Maghizh Anandan, FRCO, FRCS, MRCS, D.O
Consultant Ophthalmic Surgeon

Collagen cross-linking

Keratoconus is disease in which the corneal surface (the clear covering of the eye) becomes thinner and begins to bulge into a cone-like shape leading to blurred and distorted vision. Spectacles or contact lenses may help, but in severe cases surgery may be needed. So far there has been no effective way to stop the progression of keratoconus. It is estimated that eventually 21% of the keratoconus patients require surgical intervention to restore corneal anatomy and eyesight.
Collagen crosslinking with the help of Ultraviolet A (UVA, 365nm) and the photosensitizer riboflavin phosphate is expected to change the intrinsic biomechanical properties of the cornea, increasing its strength by almost 300%. This increase in corneal strength has shown to arrest the progression of keratoconus in numerous studies all over the world.

What is collagen cross-linking?

Collagen cross-linking (C3-R) is a new treatment for keratoconus, using a photosensitizing agent, riboflavin (vitamin B2) & Ultraviolet light (UVA, 365nm) exposure. In extensive experimental studies researchers have demonstrated a significant increase in corneal rigidity / stiffness after collagen cross-linking treatment, arresting the progression of keratoconus in treated eyes.

How is the treatment done?

This procedure is carried out under a local anaesthetic. The top layer of the cornea is first scraped slightly to help the riboflavin eye drops to be absorbed into the cornea. UVA light is then shone onto the surface of the cornea for about 30 minutes while the eye drops are applied. The aim of the procedure is to halt progression of keratoconus. Eye drops with UVA light strengthen the fibres in the cornea by a process called cross-linkage. While the cornea is healing, the person may be given painkillers, antibiotic eye drops and artificial tears to stop the cornea from becoming too dry.

Who can benefit from this treatment?
Patients with documented evidence of keratoconus progression. Collagen cross-linking treatment is not a cure for keratoconus; rather, it aims to halt the progression of the condition. This is important to understand. Patients will continue to wear spectacles or contact lenses (although a change in the prescription may be required) following the cross-linking treatment. The main aim of this treatment is to arrest progression of keratoconus, and thereby prevent further deterioration in vision and the need for corneal transplantation. However in advanced keratoconus, wherein the corneal thickness is below 350 microns, this treatment may not be possible. In such a situation other alternatives such as deep anterior lamellar keratoplasty (DALK) should be considered.

Potential Risks of C3-R Treatment for Keratoconus?
UV light is known to be damaging to cells, and the keratoconus treatment causes the stromal cells (keratocytes) in the outer layers of the treated parts of the cornea to die. However, these cells are replaced by new keratocytes which migrate from untreated parts of the cornea into the central area over a period of some months after the keratoconus C3-R® treatment. In theory the UV light could be damaging to the inner endothelial cell layer of the cornea, and this is why the corneal thickness needs to be at least 350 microns if a standard keratoconus C3-R® treatment is to be undertaken. In clinical studies carried out so far, no evidence of damage to the endothelial cell layer has been documented. Although UV is potentially damaging to the lens and retina, it is believed that the riboflavin blocks the UV transmission to an extent that no measurable damage will occur. At present the long-term effects of the keratoconus treatment are unknown. The procedure may need to be repeated.

Risks and possible problems – NICE Guidance report 2009
In the study of 49 patients (66 eyes), 1 patient had temporary inflammation of the eye 2 days after the cross-linkage procedure. At 3 days, 1 patient developed some abnormal cells beneath the surface of the cornea. This was linked to the use of rigid contact lenses too soon after the procedure. In the study of 130 patients (241 eyes), 2 patients who were also receiving other treatment for keratoconus developed patches of itchy skin (‘neurodermatitis’) within 18 to 21 months of the procedure.

One study reported a herpes simplex (‘coldsore’) virus infection in 1 patient as a result of the procedure, causing clouding in the eye that remained after 2 months. The patient’s vision was not affected. In two reports of 1 patient each, both patients had inflammation of the cornea (‘keratitis’) soon after the procedure. Both were treated with antibiotics. In another report, 1 patient had ‘corneal melting’ (a severe condition in which the fibres in the cornea break down) and inflammation caused by a bacterial infection. They received a corneal transplant and antibiotic treatment.

As well as looking at these studies, NICE also asked expert advisers for their views. These advisers are clinical specialists in this field of medicine. The advisers said that other complications of the procedure may include damage to and scarring of corneal cells, hazy vision, infection and erosion of the cornea, and the need for further procedures.

Contact Mr Anandan via his private secretary,

Sue Da Silva on Tel. 07900210191