Long-term outcomes for accelerated corneal cross-linking treatment for progressive keratoconus in a high risk cohort of patients

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Introduction:

Keratoconus is a progressive corneal ectatic condition mainly affecting teens and young adults, which can progress for 10 or even 20 years. The rate of progression tends to be faster in those under the age of 18 years[1]. A number of genetic and environmental factors have been identified which include family history, atopy and eye rubbing[2,3].

Diagnosis and monitoring is undertaken predominantly using corneal topography. The corneal curvature can be fattened surgically through the insertion of intra-corneal ring segments and there are inserts which can also strengthen and stabilise the weakened tissue[4]. However, the underlying mechanism of collagen degradation through enhanced enzymatic digestion and tissue weakening is not being addressed with these interventions alone. Invasive surgical treatment using partial or full thickness grafts will be required in approximately 12% of cases due to disease advancement, scarring or intolerance to refractive aids[5].

Photochemical collagen cross-linking is used to halt disease progression by utilising ultraviolet light in conjunction with riboflavin (a photo-sensitiser). Photochemical collagen cross-linking has been shown to significantly stiffen the cornea and make the tissue more resilient to enzymatic digestion[6]. Initially, the standard protocol was developed which involved application of ultraviolet-A (UVA) light with a wavelength of 365-nm at an intensity of 3 mW/cm^2 for 30 minutes[7]. An accelerated protocol using higher intensity UVA was developed to reduce total treatment time by reducing both light exposure and riboflavin application time. Herein, we report our clinical experience of using accelerated CXL at a tertiary centre with a large atopic population and longer follow up than most studies which have been published.

Aim:

To report long-term outcomes for accelerated corneal collagen cross-linking treatment for progressive keratoconus in a high risk cohort of patients at The Birmingham Midland Eye Centre, a tertiary referral centre.

Method:

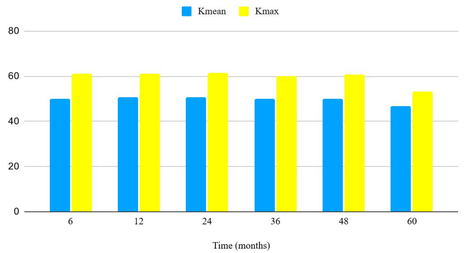
A prospective study of patients who had undergone accelerated corneal collagen cross-linking for progressive keratoconus between January 2016 to March 2017. One hundred and two treated eyes were followed up, data was collected on demographics, co-pathology, refraction, pre- and postoperative visual acuity, Pentacam corneal topography, complications and the need for repeat treatment or surgical intervention.

Surgical Methods: The corneal epithelium was removed, riboflavin applied for 20 minutes followed by UV-A irradiation (10 mW/cm2) for 9 minutes. Collagen shield or bandage contact lens was applied. Patients were discharged with topical antibiotics and cycloplegics, and topical steroids commenced at one week follow-up. Data was collected at six months, one year, two years and three years.

Table 1: Visual acuity (VA), K values and central corneal thickness (CCT) post cross-linking

Time (months)	VA (logaMAR)	Kmean (Dioptre)	Kmax (Dioptre)	CCT (microm)	Number of patients
6	0.225	50.04	61.02	461.39	70
12	0.295	50.6	61.2	442.1	47
24	0.297	50.66	61.55	442.1	36
36	0.234	49.89	60.07	440.26	32
48	0.4	50.03	60.7	436.95	14
60	0.54	46.72	53.38	427.2	5

Figure 1: Topography changes post cross-linking



Results:

Average age at initial treatment was 25 years (range 16-33), 65% of the cohort were male, majority were Asian ethnicity (80%) and 26% suffered from atopic eye disease. The number of patients whose pentacam data was collected over the three year period can be found on table 1. Mean visual acuity was 0.225 logMar preoperatively, 0.225 logMar at 6 months, 0.295 logMar at 1 year, 0.297 logMar at 2 years and 0.234 logMar at 3 years. Mean Pentacam Keratometry was 50.04 diopters at 6 months, 50.6 diopters at 1 years, 50.66 diopters at 2 years and 49.89 diopters at 3 years. No complications apart from one case of corneal haze. Repeat cross-linking was required for five patients, of which two were performed at two years and three at 3 years after the initial treatment. Of those requiring repeat treatment one patient had severe allergic eye disease and there was a history of persistent eye rubbing in all cases. No patient in our cohort required a corneal transplant.

Figure 2: Visual acuity post cross-linking

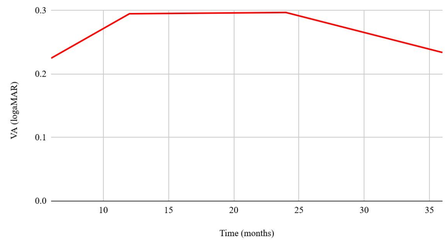
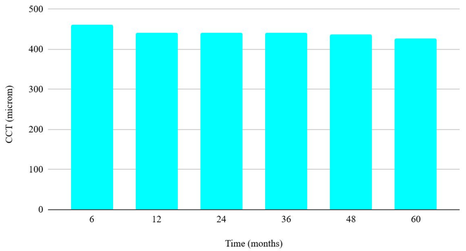


Figure 3. Central corneal thickness post cross-linking



Discussion:

Keratoconus can cause high morbidity and reduced quality of life in a young population who are otherwise fit and well. Most of the surgical treatments for correcting astigmatism do not treat the underlying pathology. Photochemical collagen cross-linking has been shown to increase corneal rigidity as well as resistance of corneal stroma to enzymatic degradation which plays a role in keratoconus development. We have presented data from our cohort of patients who have undergone photochemical cross-linking with three years follow up, which is longer than most studies published in the literature. Our cohort of patients consisted of a high proportion of patients with Indian subcontinent ethnicity, who are known to have a higher than average rate of atopy compared to other ethnicities. In our cohort 26% of the patients were documented as having atopy. Despite this visual acuity and topography have remained stable 3 years post cross-linking treatment (fig.1). The data suggests corneal flattening (fig.1) and improvement of visual acuity (fig.2) at 3 years, however we have a relatively small cohort of patients and larger data set would be required to confirm whether this was statistically significant. There was also low incidence of complications post cross-linking with only one patient developing corneal haze and five patients requiring repeat cross-linking. None of the patients in our cohort required corneal grafting.

Conclusion:

Despite a high proportion of young patients with atopic eye disease, we have demonstrated good safety and long-term efficacy of the accelerated corneal cross-linking treatment

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