CORRELATION BETWEEN FREQUENCY DOUBLING TECHNOLOGY PERIMETRY AND HUMPHREY VISUAL FIELD IN GLAUCOMA SUSPECT PATIENTS

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ABSTRACT

The aim of this study was to compare the frequency doubling technique and Humphrey visual field results for detection of early visual field defect in glaucoma suspect patients. Sixty glaucoma suspect patients were studied during one year period at Nepal medical college teaching hospital eye out patient department. All patients underwent visual field examinations with the Swedish Interactive Threshold Algorithm standard, the central 24-2 threshold test with the Humphrey field analyzer (HFA) and the frequency doubling technique (FDT) C20-1 screening program. In this study, out of 120 eyes, 48 (40%) had abnormal blocks in FDT and 72 (60%) had normal FDT. Out of 48 eyes with abnormal FDT, 43 (35.8%) had normal HFA and 5 (4.1%) had abnormal clusters in HFA. Out of 72 eyes with normal FDT, 2 (1.6%) had abnormal clusters in HFA and 70 (58.3%) had normal HFA. Altogether only 7 (5.8%) eyes showed abnormal clusters in HFA and 113 (94.2%) showed no abnormal clusters which means FDT has ability to detect early glaucomatous visual field defect than HFA which was statistically significant ($p = 0.022$). This study showed significant correlation between abnormal blocks in FDT and HFA Mean Deviation (MD), Pattern Standard Deviation (PSD) and Glaucoma Hemi field Test (GHT) ($p = 0.000$, $p= 0.000$ and $p= 0.019$) respectively. This study concluded that FDT provides a useful complement to conventional automated perimetry test and can serve as an effective initial visual field evaluation for detection of glaucomatous visual field loss in glaucoma suspect patients.

KEYWORDS

Frequency doubling technology, glaucoma suspects, humphrey visual field.

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INTRODUCTION

Glaucoma suspect describes a person with one or more risk factors that may lead to glaucoma, but this individual does not have definite glaucomatous optic nerve damage or visual field defect. These patients with suspicious findings are at increased risk of developing glaucoma. If these patients are diagnosed and monitored for earliest sign of glaucomatous damage, then the chance of vision loss due to glaucoma will be less. The FDT perimeter is a portable, relatively inexpensive instrument designed for fast and effective detection of visual field loss.[1] It offers high sensitivity and specificity in the detection of early glaucomatous damage and in other disorders ranging from ocular, retinal, neurological and neuro-ophthalmological causes.[2,3] FDT has been shown to detect glaucomatous damage earlier than the automated perimetry. Automated perimetry is currently the mainstay for evaluating functional damage related to glaucoma.[4]HFA is one of the most widely used functional devices in clinical studies, but it can diagnose glaucomatous damageif more than 40% nerve tissue is lost.[5]

This study was done to correlate the results of FDT and HFA and to study if FDT could detect field loss earlier in comparison to HFA in glaucoma suspect patients. We have conducted this study as no such study has been done earlier in our setting.

MATERIALS AND METHODS

The study was conducted in outpatient department (OPD) of ophthalmology at Nepal Medical College Teaching hospital (NMCTH) from August 2014 to September 2015 and cases of primary open angle glaucoma suspects were studied. One hundred and twenty eyes of 60 glaucoma suspect patientswere studied. Sample size was taken using formula $n=Z^2pq/d^2= (1.9)^2x0.9x (100-0.9)/25=14$. Since the sample size was very less, we took 60 patients as in previous other studies also they had included about same number of patients. This was a comparative, cross sectional hospital based study. Glaucoma suspects were those with family history of glaucoma, suspicious optic disc like enlarged cup disc ratio (CDR) ≥ 0.6 and asymmetry of CDR ≥0.2 were included in the study. Patients with primary angle closure suspects, optic disc with thinning and notching neuroretinal rim, high IOP >21mmhg, patients on antiglaucoma drugs were excluded. Informed consent was taken from each patient. Ethical clearance was taken from Nepal medical college- Research and Ethical Sub-Committee (NMC-RESC Ref:29-072/073). All patients were done an ophthalmic examination including visual acuity by Snellen visual acuity, anterior segment by slit lamp examination, intraocular pressure measurement by applanation tonometry, central corneal thickness measurement by pachymetry, gonioscopy with single mirror goniolens and evaluation of the optic discs with +90Diopter lens. One hundred and twenty eyes of 60 patients were examined with screening C-20-1 program of FDT and Humphrey visual field using 24-2 Swedish Interactive Threshold Algorithm (SITA) threshold program. Both FDT and HFA were performed on the same day. Only the reliable (fixation losses <20%, false positives and false-negatives <33%) visual fields were included in the study. All the subjects were made to wear appropriate refractive corrections for both the tests and the pupils had a diameter of at least 3 mm. In case of unreliable fields, the test was repeated after few days and was included in the study. Then the more reliable field was selected for analytical purposes. Visual fields were considered to be abnormal according to Hodapp-Parrish-Anderson criteria.[6]

PERIMETRY

1. A glaucoma hemi field test (GHT) outside normal limits;
2. Pattern standard deviation (PSD) p < 5%, or
3. Three adjacent non-edge points p < 5% in the pattern deviation probability plot of which at least one point was p < 1 % and all points were on the same side of the horizontal meridian.

FDT

The clinically significant visual field defect on FDT was defined as presence of 2 adjacent points at p<5% and one of these p<1% deviation in the pattern deviation plot in either hemisphere.

For quantification of the defect score, we used the FDT results according to the criteria devised by Quigley, in which the total defect score was assessed by the number of abnormal points in 17 zones, including the central fixation zone times the severity of the measured defect on a scale from 1 (mild) to 2 (moderate) to 3 (severe).[7] Data were collected on research proforma. Data entry and analysis was done using SPSS 20.0 version. The chi-square test was used to find association between categorical variables. Correlation between FDT and different parameters of HFA was assessed with the Pearson correlation coefficient. P value less than 0.05 was considered significant.

RESULTS

The study included 120 eyes of 60 glaucoma suspect patients whose age ranged from 20 to 85 years with mean age of 42.33 years ± 15.7 (Table-1).

Table 1: Demographic features of the study subjects

Variables	Glaucoma suspects (N=60)	P value
Age (Mean ± SD) Range	42.33 years ± 15.7 20 - 85 years	0.26
IOP (Mean ± SD) Range	13.22 mm Hg ± 2.59 10-20mm Hg	0.40
CCT (Mean ± SD) Range	546.89 µm± 36.01 462-677µm	0.34
Cup disc ratio (Mean ± SD) Range	0.68 ± 1.9 0.3:1 to 0.7:1	0.50

There were 27 (45%) males and 33 (55%) females (Figure-1).

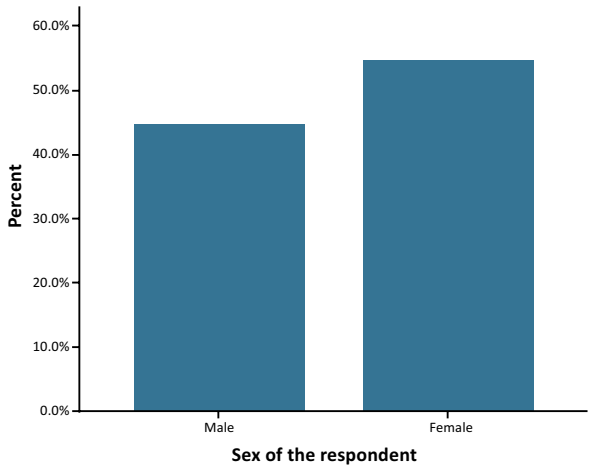

Fig. 1:
Sex distribution of glaucoma suspects

Twenty six (43.3%) were Indo-Aryan and 34 (56.7%) were Tibeto-Mongolian. Only 6 (10%) of the included glaucoma suspects had positive family history. Out of total included patients, 26 (43.3%) had enlarged CDR and 34 (56.7%) had asymmetric cup. The mean CDR was 0.68 ± 1.9 ranged from 0.3:1 to 0.7:1 (Table-1). There was a significant correlation between CDR and abnormal blocks in FDT (p= 0.020). There wereno significant correlation between CDR and HFA MD, PSD, GHT and abnormal clusters (p = 0.272, p = 0.740, p=0.287, p= 0.099) respectively (Table-2).

Table 2: Pearson correlation coefficient between CDR vs. FDT and HFA parameters Cup Disc Ratio Vs.

FDT and HFA parameters	Glaucoma suspects P value
Number of abnormal blocks in FDT	0.020
HFA MD	0.272
HFA PSD	0.740
HFA GHT	0.286
HFA abnormal clusters	0.099

Thirty (50%) had refractive error and all were myopic. Among myopic, 11 (18.33%) were of enlarged cup and 19 (31.6%) were of asymmetric cup. There was no significant correlation between myopia and suspects (p = 0.40). The mean IOP was 13.22 mm Hg± 2.59 ranged from 10-20 mmHg (Table-1). The mean CCT was 546.89 µm ± 36.01 ranged from 462 to 677µm (Table-1). There was a significant correlation between IOP and CCT(p = 0.001). The study showed no significant correlation between IOP and abnormal blocks in FDT (p= 0.107) but showed significant correlation between IOP and HFA PSD (p= 0.036) (Table-3).

Table 3: Pearson correlation coefficient between IOP vs. FDT and HFA parameters

FDT and HFA parameters	Glaucoma suspects P value
Number of abnormal blocks in FDT	0.107
HFA MD	0.093
HFA PSD	0.036
HFA GHT	0.578
HFA abnormal clusters	0.413

Out of 120 eyes, 48 (40%) had abnormal blocks in FDT and 72 (60%) had normal FDT. Out of 48 eyes with abnormal FDT, 43 (35.8%) had normal HFA and 5 (4.1%) had abnormal clusters in HFA. Out of 72 eyes with normal FDT, 2 (1.6%) had abnormal clusters in HFA and 70 (58.3%) had normal HFA. Altogether only 7 (5.8%) eyes showed abnormal clusters in HFA and 113 (94.2%) showed no abnormal clusters which means FDT has ability to detect early glaucomatous visual field defect than HFA which was statistically significant (p = 0.02). The mean abnormal blocks in FDT was 1.92 ± 3.02 (range 0-12). The mean PSD of HFA was 2.90 dB ± 2.09 ranged from 1.04 to 10.84 dB. There was a statistically significant correlation between abnormal blocks in FDT and HFA MD and PSD (p = 0.000 and p= 0.000) respectively. Out of 120 eyes 60 (50%) had within normal limit GHT in HFA, 23 (19.2%) had borderline and 37 (30.8%) had outside normal limit GHT. There was a significant correlation between abnormal blocks in FDT and HFA GHT (p = 0.019) (Table-4).

Table 4: Pearson correlation coefficient between FDT total number of abnormal blocks and HFA parameters FDT total number of abnormal blocks vs HFA parameters

	Glaucoma suspects P value
HFA MD	0.000
HFA PSD	0.000
HFA GHT	0.019
HFA abnormal clusters	0.022

Out of 48 eyes 19 (15.8%) had mild, 11 (9.2%) had moderate and 18 (15%) had severe abnormal FDT. The mean deviation (MD) of HFA was -3.4 dB ± 3.3 ranged from -0.13 to -19.53 dB. Out of 120 eyes 106 (88.3%) had MD < 6 dB, 12 (10%) had between 6-12 dB and 2 (1.7%) had > 12 dB. There was a statistically significant correlation between FDT grading and HFA MD grading (p = 0.001) (Table-5).

Table 5: Pearson correlation coefficient between FDT grading and HFA grading HFA MD grading

FDT grading		<6 dB	6-12 dB	> 12 dB	Total
	Normal	67	5	0	72
	Mild	18	1	0	19
	Moderate	8	3	0	11
	Severe	3	3	2	18
Total		106	12	2	120

*Pearson correlation significant = 0.001

So this study concluded that FDT provides a useful complement to conventional automatedperimetry and can serve as an effective initial visual field evaluation fordetection of glaucomatous visual field loss.

DISCUSSION

FDT is a method of visual field testing that relies on an optical illusion first described by Kelly in 1966.[8] The anatomical substrate of this effect has been described to the retinal ganglion cells (RGCs),[9] which are thought to be particularly susceptible to early glaucomatous damage.[10,11] This has led to the development of FDT perimetry with particular use as a glaucoma screening tool.[12,13]The FDT stimulus predominately stimulates the magnocellular ganglion cell pathway, which is primarily involved in motion detection and flicker detection. It is believed that the neurophysiological substrate for the frequency doubling illusion in humans lies in a subgroup of M cells, the proposed My cells, which show nonlinear characteristics to contrast and are thought to be preferentially lost in early glaucoma.[14]

FDT is a quick and efficient way of screening visual field with a very good sensitivity and specificity. [15] This perimetry is most likely a probe of contrast sensitivity of the magnocellular pathway.[16] This study was done to correlate FDT results with glaucomatous visual field defects, as assessed by HFA in glaucoma suspect patients. In this study, we found moderate correlation between the results of FDT and the results of HFA. Out of 120 eyes, 48 (40%) had abnormal blocks in FDT and 72 (60%) had normal FDT. Out of 48 eyes with abnormal FDT, 43 (35.8%) had normal HFA and 5 (4.1%) had abnormal clusters in HFA. Out of 72 eyes with normal FDT, 2 (1.6%) had abnormal clusters in HFA and 70 (58.3%) had normal HFA. Altogether only 7 (5.8%) eyes showed abnormal clusters in HFA and 113 (94.2%) showed no abnormal clusters which means FDT has ability to detect early glaucomatous visual field loss than HFA which was statistically significant (p = 0.02).The present study has shown that FDT can be used to detect glaucomatousvisual field loss earlier than HFA. It provides a useful complement to conventional automated perimetry test procedures and can serve as an effective initial visual field evaluation for detection of glaucomatous visual field loss. Similarly study done by S kogure *et al* showed 20% of normal HFA clusters in the HTG group showed abnormal FDT results. On the other hand, the normal HFA cluster of the NTG group had only 5% abnormal results on FDT which has suggested that FDT was more sensitive than HFA in eyes with HTG and FDT could not detect the scotoma in eyes with NTG.[17]

Another study by Nomdo M. Jansonius concluded that FDT was not able to detect glaucoma earlier than HFA but they have found a trend towards an increased risk of developing glaucomatous visual loss in patients with an abnormal baseline FDT test result.[18] Similarly another study by S kogure showed 4.0% of normal clusters of HFA with normal FDT results developed into scotoma cluster, 20.8% of normal clusters with abnormal FDT results developed into scotoma cluster with HFA at the third year which had concluded that an abnormal result in FDT shows a high risk of future scotoma on HFA after 3 years even if the original HFA perimetry showed normal results.[19] In a study by Kelly DH, the analysis of the FDT examinations during follow up revealed that in 59% of converters, the FDT abnormalities preceded SAP visual loss by as much as 4 years and the initial development of glaucomatous visual field loss as measured by SAP occurred in regions that had previously demonstrated abnormalities on FDT testing.[20]

Landers *et al*, also conducted a study to evaluate if FDT predicted future visual field loss with SAP just as it may be predicted with short wavelength automated perimetry and found that both short wavelength automated perimetry and FDT detected field loss earlier than SAP.[21]

Mean Deviation is an index of average severity of field loss and is affected by degree of loss and number of affected locations. Lower the MD, greater is the severity of field loss. This study showed significant correlation between abnormal blocks in FDT and HFA MD (p = 0.000). Pattern Standard Deviation indicates the degree to which the numbers in the total deviation plot are not similar to one another and is an index of unequalness in the amount of field loss. A larger PSD indicates a greater loss of field. There was a statistically significant correlation between abnormal blocks in FDT and HFA PSD (p = 0.000). Similarly showedsignificant correlation between abnormal blocks in FDT and HFA GHT (p = 0.019) (Table-4).This study has also shown a statistically significant correlation between FDT grading and HFA MD grading (p = 0.001) (Table-5). Similar to our study, Robert Casson study showed significant correlation between the total number of missed points on the FDT test and the Humphrey mean deviation (MD) score (p <0.001). The correlation between the total number of missed points on the FDT and the Humphrey corrected pattern standard deviation (CPSD) score was not as strong as the correlation with the MD, but was still highly significant (p<0.001).[22]

In S Patyal study the FDT showed good correlation with SAP SITA with regard to MD and PSD in the glaucoma suspect and found no significant difference in PSD between SAP SITA and FDT Matrix, with strong correlation between the devices in the glaucoma group.[23] The strong correlation between the number of missed points on the FDT perimetry and the Humphrey perimetry has been reported by Quigley HA and Patel SC and implies that counting the number of defects on the FDT may be a method of determining the presence and severity of glaucoma.[24,25] Ferreras A study showed that 20% of the patients with glaucoma suspects demonstrated functional losses in FDT and SWAP. They have concluded that FDT and SWAP detect functional losses in cases of suspected glaucoma before glaucomatous losses detected by SAP.[26] Similarly, S Lui study had concluded that FDT would be useful to monitor the onset of VF defects in glaucoma and may detect VF defects not evident in SAP.[27] Meira-Freitas D did a study to evaluate the ability of longitudinal FDT to predict the development of glaucomatous visual field loss on standard automated perimetry in glaucoma suspects and found that rates of FDT PSD change were highly predictive of the development of SAP visual field loss in glaucoma suspects.[28]

In conclusion our study suggests that a FDT screening program may help in the detection of initial visual

field damage in glaucoma suspect patients and provides a useful complement to conventional automated perimetry test. Limitation of this study is that our results are derived from cross-sectional study. Furthermore, longitudinal studies are needed to determine whether the FDT screening protocol would be useful for predicting future glaucomatous visual field defects.

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