CME PREVENTION
Details of ESCRs study testing steroids, NSAIDs and anti-VEGF for preventing CME
by Howard Larkin in Chicago

A three-year ESCRs-funded multicentre trial now getting under way could help prevent cystoid macular oedema (CME) after cataract surgery, a costly complication that is becoming more common as the incidence of diabetes rises, Dr Rudy Nuijts MD, PhD, told the ASCRS annual symposium.

The goal of the Preventing Macular Edema Post Cataract Surgery (PREMED) study is to provide evidence-based clinical guidelines for preventing CME after cataract surgery in patients with and without diabetes, said Dr Nuijts, who will direct the study with colleagues at the University Eye Clinic Maastricht, The Netherlands. The hope is to come up with CME prophylaxis and treatments that are more effective and easier to administer.

Prophylaxis especially could help ameliorate a projected spike in pseudophakic CME secondary to rising rates of diabetes resulting from ageing and overweight, Dr Nuijts said. For example, in The Netherlands, the number of people with diabetes is expected to more than double by 2025 from the current one million, or about seven per cent of the population.

Though diabetics currently make up only about 16 per cent of cataract patients, they are estimated to make up about half of postoperative CME cases. In published studies, post-cataract surgery CME rates as determined by OCT imaging range from four per cent to 20 per cent among healthy people, Dr Nuijts said. By contrast, pseudophakic CME rates run up to 31 per cent of diabetic patients with non-proliferative diabetic retinopathy without CME at baseline. Reported rates of clinically significant CME, defined as best corrected visual acuity worse than 20/40, range from zero to 5.8 per cent.

Beyond the risk of poor visual outcomes, CME increases costs by 41 per cent over uncomplicated cases, according to one study, Dr Nuijts noted. With cataract surgery rates already running from 200 to 1,600 per 100,000 annually in European countries and expected to increase, prevention is both clinically and economically desirable.

Improving on eye drops. Currently, topical NSAIDs are the treatment of choice for cataract surgery-related CME. Several large randomised controlled trials and meta-analyses have found topical NSAIDs effective in both preventing and treating pseudophakic CME. But as a drug delivery modality, eye drops suffer from inherent drawbacks, Dr Nuijts noted. These include possible fluctuations in intraocular medication concentrations, patient non-adherence rates approaching 50 per cent, and the resulting need for nurses to assist in administering drops.

Several other compounds and delivery modalities for treating CME show promise for enhancing NSAID effectiveness or provide equally effective but easier-to-administer alternatives. Case series have shown topical corticosteroids may potentiate the therapeutic effects of topical NSAIDs and that periocular injections of corticosteroids may be effective for treating CME refractory to topical treatment. One small randomised study has shown intravitreal corticosteroid injections improve anatomical, but not visual, outcomes in diabetic patients. Also, investigational studies suggest that anti-VEGF compounds may be effective in eyes that have failed other treatments. However, none of these has been extensively studied for CME prophylaxis, Dr Nuijts said.

PREMED will be the first rigorous test of a variety of approaches tailored to patients with and without diabetes. Injections will be examined in both groups in part because they have the potential for eliminating the problems of eye drops.

The non-diabetes arm, consisting of 2,400 patients, will compare a control group receiving both topical corticosteroids and NSAIDs with a group receiving topical corticosteroids only, and a group receiving subconjunctival injections of corticosteroids. The study is designed to address the questions of what value may be added by combining NSAIDs with corticosteroids, and whether a single peri-operative subconjunctival injection is non-inferior to eye drops.

The diabetes arm, involving 520 patients, will compare the control topical corticosteroid and NSAID therapy with a group receiving subconjunctival corticosteroids, a group receiving intravitreal bevacizumab, and a group receiving both types of injections. The study is designed to answer the questions of what value intravitreal or subconjunctival injections add to topical medication, and what value combining intravitreal and subconjunctival injections may add.

All patients will receive a phacoemulsification for cataract and placement of an intraocular lens. Intracameral cefuroxime will be administered at surgery followed by topical antibiotics for six days. Patients with severe diabetes will be excluded, as will patients at high risk for pre- or postoperative inflammation, Dr Nuijts said.

Follow-up visits will be at one week, six weeks and three months. Mean logMAR best-corrected visual acuity, OCT sub-analysis of macular thickness changes, intraocular pressure, vision- and health-related quality of life changes, and adverse events will be assessed. A cost-effectiveness analysis also will be conducted.

The primary endpoint in both groups will be the presence of macular oedema on OCT or clinically significant macular oedema at six weeks. Macular oedema is defined as an increase in central subfield mean thickness in the 1mm area compared with baseline. Clinically significant macular oedema is defined as an increase of more than 10 per cent compared to one week post surgery combined with a decrease in best corrected visual acuity of two or more lines on the ETDRS chart.

Dr Nuijts believes that PREMED will give cataract surgeons valuable information on controlling CME that is simply not available today.