Preventing immunological graft rejection in high-risk patients requires multi-tiered approach

Dermot McGrath

PREVENTING corneal graft rejection in high-risk patients requires a multi-pronged strategy that combines rigorous pre-, intra- and postoperative measures to reduce the possibility of immune rejection of the transplanted cornea, according to Professor Harminder Singh Dua MD.

Addressing delegates attending the first Cornea Day organised as part of this year’s ESCRS W inter Refractive meeting, Dr Dua noted that corneal transplantation is the most common type of solid tissue or organ transplant, with over 40,000 per year carried out in the US alone.

“While 80-90% of low-risk grafts succeed, between 50% and 70% of high-risk grafts fail, mainly due to immune rejection. In fact, failed graft is fast becoming the most common indication for corneal transplantation,” said Dr Dua, Department of Ophthalmology, Queen’s Medical Centre, University of Nottingham, UK.

Dr Dua said that the first step in combating graft rejection is to identify high-risk factors, including vascularised corneas, multiple previous corneal grafts, extremes of age, inflamed or infected eyes, herpes simplex viral keratitis, chemical burns and silicone keratopathy.

“In terms of preoperative care, he said that it is vital to quieten the eye as much as possible and buy time – whether by using topical steroids, ocular glue or other measures – to reduce infection and inflammation.

A second important step is to occlude as many mature blood vessels as possible.

“This is something that is not very often talked about but is very useful in preparing a solid foundation for graft surgery. Blood vessels can be occluded with an Argon laser, yellow dye laser or using my preferred technique of fine-needle diathermy,” said Dr Dua.

Describing the technique in more detail, Dr Dua said he uses a monofilament nylon needle placed along the blood vessel. The needle is then touched with the tip of a monopolar diathermy probe at a very low setting until mild blanching of the stroma occurs.

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The importance of human leukocyte antigen (HLA) matching also helps in achieving a successful corneal graft, said Dr Dua. He added that while ABO blood type matching can also be performed, this is clinically less practical.

In terms of intraoperative measures that surgeons can take to help reduce the chances of graft rejection, Dr Dua cited key factors such as graft sizing, suture management and intravenous steroids as potentially significant.

He added that management of loose or broken sutures must be done as soon as it occurs in order to prevent further complications.

Dr Dua said that there is some anecdotal evidence that applying a patch of amniotic membrane on the graft after surgery helps to lessen the risk of rejection. “There is no firm evidence for that but some people have reported success with this approach,” he said.

Postoperative measures to be taken include closely monitoring and controlling intraocular pressure, because this is a known risk factor for graft rejection in the immediate post-graft period.

Topical steroids are another essential component of the postoperative care regimen and can be used for much longer than usual – up to 18 months or 24 months – with such high-risk patients, said Dr Dua. He also advocated the use of oral acyclovir in cases of herpes simplex viral keratitis for up to 18 months after the operation.

“Our experience is that 400mg twice a day significantly reduces the incidence of herpetic eye disease and therefore of graft rejection,” he said.

Turning to the question of systemic immunosuppression, Dr Dua said that tacrolimus, a T-cell inhibitor, is his current drug of choice. The dose is from 1mg to 2mg daily, with the aim of achieving overall blood trough levels between 1 to 12 micrograms/litre.

“In the initial postoperative period we monitor regularly the blood counts, kidney function, blood pressure and tacrolimus trough levels until the dosage is stabilised. And then in the follow-up period we look closely for any signs of rejection and if they do occur, then the dosage can be altered accordingly,” he said.

Risk assessment tool

To assist in the process of assessing which patients are at greatest risk of graft rejection, Dr Dua and his co-researchers (Dr Dev Raj MD and Dr Annie Joseph MD) have pioneered a risk assessment tool based on a points system. Patients with a previous failed graft, or other complications such as stromal vascularisation, anterior synchia and preoperative glaucoma are accorded one point for each respective risk factor. Herpes simplex viral keratitis merits two points on the scale and four points are added for a chemical burn.

Dr Dua said that the efficacy of the scale has been validated by a study at the University of Nottingham of 47 high-risk patients who had received corneal grafts. In the final analysis the above protocol together with pre-, intra- and postoperative measures, graft survival improved to around 60%. Dr Dua noted that there was a strong correlation between the patients who had scored highly on the risk assessment scale and those who had subsequently experienced graft rejection.

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“Remember that 60% to 70% is usually the failure rate in this group of high-risk patients, so our protocol seems to work in terms of increasing the chances of graft survival in these particular patients,” he said.

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