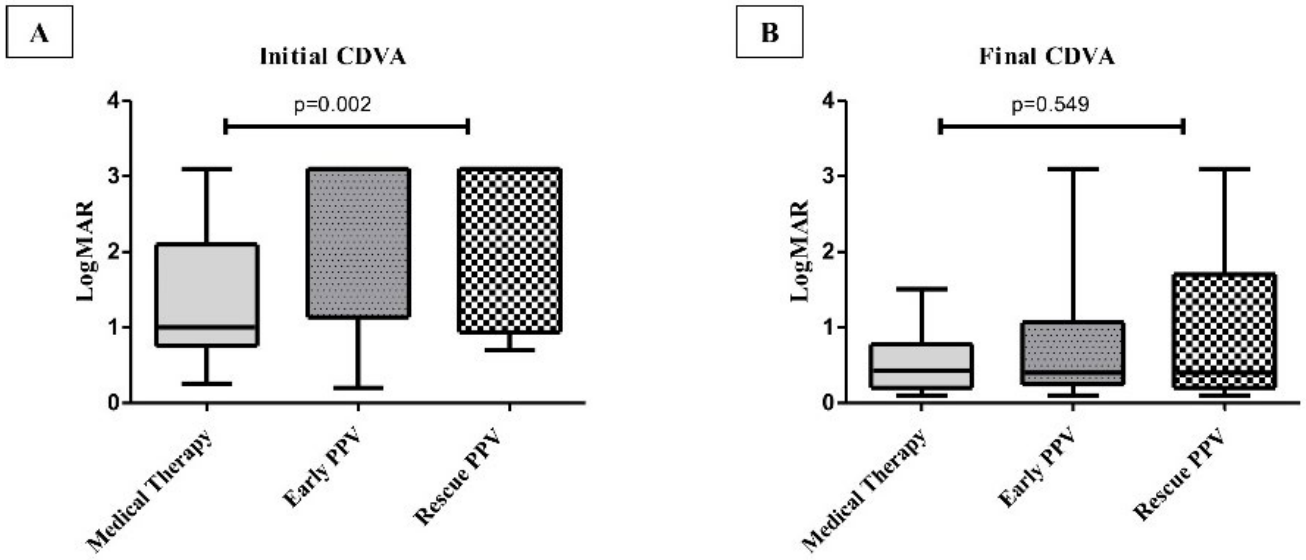

Figure 3. *Visual acuity changes in the medical and surgical treatment groups.*

Initial corrected distance visual acuity (CDVA) was poorer in the surgical groups compared to the medical group (a). Following management, visual acuity improved in both groups and no statistically significant difference was observed in the final CDVA among the groups (b). LogMAR; the logarithm of the minimum angle of resolution, CDVA; corrected distance visual acuity, PPV; pars plana vitrectomy.

Table 2. *Vitreous hemorrhage clearance and complication rates in medical and surgical groups.*

	Medical Therapy	Early PPV	Rescue PPV	(p) value
VH clearance rate (%, mean ± SD)	70±22	90±14	88±25	**0.001***
Total anti-VEGF injection (n, mean ± SD)	1.3±1.1	0.5±0.7	1.3±0.8	**0.010***
Complications (n):				
Recurrent hemorrhage	4	6	2	
Cataract		1		
IOP fluctuation		6	2	
Persistent IOP		2	1	
Epithelial defect		1		

VH, vitreous hemorrhage; (%), percent; SD, standard deviation; VEGF, vascular endothelial growth factor; IOP, intraocular pressure; *Kruskal-Kallis test

Table 3. *Subgroup analysis of medical and surgical treatment groups.*

	Medical Therapy (n)				Early PPV (n)			Rescue PPV (n)		
	Observation only (6)	IVI (19)	PRP (9)	(p) value	PPV (13)	IVI+PPV (11)	(p) value	PPV (3)	IVI+PPV (8)	(p) value
VH clearance rate (%, mean ± SD)	70±.18	69±24	72±23	0.970*	91±16	89±12	0.590**	81±37	92±18	0.788**
Initial CDVA (median [IQR] logMAR)	0.89 (0.8)	1.0 (1.3)	1.0 (1.4)	0.366*	3.1 (2.1)	2.7 (1.9)	0.932**	2.2 (2.0)	3.1 (2.3)	0.788**
Final CDVA (median [IQR] logMAR)	0.2 (0.3)	0.4 (0.6)	0.4 (0.6)	0.509*	0.4 (0.5)	0.6 (0.8)	0.266**	1.0 (2.5)	0.4 (1.1)	0.648**
Recurrent hemorrhage (n)	0	2	2		3	3		1	1	

n, patient number; IVI, intravitreal injection of anti-VEGF ; PRP, panretinal photocoagulation; PPV, pars plana vitrectomy; VH, vitreous hemorrhage; CDVA, corrected distance visual acuity; IQR, interquartile range; logMAR, logarithm of the minimum angle of resolution; *Kruskal-Wallis test; **Mann-Whitney U test

Our study revealed that patients in the surgical group presented with a longer history of VH, higher VH grade, and worse baseline CDVA. Visual acuity improved following both medical and surgical treatments, and the final CDVA was comparable across all groups. A similar study reported no significant differences in visual outcomes between PPV and intravitreal aflibercept followed by PRP [15]. A similar study reported no significant differences in visual outcomes between PPV and intravitreal aflibercept followed by PRP. It was noted that early PPV led to faster visual acuity improvement, contrasting with our findings of no significant difference in the time to achieve CDVA improvement between groups. This discrepancy may be attributed to our use of tamponade during vitrectomy, which could have influenced visual acuity. Early PPV patients required significantly fewer total intravitreal injections, and postoperative injection rates were markedly lower in the surgical group during follow-ups compared to the medical group. This suggests that applying PRP during surgery may enhance effectiveness by improving visualization of the peripheral retina. PPV was predominantly chosen for severe VH cases and instances where hemorrhage did not diminish after a two-month observation period. Factors influencing the preference for surgical intervention included patient adherence to follow-up visits, the desire for rapid visual improvement, and the condition of the fellow eye. Notably,

a quarter of patients initially treated medically ultimately underwent rescue PPV due to persistent or worsening VH. Patient expectations also played a role in the decision to transition to surgical treatment.

The most common complication observed following the treatments in our study was recurrent VH, occurring in both the medical and surgical subgroups. Recurrent VH typically signifies ongoing neovascularization, often due to inadequate PRP[17,18]. It is noteworthy that after trocar removal, particularly in cases of hypotony, mild vitreous hemorrhage may occur due to choroidal leakage at the sclerotomy ports' inner lips. This type of hemorrhage is usually mild and may go unnoticed, especially in the presence of gas tamponade. The number of preoperative anti-VEGF injections were lower in early vitrectomy group compared to rescue vitrectomy group, that might explain the difference between the recurrent vitreous hemorrhage rates. The recurrent hemorrhages in this study were not due to early postoperative hypotony, they devloped during the late follow-up of the patients. We believe that they were caused by new neovascular leasions that developed due to worsening of proliferative diabetic retinopathy. Therefore, all of these patients underwent intravitreal injections and additional PRP was performed. All recurrent VH cases in vitrectomized eyes resolved following intravitreal injections, whereas VH persisted in four patients in the medical group who subsequently underwent PPV. Eight patients in our surgical group experienced transient elevation of IOP postoperatively, with three developing glaucoma during follow-up. Typically, early postoperative IOP elevation is attributed to factors like inflammation, postoperative hemorrhage, and the use of silicone oil or gas tamponade[19]. The vitreous serves multiple roles, including acting as an oxygen scavenger[20]. Removal of the vitreous during vitrectomy allows oxygen metabolites to more easily reach the anterior segment, potentially leading to oxidative damage of the crystalline lens and trabecular meshwork. This process can contribute to the long-term development of cataracts and glaucoma[21]. Despite advancements in micro-incisional vitrectomy surgery, PPV carries risks of serious complications such as endophthalmitis, suprachoroidal hemorrhage, and ocular venous air embolism[22]. Fortunately, we did not observe any of these serious complications following PPV in our study.

The VH clearance rates and initial and final CDVA values were similar across all subgroups receiving medical and surgical treatments. However, contrary to our findings, other studies suggest a beneficial role for preoperative anti-VEGF injections before PPV. Preoperative anti-VEGF injections are reported to facilitate surgery and enhance clinical outcomes by reducing the need for extensive vitreous delamination, suppressing intraoperative bleeding, and lowering the incidence of postoperative VH [23,24]. There are also evidences that preoperative anti-VEGF treatments can improve the postoperative macular thickness and visual acuity [25].

Limitations of the present study include its retrospective design and small sample size, which particularly restrict its ability to compare clinical outcomes among subgroups of medical and surgical treatments. Larger prospective studies are required to optimize management approaches for diabetic VH. Severe anemia can cause tissue hypoxia and may be associated with retionopathy. We routinely check blood counts of our patients along with HbA1c measurements. None of our patients had severe anemia, that could potentially worsen retinopathy. However, our sample size was not suitable for subgroup analyses to test the potential impact of mild anemia on the clinical outcome.

CONCLUSION

Although VH clearance rate was higher in the surgical groups, both medical and surgical treatments showed no significant differences in the final CDVA. We suggest that the choice of treatment for uncomplicated diabetic VH should be guided by the severity of VH. Medical treatment should be considered as the initial approach for uncomplicated cases. However, in cases of persistent or severe VH, PPV may be preferred. This treatment strategy may offer a cost-effective management approach for diabetic VH and help mitigate potential adverse outcomes associated with PPV.

Statement of Ethics: This study protocol was reviewed and approved by the institutional ethics review board of Istanbul Medeniyet University Goztepe Prof. Dr. Suleyman Yalcın City Hospital, approval number [2022/0258], and written informed consent was obtained for participation in this study.

Conflict of Interest Statement: The authors have no competing interests to declare.

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Data Availability Statement: The data are available from the authors upon reasonable request.

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