Treatment to prevent or treat PVR
an elusive ophthalmic goal

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WHILE the search for effective treatments for proliferative vitreoretinopathy (PVR) continues, the key to preventing the condition is to do the best possible repair of retinal tears and detachments, and as early as possible.

This was the main message from Brooks McCuen II MD, from the Duke University Eye Centre in the U.S. He spoke here at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO). He provided an overview of various treatments that have been studied and described the current state of the field.

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“PVR can be thought of as wound healing gone wild. It is characterised by uncontrolled cellular growth within the eye, particularly over the inner and outer surfaces of the retina. It can lead to recurrent retinal detachment and significant loss of vision,” he said.

The trigger for PVR is retinal tears or detachments caused by natural aetiology, trauma or other reasons. While the vast majority (90%) of retinal detachment repairs are successful, most of the ones that can’t be repaired are due to PVR. Once PVR develops, patients have a poorer prognosis for future repair.

Pharmacological treatment to either prevent or treat existing PVR is an important goal in ophthalmology, and several approaches have been studied to date. Dr McCuen divided pharmacologic treatment approaches into two categories: those designed to prevent PVR, and those intended to treat existing disease.

Current treatment options yield disappointing results

Systemic steroids appeared early as a treatment option to prevent PVR, starting with a pivotal trial in the 1980s showing they reduced the incidence of postoperative retinal fibrosis after scleral buckling.

In 2001, work was done using combination therapy with 5-fluorouracil (5-FU) and low molecular weight heparin (LMW H) for prevention. Researchers showed in one study that there were significant reductions in postoperative PVR and lowered re-operation rates in treated eyes.

“When they confirmed that the PVR eyes had a worse final visual acuity than eyes without postoperative PVR, there was no ultimate difference in final visual acuities between the treatment and control groups,” Dr McCuen said.

This treatment approach is even more disappointing with even newer research. Dr McCuen noted a study presented at this year’s ARVO conference in a series of over 600 eyes randomised to LMW H, 5-FU or placebo. Here, researchers concluded that LMW H and 5-FU should not be used routinely for primary retinal detachment surgery but should be reserved only for high-risk cases.

No proven treatment for established PVR

When it comes to the treatment of established PVR, there are still no ideal methods or drugs. The primary pharmacologic agents studied in human trials generally fall into drugs that are anti-metabolite, anti-inflammatories, oligonucleotides or combinations. 5-FU was the first anti-metabolite studied, but interest waned with concerns over safety — though it’s not completely out of the picture, he noted.

Daunorubicin, another anti-metabolite, has also been studied, and a non-randomised study showed relatively high success rates. However, a subsequent multicentre randomised clinical trial in patients who had one-year follow-up showed that even though there was a reduction in the number of re-operations with daunorubicin, there were no differences in the final anatomic or visual results, he said.

In 1996, a study was published where randomised patients were given a combination of heparin and dexamethasone in the infusion fluid of eyes undergoing PVR surgery. This study showed there was a trend toward reduced re-proliferation in treated eyes; these eyes also had increased risk for postoperative haemorrhage.

Results with intravitreal triamcinolone have also been discouraging. Dr McCuen said. A small series of patients in a study from 2003 suggested that use of 25mg of intravitreal triamcinolone led to a relatively high rate of PVR recurrence. The researchers advised caution with the use of this drug for this purpose.

Another study using 5-FU in combination with LMW H for existing PVR showed a high rate of single operation success. However, even this study had a downside when the researchers noted that cystoid macular oedema occurred more frequently than expected.

British researchers published a study in 2004 using the “British Cocktail”, combining 5-FU and LMW H. This was a prospective, randomised clinical trial of 157 eyes followed for six months.

“Unfortunately in established PVR there proved to be no significant difference in the single operation retinal reattachment rate, the final reattachment rate, the final visual acuity or the rate of complications between the treated and control groups. There was a strong trend, however, for less macular puckers in the treated eyes,” Dr McCuen said.

Promising new agent yields no benefit

In more recent years, a promising agent called VIT-100 (Immusol) entered into some preliminary trials. The compound is a chimeric ribozyme to proliferating cell nuclear antigen or PCNA. It is supposed to inhibit growth of the cells in PVR.

While VIT-100 appeared to be successful in animal models of PVR, phase-1 and phase-2 human trials haven’t been quite so promising.

“VIT-100 showed no statistically significant benefit over placebo in the treatment of PVR and its use for this indication has been abandoned,” he said.

“There are no cut-and-dry answers at this point in time... each physician dealing with PVR must come to his or her own conclusions,” he said.

Dr McCuen’s own general approach is to treat or prevent PVR in patients with a short course of systemic steroids starting the day prior to vitrectomy. During surgery, the patients are given a bolus of intravenous steroid.

“In addition, I generally add low molecular weight heparin to the infusion fluid both to inhibit PVR as well as to reduce the postoperative fibrin reaction common with extensive dissection of the vitreous base,” he said.

After surgery, patients are given a topical steroid, and systemic steroids are reduced. If the patient develops a significant fibrin reaction, he’ll consider using intracameral TPA.

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