The prospects for new treatments in age-related macular degeneration

The prospect that interferon alfa might be shown to have a role in the management of age-related macular degeneration is given further support in two papers in this issue of the journal. The exact mechanism involved remains unclear but there is in vitro evidence that interferon alfa inhibits endothelial cell proliferation and migration. In experimental animals it has been shown to inhibit leucocyte induced angiogenesis and its role in the management of life threatening haemangiomas in children is also recognised. Converted into the management of age-related macular degeneration it might be hoped that it would influence the developing neovascular membrane thereby avoiding foveolar destruction and consequent visual loss.

These studies report interferon alfa treatment of patients with membranes within the avascular zone. Although the number of patients with neovascular membranes showing improvement, in terms of visual acuity, membrane size, or angiographic appearance is relatively small the fact that nine out of 50 did show early benefit is noteworthy. Equally, 29 out of 50 retained their pretreatment acuity and 17 out of 50 showed no change in the clinical appearance. The treatment period was short in both studies (4–6 weeks) but the patients were observed for an extended period (7–6–10 months) to collect the data. The apparent effect on the function of the second eye during treatment and worsening of symptoms and clinical findings on stopping interferon therapy would suggest that there may be an effect that might be more clearly demonstrated with a longer period of treatment. Neither of these reports is of a controlled trial and the benefit identified must be seen in this light.

Ophthalmologists managing disciform disease have long recognised the variability of response to laser treatment, the development of recurrences, and the failure of some lesions to progress. If there is a plastic period in the development of a membrane then correctly manipulated therapy aimed at those cytokines and angiogenic factors involved might arrest the developing membrane and modify the visual outcome. At the same time it is interesting to speculate on the role that teletherapy, as reported by Chakravarthy et al earlier this year, might play in the future management of the degenerative process. Would either of these new options have a role as an adjuvant to photocoagulation thereby reducing the incidence of recurrent disease?

Interferon is not without its side effects but it could reasonably be expected that these might be, at least in part, dose related. Kirkpatrick et al report few side effects, and those relatively minor, on their regimen of 1.5 rising to 3.0 \times 10^6 units per m2 of body area. Gillies et al report three treatment regimens involving 9, 15, and 21 \times 10^6 units per week in divided doses. A cardiac arrest and subsequent death due to myocardial infarction occurred in the absence of any previous history and may be unrelated but this patient was on the highest dose regimen, which was also true for the patient with the perforated peptic ulcer, Gillies et al identify that the lower doses were better tolerated and this is supported by Kirkpatrick and coworkers. Careful selection of patients for treatment, avoiding those with a history of cardiovascular disease or depressive illness, should avoid such major complications. The other problems involving thrombocytopenia, leukopenia, liver function, and biochemical abnormalities should be identified by routine screening of the patients before and during treatment.

Teletherapy and interferon treatment offer new prospects for the management of macular degeneration. It is essential that they are evaluated by a properly structured prospective controlled clinical trial before they are considered as established treatment. Experience in earlier controlled trials has shown that adequate numbers for study are often difficult to achieve and may be beyond the resources of a single unit. If such studies are to be successfully undertaken interested ophthalmologists will need to group their energies and expertise and must be adequately funded and led.

There is a real opportunity to move forward in the management of age-related macular degeneration which affects most of the one million people identified by the Royal National Institute for the Blind as being visually handicapped in Britain. The social cost of this handicap is high and the potential for benefit within the community by reducing dependence significant. The cost of establishing a properly funded group of workers to pursue these new treatment proposals may be high but the cost of not doing so could be even higher. Even if neither teletherapy nor interferon prove to be the ultimate answer, the knowledge gained by studying these aspects in depth will be enormous. Just as assessing the role of laser photocoagulation moved us forward significantly in the management of retinal disease, the investigation of interferon and teletherapy will serve as a stimulus to new knowledge.

The data presented in these papers support the need to investigate further the possibility of tackling neovascularisation by influencing the cytokines that stimulate the membrane and the endothelial and pericyte proliferation that
Choice in local anaesthesia

A recent Medline database search selected more than 100 articles in the last 3 years relevant to local anaesthesia in ophthalmic surgery. Techniques described included retrobulbar, peribulbar, subconjunctival, one quadrant, and four quadrant sub-Tenon’s injections, and their variants. Phacoemulsification using topical anaesthesia only has also been reported, and the anaesthetic solution has been ‘doctored’ to reduce stinging.1 What should the ophthalmic surgeon in training derive from this wealth (or minefield) of data?

The complications of local anaesthesia have been well documented. Studies using computed tomography2 and magnetic resonance imaging3 have improved our understanding of anatomical relations in the orbit, though they have yet to prove their value in terms of lowered complication rates. Other obvious topics for investigation have been the efficacy of anaesthesia and akinesia, safety, and long term morbidity. However, many papers can be criticised for inadequate scientific methodology, particularly with regard to assessment of akinesia and pain.

In this issue of the journal, Ali-Mellkilia et al report on the comparison of three techniques of local anaesthesia which raises several important issues. The blocks were administered by anaesthetists rather than the surgeon. Is this ideal? There may be a clear conflict between improving ‘turnover time’ in theatre and the desirability of close quarter observation of the initial reaction to pain stimuli and periocular manipulation. Personal administration of the block promotes the best chance of observing orbital haemorrhage or other complications before draping the patient and incising the eye.

The use of a scoring system for akinesia is desirable in a research setting, but preset criteria seem to have resulted in reblock rates (11% to 19%) that are high in our experience. The norm in usual practice is close to 0%. We look forward to studies using peroperative video monitoring and subsequent assessment by an independent observer. It is likely that surgeons quickly develop a personal tolerance to eye movement that is preferable to running the gauntlet of peribulbar injection again. The recti muscles are not the only muscles to be considered in local anaesthesia. Lid squeezing against the speculum can be disastrous when the eye is open. Unless very confident of tissue diffusion and sufficient time, the very low risk and low volume of Lint injection should be considered for every case.

Discomfort and pain should be scored soon after the operation, preferably on a visual analogue scale. These should include the discomfort and stinging arising from the administration of the block, peroperative pain with particular reference to placement of the superior rectus suture where one is used, expression of the lens nucleus, and suturing of the wound, as well as postoperative pain.

The volume of anaesthetic agent used is greater with ‘peribulbar’ methods and the maximum safe volume is partly dependent on body weight – for example, 7.5 ml of 2% lignocaine for a 50 kg patient. Signs of toxic reaction include circumoral numbness and tingling, followed by dizziness, tinnitus, slurred speech, and aggressive behaviour before the onset of convulsions and collapse. Lonsdale et al raise strong objections to the use of bupivacaine, which is said to have a specific cardiac toxicity, with a lengthening of the QT interval and a lowering of ventricular tachycardia threshold. This has to be weighed against the advantage of its long duration of action. Strangely, the least toxic, prilocaine, is largely ignored in the ophthalmic literature.1 It does, however, reduce haemoglobin to methaemoglobin and this may bias pulse oximeter saturation readings.

The trainee surgeon’s attention should be drawn to the report of the Joint Working Party on Anaesthesia in Ophthalmic Surgery4 and the recommendations for intravenous access and monitoring (pulse oximetry, electrocardiography, and blood pressure measurement). An editorial review of pulse oximetry, its pitfalls, and basic respiratory physiology has been given by Hutton.5 The essential message is that pulse oximetry is a poor measure of hyperventilation when the concentration of inspired oxygen is high. The surgeon should consider whether oxygen supplementation under the drapes is strictly necessary, and whether transparent drapes will assist in observation of chest wall movement.

The administration of local anaesthesia has always been more than just deciding on the right place to inject. Decisions range from costs, time efficiency, safety, efficacy, and monitoring to postoperative analgesia. It is unlikely that any single approach will be ideal. However, where a peribulbar technique is chosen, it would make sense to use the medical compartment of the orbit as the site of the second injection as it works well, does not run the risk of damage to the trochlea, and reduces the risk of globe perforation.

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