PREVENTING BLINDNESS
Development of better diagnostics and therapeutics key to progress
by Cheryl Guttman Krader in Fort Lauderdale

The development of new diagnostic methods should help to reduce the toll of angle-closure-glaucoma (ACG)-related blindness before the decade concludes. However, preventing blindness from open-angle glaucoma (OAG) presents a more difficult challenge, according to Harry A Quigley MD.

Dr Quigley is A. Edward Maumenee Professor of Ophthalmology, The Johns Hopkins University School of Medicine, Baltimore, MD. He spoke at the annual meeting of the Association for Research in Vision and Ophthalmology during a mini-symposium focusing on research priorities to enable Vision 2020 to reach its goal of eliminating avoidable blindness.

Dr Quigley noted that the biggest challenge to preventing ACG blindness is a lack of predictors for identifying what patients with angle closure will develop the disease. Only about 10 per cent of persons with a narrow angle develop ACG, and about three-fourths of persons with ACG are asymptomatic, he explained.

Recent research suggests that measuring changes in choroidal volume and iris volume during provocative testing may better identify angle closure suspects at risk for developing disease compared with current approaches using gonioscopy and ultrasound biomicroscopy to study angle anatomy.

“We know we should be measuring something physiological, and gonioscopy and ultrasound biomicroscopy are inadequate because they provide only a static view of a dynamic process,” Dr Quigley said.

Research conducted by Dr Quigley and others using anterior segment OCT has shown that iris volume after pupil dilation changes less in eyes with ACG than in controls with normal angles or even in fellow eyes having narrow angles without ACG.

“The iris is like a sponge that loses water to the aqueous with pupil enlargement, and it’s not surprising that the amount of water lost may differ among eyes depending on iris structure. Minimal change in iris volume during pupil dilation in an eye with a narrow angle can predispose to angle closure glaucoma,” Dr Quigley explained.

Choroidal expansion is also being considered as a pathogenic mechanism for the development of angle closure glaucoma and a potential diagnostic target for identifying angle closure suspects. Research has shown the presence of a space between the choroid and sclera in eyes with ACG but not in normal eyes. This space may represent choroidal expansion that has also been observed to be more common in ACG eyes than normal controls. Choroidal expansion could increase pupillary block in an eye with a narrow angle as a result of increased IOP causing anterior movement of the lens and iris.

Validation of the role of these new diagnostic approaches requires their investigation in longitudinal studies. One such trial is currently under way in Guangzhou, China. The study has enrolled 850 subjects with narrow angles who undergo iridotomy in one randomly selected eye after baseline physiological measurements of iris volume and choroidal thickness. The subjects will be followed for three years.

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OAG more challenging. Success in reducing the blindness burden of OAG faces more complex challenges considering the deficiencies of existing therapies. Results from numerous studies highlight that poor adherence limits the effectiveness of medical therapy among affluent populations in Western countries as well as in the developing world. This issue may be overcome by novel delivery methods, and technologies are being developed, but are not yet in human trials. Various strategies have also been shown effective for motivating patients to take their drops more often, but while adherence improves, it remains suboptimal.

Laser angle surgery is a well-tolerated minimally invasive procedure with a favourable safety profile. However, it causes minimal IOP-lowering, and with its high instrument cost and requirement for operator skill, its applicability in the developing world is limited. Nevertheless, en masse laser treatment might be worthwhile even if the benefit is IOP-lowering by a few mmHg. Dr Quigley said.

An alternative to trabeculectomy that does not require high-level training, causes fewer side effects, and has higher success rates, is needed for surgery to become a viable solution. Dr Quigley proposed that building experience with new surgical techniques in the developing world might be achieved by focusing on regions with established cataract treatment programmes where patients receiving cataract surgery and who are found to have co-morbid glaucoma can simultaneously undergo glaucoma surgery.

Dr Quigley’s list of research priorities for successful elimination of glaucoma-related blindness also included a need for more data on the risk and cost of glaucoma treatment, the development of better tools to guide selection of treatment that will maximise outcome and minimise cost, and conduct of clinical trials of potential neuroprotective agents.

He noted that results from animal studies suggest a host of candidate compounds with dual activity for lowering IOP and protecting retinal ganglion cells. Recognising the lack of industry interest in developing neuroprotective drugs for glaucoma, Dr Quigley encouraged academicians and clinicians to establish their own clinical trial networks to investigate the efficacy and safety of new drugs for preventing glaucoma blindness.

“It’s said that neuroprotective trials take too long and need too many patients,” he noted.

However, using data published by Chauhan et al., Dr Quigley estimated that a 50 per cent treatment effect could be detected in two years in a study enrolling fewer than 200 patients if the visual fields are repeated quarterly.