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Role of blue or yellow perimetry in early detection of glaucomatous damage

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Abstract
Aim: Aim of the study was to detect early damage of the optic nerve head in patients with glaucoma with the help of blue on yellow perimetry, and to correlate the functional indices measured by blue on yellow perimetry with the structural parameters measured by optical coherence tomography.
Materials and Methods: This is a prospective cross sectional study conducted in the Department of Glaucoma, Regional Institute of Ophthalmology, and Chennai. 180 eyes of 93 subjects were screened. Out of 180 eyes, 158 eyes were glaucoma suspects who were referred with either suspicious disc, increased IOP, or with other risk factors. Complete glaucoma evaluation including standard white on white, blue on yellow perimetry, and optical coherence tomography was done, and the results were analysed.
Results: Out of 158 eyes, 137 eyes showed normal fields, 16 were borderline, five had abnormal fields in white on white (W-W) perimetry. With blue on yellow (B-Y) perimetry. 54 eyes were found to be normal, 36 eyes were borderline, and 68 eyes were abnormal. All the 137 eyes with normal fields in W-W perimetry were subjected to B-Y perimetry and analysed. 50 eyes had normal fields, 29 eyes had borderline fields, and 58 eyes had abnormal fields. Out of 16 eyes with borderline fields in W-W perimetry, 10 were abnormal, five were borderline and one turned out to be normal B-Y perimetry. All five eyes with abnormal fields in W-W Perimetry were abnormal in B-Y Perimetry. Retinal nerve fibre layer (RNFL) values by OCT and global indices in blue on yellow perimetry had a statistically significant correlation.
Conclusion: Blue on Yellow perimetry detects glaucomatous damage earlier in suspected glaucoma patients, compared to standard white on white perimetry. The functional parameters presented in the form of global indices in B-Y perimetry correlate with structural parameters given by optical coherence tomography.

Keywords: glaucoma suspects, standard automated perimetry, blue on yellow perimetry, optical coherence tomography, early detection of glaucoma

Introduction

Glaucoma is defined as a disturbance of the structural and functional integrity of the optic nerve that can usually be arrested or diminished by adequate lowering of the intraocular pressure [1]. Functional loss is recorded with visual field analysis by standard automated perimetry which is both sensitive and specific to detect field loss and it is a widely used technique that is arguably the gold standard to evaluate glaucomatous neuropathy and to monitor disease progression. It has been documented that upto 40 percent of the ganglion cells may be lost before a defect is apparent on the standard visual fields [2, 3]. Also numerous studies have shown that glaucomatous field abnormalities may be preceded by structural changes of optic nerve head and nerve fibre layer. Because glaucomatous damage is largely irreversible it is imperative to identify accurately eyes with early damage because they are at risk of continued injury. So newer advances in field examination have come into practice, which can detect field defects earlier before becoming evident on standard white on white automated perimetry. The visual function specific psychophysical strategies for detecting glaucomatous field defects, such as Blue on yellow perimetry, have greater sensitivity to early glaucoma than standard achromatic automated perimetry, a non-discriminative method for ganglion cell testing for glaucoma diagnosis [4, 5]. The ability of Blue on yellow perimetry to isolate a specific visual function associated with a subset of retinal ganglion cells might allow it to detect glaucomatous defects earlier and more extensively than Standard automated perimetry. This study is to find the role of short wavelength perimetry (blue on yellow perimetry) in early detection of glaucomatous damage.

Objectives of the Study

This study mainly evaluate the role of Blue on Yellow perimetry in the early detection of glaucomatous damage and establish whether the functional indices measured by the Blue on Yellow perimetry correlate with the structural parameters measured by Optical Coherence Tomography.

Materials and Methods

This is a cross sectional study prospectively planned. 180 eyes of 93 subjects who attended the glaucoma services in regional institute of ophthalmology were enrolled in this study. The study subjects were divided into two groups, glaucoma suspect and

established glaucoma groups. Out of 93 subjects, 82 subjects with 158 eyes were glaucoma suspects who were referred with either suspicious disc or IOP and other risk factors. 11 patients with 22 eyes were established primary open angle glaucoma on medical management.

Inclusion Criteria for Glaucoma Suspects

Subjects with open angles > 2 by Shaffer's grading, best corrected visual acuity >6/12 or better, refractive error not more than +/- 3 Dsph and +/-*2*Dcyl with any one of the following: positive family history, central corneal thickness corrected IOP >21 and <30 mmHg or Suspicious disc changes CD >/= 0.5, CD asymmetry between. the two eyes >0.2, splinter hemorrhage, focal notching, narrowing of neuroretinal rim, suspicious alteration in nerve fibre layer were included in this study.

Inclusion Criteria for Established Glaucoma Patients

Subjects with open angles >2, best corrected visual acuity > 6/12 or better, refractive error not more than +/- 3 Dsph and +/-*2*Dcyl, with at least three or more occasions of elevated IOP > 21 mmHg now on medical control, significant optic nerve head changes and definitive glaucomatous field defects as suggested by anderson's criteria were included.

Exclusion Criteria

The patients with closed/narrow angles by gonioscopy, congenital glaucoma, secondary glaucoma, patients who have undergone intraocular surgery or laser, high refractive errors, media opacities like cataract >grade II nuclear sclerosis, vitreous haemorrhage, patients who had evidence of retinal pathology like retinitis pigmentosa, diabetic or hypertensive retinopathy, age related macular degeneration, congenital colour vision defects were excluded from this study.

Recording of Visual Fields

Visual field analysis both standard white on white and blue on yellow perimetry was performed with octopus 311 perimeter. All the individuals were subjected to the tests under standard lighting conditions and in the same room. The refractive correction was done with trial lenses of 40 mm diameter. All the study subjects were briefed about the procedure and the tests were repeated if necessary. It was made sure that the patient's eye that is to be tested is wide open to avoid artifact defects. The eye occlude was applied in such a way that the patient feels comfortable. The patient was positioned with the eye close to the trial lens to avoid artifact (ring) scotomas. The reliable fields were taken for the study. Standard white on white perimetry was carried out with TOP (tendency oriented perimetry) using Goldmann type III stimulus. Blue on yellow perimetry was done with same fast threshold strategy TOP using yellow background and Goldmann target size V. The tests were repeated twice with an interval of two weeks to get a reliable field. An interval of one week was allowed between the white on white and blue on yellow perimetric tests. An abnormal field was defined as mean defect > 2, LV >6, Bebie's curve showing generalized depression with a focal dip, corrected probability plot showing three or more non edge points with P<5 of which one with P<1 and good reliability. RNFL analysis was done with Scanning laser ophthalmoscope - Optical coherence tomography (SLO-OCT OTI Tech) version VI.37 only in the glaucoma suspect group. The temporal delay of backscattered low coherence light (840 nm) from the anterior and posterior RNFL is measured by OCT. RNFL thickness is obtained as an average value and also in individual quadrants.

Results

180 eyes of 93 subjects were taken for the study, of which 158 eyes of 82 patients were categorized as glaucoma suspect group and 22 eyes of 11 patients were taken as the established glaucoma group.

Glaucoma Suspect Group

The age distribution of the subjects in the glaucoma suspect group was in the range of 18-74 years with a mean age of 46.12 years. The ratio of males to females in the glaucoma suspect group was 0.9:1 with a predominance of females. Out of the 82 glaucoma suspects, 6 patients were one eyed who lost the other eye because of a non-glaucomatous cause. In the total 158 eyes of the glaucoma suspect group, 30 eyes were having increased IOP >21 mmHg and <30 mmHg (CCT corrected), 116 eyes were having suspicious disc changes (enlarged CD ratio =/> 0.5, focal notching, narrowing of neuroretinal rim, disc haemorrhage, suspicious alteration in NFL), 12 eyes were with strong positive family history but having subtle features of glaucoma, 21 eyes were having suspicious fields in standard W-W perimetry.

The best corrected visual acuity of the eyes in the glaucoma suspect group was in the range of 6/6- 6/12, with exclusion of refractive errors more than +/- 3 Dsph and *+1-2* Dcyl, and media opacities like > grade II nuclear sclerosis.

Table 1: IOP Distribution

IOP mm Hg	Number of eyes	Percentage
10-15	56	35
16-20	72	46
>21	30	19
Total	158	100

The CCT corrected intraocular pressure in the glaucoma suspect group was in the range of 10 - 28 mmHg with a mean IOP of 17.20 mmHg with a standard deviation of 4.42.

Table 2: Cup disc ratio

CD RATIO	Number of Eyes	Percentage
0.3-0.4	36	23
0.5-0.6	94	59
0.7-0.8	28	18
Total	158	100

The disc changes noted were CD >/= 0.5, CD asymmetry between the two eyes >0.2, splinter hemorrhage, focal notching, narrowing of neuroretinal rim, suspicious alteration in nerve fibre layer. The CD ratio of the glaucoma suspect group was in the range from 0.3-0.8 with 59% eyes having CD ratio of 0.5-0.6.

Results of Standard W-W Perimetry

In the glaucoma suspect group, out of 158 eyes, 137 eyes showed normal fields, 16 showed borderline, 5 had abnormal fields. The mean duration taken for the subjects to perform the standard W-W perimetry was 2.53 minutes. The normal field showed mean defect < 2, loss variance (LV) <6, Bebie's curve within 2 SD,

corrected probability plot showing P > 5 and good reliability. Borderline fields showed borderline elevation of LV, depressed sensitivity in the locations suggestive of glaucoma with few relative and absolute defects. The abnormal fields showed mean defect > 2, LV >6, Bebie's curve showing generalized depression with a focal dip, corrected probability plot showing three or more non edge points with P<5 of which one with P<1 and good reliability.

The average values of the global indices with their standard deviation revealed elevation of mean defect and loss variance in borderline and abnormal fields. In Octopus abnormal mean defect is given as a positive number.

Table 3: Global indices

Standard W- W perimetry in glaucoma suspect group	Global indices					
	MS (mean sensitivity)		MD (Mean defect)		LV (loss variance)	
	Average	SD	Average	SD	Average	SD
Normal	26.92	2.23	0.98	1.72	3.6	1.84
Borderline	24.67	1.47	3.08	1.43	8.19	1.25
Abnormal	24.6	1.33	3.8	0.80	14.58	5.20

The Standard W-W perimetry was found normal in 87 % of eyes, borderline in 10 %, abnormal in 3%.

Results of Blue on Yellow Perimetry

Blue on yellow perimetry was done with the same TOP (tendency oriented perimetry) strategy with Goldmann type V stimulus for all 158eyes within one week from W-W perimetry. The reliable fields were taken for the study. Blue on yellow perimetry was found normal in 54 eyes, abnormal in 68 eyes, borderline in 36 eyes out of 158 eyes. The mean duration taken for blue on yellow perimetry was 2.83 minutes. The field was defined as normal when mean defect <2, LV<6, Bebie's curve within 2 SD, corrected probability plot showing deviation of P>5 with good reliability indices.

The abnormal field was represented by mean defect >2, LV >6, generalized depression with a focal dip, corrected probability plot showing three or more non edge points of P<5, of which one value P<1.Borderline fields showed borderline elevation of mean defect and LV, areas of depressed sensitivity in the locations suggestive of glaucoma, presenting as few relative and absolute defects.

The blue on yellow perimetry showed greater mean defect and loss variance in abnormal fields with reduction in mean sensitivity compared to normal fields in B-Y perimetry.

Table 4: Global indices

Blue on yellow perimetry in glaucoma suspect group (n=158)	Global indices					
	MS		MD		LV	
	Average	SD	Average	SD	Average	SD
Normal	22.95	2.53	1.56	1.95	3.97	1.49
Borderline	19.93	3.90	4.72	3.05	7.84	1.68
Abnormal	16.38	4.00	6.94	2.74	14.78	3.89

Comparison of W-W and B-Y Perimetry

The mean duration taken for the W-W and Blue on yellow perimetry was 2.53 and 2.83 minutes respectively. It shows that the time difference between the two perimetric tests is very minimal since both tests were done with the TOP strategy. The average values of global indices obtained from the two perimetric tests were compared. It showed lesser values of mean sensitivity and larger values of mean defect in Blue on yellow perimetry compared with W-W perimetry. The loss variance is lesser in borderline blue on yellow field, greater values in normal and abnormal blue on yellow field.

Table 5: Comparison of Global indices in W-W and B-Y perimetry

Fields	MS		MD		LV	
	W-W	B-Y	W-W	B-Y	W-W	B-Y
Normal	26.92 N=137	22.95 N=54	0.98	1.56	3.6	3.97
Borderline	24.67 N=16	19.93 N=36	3.08	4.72	8.19	7.84
Abnormal	24.6 N=5	16.38 N=68	3.8	6.94	14.58	14.78

137 eyes which showed normal fields in Standard W-W perimetry turned out to be abnormal in Blue on yellow perimetry in 58 eyes, normal in 50 eyes, and borderline in 29 eyes. 16 eyes which showed borderline fields in W -W perimetry turned out to be borderline in 5 eyes, abnormal in 10 eyes, normal in 1 eye with Blue on yellow perimetry.5eyes which showed abnormal fields in W-W perimetry and a suspicious disc, turned out to be normal in three eyes and borderline in two eyes.

The results of the two perimetric tests showed 50 eyes with normal fields, 5 eyes borderline, in both standard W-W perimetry and B-Y perimetry.

58 eyes and 29 eyes turned out to be abnormal and borderline respectively in B-Y compared with normal fields in W-W perimetry. 10 eyes with borderline fields in W-W perimetry turned out to be abnormal in B- Y perimetry. The eyes which showed abnormal fields in B-Y perimetry had increased IOP in 11 eyes, family history in 3 eyes, suspicious disc findings in 56 eyes, suspicious fields in 10 eyes. All the 6 one eyed suspects showed abnormal fields in B-Y perimetry. 10 eyes with borderline defects in W-W showed abnormal fields in B-Y perimetry

Rnfl Analysis in Glaucoma Suspect Group

RNFL thickness is measured as an average and in individual quadrants with optical coherence tomography. The overall average of the RNFL average obtained for the glaucoma suspect group was 115.81 microns with a standard deviation of 9.18. The

RNFL thickness values in the eyes which had abnormal fields in B-Y perimetry showed average RNFL of 110 microns with a standard deviation of 8.96. The RNFL thickness values in the eyes which had normal fields in B-Y perimetry showed average RNFL thickness values of 121.33 microns with a standard deviation of 8.03.

Correlation of Rnfl Thickness with Global Indices in B-Y Perimetry

The functional parameters presented in the form of global indices in B-Y perimetry are correlated with structural parameters given by optical coherence tomography as RNFL average using pearsons correlation coefficient.

Table 6: Correlation of RNFL thickness with global indices in B-Y perimetry

N=158 Eyes Global Indices of B-Y Perimetry	Rnfl Average		Superior Quadrant		Inferior Quadrant		Nasal Quadrant		Temporal Quadrant	
	R	P	r	P	R	P	R	P	r	p
MS	0.473	0.000	0.41	0.00	0.29	0.00	0.20	0.005	0.09	0.1
MD	-0.39	0.000	-0.353	0.00	-0.21	0.00	0.231	0.001	-0.03	0.3
LV	-0.49	0.000	-0.44	0.00	-0.33	0.0001	-0.21	0.003	-0.05	0.2

Correlation -r, probability –p

The mean defect and loss variance showed a negative correlation with the RNFL values.

The significant correlation between the structural and functional parameters improves the sensitivity of the B-Y perimetry in detecting glaucomatous damage.

Results of Standard W-W Perimetry

22 eyes of 11 subjects showed abnormal fields consistent with glaucomatous damage with mean defect >2, LV >6, generalized depression with a focal dip in Bebie's curve, more than three non-edge points depressed at the level of P< 5 and P<1. The time taken for the Standard W-W perimetry was 2.5 minutes.

The average of the global indices given by the standard W-W perimetry in the established glaucoma group.

Table 7: Global indices in W-W perimetry

Global Indices in W-W Perimetry	Average
Mean sensitivity	22.11
Mean defect	5.4
Loss variance	14.06

Results of Blue on Yellow Perimetry

22 eyes underwent Blue on yellow perimetry in the same machine Octopus 311 with an interval of one week from the standard W-W perimetry.

The subjects were already exposed to both Standard W-W and B-Y perimetry eliminating the learning effects. The time duration for performing the test in the established glaucoma group was 2.9 minutes using TOP strategy. The average values of the global indices showed lesser values of mean sensitivity and greater values of mean defect and loss variance compared to Standard W-W perimetry.

Table 8: Global indices in B-Y perimetry

Global Indices in B-Y Perimetry	Average
Mean sensitivity	14.25
Mean defect	8.89
Loss variance	19.01

The comparison of global indices in standard W-W perimetry and Blue on yellow perimetry showed that the defects shown in the B-Y perimetry were larger and deeper than the defects obtained in standard W-W perimetry.

Table 9: Comparison of global indices in standard W-W perimetry and Blue on yellow perimetry

Global Indices	W-W	B-Y
Mean sensitivity	22.11	14.25
Mean defect	5.4	8.89
Loss variance	14.06	19.01

In established glaucoma group the mean defect and loss variance given by the B-Y perimetry showed positive correlation with the loss variance obtained from the W-W perimetry. The correlation of loss variance of W-W and loss variance of B-Y was statistically significant. Outcomes: Blue on yellow perimetry detects glaucomatous damage earlier in suspected glaucoma patients compared to standard white on white perimetry. The functional parameter correlate with structural parameters showing the role of Blue on yellow perimetry in screening the patients with positive risk factors for glaucoma

Discussion

Blue on yellow perimetry is a modification of standard automated perimetry using the same perimeter and programs. It utilizes a 440 nm, goldmann type V stimulus at 200 milliseconds duration on a 100 candelas/m2 yellow background to test selectively the short wavelength sensitive cones and their connections. The test is most likely processed by the small bistratified blue- yellow ganglion cells, which encompass approximately 5% of the total population of retinal ganglion cells.

The study has been done with the aim of evaluating the utility of Blue on yellow perimetry in early detection of glaucoma. Although the standard W-W perimetry is the current gold standard for examining the fields in glaucoma, newer perimeters are developed to detect the glaucomatous damage in earlier stages. The ability of Blue on yellow perimetry to isolate a specific visual function associated with a subset of retinal ganglion cells might allow it to detect glaucomatous defects earlier and more extensively than standard automated perimetry. The primary strength of the study is that all examinations were done in a single population. The advantage of examining the performance of an instrument in a single population is that population based variables are eliminated, thus allowing direct comparison of the results obtained with different instruments.

The tests were repeated twice with an interval of two weeks to get a reliable field. An interval of one week was allowed between

the white on white and blue on yellow perimetric tests. An abnormal field was defined as mean defect > 2, LV >6, Bebie's Blue on yellow perimetry done in the glaucoma suspect group showed abnormal fields in 68 eyes (43%), normal fields in 54 eyes (34 %) and borderline fields in 36 eyes (23%). 42 % of normal W-W perimetry in 137 eyes turned out to be abnormal in B-Y perimetry. The 21% and 37 % of normal fields in W-W perimetry turned out to be borderline and normal in B-Y perimetry. The 16 eyes which showed borderline field in W-W perimetry turned out to be abnormal in 10 (63 %), normal in 1(6%), borderline in 5(31%). 5 eyes which showed abnormal fields in W-W perimetry turned out to be normal in 3 eyes and borderline in 2 eyes with B-Y perimetry. Both W-W and B-Y perimetry were found normal in 50(32%), borderline in 5(3%) of eyes. In this study most of the subjects who have been included had normal W-W perimetry. Abnormal fields were found in 68 (43%) in B-Y perimetry which showed normal and borderline fields with 37 % and 6% in W-W perimetry respectively. The results of B-Y perimetry are consistent with previous studies. Mansberger *et al.* published in a study comprising 86 patients with large CD ratio, that standard W-W and Blue on yellow perimetry results were abnormal in 44 (51%) and 52 (60%) of 86 patients, respectively [6]. Sanchez *et al*, showed a significant correlation between RNFL average in stratus OCT and MD and PSD values in Humphrey Short wavelength perimetry [7].

The learning effect may have an impact on the abnormal fields obtained with B-Y perimetry but normal W-W perimetry, since B-Y perimetry has learning effects till the sixth examination which can result in apparent reduction in retinal sensitivity. Wild *et al*. reported that care should be taken to ensure that, during the initial examinations, apparent field loss with Blue on yellow perimetry in patients exhibiting a normal field by standard W-W perimetry is not the result of inexperience in Blue on yellow perimetry [8]. Apparently deeper or wider field loss in the initial examinations with Blue on yellow perimetry compared with that exhibited by standard W-W perimetry in glaucoma also may arise from inexperience in Blue on yellow perimetry.

All the one eyed suspects showed abnormal fields in B-Y but normal and borderline in W-W perimetry helping to start treatment earlier and not waiting for the defects to appear in W-W perimetry. The subjects with normal fields obtained with B-Y perimetry and W-W perimetry are relieved of the anxiety of having glaucoma and avoiding unnecessary tests, but they are not totally free from the chance of developing glaucoma. The significant correlation between the functional indices and structural parameters improves the sensitivity and specificity of the B- Y perimetry in those situations. The mean defect and loss variance are greater in B-Y than W-W perimetry. The field defects estimated by B on Y were reproducible and larger compared to the W-W which is in par with previous studies.

The limitations of the study are being the study does not include the patients with lens opacity or high refractive errors. In those situations, the test gives unreliable reports and sometimes it is not possible to do the test. So in such patients the test has limited value. It is a pilot study in which the study sample is less, the duration of the study is shorter. The longitudinal studies comprising large group of subjects need to be done to improve the diagnostic accuracy of the test. The inherent problems of short term and long term fluctuations, test retest variability are not dealt in the study.

Conclusion

Blue on Yellow perimetry detects glaucomatous damage earlier in suspected glaucoma patients compared to standard white on white perimetry. The functional parameters correlate with structural parameters showing the role of Blue on Yellow perimetry in screening the patients with positive risk factors for glaucoma. It can confirm or exclude glaucoma in three fourth of suspects showing that the test is sensitive and also specific in diagnosis of glaucomatous damage. In conclusion, even though standard perimetry remains the gold standard in detecting glaucomatous damage, Blue on yellow perimetry proves to be a valuable tool in detecting the damage earlier in glaucoma suspects without lens opacities and starting the treatment to prevent irreversible visual loss but needs further longitudinal studies comprising large sample.

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