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Research article

ELECTROPHYSIOLOGICAL CHANGES IN LATENCY IN DIABETIC RETINOPATHY: AN OBSERVATIONAL STUDY

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ABSTRACT

Purpose: Multifocal ERG is a useful indicator of diabetic retinopathy. The significant delay in local responses provides a chance for the detection and understanding of the various stages of diabetic retinopathy. **Materials and Methods:** This is a cross sectional study conducted in ERG clinic at M&J Western regional institute of ophthalmology, Ahmedabad from January 2013 to September 2015 who were more than 35yrs of age. **Results:** In our study, we studied 45 eyes of diabetic patients and 20 eyes of normal subjects. In our study the mean values of the various parameters was calculated in the control group with N1, P1 and N2 latency being 14.09ms. 29,76ms and 45.55ms respectively. The N1, P1 and N2 amplitude was found to be 31.52nV, 73.61nV and 90.38nV respectively. The maximum delay in N1, P1 and N2 latency was seen to be 3.24ms, 7.11ms and 8.40ms respectively from the normal value. We also found a decrease in amplitude of the ERG waveform with N1, P1 and N2 amplitude being 20.98nV,61.48nV and 76.4nV respectively from the normal value. Also it is helpful in cases with clinically significant macular edema where responses are remarkably delayed suggesting local retinal dysfunction and macular pathology. It provides us information regarding the condition of the macula and some ideas about the extent of ischemia affecting this area. **Conclusion:** In conclusion, we can say that the delayed responses obtained indicate abnormal retinal function corresponding to local discrete retinal lesions. It provides a very sensitive and objective assessment of the local retinal condition in various stages of diabetic retinopathy.

KEYWORDS: Diabetes mellitus, Diabetic retinopathy, Multifocal electroretinogram.

INTRODUCTION

Diabetes Mellitus (DM) is a heterogenous group of metabolic disorder characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both[1]. The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010. Chronic diabetes results in the development of tissue complications, mainly microvascular (retinopathy, nephropathy and neuropathy) and macrovascular disease (atherosclerosis)[2]. Microangiopathy is characterized by progressive occlusion of the capillary lumen with subsequent impaired tissue perfusion, increased vascular permeability and increased production of extracellular material by perivascular cells, resulting in basement membrane thickening and loss of pericytes[3].

Retinopathy is the most common microvascular complication of diabetes, and it remains a major cause of new onset blindness in age group of 20-74 years of patients worldwide. Vascular lesions in the early stages of diabetic retinopathy are characterized by the presence of capillary microaneurysms, pericyte deficient capillaries, and obliterated and degenerated capillaries. Proliferative diabetic retinopathy is the more advanced form of the disease, when circulation problems cause the retina to become hypoxic. As a result, new fragile blood vessels can begin to grow in the retina and into the vitreous.

Electroretinogram (ERG)[4] is the neurophysiological test used in order to measure electric changes that happen in the retina after a light stimulus. Full-field electroretinogram

(ERG) has been used as an objective tool to detect alterations of retinal function during the early stages of diabetes, to predict the progression of diabetic retinopathy and to monitor the treatment effects. The sensitivity of the full-field ERG is limited, precisely because it reflects the activity of the entire retina. Even advanced disease, if confined to small, discrete patches, can remain undetected by the full-field ERG. (e.g., focal edema and capillary non perfusion).

In contrast, the Multifocal electroretinogram (mfERG) developed by Sutter[5] and Tran and Bearse[6] and Sutter enables assessment of up to hundreds of distinct retinal areas, posterior region around macula within approximately 8 minutes per eye.

Aims & Objectives

Retinopathy is one of the most important complications of chronic diabetes. It increases gradually and sometimes seen at a very late stage when visual symptoms become obvious or when fundus findings are noted.

Through this study, we would like to assess:

1. The effect of diabetes on multifocal ERG findings.
2. The effect of different stages of diabetic retinopathy on multifocal ERG findings.

MATERIALS & METHODS

Study Design/Place of study: It was a cross sectional study

Study location: The study was conducted at M & J Western Regional institute of Ophthalmology, Ahmedabad from January 2013 to September 2015.

Inclusion criteria: Patients who had mild to moderate non proliferative diabetic retinopathy (NPDR) with clinically significant macular edema (CSME) age between 35-65 years of both sexes.

Exclusion criteria: Following subjects were excluded from the study: History of glaucoma, addiction of alcohol, addiction of smoking, retinal detachment due to any reason, Visual acuity <6/60 and mentally challenged patients

Sample Size:

On the basis of clinical evaluation and fundus examination, the subjects were divided into 3 groups -

GROUP 1: 20 eyes of patients who did not have diabetes were taken as control.

GROUP 2: 25 eyes of patients who had mild to moderate non proliferative diabetic retinopathy (NPDR) with clinically significant macular edema (CSME).

GROUP 3: 20 eyes of patients who had severe NPDR with CSME.

Method of data collection:

The data was collected by means of a personal interview by history taking, physical examination and performing the tests. The procedure of examination performed was explained to all the cases and written consent was taken prior to examination.

Visual acuity: Taken on Snellen's chart[7,8].

Slit lamp examination: It was done to examine the anterior segment as well as fundus using 90 D lense.

Fundus examination: It was done using slit lamp biomicroscopy,direct and indirect ophthalmoscopy.

Fundus fluorescein angiography: It was also done to completely evaluate the vascular system of retina.

Multifocal electroretinogram: It was done in each patients under same condition using ISCEV[9] Standards.

Classifications and cut-offs parameters

HBA1C: Patients with HbA1C >6.5 %(48 mmol/mol) were taken as diabetics.

Fasting and Post Prandial Blood Sugar: Diabetics: Subjects with fasting blood sugar >126mg/d1 or >7.0 mmol/1 and post prandial blood sugar >200 mg/dl or >11.1 mmol /1 and known cases of diabetes irrespective of their current treatment status and glycemic control status. All others were considered as non-diabetics.

Visual Acuity: Subjects with Visual Acuity 6/6 to 6/12 were taken in the control group. Visual acuity more than 6/60 were taken in diabetic group.

Statistical analysis: The data was analyzed using Microsoft excel by applying unpaired t-test for quantitative data and using Epi Info 7 version 7.0.8.3 by chi- square test for qualitative data . Correlation coefficients and Odds ratio were calculated for the different variables. Significance level was taken as $p < 0.05$.

RESULTS

Table 1. Age wise distribution of the subjects

AGE GROUP (Years)	GROUP 1	GROUP 2	GROUP 3
35-45	2	0	1
45-55	8	11	6
55-65	10	14	13

Table 2. Sex wise distribution of subjects

SEX	GROUP 1	GROUP 2	GROUP 3
MALE	12	10	14
FEMALE	8	15	6

Figure 1 shows higher values of FBS, PPBS and HbA1C in the diabetic group as compared to the control group and the difference was found to be statistically significant with the P value being less than 0.0001 for all the parameters. It shows a linear increase in the mean values of FBS, PPBS and HbA1C from group 1 to group 3 as the severity of the disease increases.

Comparison of latency and amplitude of erg in 3 groups: A mean value of the local responses in multifocal ERG was calculated in terms of N1, P1, N2 latencies and amplitudes of all the subjects and was analyzed.

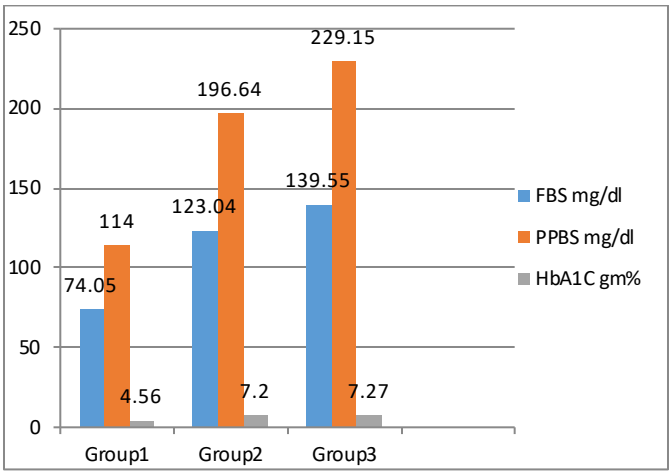

Figure 1. COMPARISON OF FBS(mg/dl) , PPBS (mg/dl) and HbA1C (gm%) in 3 groups

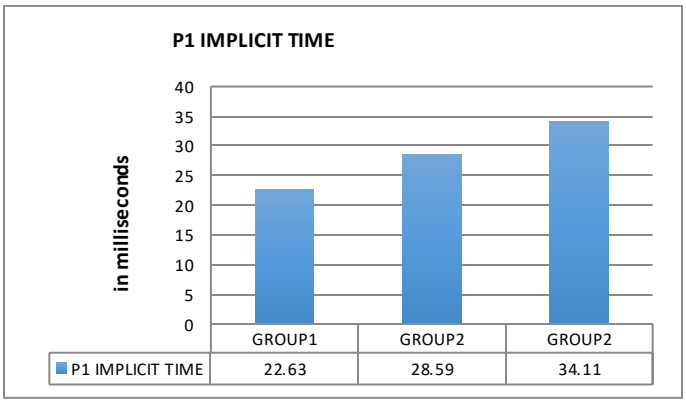

Figure 2. Comparison of p1 implicit time in 3 groups

Figure 2 shows an increase in the P1 implicit time from 22.63ms in group 1 to 28.59ms in group 2. A further increment was noted in group 3 where it is 34.11ms.

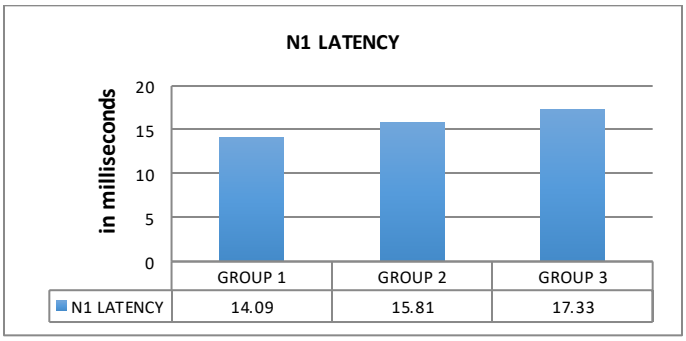

Figure 3. Comparison of n1 latency in 3 groups.

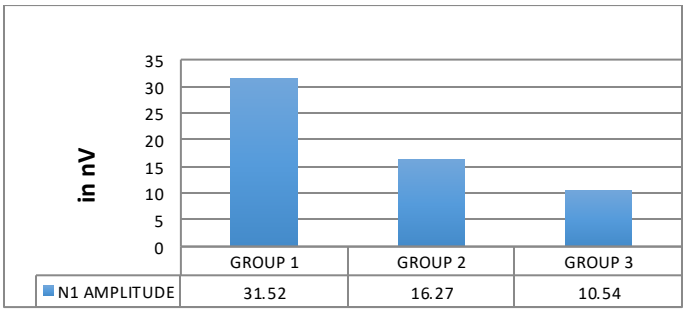

Figure 4. Comparison of n1 amplitude in 3 groups

Above figures (Figure 3 & 4) show an increase in N1 latency of 3.24ms and a decrease in N1 amplitude of 20.98nV from group 1 to group 3 suggesting that the latency increases and the amplitude increases as the severity of the disease increases.

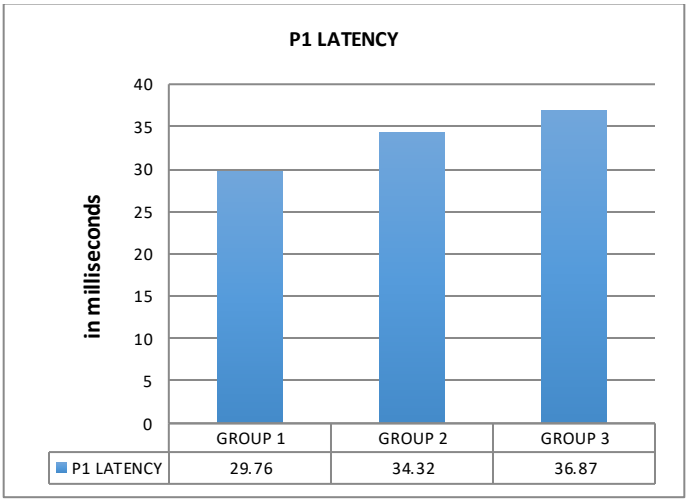

Figure 5. Comparison of p1 latency in 3 groups.

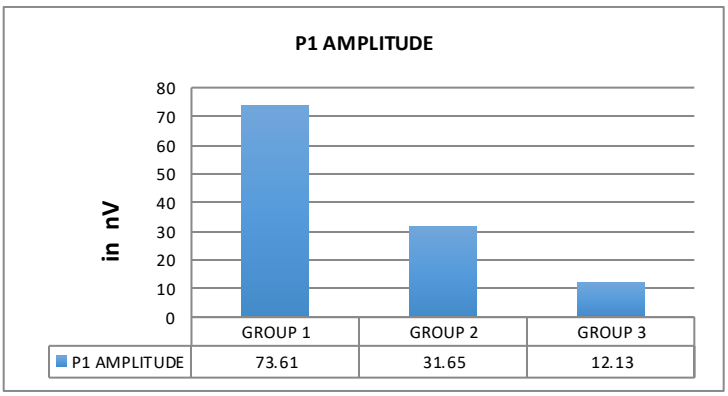

Figure 6. Comparison of p1 amplitude in 3 groups

The figures above (Figure 5 & 6) suggest that the P1 latency increases with the difference of 4.56 ms between group 1 and group 2 and difference of 2.55ms between group 2 and group 3. The P1 amplitude decreases significantly with a difference of 61.48 between group 1 and group 3.

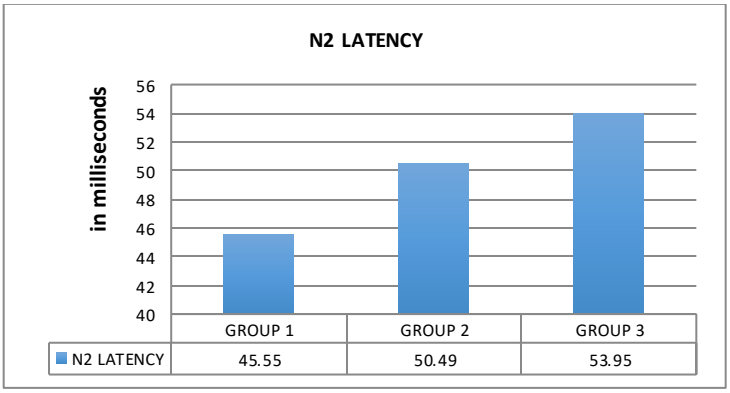

Figure 7. Comparison of n2 latency in 3 groups

The Figure 7 & 8 show an increase in the N2 latency and a decrease in N2 amplitude from group1 to group3.

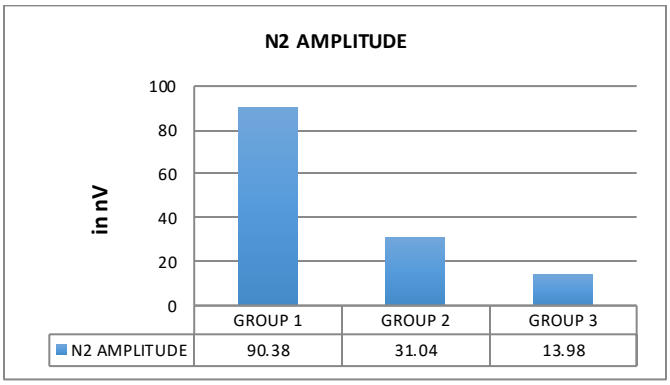

Figure 8. Comparison of n2 amplitude in 3 groups

DISCUSSION

Various studies have been done on patient with diabetic mellitus correlating the retinal function and potentials with severity and duration of diabetes using Multifocal ERG technique. Palmowski et al[10], in his study patients underwent multifocal ERG testing reporting that implicit times of Multifocal ERGs, averaged across the whole retina, were significantly delayed in some diabetic eyes without retinopathy. Whole field response delays were greater in magnitude and more prevalent among their group eyes with NPDR. It was seen that in patients with NPDR, N1 latency was delayed (mean=17.1ms), P1 latency (mean=32.3ms) and N1 amplitude was decreased (mean=19.9nV). In our study in severe NPDR, the N1 latency was 17.33ms, P1 latency was 36.87ms and the N1 amplitude was 10.54nV. Similarly the P1 implicit time in this study was delayed (27.7ms) which was found to be 28.59ms in our study in patients with mild to moderate NPDR and further delayed to 34.11ms in severe NPDR.

BRAD FORTUNE et al,[11] 1999, patients with non-proliferative diabetic retinopathy (NPDR) and patients without retinopathy compared with 16 age-matched, non-diabetic subjects found that in eyes with NPDR, the implicit time of responses was markedly delayed (e.g., up to 7 mSec from normal).

The results demonstrated that Multifocal ERG[12] implicit time analysis is highly sensitive method of assessment of local retinal function in diabetics. The range of local ERG implicit time observed for the normal eyes in this study was very narrow, consistent with the findings of other Multifocal ERG studies. Consequently, local ERG delays as small as 2.5mSec may be regarded as representing significant local retinal dysfunction in diabetic eyes.

In eyes with NPDR, delays of local responses were greater and were found throughout most of the retina than in eyes without retinopathy. Response delays were progressively worse towards the center of discrete ophthalmoscopic lesions in the retinopathic eyes. Local ERGs delayed by 4 msec or longer were found only in, or immediately adjacent to, diabetic retinal lesions. Local ERG amplitudes were more variable than implicit times - between normal eyes (10 times) and within normal eyes (5 times).

In our study the P1 implicit time was delayed by 11.48ms in severe NPDR and by 5.96ms in mild-moderate NPDR as compared to control. Similarly, the N1 latency delay was more than 3ms, N2 and P1 latency delay was more than 7ms as concluded by this study.

YING HAN ET AL,[13] 2004 concluded that the relative risk of development of new retinopathy over 1 year in the areas with abnormal baseline Multifocal erg implicit times was approximately 21 times greater than that in the areas with normal baseline Multifocal ergs. Mohamm.ad-sadegh farahvash,[14] 2006, studied forty-one eyes with clinically significant macular edema, tested and compared with 13 non diabetic subjects and found that local electroretinogram responses were significantly delayed and decreased in amplitude in patients with clinically significant macular edema.

CONCLUSION

Multifocal ERG is a useful indicator of diabetic retinopathy. The significant delay in local responses provide a chance for the detection and understanding of the various stages of diabetic retinopathy.

The normal values of the various parameters of mfERG are considered to be within a range rather than a discrete value. In our study the mean of these values was calculated in the control group with N1, P1 and N2 latency being 14.09ms, 29.76ms and 45.55ms, respectively. The N1, P1 and N2 amplitude was found to be 31.52nV, 73.61nV and 90.38nV, respectively. The maximum delay in N1, P1 and N2 latency was seen to be 3.24ms,7.11ms and 8.40ms respectively form the normal value. We have also found a decrease in the amplitude of the ERG waveform with the N1, P1 and N2 amplitude being 20.98 nv,61.48nV and 76.4 nV respectively from the normal value. Also, it is helpful in cases with clinically significant macular edema where the responses are remarkably delayed suggesting local retinal dysfunction and macular pathology. It provides us information regarding the condition of the macula and some idea about the extent of ischemia affecting this area.

In conclusion, we can say that the delayed responses obtained indicate abnormal retinal function corresponding to local discrete retinopathic lesions. It provides a very sensitive and objective assessment of the local retinal condition in various stages of diabetic retinopathy.

REFERENCES

1. Peter H Bennett, Williams C. Knowler: Joslin's Diabetes mellitus, 13th edition. Definition, diagnosis and classification of diabetes mellitus and glucose homeostasis, chapter 19, 331-339.

2. International diabetes federation. Global press release for world diabetes day. 2012.
3. Paul Zimmet, Jonathan Shaw: Joslin's Diabetes mellitus, 13th edition; Diabetes-A world wide problem, chapter 30, 525-52.
4. Yonemura D, Aoki T, Tsuzuki K. Electroretinogram in diabetic retinopathy. Arch Ophthalmol. 1962;68:19 —24.
5. Sutter EE, Tran D. The field topography of ERG components in man, I: the photopic luminance response. Vision Res. 1992;32: 433-446.
6. Bearse MA, Sutter EE. Imaging localized retinal dysfunction with the multifocal electroretinogram. J Opt Soc Am A. 1996;13:634- 640.
7. Odom JV, Bach M, Brigell M, Holder GE, McCulloch DL, Tormene AP (2010) ISCEV standard for clinical visual evoked potentials (2009 update). Doc Ophthalmol 120:111–119
8. "Visual acuity measurement standard" (PDF). www.icoph.org. Retrieved 2015-05-29.
9. Donald CH, Michael B (for the International Society For Clinical Electrophysiology of Vision). Standard for Clinical electroretinography (2011 update). Doc Ophthalmol. 2012 124:1-13
10. Palmowski AM, Sutter EE, Bearse MA, Fung W. Mapping of retinal function in diabetic retinopathy using the multifocal electroretinogram. Invest Ophthalmol Vis Sci. 1997;38:2586-2596
11. Brad Fortune, Multifocal Electroretinogram Delays Reveal Local Retinal Dysfunction in Early Diabetic Retinopathy Investigative Ophthalmology & Visual Science. 1999; Vol.40, 2638-2651
12. Seeliger MW, Kretschmann UH, Apfelstedt—Sylla E, Zrenner E. Implicit time topography of multifocal electroretinograms. InvestbOphthalmol Vis Sci. 1998;39:718-723.
13. Ying Han, Anthony J. Adams Multifocal Electroretinogram Delays Predict Sites of Subsequent Diabetic Retinopathy Investigative Ophthalmology & Visual Science. 2004;45(3), 948-954.
14. Mohammad-Sadegh Farahvash, Shiva Mohammadzadeh Pharm D. Multifocal eJectroretinogram in clinically significant diabetic macular edema, Arch Iranian Med. 2006; 9 (3): 261 — 265.