Potential applications for corneal cross-linking in ophthalmology

Corneal cross-linking has been shown to be a useful tool for arresting corneal melting and stabilising the cornea in companion animals.

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Corneal cross-linking (CXL) is an exciting new treatment modality available in veterinary ophthalmology. Studies into the use of CXL started in the late 1990s in human ophthalmology and the technique is now in widespread use in the human field.

The stroma of the normal cornea is comprised predominantly of collagen fibrils arranged in parallel bundles. There is a natural degree of “cross-linking” between adjacent collagen fibrils; these cross-links are covalent bonds that “anchor” the fibrils together, improving the biomechanical stability of the cornea. An increase in corneal cross-linking occurs naturally with age.

The aim of medical CXL is to increase the number of covalent bonds between the collagen fibrils – this is achieved by exposing riboflavin (vitamin B2) soaked collagen to ultraviolet light, thus inducing bonds to form.

The riboflavin acts as a photosensitiser when exposed to UV-A light, with a wavelength at the riboflavin absorption peak of 370nm. Free oxygen radicals are generated, resulting in a photopolymerisation process, which introduces the additional cross-links within and between collagen fibres up to a depth of 300μm.

With increasing cross-linking, the treated corneas are stiffer and more resistant to enzymatic digestion (increased biomechanical and biochemical stability). Additionally, there is reactive oxygen species-induced damage to microorganisms in the irradiated area.

The technique is used primarily to treat keratoconus in people. At Moorfields Eye Hospital, for example, many patients have been treated with great success – of 4,620 treatments performed, only two eyes went on to require corneal transplants. Prior to the availability of CXL, 20 percent of patients with keratoconus would eventually require a corneal transplant. However, there has also been some research into the use of CXL as an adjuvant treatment to treat infectious, melting keratitis.

**BASIC PROTOCOL FOR CXL USING THE PESCHKE VET SYSTEM:**

1. Sedate or anaesthetise patient.
2. Apply riboflavin to cornea: one drop every two minutes for 15 to 20 minutes (to saturate cornea) (Figure 1).
3. Inspect anterior chamber for yellow discolouration (indicates good saturation of cornea with riboflavin – apply more drops if insufficient saturation).
4. Insert eyelid speculum.
5. Rinse cornea with saline to remove excess riboflavin (to avoid riboflavin shielding).
6. Set UV power – 45mW/cm².
7. Turn on CXL system, focus beam on cornea (45 to 55mm distance between CXL unit and eye) (Figure 2).
8. Adjust beam diameter to irradiate desired area.
9. Illuminate cornea for two minutes (unit will automatically stop) (Figure 3).
10. Continue medical treatment (eg topical chloramphenicol, atropine or serum, as clinically indicated).
11. Monitor carefully while healing takes place.

**FIGURE (1)** The riboflavin is formulated with HPMC to create a viscous eye drop.