

THE SENSITIVITY AND SPECIFICITY OF TOP, FDP AND GDx IN SCREENING FOR EARLY GLAUCOMA

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SUMMARY:

The purpose of this study was to evaluate the efficacy of three screening tests in detecting glaucoma in its early stage: the Tendency Oriented Perimetry (TOP) and Frequency Doubling Perimetry (FDP) visual field tests, and the Glaucoma Diagnostic (GDx) nerve fibre layer analyser. Eighteen patients with glaucoma who showed an early defect on HFA c 24-2 and twenty normals underwent the three tests. TOP showed a sensitivity of 94.4 % and a specificity of 75 %, FDP showed a sensitivity of 72.2 % and a specificity of 100%, and GDx a sensitivity of 77.7 % and a specificity of 60 %.

RÉSUMÉ:

Le but de cette étude était d'évaluer l'efficacité de trois tests de dépistage du glaucome à un stade précoce: les tests du champ visuel Tendency Oriented Perimetry (TOP) et Frequency Doubling Perimetry (FDP), et l'analyseur de la couche de fibres optiques Glaucoma Diagnostic (GDx). Dix-huit patients glaucomateux qui présentaient un déficit débutant du champ visuel au HFA c 24-2 et vingt patients normaux ont subi les trois tests. Le TOP montrait une sensibilité de 94,4 % et une spécificité de 75 %, le FDP montrait une sensibilité de 72,2 % et une spécificité de 100 %, et le GDx une sensibilité de 77,7 % et une spécificité de 60 %.

SAMENVATTING:

Deze studie had tot doel de efficiëntie van drie screening tests voor de opsporing van glaucoom in het vroege stadium na te gaan: de gezichtsveld tes-

ten Tendency Oriented Perimetry (TOP) en Frequency Doubling Perimetry (FDP), en de zenuwvezellaagdijktometer Glaucoma Diagnostic (GDx). Achttien glaucoom patiënten die een beginnend defect vertoonden op het HFA c 24-2 gezichtsveld en twintig normalen ondergingen deze drie tests. De TOP toonde een sensitiviteit van 94,4 % en een specificiteit van 75 %, de FDP een sensitiviteit van 72,2%, en een specificiteit van 100 % en de GDx een sensitiviteit van 77,7 % en een specificiteit van 60 %.

KEYWORDS

Glaucoma, Screening, Tendency Oriented Perimetry, Frequency Doubling Perimetry, Nerve fibre Layer Analyser

MOTS-CLÉS

Glaucome, Dépistage, Tendency Oriented Perimetry, Frequency Doubling Perimetry, Analyseur de la couche de fibres optiques.

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received 29.10.99
accepted 03.01.00

INTRODUCTION

By the year 2000 primary glaucoma will affect 66.8 million people in the world, with 6.7 million suffering from bilateral blindness (7). This makes primary glaucoma the second largest cause of bilateral blindness after cataract. The fact that glaucoma blindness is irreversible, but often installs after a slowly progressive asymptomatic stage, calls urgently for the development of improved methods of screening (7). Indeed, it is estimated that in developed countries only half of the glaucoma patients are aware of their disease, a number which is even lower in developing countries.

Although screening for glaucoma appears logical, the cost-effectiveness of the current methods has been questioned (1,3): tonometry only detects fewer than half of the glaucoma patients (8).

Functional tests of peripheral visual function have proved to be excellent for follow up of glaucoma and are now also used as potential screening approaches. We studied the screening value of two new visual field tests: the Tendency Oriented Perimetry (TOP, part of the Octopus program, Interzeag), and the Frequency Doubling Perimetry (FDP, manufactured by Humphrey instruments).

We compared the results to a third test, the Glaucoma Diagnostic (GDx, manufactured by Laser Diagnostic Technologies), which is being used to detect glaucomatous damage by measuring the nerve fiber layer (NFL) thickness.

While other authors have already discussed the effectiveness of FDP and GDx in detecting glaucoma in general, without differentiating on the stage of disease, we decided to evaluate the efficacy of the three tests in detecting glaucoma in its early stage (6,10).

SUBJECTS, MATERIALS AND METHODS

We compared a group of patients with early glaucoma to a normal control group.

The inclusion criteria for the normal subjects are shown in table 1. They all performed a reliable Humphrey c 24-2 SITA Standard visual field test (HFA) which was defined as normal if (1) both the Mean Deviation (MD) and Pat-

tern Standard Deviation (PSD) were below 2 dB, and (2) the Glaucoma Hemifield Test was normal or borderline.

From our outpatient clinic we selected the subjects with glaucoma. They were included if they showed a glaucomatous optic disc and an early defect on the HFA, which correlated with the optic disc appearance. An early defect was defined as an abnormal Glaucoma Hemifield Test in combination with a PSD between 2 and 20 dB and a MD lower than 7.5 dB. The patient was only selected if the same defect was reproducible at least twice. Only one eye per patient was included.

The selected subjects of the two groups underwent the three following screening tests on the same day and in random order:

1. The TOP program of the Octopus visual field analyser. This program presents each test location only once and calculates the threshold using the principal of correlations between neighbouring testlocations (5).
2. The c-20 supra threshold screening modality of FDP. This visual field test uses a target consisting of a low spacial frequency sinusoidal grating which undergoes a high temporal frequency counterphase flicker, causing the grating to appear twice its actual spatial frequency. This phenomenon is called frequency doubling illusion and is believed to be mediated by mechanisms in the magnocellular pathway, in particular the My ganglion cells. (2, 4) In this screening test 17 visual field locations are tested. The subject is asked to press the response button when a target consisting of flickering vertical black and white bars appears on the screen. An abnormal response will appear as a shaded testlocation on the printout.
3. The GDx, which is a nerve fibre layer analyser. It is a scanning laser polarimeter which calculates the thickness of the nerve fibre

Table 1: *Inclusion Criteria for normal subjects.*

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1. Refraction $< \pm 6$ Diopters
 2. No previous intraocular surgery
 3. No ocular pathology
 4. No or discrete lensopacities
 5. Normal optic nerve head
 6. Age of 50 years or older
 7. Intraocular pressure ≤ 22 mmHg
 8. Normal HFA c 24-2 Sita Standard visual field test.
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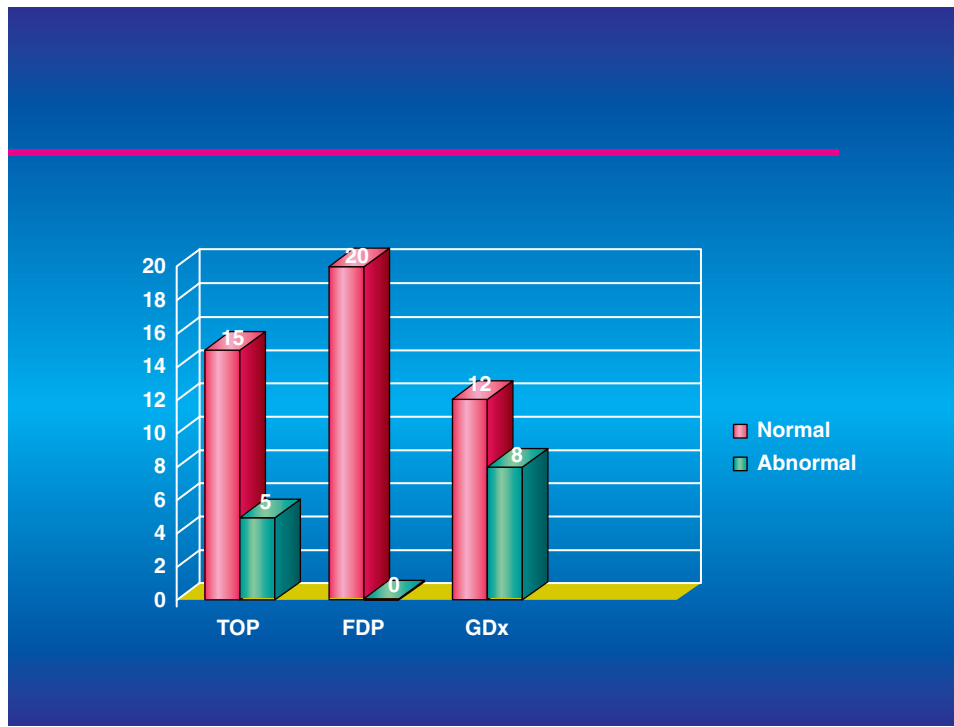


Fig. 1: TOP, FDP and GDx results in the normal group. (n=20)

layer by measuring the phase shift of incoming light, presumably caused by the microtubules of the retinal ganglion cells(9). It is a structural test, which means that it is not dependent on the patient's response as are visual field tests.

Five consecutive GDx measurements were taken per patient and the one with the highest quality score was selected. The visual field tests TOP and FDP were only allowed to be performed once, as would be done in a screening setup.

For each group, the three tests were then protocolled as normal or abnormal by the following criteria of abnormality:

- (1) The TOP was considered abnormal if the Loss Variance (LV), was greater than 6 dB,
- (2) The FDP, if at least one out of the 17 test locations appeared shaded on the print-out, and
- (3) The GDx, if at least one of the four following parameters resulted borderline or out-

side normal limits: the "symmetry", which reflects the symmetry between the thickness of the superior and the inferior quadrant, the "superior average" and "inferior average", and the "number", an experimental number between 0 and 100 which is a reflection of all the 215 parameters obtained by the GDx scan. The number was considered as borderline between 30 and 70, and outside normal limits above 70.

RESULTS

Twenty normals and eighteen glaucoma patients were included in the study and completed all the tests in a reliable way.

The mean age of the normals was 65,3 years (range 55 -79 yrs). Nine were females and eleven were males. The mean (\pm SD) MD and PSD on the HFA were respectively 0,87 (\pm 0,95) and 1,57 (\pm 0,25).

On average the glaucoma patients were 8 years older (mean 73 yrs, range 60 - 83 yrs).Five

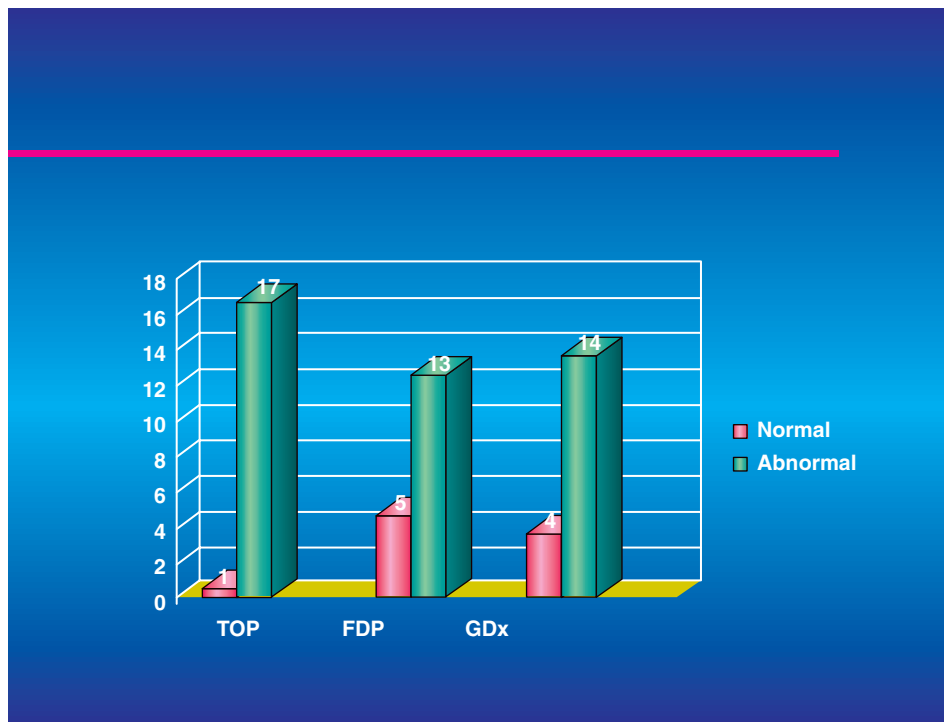


Fig. 2: TOP, FDP and GDx results in the glaucoma group. (n=18)

were females and thirteen were males. The mean (\pm SD) MD and PSD on the HFA were respectively 3,42 (\pm 2,13) and 5,13 (\pm 2,64). Thirteen patients had primary open angle glaucoma, three chronic angle closure glaucoma, one pseudoexfoliative glaucoma and one normal tension glaucoma.

The results of the tests for both groups are presented in figure 1 and 2, and the resulting sensitivity and specificity for the three tests in figure 3. Using the criteria of abnormality mentioned above, the TOP was normal in 1 of the 18 glaucoma patients and 15 of the 20 normals. This represented a sensitivity of 94,4% and a specificity of 75 % respectively.

The FDP screening test was normal in 5 of the 18 glaucoma patients and in all of the 20 normal subjects. (sensitivity of 72,2 % and specificity of 100 % respectively)

The GDx was normal in 4 of the 18 glaucoma patients and 12 of the 20 normals. (sensitivity

of 77,7 % and specificity of 60 % respectively)

The according diagnostic precision was 0.71 for the TOP, 0.72 for the FDP, and 0.47 for the GDx. (Fig. 4) This difference was not statistically significant.

The diagnostic precision is the sum of the true positives (the number of glaucoma patients detected as abnormal by the test) and the true negatives (the number of normals detected as normal by the test) divided by the sum of the total number of glaucoma patients and the total number of normals included in the study.

The mean test time in the normal group was 42 seconds for the FDP and 2 minutes and 16 seconds for the TOP. The GDx took approximately 5 minutes per patient.

In all the glaucoma patients who were detected by TOP and FDP, the visual field defects were congruent with the defects detected by the HFA.

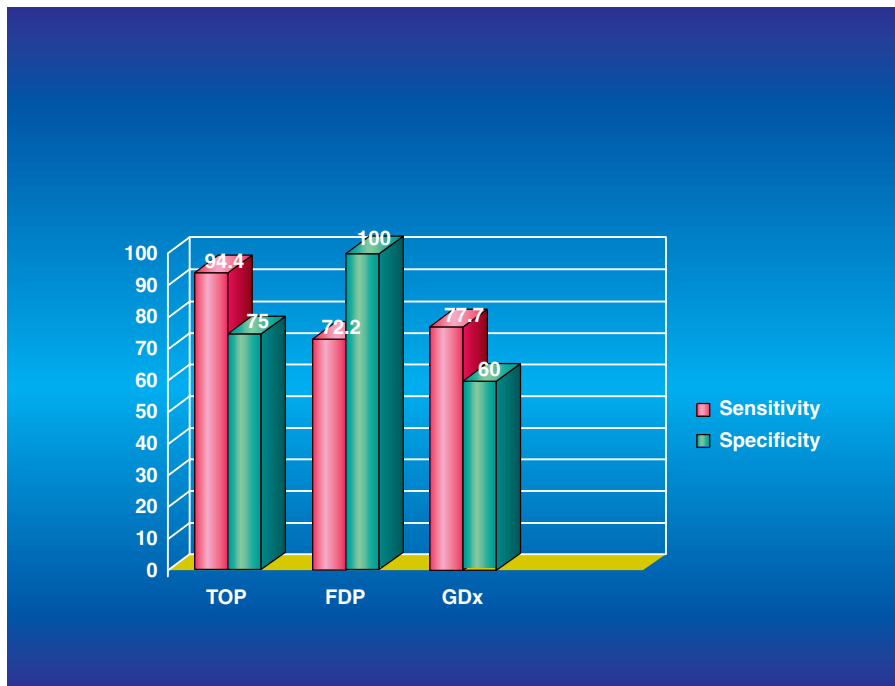


Fig. 3: Sensitivity and specificity of TOP, FDP and GDx (%)

Diagnostic Precision

TOP	0.71
FDP	0.72
GDx	0.47

Fig. 4: Diagnostic precision of TOP, FDP and GDx.

DISCUSSION

Our study showed that TOP and FDP had a high diagnostic precision in detecting early glaucoma. Surprisingly the GDx showed the lowest diagnostic precision and a sensitivity lower than the TOP and comparable to the FDP. Since structural damage usually precedes functional damage, one would expect the GDx to be the most sensitive of the three tests in detecting early glaucoma (11). Yet it failed to detect NFL damage in 4 of the 18 patients. One explanation might be the fact that the results depend on the definition of the criteria of abnormality. The GDx software looks at 215 parameters in total, 15 of which are shown on the printout. This obliges the examiner to make a selection of the parameters to be used for interpretation of the results. Until now, there is no consensus on which parameters to use. We chose the number, the symmetry, the inferior average and the superior average, as recommended by the manufacturer. Our GDx apparatus did not show the inferior to nasal ratio, a parameter used by Lemij et al., who found a surprisingly high sensitivity (96 %) and specificity (93 %) (10). Another explanation for our lower sensitivity and specificity might be the fact that we only included patients with early glaucoma, whereas Lemij et al included patients with early, moderate and advanced glaucoma.

The same applies for the FDP: Quigley et al studied the efficacy of the screening modality of the FDP on 76 glaucoma patients and found a sensitivity of 91 % and a specificity of 94 %. These high percentages might also be explained by the fact that they did not differentiate on the stage of glaucoma when including the patients. (6) In our study the supra-threshold modality of the FDP had the highest diagnostic precision, but the lowest sensitivity. This might be surprising since several hypotheses concerning early glaucoma, such as the large diameter ganglion cell hypothesis and the reduced redundancy hypothesis, suggest that FDP should be particularly sensitive in detecting beginning glaucoma (2,4). Our study is too small to make final conclusions, but using the full threshold instead of the supra-threshold modality, the FDP would probably have had a higher sensitivity, without losing the advantage of a short

testing time. (The full threshold FDP test takes approximately 3 minutes.)

Indeed, the easiness to perform the test is one of the important aspects in screening. The ideal test would be rapid, inexpensive, applicable to most subjects and easy to perform. It should also be easy to interpret and have a high sensitivity and specificity (6).

Important advantages of the FDP are: the short test time and the resistance to blur effect (no correction needed for refraction errors of up to ± 7 D) and to pupil size change. The opposite eye is automatically occluded and no skilled operator is required to perform the examination. The instrument is light, easy to carry and relatively cheap. The disadvantages are: insufficient fixation check and rather poor test reproducibility in borderline cases (2).

As the TOP needs to present each test location only once to calculate the threshold value, the test takes less than three minutes. This means a significant reduction of exploration time compared to the other full threshold Octopus programs (5). In our study TOP also had a high sensitivity and high diagnostic precision.

GDx is a test which does not take long, does not depend on patient cooperation and does not require pupil dilation. The technique is still questioned and there is a lack of consensus on the interpretation of the results.

CONCLUSION

In this study, TOP and FDP had a high and comparable diagnostic precision in detecting early glaucoma. TOP had the highest sensitivity. The lower specificity however will result in overscreening. The FDP supra-threshold strategy on the other hand, had a specificity of 100 %, but the test will fail to detect some patients with early glaucoma due to the lower sensitivity. GDx showed a sensitivity comparable to that of the FDP, but the lowest specificity and diagnostic precision.

Although the number of patients is rather small, our study suggests that TOP and FDP can be efficient screening methods for early glaucoma.

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