Research Article

Electrophysiological study of changes in retinal function following pan retinal photocoagulation in patients with diabetic retinopathy

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Abstract

Purpose: To Quantify the loss of Retinal Function due to Pan Retinal Photocoagulation in Diabetic Retinopathy patients using Full Field Electroretinography. **Methods:** This was a prospective observational study of 53 patients (105 eyes) with Diabetic Retinopathy selected for Pan Retinal Pan Retinal Photocoagulation (PRP) in a tertiary eye care centre. In all these patients Full Field ERG were done prior to PRP and then at 1 month and 3 months after PRP. The mean amplitudes and implicit times for different wave parameters at each visit (pre laser, 1 month and 3 months) were calculated. The values were paired as pre and 1 month, Pre and 3 month and 1month and 3 month and the mean differences of the pairs were calculated. Paired t test was used to calculate the significance of the variations. **Results:** It was found that the PRP produced a global loss of retinal function which was variable and was reflected in the statistically significant reduction in amplitudes of the Full field ERG waves. The average loss of amplitude at 3 months was 27.2% for "A" waves and 14.4% for "B" waves. The changes to the implicit time were not of much significance. As far as the visual results are concerned, Stabilisation (defined as no change in vision or a loss of vision less than 2 lines) or improvement of visual acuity could be achieved in 95% of the eyes. **Conclusions:** The amplitudes of the different waves of the Full Field ERGs can be used effectively in order to quantify the loss in Global Retinal function as a result of PRP. The implicit times however did not prove to be a reliable parameter to measure the change in retinal function.

Keywords: Amplitude; Diabetic Retinopathy; Electroretinography; ERG; Implicit Time; Pan Retinal; Photocoagulation; PRP; Retinal Function;

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INTRODUCTION

The study of Diabetic Retinopathy is always relevant because it is one of the leading causes of visual disability and blindness in the developed world, accounting for 10% of all new cases of blindness in the United States.[1] In a population-based study in South India,[2] diabetic retinopathy was detected in 1.78% of the patients screened, and was projected to become a significant cause of blindness in the coming decade. This blindness usually results from non-resolving vitreous haemorrhage, tractional retinal detachment and diabetic macular oedema. Of this the first two are the major causes of severe visual loss (defined as Visual acuity of <5/200) in the stage of Proliferative diabetic retinopathy[3,4,5.] Pan Retinal Photocoagulation has become the standard treatment for Diabetic patients with Proliferative Retinopathy, aimed at reducing the risk of blindness[3-14]. However one major side effect of the procedure is the destructive effect on the various layers of the Retina. This can result in some loss of visual function. Accurate functional assessment of the same can be done by using electrophysiological testing like ERG. Such assessment can help in titration of the laser burns so as to get the

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optimum result while minimizing the damage due to the laser. Effects due to different wavelengths of laser can be compared and the optimum wavelength can be arrived at. Most of the studies done are for Argon Laser which is not widely used now[15,16,17,18,19,2021,22]. The type of Lasers presently used are the DIODE Laser and Double Frequency Yag Laser. Not many studies have been done to quantify electrophysiologically the functional loss produced by DIODE Laser and Double Frequency YAG Laser during Pan Retinal Photocoagulation. The effect of these lasers on the photoreceptor layers and other layers of retina is not yet fully known. Knowing the damage to the different layers of the Retina will help us to device newer treatment modalities and newer laser management protocols to minimize the collateral damage to the Retina happening during the procedure. Our study aims to find out how Laser photocoagulation affects the various retinal layers.

AIMS OF THE STUDY

1. To quantify the amount of Loss of Retinal function due to PRP with Double Frequency YAG Laser in terms of Full Field ERG changes in "a" wave and "b" wave in rod response, mixed response andstandard white responses of ERG
2. To assess the effectiveness of Laser PRP in terms of stabilization of vision and prevention of severe visual loss

MATERIALS AND METHODS

This prospective observational study was conducted in the Retina Clinic of a Tertiary care hospital in Kerala, India from March 2012 to September 2013 (18 months duration). All patients in the age group 18 yrs to 70 yrs with Diabetic retinopathy posted for Pan Retinal Photocoagulation (PRP) during this period constituted the study population and patients were recruited consecutively till the calculated sample size of 105 eyes were reached. The following patients were excluded

Exclusion Criteria

1. Patients with Significant Cataracts which might interfere with electrophysiological testing
2. Very sick patients who cannot co operate for the electrophysiology testing
3. Patients with other co existing retinal problems like age related macular degeneration, Retinitis pigmentosa ; Vitreous Hemorrhage
4. Those who had undergone only grid laser

The above sample size of 105 eyes was calculated using the formula ***Sample Size (N)= $4\sigma^2/L^2$*** , where σ is the Standard deviation (SD) ; L is the allowed deviation. In calculating the sample size the values obtained by Liang *et al* [(20)] for the ERG reduction with respect to the amplitude of the "a" waves were used.(Implicit time variations were found to be not of much use and theortically a wave is supposed to be affected more by Laser).The sample size calculated was 105 for 5% allowed deviation and 95% confidence intervals and hence was fixed as 105 eyes. Patients selected for PRP and satisfying the inclusion criteria were selected for the study. In all these patients Full Field ERG was done prior to PRP and then at 1 month and 3 months after PRP. The ERG was done as per the ISCEV (International Society of Clinical Electrophysiology for vision) guidelines. For Full Field ERG Amplitudes and Implicit times of "A" and "B" waves were measured in dark adapted and light adapted conditions to get 3 set of values viz Rod response; Combined response and Cone response. Best Corrected Visual Acuity was recorded prior to laser and at each follow up using Snellen's chart.

Statistical Analysis

The values were entered in SPSS .The mean values for the different Wave parameters at each visit (pre laser, 1 month and 3 months) were calculated. The values were paired as pre and 1 month, Pre and 3 month and 1month and 3 month and the mean differences of the pairs were calculated. Paired t test was used to calculate the significance of the variations.

OBSERVATIONS AND RESULTS

105 eyes of 53 patients planned for Pan Retinal Photocoagulation were selected.(Patient NO: 19 only 1 eye was eligible as the other eye Diabetic Retinopathy did not require PRP.). Of the 53 patients 35(66%) were male and 18 (34%) were female. The age distribution of the sample is illustrated below in Table 1

Table 1: Percentage distribution of the sample according to age (Range 36 to 74 years)

Age	Count	Percent
<50	13	24.5
50-59	28	52.8
>=60	12	22.6
Mean ± SD	53.6 ± 7.4	

**: Significant at 0.01 level *: Significant at 0.05 level

The amount of Loss of Retinal function due to PRP in terms of Full field ERG waves was measured by calculating the mean values and finding the difference as shown in the following tables.

Table 2: Change in Full Field "A" Wave amplitude due to PRP

"a" amplitude		Mean	SD	N	Pair	Mean difference	Paired t	p
Rod	Pre	-8.5	9.0	92	Pre and 1M	2.7	2.51*	0.014
	1 Month	-5.9	8.9	92	Pre and 3M	3.5	2.33*	0.022
	3 Month	-5.0	12.8	91	1M and 3M	0.9	0.58	0.567
Con	Pre	-43.3	29.8	92	Pre and 1M	4.7	1.66	0.101
	1 Month	-38.6	15.4	92	Pre and 3M	9.9	2.92**	0.004
	3 Month	-33.6	19.5	91	1M and 3M	5.2	2.38*	0.020
Combined	Pre	-181.0	94.8	92	Pre and 1M	11.9	2.24*	0.028
	1 Month	-169.1	86.8	92	Pre and 3M	31.3	3.54**	0.001
	3 Month	-148.6	106.9	90	1M and 3M	20.5	2.51*	0.014

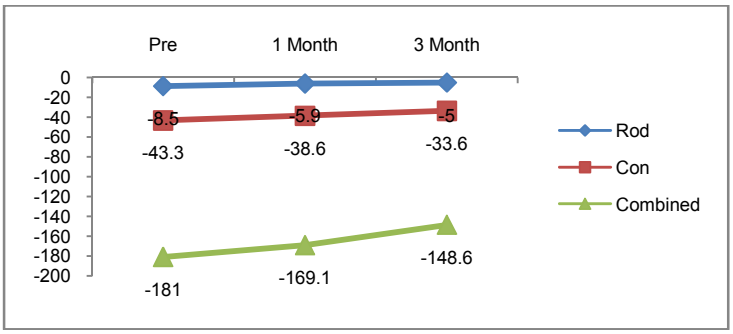

Figure 1: Mean FF ERG "A" amplitudes

The loss of retinal function given by the mean difference in the amplitudes of the "A" waves of Post PRP Full field ERG with respect to the Pre PRP ERG was found to be significant except in the case of the 1 month cone response. The change between the 1 month and 3 month values were also found to be significant except for the Rod response.

Table 3: Change in Full Field "a" implicit time due to PRP

a implicit time		Mean	SD	N	Pair	Mean difference	Paired t	p
Rod	Pre	50.5	18.4	92	Pre and 1M	1.1	0.49	0.623
	1 Month	49.3	24.4	92	Pre and 3M	6.0	3.05**	0.003
	3 Month	44.9	20.3	90	1M and 3M	4.8	2.17*	0.033
Con	Pre	24.1	6.5	92	Pre and 1M	0.8	1.21	0.230
	1 Month	23.4	4.7	92	Pre and 3M	0.6	1.12	0.264
	3 Month	23.5	7.4	90	1M and 3M	0.2	0.26	0.794
Combined	Pre	29.0	4.7	92	Pre and 1M	0.2	0.36	0.723
	1 Month	28.8	5.0	92	Pre and	1.0	1.68	0.096

	3 Month	27.9	5.1	90	3M 1M and 3M	0.8	1.38	0.171

**: Significant at 0.01 level *: Significant at 0.05 level

So when it came to implicit time the mean differences were not as significant as only the rod implicit time showed a significant change and that too only with the 3rd month values.

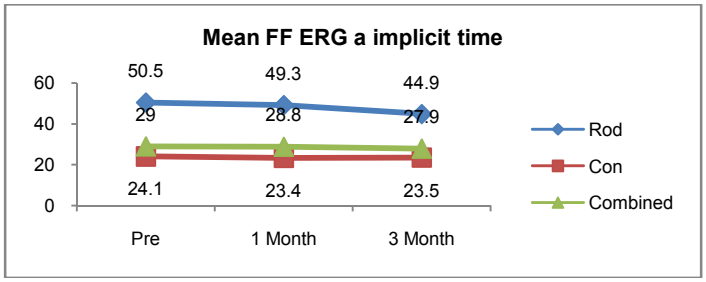

Figure 2: Graph showing the change in "a" implicit time

Table 4: Change in Full Field b amplitude due to PRP

b amplitude		Mean	SD	N	Pair	Mean difference	Paired t	p
Rod	Pre	38.5	43.9	92	Pre and 1M	3.8	2.36*	0.021
	1 Month	34.7	42.2	92	Pre and 3M	3.9	2.31*	0.023
	3 Month	35.4	38.2	90	1M and 3M	0.0	0.02	0.986
Con	Pre	99.2	57.1	92	Pre and 1M	14.1	2.34*	0.021
	1 Month	85.0	43.6	92	Pre and 3M	14.8	3.28**	0.001
	3 Month	82.2	35.4	90	1M and 3M	4.0	1.47	0.144
Combined	Pre	356.3	141.0	92	Pre and 1M	39.3	4.3**	0.000
	1 Month	317.0	129.9	92	Pre and 3M	64.6	6.13**	0.000
	3 Month	297.2	110.2	90	1M and 3M	24.5	3.51**	0.001

**: Significant at 0.01 level *: Significant at 0.05 level

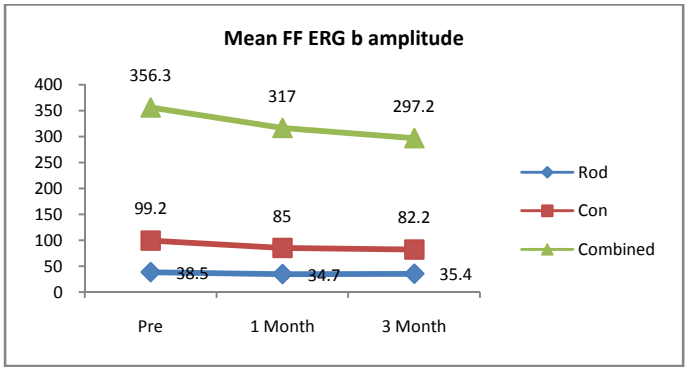

Figure 3: Graph showing the change in the b wave amplitude

Drop in the "B" wave amplitude from Pre PRP values to 1 month and 3 month values noted .These differences were found to be significant for at least 0.05 levels in all values except the 1 month to 3 month comparison.

Table 5: Change in Full Field b implicit time due to PRP

b implicit time		Mean	SD	N	Pair	Mean difference	Paired t	p
Rod	Pre	90.0	26.2	92	Pre and 1M	2.8	1.48	0.142
	1 Month	87.1	27.6	92	Pre and 3M	11.3	5.17**	0.000
	3 Month	79.1	28.6	90	1M and 3M	8.7	4.17**	0.000
Con	Pre	45.4	6.8	92	Pre and 1M	0.3	0.53	0.597
	1 Month	45.1	6.3	92	Pre and 3M	1.4	2.11*	0.037
	3 Month	43.9	7.1	90	1M and 3M	1.1	2.32*	0.022
Combined	Pre	56.4	8.2	92	Pre and 1M	1.0	1.23	0.221
	1 Month	55.4	8.8	92	Pre and 3M	3.4	3.68**	0.000
	3 Month	53.0	8.9	90	1M and 3M	2.4	3.91**	0.000

**: Significant at 0.01 level *: Significant at 0.05 level

The implicit time changes between the Pre PRP values and 1 month values were not found to be significant where as those between Pre PRP values and 3 month values were found to be significant. Thus it was the loss in amplitudes that were found to be significant and the %ge loss of the mean amplitudes with respect to the Pre Laser values were found and charted as shown in Figures 4(a) and 4 (b) . Maximum loss was seen in Scotopic A amplitudes responses at both 1 month and 3 month. 3 month loss was higher than 1 month. (see fig 4 (a)

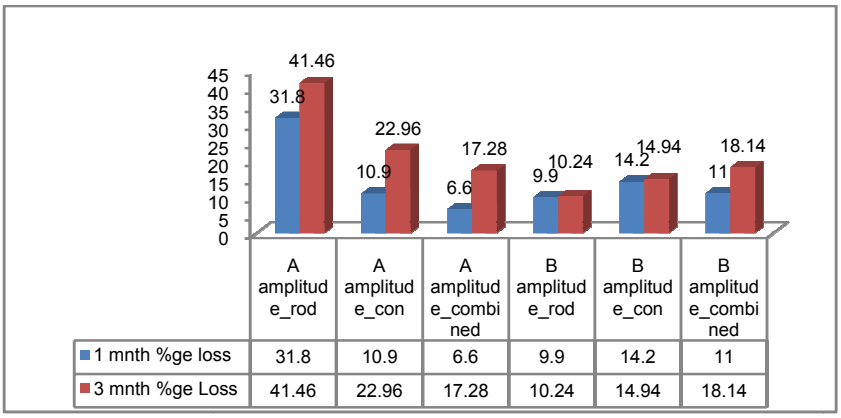

Figure 4(a): Graph showing loss of mean amplitude as a %age of pre laser mean values

When the total mean loss was compared "A" wave amplitude loss was found to be higher than the "B" wave amplitude loss. (See Fig 4 (b)

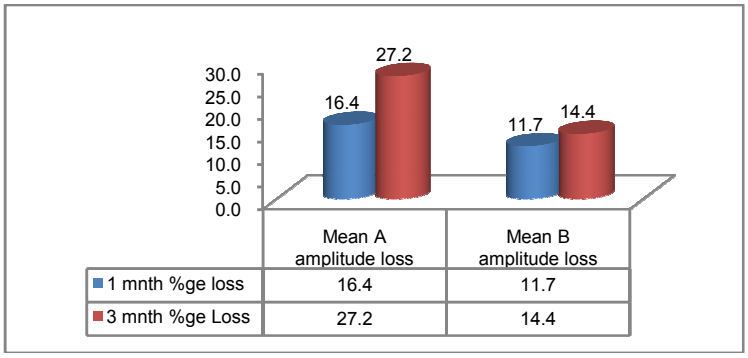

Figure 4(b): Mean Full Field ERG Amplitude Loss after PRP as %ge of Pre PRP Mean

The pre laser Snellen visual acuity was compared with 3 months post laser visual acuity and the results are classified as follows

Table 6: Visual outcome at 3 months after prp

	Number of Eyes	%Percentage
>2 lines drop in vision	5	5.1%
Same or 1 line drop (Stabilisation)	73	74.5%
Improved by more than 1 line	20	20.4%
Total	**98**	

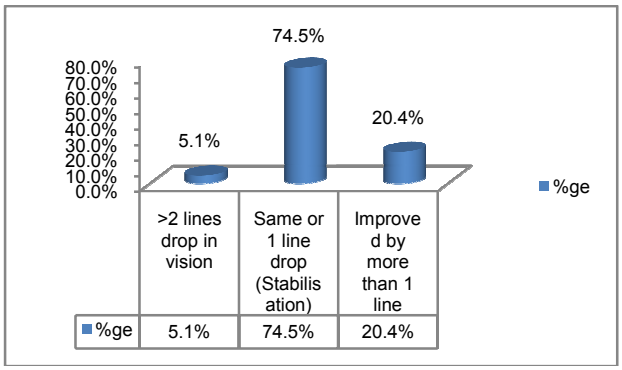

Figure 5: Visual outcome at 3 months Post PRP in terms of % ge of eyes

Thus Visual acuity deteriorated in only 5 eyes (5.1%). 20.4% eyes showed improvement of at least 1 line while the vision was stabilised in 74.5% eyes.

DISCUSSION

105 eyes of 53 patients planned for Pan Retinal Photocoagulation were recruited for the study.(In Patient NO: 19 only 1 eye was eligible as the other eye Diabetic Retinopathy did not require PRP.). Of the 53 patients 35 were male and 18 were female. The age of the patients enrolled ranged from 36 years to 74 years with a mean of 53.6 ± 7.4.Maximum number of patients belonged to the 50-58 age group (52%).This is similar to the results of a study conducted by Mousumi Bhattacharya[25], done among 350 diabetic patients attending two urban hospitals at Varanasi district, which concluded that the mean age of Type 2 diabetic patients(both male and female) were 50.97±9.74. In another study of Southern urban community [26], the average age of Type 2 diabetic patients were found to be 55.60±9.50 years which is also similar to our study. Out of this 6 patients(12 eyes) did not come for follow up after the laser and hence had to be discarded from the sample.1 eye developed vitreous hemorrhage and had to be taken up for vitrectomy and hence could not be studied further. It was found that PRP produced a global loss of retinal function which was variable and was reflected in the reduction in amplitudes of the Full field ERG waves. This reduction in amplitude was statistically significant in both "A" waves and "B" waves in different stimulus settings except in the case of 1 month cone response of "A" wave amplitude. This was probably because cone response gets more contribution from the central macular area which is relatively spared in Pan Retinal Photocoagulation. The magnitude of reduction of amplitude was more in the case of "A" waves as can be seen from Fig 4(b). The average loss of amplitude at 3 months was 27.2% for "A" waves and 14.4% for "B" waves. Previous studies have also reported widely variable results. E.g. 40% reduction as per Frank *et al*[16] and 10-95 % as per Ogden and associates[17]. But these values were for Argon Laser where as the Laser used in this study was Double frequency Yag. Thus the functional loss was found to be lesser than the studies with argon laser. The fact that the "A" waves were more affected suggests that the photoreceptors were preferentially affected when compared to the rest of the retina. This is in accordance with the findings of Perlman *et al*[15] and Gjotterberg M *et al*[19]. The changes to the implicit time were not of much significance. This was in agreement with the observations of Liang JC *et al*[20]. As far as the visual results are concerned, Stabilisation defined as no change in vision or a loss of vision less than 2 lines was achieved in 74.5% eyes (73 eyes) .Visual acuity improved by at least 1 line in 20.4% eyes (20 eyes).Only 5.1% (5 eyes) of the photocoagulated eyes lost at least 2 lines . Thus stabilisation or improvement of visual acuity could be achieved in 95% of the eyes. The corresponding number in other similar studies were 70%, 77% and 88 % [27,28,29]. Thus we could achieve results which were similar to or even better than other studies as far as visual acuity was concerned.

CONCLUSIONS

1. Some amount of functional loss occurs in the retina as a whole as a result of Pan Retinal Photocoagulation and this can be quantified using Full Field Electroretinogram.
2. The amplitudes of the different waves of the Full Field ERGs can be used effectively in order to quantify the loss in Global Retinal function as a result of PRP.
3. The implicit times however did not prove to be a reliable parameter to measure the change in retinal function.
4. Inspite of the functional loss induced, Pan Retinal Photocoagulation remains an effective tool in preserving vision in patients with Proliferative Diabetic Retinopathy.
5. The objective measurement of the ERG wave amplitudes can be used effectively in designing titrated PRP protocols intended to minimise the decline in retinal and macular function as a result of PRP. The same can also be used to arrive at ideal Laser wavelengths which can give optimal results with minimum loss of retinal function which is the need of the hour in Laser treatment of Diabetic Retinopathy.

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