Emmetropic eyes without PVD at risk of retinal detachment following cataract surgery

Robbeard O’hEineachain in Monte Carlo

EVEN emmetropic eyes may be at a significantly increased risk of retinal detachment following uneventful cataract surgery if no posterior vitreous detachment (PVD) is present pre-operatively, according to Mario Stirpe MD, Fondazione G B Bietti-IRCCS, Rome, Italy.

In a study involving 450 emmetropic eyes of 265 patients who underwent phacoemulsification and IOL implantation, the rate of retinal detachment was 7.7 per cent among eyes without pre-operative PVD but only 1.5 per cent of eyes with pre-operative PVD postoperatively. That compared to a postoperative retinal detachment rate of only 1.1 per cent among eyes which had pre-operative PVD, Dr Stirpe told the 7th EURETINA Congress.

“In cataract surgery the introduction of phacoemulsification has lowered the risk of intraoperative complications, however, retinal detachments still occur in myopic eyes due to the vitreous detachments the procedure can induce. Our data suggests there is a major risk of retinal detachment following phacoemulsification in emmetropic eyes without PVD prior to surgery,” he said.

The patients in the study included 143 men and 122 women with a mean age of 62 years. N one included in the study had glaucoma, uveitis, previous eye surgery, retinal laser treatments, ocular trauma, diabetes, general vascular disorders, or postoperative YAG laser capsulotomy. However eyes with asymptomatic peripheral retinal degenerations were included in the study so long as these involved only one retinal quadrant.

All underwent uneventful phacoemulsification with IOL implantation between October 1999 and December 1999 and had a follow-up of five years. Pre- and postoperative examinations included biomicroscopy with + 90 D lens, B-scan ultrasonography and optical coherence tomography (OCT 1, Ili Stratus).

Elevated retinal detachment risk following postoperative PVD

Pre-operative PVDs were present in 265 (58.9 per cent) eyes of 156 patients. The age difference between those with and those without PVD was statistically significant (p<0.0001) with mean values of 63.44 years and 60.02 years, respectively.

There was no statistically significant difference between those with and those without PVD as regards peripheral retinal lattice degeneration. The condition was present in 53 eyes (20.7 per cent) with and 47 eyes (25.4 per cent) without pre-operative PVD.

Among the 185 eyes with no pre-operative PVD, a PVD occurred in 147 (79.5 per cent) between two days and 34 months postoperatively. Among those eyes, retinal detachment occurred in 11 eyes (7.7 per cent) seven days to 18 months postoperatively (median 6.3 months). In contrast, only three (1.1 per cent) of the 265 eyes with pre-operative PVDs had a retinal detachment 16 to 49 months postoperatively.

The retinal detachments occurring in eyes without pre-operative PVDs included horse-shoe retinal tears on lattice areas of the superior quadrant in 10 eyes and small retinal holes in the inferior quadrant in one eye without areas of lattice degeneration. The time between PVD and retinal detachment ranged from two days to three months in 10 eyes and 13 months in one eye.

In eyes with pre-operative PVD, the retinal detachments included retinal breaks in the area of lattice degeneration in the inferior quadrant in one eye, and small, barely identifiable retinal holes in the inferior quadrant with no lattice degeneration.

“Peripheral asymptomatic retinal degenerative areas may originate retinal breaks after phacoemulsification, especially in eyes without a previous PVD. In this study more retinal detachments involved peripheral retinal degenerative areas located in the superior quadrants. This raises the question of whether we should consider prophylactic laser treatments on lattice areas, including those which are asymptomatic, in eyes without PVD who are candidates for phacoemulsification,” Dr Stirpe noted.

Commenting on the study, Thomas Wolfensberger MD, Switzerland, suggested that the risks might outweigh the benefits if laser prophylaxis were to be carried out on all patients with lattice degenerations but without PVDs who are undergoing phacoemulsification.

“I am not sure that prophylactic treatment should be advised because if you look at the percentages you’d probably have to treat several hundred patients to get a benefit. I might instead suggest that these patients receive more ‘passive’ prophylaxis being advised of the early signs of symptoms of retinal detachment, and their general ophthalmologists should also be advised of the risk,” he said.

Continued from page 26

Around the same time that gene therapy was effective in patients with X-linked SCID, Prof Ali’s team were demonstrating a gene therapy rescue in an rds mouse model and others showing retroviral vectors and some have used adenovirus is that it tends to be short-lived following intravitreal injection in the eye.

However eyes with asymptomatic peripheral retinal degenerations were included in the study so long as these involved only one retinal quadrant.

All underwent uneventful phacoemulsification with IOL implantation between October 1999 and December 1999 and had a follow-up of five years. Pre- and postoperative examinations included biomicroscopy with + 90 D lens, B-scan ultrasonography and optical coherence tomography (OCT 1, Ili Stratus).

Elevated retinal detachment risk following postoperative PVD

Pre-operative PVDs were present in 265 (58.9 per cent) eyes of 156 patients. The age difference between those with and those without PVD was statistically significant (p<0.0001) with mean values of 63.44 years and 60.02 years, respectively.

There was no statistically significant difference between those with and those without PVD as regards peripheral retinal lattice degeneration. The condition was present in 53 eyes (20.7 per cent) with and 47 eyes (25.4 per cent) without pre-operative PVD.

Among the 185 eyes with no pre-operative PVD, a PVD occurred in 147 (79.5 per cent) between two days and 34 months postoperatively. Among those eyes, retinal detachment occurred in 11 eyes (7.7 per cent) seven days to 18 months postoperatively (median 6.3 months). In contrast, only three (1.1 per cent) of the 265 eyes with pre-operative PVDs had a retinal detachment 16 to 49 months postoperatively.

The retinal detachments occurring in eyes without pre-operative PVDs included horse-shoe retinal tears on lattice areas of the superior quadrant in 10 eyes and small retinal holes in the inferior quadrant in one eye without areas of lattice degeneration. The time between PVD and retinal detachment ranged from two days to three months in 10 eyes and 13 months in one eye.

In eyes with pre-operative PVD, the retinal detachments included retinal breaks in the area of lattice degeneration in the inferior quadrant in one eye, and small, barely identifiable retinal holes in the inferior quadrant with no lattice degeneration.

“Peripheral asymptomatic retinal degenerative areas may originate retinal breaks after phacoemulsification, especially in eyes without a previous PVD. In this study more retinal detachments involved peripheral retinal degenerative areas located in the superior quadrants. This raises the question of whether we should consider prophylactic laser treatments on lattice areas, including those which are asymptomatic, in eyes without PVD who are candidates for phacoemulsification,” Dr Stirpe noted.

Commenting on the study, Thomas Wolfensberger MD, Switzerland, suggested that the risks might outweigh the benefits if laser prophylaxis were to be carried out on all patients with lattice degenerations but without PVDs who are undergoing phacoemulsification.

“I am not sure that prophylactic treatment should be advised because if you look at the percentages you’d probably have to treat several hundred patients to get a benefit. I might instead suggest that these patients receive more ‘passive’ prophylaxis being advised of the early signs of symptoms of retinal detachment, and their general ophthalmologists should also be advised of the risk,” he said.

Continued from page 26

Around the same time that gene therapy was effective in patients with X-linked SCID, Prof Ali’s team were demonstrating a gene therapy rescue in an rds mouse model of retinal degeneration (an animal model with a mutation in the peripherin gene which leads to complete photoreceptor cell death within approximately 250 days of birth).

Prof Ali’s research report stimulated similar pre-clinical testing and there have since been a number of studies completed both in the rds model and others showing gene therapy mediated rescue of a degenerative condition. Two notable gene therapy trials in the eye, one from Richard Hurwitz’s lab in Texas has looked at adenoviral mediated delivery of thymidine kinase in retinoblastoma in children who had already had advanced retinoblastoma with the idea of transducing seedlings followed by injection of ganciclovir.

AMDA research

More recently, in a Phase I clinical trial for the treatment of neovascular age related macular degeneration, Dr Peter Campochiaro of the Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore used an adenoviral delivered PEDF (pigment epithelium derived factor) to act as an antagonist of VEGF. PEDF is an important angiostatic agent that may prove useful for treating AMD in the future and this trial established the potential viability for such an approach following intravitreal injection in the eye. However, one of the disadvantages of adenovirus is that it tends to be short-lived and so expression over the long term may not be feasible.

During the last decade or so there have been a huge number of clinical trials many of which have been conducted for cancer gene therapy, a few for cardiovascular disease and only a minority, less than 10 per cent, for monogenic diseases such as LCA.

The majority of these gene therapy clinical trials to date have been registered in the US, the UK and Germany and most of the trials have used adenoviral and retroviral vectors and some have used naked plasmid while adeno-associated virus (AAV) (used for the LCA study) represent only 3.7 per cent of studies performed so far.

The eye of course has many unique advantages for gene therapy; viral vectors stably transduce ocular tissues, treatment may be delivered to an immune privileged enclosed compartment, comprised almost exclusively of non-dividing cells.

In addition, proof of principle has been demonstrated for many treatments aimed at ocular conditions and so the next logical step is to attempt to advance the technology of gene therapy for inherited retinal degenerations into the clinic.

Two key questions to be addressed when preparing the technology for human trials are (1) can gene therapy proof of principle established in animal models be replicated in humans? and (2) what are the risks and safety issues involved? Many of these applications require subretinal delivery of vector and therefore consideration needs to be given to potential inflammatory immune responses from the surgical procedure. Furthermore, as was seen in a number of the X-linked SCID studies, there are potential risks with regard to insertional oncogenesis in the eye, but constantly improving vector technology continues to minimise this risk.

Practitioners at the coalface of this technology are additionally mindful of the requirements should be for the first target of application for gene therapy in the eye.

They concluded that it was important to target a single gene disorder, specifically a recessive disease so that you might be reasonably confident of the result. Having a sound biological and medical understanding of the disease and the experimental models available for extensive pre-clinical testing also constrained the list of potential targets. In addition it was thought preferable to have access to large animal models in order to assess the likelihood that the intervention would provide real medical benefit.

A further level of constraint in choosing where the first gene therapy trial should be focused is that there should be a window of opportunity for the intervention before the disease is too far advanced. Ideally a gene therapy intervention should go beyond simply delaying disease progression, which could take a long time to demonstrate, but rather it should aim to improve retinal function in the shorter term.