

Primary open-angle glaucoma

Early diagnosis of this otherwise progressive, asymptomatic process is essential

GLAUCOMA IS THE MOST COMMON neurodegenerative disease of the optic nerve, with a prevalence of about 3%.¹ This means that about 150 000 Australians, about 75% of whom are aged over 70, have glaucoma. This number will double over the next 30 years as our population ages.² After macular degeneration, glaucoma is the second most common cause of irreversible blindness in our community,³ and the commonest cause of preventable blindness.

The basis for the most common form of glaucoma is multifactorial. Genetic linkage analysis has isolated several putative genes for open-angle glaucoma, but these account for only a small percentage of cases. Risk factors for open-angle glaucoma identified in Australian cross-sectional analyses include age and intraocular pressure, family history of glaucoma,⁴ myopia, systemic hypertension and diabetes.⁵

In glaucoma there is a relatively slow loss of retinal ganglion-cell axons. Early loss is usually in the mid-peripheral visual field. The disease becomes symptomatic at a relatively late stage when central vision is affected and the visual acuity declines, or extensive loss of peripheral vision leads to problems with mobility. However, because progression of the visual field loss is relatively slow, glaucoma is responsible for a relatively small number of the new cases of visual acuity impairment detected annually.⁶

Underpinning the treatment of glaucoma is a reduction in intraocular pressure. Recent reports^{7,8} provide evidence for setting a target intraocular pressure level for each patient, depending on the assessed risk of progressive visual damage, such as extent and rate of prior damage, proximity of the visual damage to the point of fixation (most sensitive central vision), likely number of years of life remaining for the patient, family history, and the level of intraocular pressure at which damage has occurred.

Usually, topical drug therapy is used first. Newer drugs such as prostaglandin F_{2α} agonists (latanoprost, travoprost), prostamides (bimatoprost), topical carbonic anhydrase inhibitors (dorzolamide, brinzolamide), β-blockers (timolol, laevobunolol, betaxolol) and α₂-agonists (brimonidine, apraclonidine) have tended to replace pilocarpine and adrenalin-related compounds. Since drugs are absorbed directly from the nasal mucosa into the venous circulation with hepatic by-pass, topical agents mimic intravenous drugs — their safety margin can be widened by simple eyelid closure and digital occlusion of the tear duct for at least two minutes after instillation. Non-compliance and difficulties with instillation techniques remain major challenges for the long-term treatment of this incurable and asymptomatic condition.

Failure to achieve target intraocular pressures by medical means usually leads to laser procedures. Laser trabeculoplasty techniques offer a 75% chance of helpful intraocular pressure reduction, with a 50% chance of continuing benefit for up to five years. Lasers are also used to achieve peripheral iridectomies for angle-closure glaucoma, and to

inhibit aqueous inflow by ciliary-body destruction in blind, painful eyes. If medical and laser treatments fail, incisional surgery is performed to create an alternative pathway for the aqueous humor onto the scleral surface. Augmented with antifibrotic agents (5-fluorouracil, mitomycin-C), a long-term success rate of up to 90% can be achieved. For patients with exaggerated healing responses (glaucoma secondary to uveitis or rubeosis), intraocular pressure reduction can be achieved with plastic tubes draining into plastic reservoirs (there are three types of implants — Molteno [Molteno Ophthalmic, Dunedin], Baerveldt [Pharmacia, Kalamazoo, Mich, USA], and Ahmed [New World Medical, Rancho Cucamonga, Calif, USA]).

Beyond intraocular pressure reduction lies the hope of neuroprotection — an attempt to prevent initiation or progression of intracellular processes resulting in retinal ganglion-cell apoptosis (induced cell suicide). A large international multicentre prospective randomised clinical trial of the NMDA [*N*-methyl-D-aspartate]-receptor antagonist memantine is under way, with results expected in 2006.

Our conventional approach of looking for visual field defects, or for their progression, with white-on-white automated perimetry is still the main method of monitoring for glaucoma stability, but a large proportion of the nerve fibres can be lost before an initial defect is seen. (In white-on-white automated perimetry, a white light target is projected into a white background bowl — the patient responds when the light is just seen and its intensity is varied until the threshold for seeing has been crossed, which determines the sensitivity of the retina at that point.) There are now several new techniques for the detection of glaucoma which are specifically designed to detect change at earlier stages of the disease. Psychophysical tests are available which target smaller subpopulations of ganglion cells, such as frequency-doubled perimetry, and short-wavelength automated perimetry (blue target/yellow background). Multifocal objective perimetry, recently developed at the Save Sight Institute,⁹ records a multifocal visual evoked potential and removes the need for patients' subjective responses. Optic disc and nerve fibre imaging techniques using scanning laser ophthalmoscopes (eg, Heidelberg retina tomograph [HRT, Heidelberg Engineering, Heidelberg, Germany]; GDx Access [Laser Diagnostic Technologies, Jackson, FL, USA]) or optical coherence tomography can provide objective measures of structural change.

Glaucoma blindness is largely preventable. While the visual damage is not reversible, it can usually be arrested. To achieve this, early diagnosis of this otherwise progressive, asymptomatic process is essential. Ninety per cent of the Australian population visits a general practitioner annually, yet 50% of patients with glaucoma identified in population surveys are undiagnosed and untreated.³ Clinically, the first changes occur at the optic disc and it is vital that clinicians

look for the characteristic sign of optic disc cupping. Every GP should view a patient's optic disc with an ophthalmoscope from time to time, especially if one or more risk factors are present. Anyone with significant optic disc cupping, or asymmetry between the optic discs of the two eyes, should be referred for investigation.

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Epidural block and outcome after major surgery

Patients at increased risk of postoperative respiratory complications may benefit

PATIENTS UNDERGOING SURGERY need good advice not only about whether a particular elective procedure is truly necessary and likely to be of benefit, but also about the nature and chances of an adverse outcome from the surgery itself. Those with heart failure, coronary artery disease, diabetes or emphysema are more likely to suffer serious complications or death after major surgery. Epidural anaesthesia and analgesia may be a preferable technique in such patients,¹ as epidural block can attenuate the neurohumoral stress response to surgery,² potentially improving postoperative cardiorespiratory function and reducing complications.

Many small randomised controlled trials (RCTs) have supported this conjecture, but, because most serious complications after anaesthesia and surgery are rare, none has had sufficient power to demonstrate whether epidural block significantly improves postoperative outcome. A solution to this problem is to combine the results of all available trials in a meta-analysis. Applying this approach to data from 141 RCTs involving 9559 patients, Rodgers et al showed that the use of epidural or spinal block (with or without general anaesthesia) resulted in a significant 30% reduction in mortality after surgery.³ Outcomes causing major morbidity (major morbidity endpoints) such as thromboembolism and pneumonia were also reduced. Another recent systematic review found that epidural block reduces postoperative myocardial infarction.⁴ Although these findings are supportive, they were based exclusively on small RCTs, and meta-analyses sometimes give conflicting results when compared with large RCTs.⁵

In 1984, Yusuf et al explained how large, simple randomised trials can reliably detect moderate effects on important but uncommon outcomes such as death or major morbidity after surgery.⁶ Two of us are part of an Australian group that has recently published the results of a large

multicentre RCT of epidural block in 888 high-risk patients undergoing major abdominal surgery (the MASTER trial).⁷ Patients were randomly allocated to receive general anaesthesia with or without epidural block. The epidural block was established before the commencement of surgery (epidural anaesthesia) and epidural analgesia was continued for three days after surgery. All other care was left to the discretion of the anaesthetist and surgical team: most patients were managed in general surgical wards after surgery, although some required high-dependency or intensive care. Thus, our trial was a test of effectiveness in routine practice and its results can be generalised.

There was no significant difference in mortality at 30 days or in overall morbidity — 57% of epidural and 61% of control group patients had at least one morbidity endpoint (sepsis, respiratory failure, myocardial infarction, heart failure, renal failure, gastrointestinal [bleeding or need for parenteral nutrition], hepatitis, or haematological [anaemia, leukopenia, or thrombocytopenia]) or died ($P=0.30$). Mortality at 30 days was low in both groups (epidural, 5.1%; control, 4.3%). Of the eight morbidity endpoints studied, only one, respiratory failure, occurred less frequently in patients managed with epidural block (epidural, 23%; control, 30%; $P=0.03$). Another large RCT published recently showed similar results.⁸ Thus, there is no evidence that epidural block improves outcome in most patients undergoing major abdominal surgery with general anaesthesia, other than for respiratory complications.

Nevertheless, in the MASTER trial, pain scores over the first three days after surgery were significantly lower in the epidural group. This difference occurred despite most participants in the control group receiving multimodal analgesia.¹ This demonstrates some benefit from epidural block: a reduction in pain may assist deep breathing and coughing