New diagnostic technologies show potential in screening for glaucoma

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in Vilamoura, Portugal

A COMBINATION of scanning laser polarimetry and Humphrey Matrix frequency doubling technology perimetry (Carl Zeiss Meditec) for mass glaucoma screening, said Gabor Hollo MD, PhD, DSc, Department of Ophthalmology, Semmelweis University, Budapest, Hungary.

In a study involving 233 volunteers in a seven-day glaucoma screening programme, analysis of data from the two diagnostic devices could detect early glaucoma with moderate sensitivity and high specificity, he told a meeting of the European Association for Vision and Eye Research.

Dr Hollo noted that there is an urgent need for easy-to-use and reliable means of detecting early glaucoma. The population of most countries of the developed world is ageing and the prevalence of glaucoma is likely to increase, he said.

Several studies have demonstrated that early detection and treatment can slow the progression of the disease and preserve vision. However, at present 50 per cent of glaucoma cases go undetected until irreversible vision loss has already occurred. One reason for that is the healthcare services of most countries are not up to the task of clinically examining the total population or even those who are most at risk for glaucoma.

“Early treatment can be much more useful than treatment of advanced cases. But we should avoid diagnostic techniques which yield a lot of false positives and overload the health service system by instead using very specific tests and population-based glaucoma screening if ophthalmologists go out into different areas and try to screen patients one by one it can be very precise but it is not cost-effective and cannot be used for mass screening, so we need something different,” he said.

Local screening programme

The Hungarian researchers advertised their screening programme in advance in local newspapers and on the radio, emphasising its particular relevance to individuals with such risk factors for glaucoma as age over 60 years and a family history of the disease.

Of the total group, 181 participants underwent testing with both GDx-VCC and Matrix frequency doubling technology perimetry (M-FDT) by examiners masked as to the clinical findings, while the remaining patients proved unsuitable for such tests.

The GDx-VCC is a fifth-generation scanning laser polarimeter that scans the back of the eye using a polarised light beam to provide imaging of the retinal nerve fibre. The Matrix Frequency doubling technology perimetry uses two low spatial frequency sinusoidal gratings, which alternate to produce a “frequency doubling illusion”. The instrument automatically varies the contrast between dark and light portions of the target to determine the contrast at which the flickering target can be detected.

To determine the accuracy of the diagnostic instruments, a glaucoma specialist carried out an examination of all participants. The specialist measured visual acuity and IOP and performed slit-lamp and optic nerve head examinations.

Anyone who tested positive and whom the clinical examination indicated as a glaucoma suspect underwent a more detailed clinical examination within three months of the screening so that the final diagnosis was available for analysis of the study’s results. The parameters assessed in the study included sensitivity, specificity, accuracy, likelihood ratio for the different instrument-provided data including nerve fibre indicator (NFI) and localised nerve fibre defect, Dr Hollo said.

He explained that the positive likelihood ratio compares the probability of a specific test result in a glaucoma patient to the probability of the same result in a patient without the disease. The NFI provides an overall measure of the probability of glaucoma in an eye while the nerve fibre defect parameter provides a measure of localised damage.

The researchers found that glaucoma was present in 39 eyes of 28 participants among the 345 eyes of 181 participants that underwent GDx-VCC and M-FDT measurements. That amounted to a prevalence of 11.3 per cent. All but two of the glaucomatous eyes had early damage.

The glaucoma cases included two cases of primary open-angle glaucoma, 17 cases of normal tension glaucoma, one case of pigmentary and four of exfoliative glaucoma and one case of angle closure glaucoma.

“The incidence of glaucoma in this study population was rather high and that may have been because we stressed the importance of risk factors for the disease. I should point out that normal tension glaucoma was represented in more than 40 per cent, and more frequently than high tension POAG,” Dr Hollo noted.

He added that single IOP readings had positive likelihood ratio of around 1.0, which suggested that this measurement had no predictive value and provided no information.

Combined measurements best

When the tests were evaluated separately, the GDx-VCC nerve fibre indicator (NFI) findings performed best with 25.6 per cent sensitivity, 97 per cent specificity, and 89 per cent accuracy, and a positive likelihood ratio of 8.5. Matrix-FDT testing was of no predictive value on its own but seemed to complement the findings of laser polarimetry.

That is, when M-FDT screening, GDx-VCC NFI and nerve fibre defect parameters were measured separately, the sensitivity increased to 41.7 per cent, accuracy and specificity remained high at 92 per cent and 97 per cent, respectively, and the positive likelihood ratio was clinically significant at 13.6.

Dr Hollo noted that the sensitivity of the testing was not ideal, but he pointed out that unlike any other form of ophthalmic examination, it could be performed by trained technicians without medical qualifications.

“This kind of combination GDx-VCC and Matrix FDT might be suitable for glaucoma screening where we screen for early cases which are so difficult to differentiate from normal eyes”

Gabor Hollo MD, PhD, DSc

“This kind of combination GDx-VCC and Matrix FDT might be suitable for glaucoma screening as their role in management of glaucoma patients and also glaucoma suspects,” he said.

To assess the effectiveness of the approach, Dr Malik and her associates conducted a retrospective review of the accuracy of new optometrist referrals to a specialist glaucoma clinic over a six-month period.

The optometrists’ guidelines for referring patients to ophthalmologists for glaucoma assessment included the finding of IOP greater than 21.0 mmHg with visual field changes and/or a characteristic disc change, such as, cup/disc ratio asymmetry greater than 1.2.

The referral guidelines were the same for normal tension glaucoma and ocular hypertension, except that IOP could be less than 21 mmHg for normal tension glaucoma but had to be greater than 21 mmHg without disc or field for ocular hypertension.

High proportion of false positives

Dr Malik and her associates found that only slightly over a third (102 patients referred by optometrists actually had glaucoma. About two thirds of patients were referred on the basis of a single suspicious finding, the rest were referred on the basis of two findings.

The most common cause for referral was IOP greater than 21 mmHg. GDx-VCC patients referred for this finding only 24 were confirmed to have glaucoma (positive predictive value 0.39). Moreover, the mean IOP of referred patients was 24 mmHg when measured by optometrists – who used non-contact tonometry in nearly all cases – but was only 17 mmHg when measured in hospital (p=0.001).

Similarly, among 23 with visual field changes, only 10 were confirmed to have the disease (PPV 0.43). Ophthalmic disc abnormalities was the second most common cause for referral and had the highest predictive value of any single finding. Among the 53 patients for whom optometrists recorded this finding 30 were confirmed to have glaucoma (PPV 0.56).

Referrals for more than one suspicious value had the highest positive predictive value of 0.58. Among 34 referred for more than one suspicious finding 20 were confirmed as having glaucoma.

“Referral accuracy for glaucoma improves when more than one suspicious finding is documented. Non-contact tonometry and perimeter results from a single patient visit are a major source of unnecessary referrals. Emphasis on specific training and equipment use for community optometrists will be required as their role in management of glaucoma increases,” Dr Malik concluded.

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