

Function Evaluation of Diabetic Vitreous Hemorrhage after Vitrectomy

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ABSTRACT

Purpose: The aim of this study is to evaluate electrophysiological changes before and after pars plana vitrectomy for diabetic vitreous hemorrhage.

Subject & Method: This study included 30 eyes of 30 patients with diabetic vitreous hemorrhage undergoing pars plana vitrectomy. All subjects underwent complete ophthalmological examination, Ultrasonography, Visual evoked potential, Electroretinography before and after vitrectomy (at 1 week & 3 months). **Results:** There was a statistically significant improvement in the Uncorrected Visual Acuity (UCVA) and the Best Corrected Visual Acuity (BCVA) along the study period ($p < 0.001$). There was statistically significant improvement in the mean latency and mean amplitude of Flash VEP. There was a statistically significant increase in the mean amplitude of all ERG parameters at 3 months postoperative.

Conclusion: Electrophysiological test is an important tool in detection improvement of retinal function after vitrectomy.

INTRODUCTION

Diabetic vitreous hemorrhage is a cause of severe visual loss in diabetic patients. Pars plana vitrectomy with endolaser pan retinal photocoagulation remains the procedure of choice for non-clearing vitreous hemorrhage [1]. However, removing the vitreous body has considerable consequences for eye physiology. Oxygen transport and local availability of growth factor may both be altered [2]. The electroretinogram (ERG) reflects the summed electrical activity of the retina. Full-field electroretinography evaluates global retinal function, while multifocal ERG (mf-ERG) provides a topographic measure of retinal electrophysiological activity [3]. Visual evoked potential (VEP) is an electrical signal generated by the occipital cortex in response to light stimulation of the retina. The importance of the VEP is the diagnosis of optic nerve diseases and other ocular diseases [4]. The aim of this study is to evaluate electrophysiological (ERG, mf-ERG, VEP) changes before and after pars plana vitrectomy for diabetic vitreous hemorrhage.

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SUBJECT & METHOD

This prospective study included 30 eyes of 30 patients with diabetic vitreous hemorrhage undergoing pars plana vitrectomy attending the Outpatient Clinic of Mansoura Ophthalmic Center during the period from January 2018 to September 2020. The following were excluded: Vascular occlusive disorders. Bleeding coagulopathies, Tractional retinal detachment.

Patients were informed verbally and in writing of the potential risks and benefits, and those who agreed to participate signed a written informed consent form.

All patients underwent complete ophthalmic evaluation using slit lamp biomicroscopy with special reference to lens status, intraocular tension and retinal status, Ultrasonography, Visual evoked potential.

ELECTRORETINOGRAPHY

Technique of Electroretinography (ERG)

Full field ERG was recorded using Ronald Consult (Ronald Consult, Electrophysiologische Diagnostik Systeme, Brandenburg, Germany).

ERG, mf-ERG were performed according to ISCEV 2015 guidelines [5]. Pupils were fully dilated (>7mm) using 1% tropicamide and 2.5% phenylephrine. Before placing electrodes, the skin was cleaned. Topical corneal anesthesia (Benoxinate hydrochloride 4%) was instilled and a Dawson, Trick and Litzkow (DTL) electrode (positive electrode) was placed contacting corneal limbus, a ground electrode was placed on the forehead and a negative electrode was placed near the orbital rim. The electrodes were placed under dim red light and after dark adaptation for 20 minutes. The recording was monocular and the contralateral eye was occluded with light pressure to suppress blinking. Prior to beginning the patients had to be in a comfortable body position, the head was still before stimulation and the eyes fixated on red light within the Ganzfeld globe. Subsequently the test was started and recorded.

Technique of VEP

Standard silver chloride electrodes of 1cm diameter were used for recording. Active (positive) electrode was connected to midline of head two finger breadth above inion (projection at backhead). Ground electrode was connected in midline of head at level of ear lobule. Negative electrode was connected to middle of forehead. The sites of electrode were cleaned with cleaning cream before putting the electrodes. The

electrodes (silver, cup-shaped) were filled with connecting gel before putting in their sites. Impedance was kept below (10 K). For each eye two recordings were obtained. Participants were made to sit in a chair comfortably with chin in headrest to avoid muscle artifacts. The room was dimly lit with ambient light. White stimulus was given through xenon light kept at a distance of 30cm, at 2Hz frequency given for each eye separately with the eye open while the other eye being covered with an opaque patch. Subjects were asked to fix their gaze on the flash generated. They were watched for any gross eye movement or attention lapse during the procedure through the camera in the monitor. Two trials were given for each eye. The resultant curve of the flash VEP waveform consists of a series of negative N and positive P components.

Surgical technique of vitrectomy

All the surgeries are performed by the same surgeon. A standard 23 G, 3 ports Pars plana vitrectomy approach is adopted. Cases are operated under either general anaesthesia or retrobulbar anesthesia. LUMERA 700 Zeiss operating microscope (Carl Zeiss, Meditec AG, Germany) was the Resight 700 as a fundus viewing system together with Oertli vitrectomy machine (Oertli, Berneck, Switzerland).

Surgical details

- Initially, Core vitrectomy and posterior hyaloid separation was done.
- Posterior vitreous detachment was done by the vitrectomy probe in the aspiration mode only.
- Complete peeling of the posterior hyaloids was confirmed by injection of triamcinolone acetonide (Kenacort-A 40 Suspension for injection, Bristol-Myers Squibb).
- Then vitreous gel was trimmed towards the periphery. Brilliant blue G (Brillant PeelR, DORC, Rotterdam, Netherlands) was applied after partial air fluid exchange for 60 second. A 23 G (0.6mm) symmetrical end gripping micro forceps (Eckardt forceps, DORC, Rotterdam, Netherlands)) was used to create an edge of the ILM near the arcade and then used to complete the peeling maneuver to create a maculorrhexis about two disc diameter centered around the hole.
- Peripheral retinal indentation and examination for any detected breaks, peripheral holes, lattice degenerations or localized detachment.
- Endolaser photocoagulation is applied accordingly when

needed. Fluid-air then air-gas exchange is done with either 12% C3F8, 16% C2F6 or 20% sulfur hexafluoride using 100 ml syringe to flush the vitreous cavity and ensure adequate air-gas exchange.

- Tight closure of the sclerotomies is done by vicryl 7/0 suture to guard against postoperative hypotony.
- Simultaneous phacoemulsification was done in the coexistence of grade II/VI to, III/VI and grade IV/VI nuclear cataract according to LOCSII.

Post-operative care

The postoperative treatment regimen included topical antibiotics (moxifloxacin hydrochloride 0.5% ophthalmic solution (VIGAMOX®)), topical steroids (prednisolone acetate 1% ophthalmic suspension, (PRED FORTE®)) and cycloplegic eye drops (cyclopentolate hydrochloride 1%.

Systemic steroids are not prescribed unless the patient develops anterior segment inflammatory reaction with special reference to the patient physician.

Postoperative follow-up

Patients were followed up at 1st week and 3rd month postoperatively.

The following was done

Assessment of Visual acuity and best corrected distant visual acuity (BCVA), Slit lamp Biomicroscopy, Measurement of ocular tension using Goldmann applanation tonometer, Visual Evoked Potential (VEP), Electroretinography (ERG).

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Quantitative data were expressed as mean ± SD (Standard deviation) or median (range) according to distribution (parametric and non-parametric respectively). Paired samples t-test was used to compare between two dependent groups of normally distributed variables (parametric data) while Wilcoxon-Signed rank test was used for non-normally distributed Data (non-parametric data. The level of significance was tested, expressed as the probability of (p-value); significant if the p value is ≤ 0.05.

RESULTS

The study was conducted on 30 eyes with diabetic vitreous hemorrhage. The demographic features of the studied population were included in Table 1.

Table 1. The demographic feature of the studied population.

	Range	Mean ±SD
Age (years)	46–64	55.9±4.6
Sex (n, %)		
Females	10, 33.3%	
Males	20, 66.7%	
Duration of diabetes (years)	18–25	20.9±2.3
HBA1c%	5.7–9.7	7.5±1.1
Treatment for diabetes (n, %)		
Insulin injection	14, (46.7%)	
Oral hypoglycemic	16, (53.3%)	

N: Number; SD: Standard Deviation.

There was a statistically significant improvement in the Uncorrected Visual Acuity (UCVA) along the study period (p <0.001). The mean UCVA (log MAR) was 1.62 ±0.30,

1.41 ±0.39 and 1.06 ±0.31 at baseline, 1 week and 3 month postoperative (p<0.0001, Figure 1A).

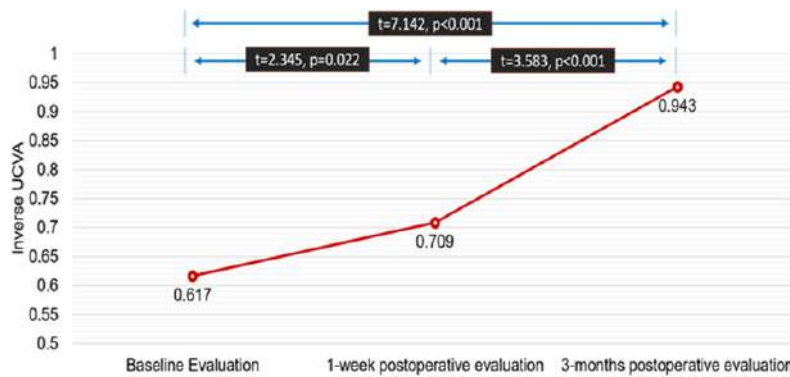


Figure 1(A). Post hoc test for the comparison of the UCVA.

There was a statistically significant improvement in the Best Corrected Visual Acuity (BCVA) along the study period ($p < 0.001$). The mean BCVA (log MAR) was 1.62 ± 0.30 , 1.45 ± 0.33 and 1.08 ± 0.32 at baseline, 1 week and 3 months postoperative. ($p < 0.0001$ Figure 1B)

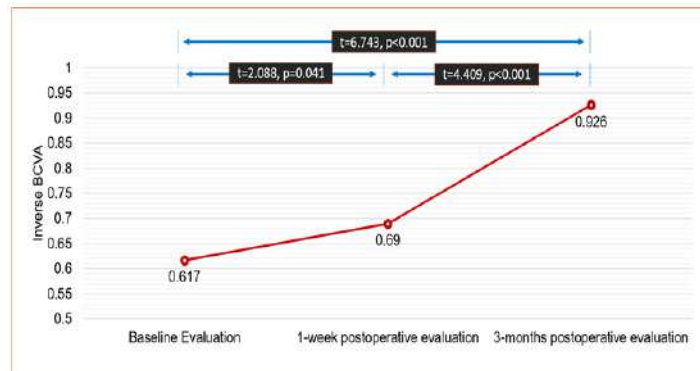


Figure 1(B). Post hoc test for the comparison of the BCVA.

There was statistically significant improvement in the mean latency and mean amplitude of Flash VEP 2 Hz at 3 months postoperative as compared with the baseline value ($p = 0.029$, 0.026 respectively). Table (2), Figure (2)

Table 2. Comparison of the FVEP parameters recordings between baseline and 3-months postoperative

	FVEP Parameters		Student's t test	
	Baseline	3-months postoperative	t	p
Flash VEP 2 HZ				
Latency P2 (ms)				
• Range	121 - 190	105 - 188	2.236	0.029
• Mean \pm SD	150.6 \pm 22.6	136.6 \pm 25.8		
Amplitude N2-P2 (μv)				
• Range	1.63 - 15.20	3.07 - 18.91	2.284	0.026
• Mean \pm SD	6.50 \pm 3.55	8.93 \pm 4.66		

FVEP, Flash Visual Evoked Potential; ms, millisecond; μ v, microvolt

This table shows that there was significant improvement in FVEP parameters.

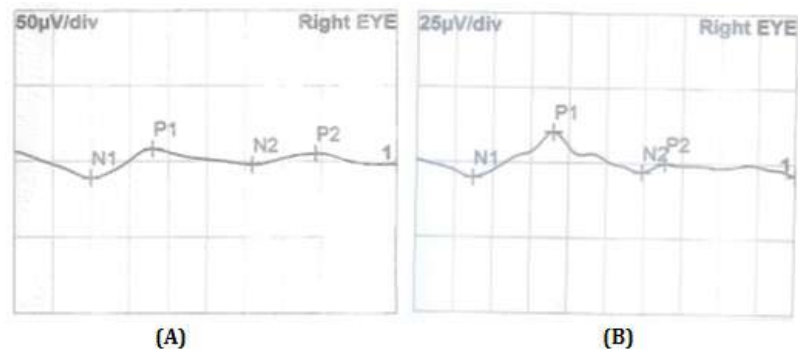


Figure 2. (A) Preoperative FVEP. **(B)** postoperative FVEP.

There was a statistically significant increase in the mean amplitude of all ERG parameters at 3 months postoperative as compared with the baseline value ($p < 0.05$). There was no statistically significant difference in the mean latency of Scotopic b-wave, combined b-wave and 30 Hz Flicker at 3 months postoperative as compared with the baseline value.

However, there was a statistically significant increase in the mean latency of Oscillatory Potentials and Photopic b-wave at 3 months postoperative as compared with the baseline value (Table 3 & Figure 3). Among the 30 patients enrolled in the study, there were 36.7% ($n=11$) had b/a ratio < 1 and 63.3% ($n=19$) had b/a ratio > 1 .

Table 3. Comparison of the ERG parameters recordings between baseline and 3-months postoperative

	ERG Parameters		Student's t test	
	Baseline	3-months postoperative	t	p
Scotopic b-wave				
Latency (ms)				
Range	33 - 105	61 - 92		
Mean \pm SD	82.3 \pm 18.9	78.7 \pm 9.5	0.941	0.351
Amplitude (μ v)				
Range	3.88 - 16.70	9.50 - 17.60		
Mean \pm SD	10.18 \pm 4.47	13.76 \pm 2.64	3.777	<0.001
Combined b-wave				
Latency (ms)				
Range	42 - 61	20.9 - 61		
Mean \pm SD	49.9 \pm 5.2	48.4 \pm 10.2	0.726	0.471
Amplitude (μ v)				
Range	22.3 - 90.7	42.1 - 111.3		
Mean \pm SD	61.6 \pm 22.5	77.3 \pm 20.5	2.825	0.006
Oscillatory PotentialS				
Latency (ms)				
Range	23.6 - 39.9	17.3 - 36.3		
Mean \pm SD	31.1 \pm 5.6	27.0 \pm 6.9	2.527	0.014
Amplitude (μ v)				
Range	2.2 - 8.1	3.9 - 8.8		
Mean \pm SD	4.8 \pm 1.7	6.3 \pm 1.4	3.731	<0.001
Photopic b-wave				
Latency (ms)				
Range	32 - 46	30 - 41.1		
Mean \pm SD	38.5 \pm 4.2	34.9 \pm 3.09	3.862	<0.001
Amplitude (μ v)				
Range	14.5 - 38.9	21.0 \pm 51.3		
Mean \pm SD	25.8 \pm 7.6	34.3 \pm 9.5	3.827	<0.001
30 Hz Flicker				
Latency (ms)				
Range	38 - 107	45 - 75		

Mean \pm SD	64.5 \pm 20.1	64.5 \pm 11.5	0.007	0.994
Amplitude (μ v)				
Range	5.1 – 17.5	11.9 – 29.7		
Mean \pm SD	12.2 \pm 3.8	20.0 \pm 5.9	6.088	<0.001

ERG: Electroretinogram; SD: standard deviation; ms: millisecond; μ v: microvolt

There was a statistically significant positive correlation between final BCVA, UCVA with Preoperative BCVA, UCVA and at 1-week BCVA, UAVA (Table 4 & Figure 4).

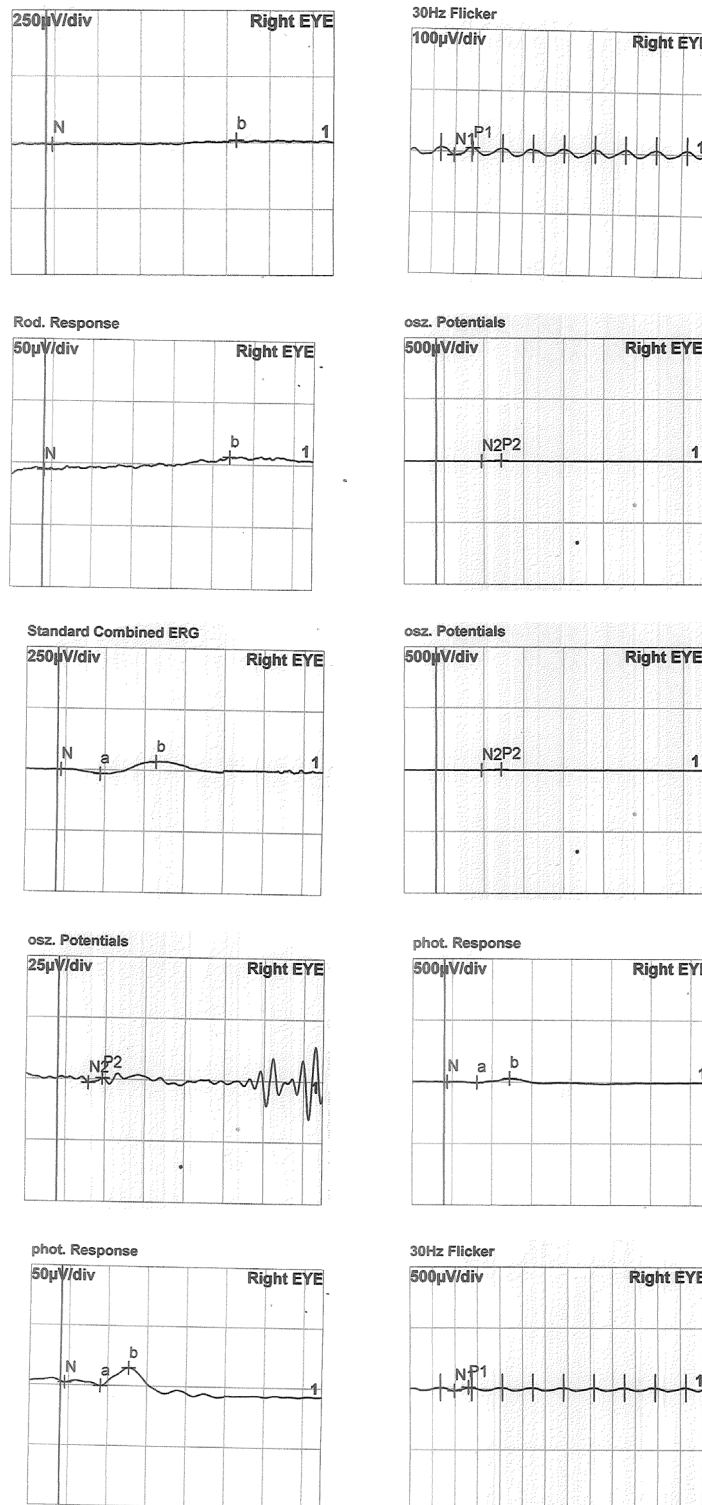


Figure3. ERG before and after vitrectomy

Table 4. Correlation of final UCVA and BCVA at 3-months postoperative with preoperative and at 1-week

Correlation of final UCVA at 3-months postoperative with	r	p
• Preoperative UCVA	0.517	0.003
• UCVA at 1-week postoperative	0.711	<0.001
Correlation of final BCVA at 3-months postoperative with		
• Preoperative BCVA	0.481	0.007
• BCVA at 1-week postoperative	0.807	<0.001

UCVA: Uncorrected Visual Acuity; BCVA: Best Corrected Visual Acuity

This table shows that there was a statistically significant positive correlation between **final UCVA** with **preoperative UCVA** and **UCVA at 1-week**.

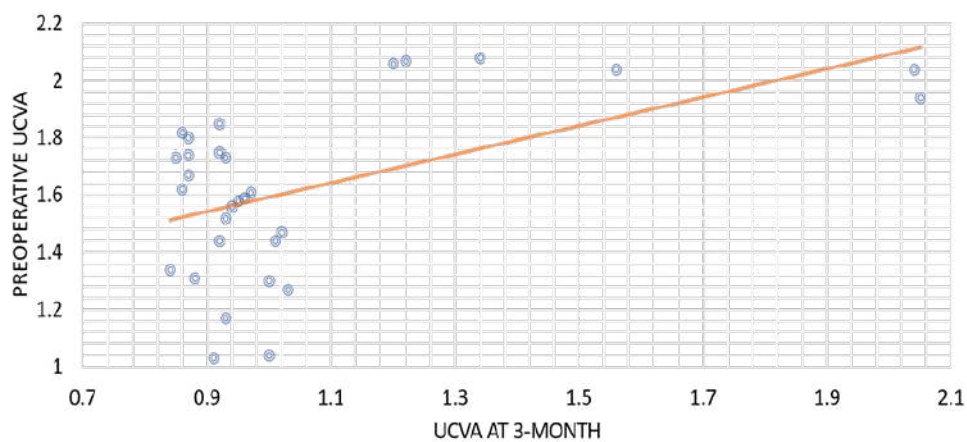


Figure 4(A). Correlation of UCVA at 3-month with preoperative UCVA.

This figure shows statistically significant positive correlation between UCVA at 3-month and preoperative UCVA.

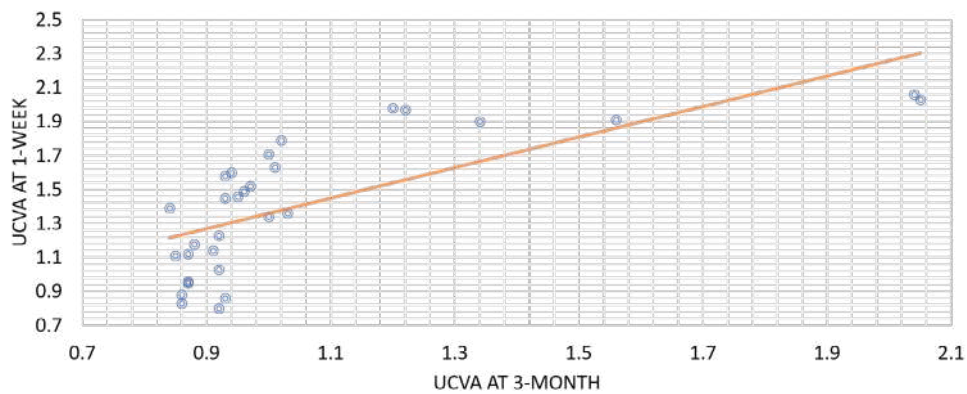


Figure 4(B). Correlation of UCVA at 3-month with 1-week UCVA.

This figure shows statistically significant positive correlation between UCVA at 3-month with 1-week UCVA.

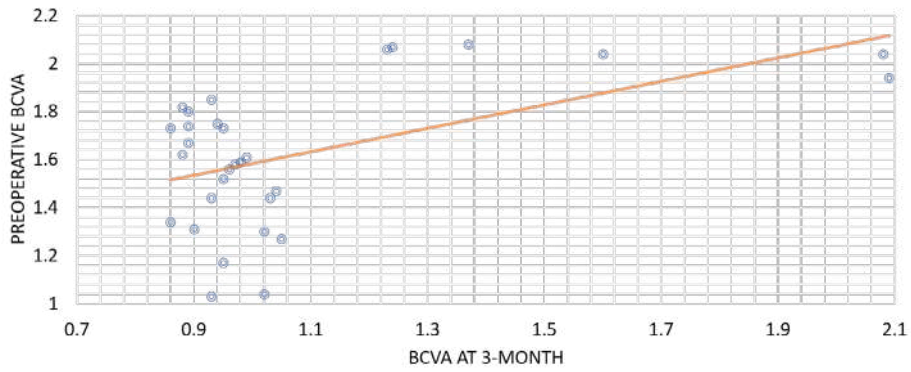


Figure 4(C). Correlation of BCVA at 3-month with preoperative BCVA.

This figure shows statistically significant positive correlation between BCVA at 3-month and preoperative BCVA.

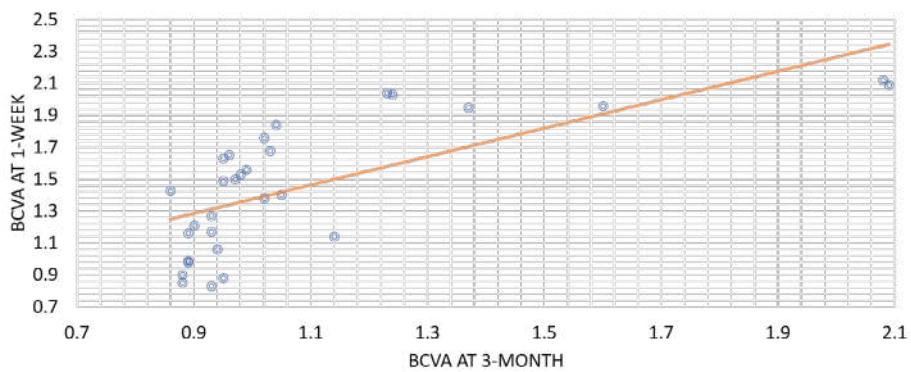


Figure 4(D). Correlation of BCVA at 3-month with 1-week BCVA

This figure shows statistically significant positive correlation between BCVA at 3-month with 1-week BCVA.

There was a statistically significant difference in the postoperative in the patients stratified by the b-wave/a-UCVA,BCVA between the preoperative and 3 months wave ratio into b/a ratio <1 and b/a ratio > 1 (Table 5 & 6).

Table 5. Change of the UCVA from preoperative to 3-month evaluation in patients stratified by the b-wave/a-wave ratio

	UCVA		Δ change [95% CI]	Student's t test	
	Preoperative	3-month postop.		t	p
b/a ratio <1 (n=11)	1.65 ±0.39	1.27 ±0.44	0.38 [0.01, 0.75]	2.144	0.045
b/a ratio ≥1 (n=19)	1.60 ±0.25	0.93 ±0.08	0.67 [0.55, 0.79]	11.126	<0.001

N: Number; UCVA: Uncorrected Visual Acuity; CI: confidence interval

This table shows that there was a statistically significant difference in the UCVA between the preoperative and 3 months postoperative in the patients stratified by the b-wave/a-wave ratio into b/a ratio <1 and b/a ratio > 1.

Table 6. Change of the BCVA from preoperative to 3-month evaluation in patients stratified by the b-wave/a-wave ratio

	BCVA		Δ change [95% CI]	Student's t test	
	Preoperative	3-month postop.		t	p
b/a ratio <1 (n=11)	1.64 \pm 0.33	1.29 \pm 0.42	0.35 [0.01, 0.69]	2.173	0.042
b/a ratio \geq1 (n=19)	1.61 \pm 0.25	0.92 \pm 0.08	0.67 [0.57, 0.81]	11.458	<0.001

N: number; UCVA: Uncorrected Visual Acuity; CI: Confidence Interval

Table 6 shows that there was a statistically significant difference in the BCVA between the preoperative and 3 months postoperative in the patients stratified by the b-wave/a-wave ratio into b/a ratio <1 and b/a ratio >1.

DISCUSSION AND CONCLUSION

Diabetic retinopathy (DR) is a common and devastating complication of diabetes mellitus (DM) and one of the commonest causes of legal blindness and visual impairment in the western world [6].

As the lifespan of diabetic patients has increased with the widespread use of antidiabetic medications, ocular and systemic microvascular complications of diabetes are more commonly encountered by the health care individuals [7]. In type 1 DM, the frequency of PDR increases up to 41% when the duration of diabetes exceeds 15 years. In type 2 DM, on the other hand, the rate of PDR is 3% when the duration of the disease exceeds 10 years [8].

It is estimated that the number of people with diabetic retinopathy (DR) in developed countries will increase from 126.6 million in 2011 to 191 million by 2030 [9].

Vitreous hemorrhage (VH) is the commonest complication of PDR. Depending upon the severity of hemorrhage, it can cause significant reduction in vision and make the examination and treatment more difficult [10].

Pars plana vitrectomy (PPV) remains the treatment of choice for eyes in which the vitreous hemorrhage is not spontaneously resolving [11] and if vitreous hemorrhage fails to clear despite laser photocoagulation and anti-proliferative drugs (anti-VEGF) [12].

In this study, electrophysiological changes before and after pars plana vitrectomy for diabetic vitreous hemorrhage were studied and whether electroretinogram (ERG) can predict the postoperative outcome in diabetic cases where massive vitreous hemorrhage precludes fundus observation. 30 eyes of 30 patients with diabetic vitreous hemorrhage underwent pars plana vitrectomy; 11 eyes with b/a ratio <1

(group 1) and 19 eyes with b/a ratio >1 (group 2). All were followed up 3 months postoperative by ERG and VEP.

Visual acuity results

There was a statistically significant improvement in the BCVA at 1 week following the surgery (1.45 \pm 0.33) as compared with the preoperative value (1.62 \pm 0.30) ($p=0.041$) and there was more further improvement in the value of BCVA at 3 months after the surgery (1.08 \pm 0.32) with high statistically significant difference as compared with the preoperative value ($p < 0.001$).

Similar results were reported by Iqbal et al. (2016) who showed that pre-operative and final post-operative mean BCVA LogMAR was 1.01 \pm 0.17 and 0.74 \pm 0.25 respectively. The difference in pre and postoperative BCVA was 0.045 which was statistically significant ($p < 0.05$) [12].

Also, Othman et al. (2014) reported final visual acuity showed improvement in 17 eyes (85%), whereas postoperative best-corrected visual acuity remained unchanged in three eyes (15%). The mean preoperative corrected visual acuity was 1.47 \pm 0.73 logMAR units.

A statistically significant increase in the mean corrected visual acuity was observed in all study eyes at 3 months after surgery (0.60 \pm 0.48 logMAR units; $P < 0.001$) [13].

However, Wu et al. (2017) conducted a study that included 82 eyes of 82 patients with vitreous haemorrhage or opacity due to ocular trauma, retinal detachment or retinal vascular diseases including diabetic retinopathy (non selective cases) and they compared these results with the values 2 weeks after vitrectomy operation. The authors revealed that there was no improvement or reduction in postoperative visual acuity [14].

VEP results

In this study, according to the analysis of Flash VEP parameters, there was statistically significant improvement in the mean latency of Flash VEP at 3 months postoperative as compared with the baseline value ($p=0.029$). Similarly,

there was statistically significant improvement in the mean amplitude of Flash VEP at 3 months postoperative as compared with the baseline value ($p=0.026$).

In the study conducted by Kim et al. (2017) the mean VEP P2 amplitude was $13.09 \pm 4.63 \mu\text{V}$ in the eyes with vitreous haemorrhage and PDR which was statistically significant lower as compared with the normal eyes ($18.43 \pm 8.96 \mu\text{V}$) ($p=0.024$). Also, they showed that the mean VEP P2 peak time was $125.17 \pm 12.26 \text{ ms}$ in the eyes with vitreous haemorrhage and PDR which was statistically significant longer as compared with the normal eyes ($18.43 \pm 8.96 \mu\text{V}$) ($p= 120.88 \pm 8.08$) [15].

ERG results

Dense vitreous haemorrhage and other media opacities affect electrophysiological responses by absorbing, reflecting and scattering the incoming light stimulus. In addition to removing the media opacity, vitrectomy has also considerable consequences for eye physiology as oxygen transport.

In our study, the analysis of the different parameters of full field ERG has revealed statistically significant improvement in all the tested parameters following vitrectomy as compared with the preoperative values.

Regarding the analysis of Scotopic b-wave in the study cases, the mean preoperative latency duration was $82.3 \pm 18.9 \text{ ms}$ which was longer as compared with the 3-month postoperative latency duration ($78.7 \pm 9.5 \text{ ms}$), but it didn't reach a statistically significant value ($p=0.351$). The mean 3-month postoperative amplitude was $13.76 \pm 2.64 \mu\text{v}$ which was statistically significant improved as compared with the mean preoperative amplitude ($10.18 \pm 4.47 \mu\text{v}$) ($p< 0.001$).

The analysis of Combined b-wave in the study cases, the mean preoperative latency duration was $49.9 \pm 5.2 \text{ ms}$ which was slightly longer as compared with the 3-month postoperative latency duration ($48.4 \pm 10.2 \text{ ms}$), but it didn't reach a statistically significant value ($p=0.471$). The mean 3-month postoperative amplitude ($77.3 \pm 20.5 \mu\text{v}$) which was statistically significant improved as compared with the preoperative amplitude which was $61.6 \pm 22.5 \mu\text{v}$ ($p< 0.006$).

The analysis of Oscillatory Potentials in the study cases, the mean preoperative latency duration was $31.1 \pm 5.6 \text{ ms}$ which was statistically significant longer as compared with the 3-month postoperative latency duration ($27.0 \pm 6.9 \text{ ms}$) ($p=0.014$). The mean 3-month postoperative amplitude ($6.3 \pm 1.4 \mu\text{v}$) was statistically significant improved as compared with the preoperative amplitude ($4.8 \pm 1.7 \mu\text{v}$) ($p=0.001$).

The analysis of photopic b-wave in the study cases, the mean preoperative latency duration was $38.5 \pm 4.2 \text{ ms}$ which was statistically significant longer as compared with the 3-month postoperative latency duration ($34.9 \pm 3.09 \text{ ms}$) ($p< 0.001$). The mean 3-month postoperative amplitude ($34.3 \pm 9.5 \mu\text{v}$) was statistically significant improved as compared with the preoperative amplitude ($22.8 \pm 7.6 \mu\text{v}$) ($p< 0.001$).

The analysis of 30 Hz Flicker in the study cases, the mean preoperative latency duration was $64.5 \pm 20.1 \text{ ms}$ and at the 3-month postoperative latency duration ($64.5 \pm 11.5 \text{ ms}$) with no significant difference. The mean 3-month postoperative amplitude ($20.0 \pm 5.9 \mu\text{v}$) which was statistically significant improved as compared with the preoperative amplitude ($12.2 \pm 3.8 \mu\text{v}$) ($p< 0.001$).

In agreement of our results, Abdelkader et al. [16] carried out a study on 25 eyes of 25 patients with diabetic macular edema to evaluate the effect of successful vitrectomy on retinal function in diabetic patients. At 3 month postoperative, the amplitude responses were increased compared to preoperative value [16]. Our study confirmed that preoperative UCVA, BCVA and b/a ratio had statistically significant association with postoperative visual outcome.

There was a statistically significant difference in both UCVA and BCVA between the preoperative and 3 months postoperative in the eyes stratified by the b-wave/a-wave ratio into b/a ratio <1 and b/a ratio >1 . The eyes with a b/a ratio >1.0 had better postoperative visual acuity than eyes with a b/a ratio <1.0 . Within the same context, the Japanese study of Hiraiwa T. [17] detected that eyes with b/a ratio <1.0 had worse postoperative visual acuity than eyes with a b/a ratio >1.0 [17].

Results were also in harmony with Wu et al. [14] who showed that preoperative visual electrophysiology was significantly correlated with the effectiveness of the operation. It is helpful in the prognostic assessment of postoperative visual outcome [14].

CONFLICT OF INTEREST

No Authors has proprietary interest.

FINANCIAL SUPPORT

Mansoura University Ophthalmic Center, Egypt.

ETHICAL APPROVAL

This study was approved by the Human Subjects Committee of the University of Mansoura, and adhered to the Declaration of Helsinki. Written informed consent was obtained from all participants.

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