Original Article

KERATOCONUS

Ahmed M Khalafallah MD[1] , Ahmed A Abdelghany MD[1] , Ahmed M Sabry MD[1] , Yahia M Khairat MD[1] , Mohamed F. Abdelkader MD[1]

[1] Ophthalmology Department, Faculty of Medicine, Minia University, Minia, Egypt
Email:drahmedmaher1988@gmail.com
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Abstract

Keratoconus is a progressive noninflammatory ectatic disease of the cornea with onset at puberty in most cases. Both genetic and nongenetic or environmental factors have been implicated. Keratoconus has been associated with numerous genetic systemic disorders. many keratoconus-associated syndromes have a high incidence of eczema and atopy, such as Down syndrome, hyper-IgE syndrome, ichthyosis, and oculodentodigital syndrome, Turner syndrome (conjunctival lymphangiectasia), autographism and Mulvihill–Smith syndrome. In each of these syndromes associated with atopy and eczema, associations are known to include both keratoconus and eye rubbing. Keratocyte density, possibly from IL-1–induced apoptosis, is reduced in keratoconus and can be demonstrated as well with eye rubbing and with contact lens wear. A recently developed treatment for keratoconus is corneal collagen crosslinking (CXL). In CXL, stromal fibers are photopolymerized by the combined action of a photosensitizing substance (riboflavin or vitamin B2) and ultraviolet rays A.

Keywords : Keratoconus – Intracorneal ring segment – Corneal collagen crosslinking

INTRODUCTION

Keratoconus is a progressive noninflammatory ectatic disease of the cornea with onset at puberty in most cases.[1] The etiopathogenesis of keratoconus is still unknown, but it is generally accepted that keratoconus is a multifactorial condition or that it represents the final stage of a variety of different pathological processes. Both genetic and nongenetic or environmental factors have been implicated. There is strong evidence for genetic factors in the literature. Although usually sporadic, a family history of keratoconus is not unusual with about 15% of patients.[2] Topography in first degree relatives of keratoconus patients is also more likely to show patterns resembling keratoconus.[3] Ioti et al[4] found keratoconus or keratoconus suspect patterns in 60.2% of family members of Japanese keratoconus patients by topography and/ or Orbscan.[5]

Keratoconus has been associated with numerous genetic systemic disorders. These genetic disorders and syndromes have some unifying factors when they are reclassified. The majority of genetic syndromes associated with keratoconus fall into one of the following 4 groups: connective tissue disorders with abnormal collagen elasticity, abnormal retinal function with oculodigital stimulation, associated with atopy or eczema and eye rubbing, or low mental function associated with oculodigital stimulation. A number of these keratoconus-related disorders involve abnormalities of collagen elasticity and connective tissue, including brittle cornea syndrome, congenital hip dysplasia, joint hypermobility, nail patella syndrome, osteogenesis imperfecta, Ehlers–Danlos syndrome, false chordae tendineae of the left ventricle, Marfan syndrome and pseudoxanthoma elasticum. In addition, many keratoconus-associated syndromes have a high incidence of eczema and atopy, such as Down syndrome, hyper-IgE syndrome, ichthyosis, and oculodentodigital syndrome, Turner syndrome (conjunctival lymphangiectasia), autographism and Mulvihill–Smith syndrome. In each of these syndromes associated with atopy and eczema, associations are known to include both keratoconus and eye rubbing.[6]

Specific genetic defects have been found in small numbers of keratoconus families such as a VSX-1 mutation but have not been found in most others. [7] A deletion in the SOD-1 gene has been reported in 2 families. [8] HLA-A26, B40, and DR9 have been associated with early-onset keratoconus in Japan. [9] Various loci have been linked with keratoconus susceptibility, including those on chromosomes 2, 3, 5, 6, 9, 13, 15, 16, 17, and 20. Genome-wide association studies have identified 2q21.3 as a highly significant susceptibility region for keratoconus. All these findings strongly suggest a genetic component to the development of keratoconus. [10]

Environmental factors, however, have also been strongly associated with keratoconus. Atopy has been shown to be associated in many studies. The association may be because of eye rubbing in people with allergic symptoms, leading to corneal ectasia. In a case–control study by Bawazeer et al [11], univariate analysis suggested that atopy, eye rubbing, and keratoconus family history were all associated with keratoconus development, but multivariate analysis showed that only eye rubbing was statistically significant. McMonnies extensively reviewed the topic of possible mechanisms for the association between what he termed chronic habitual eye rubbing and the development of keratoconus. He described a number of possible mechanisms including temperature increase from eye rubbing, leading to increased activity of inflammatory mediators and enzymes; hydrostatic pressure increases combined with enzyme activation "tenderizing" the cornea; reduction of corneal shear strength; reduction of proteoglycan viscosity and displacement of proteoglycans from the corneal apex; and induction of keratocyte apoptosis from eye rubbing. [12]

Wilson et al [13] demonstrated that epithelial trauma could lead to interleukin-1 (IL-1)–mediated apoptosis and postulated that this could take place in keratoconus. Fabre et al [14] showed that IL-1 receptor sites are increased in cultured keratoconus stromal cells. Interestingly a recent study showed the presence of IL-1B promoter mutations in Korean keratoconus patients. [15]

Keratocyte density, possibly from IL-1–induced apoptosis, is reduced in keratoconus and can be demonstrated as well with eye rubbing and with contact lens wear. Indeed, contact lens wear has been associated with increased keratoconus risk. [16] Also, keratoconus patients wearing rigid contact lenses seem to express proinflammatory cytokines much more than normal myopic contact lens wearers. [17]

Factors that may reduce keratoconus risk include smoking, which seems to have a reduced prevalence in keratoconus patients and perhaps reduces the risk by increasing corneal collagen cross-linking. [18] Diabetic hyper-glycemia may also increase corneal collagen cross-linking, and it seems that diabetic patients with keratoconus have less severe disease. [19]

A recently developed treatment for keratoconus is corneal collagen crosslinking (CXL). In CXL, stromal fibers are photopolymerized by the combined action of a photosensitizing substance (riboflavin or vitamin B2) and ultraviolet rays A.[20] Photopolymerization increases the rigidity of corneal collagen. The aim is to slow or arrest progression of the disease to delay or avoid keratoplasty.[21]

Intrastromal corneal ring segments (ICRS) have been proposed as an additive surgical procedure for keratoconus correction to delay, if not prevent, the need for corneal grafting.[22–24] The goal of ICRS implantation is to regularize the front surface of the cornea while maintaining the existing biomechanical status of the underlying stroma.[25]

Femtosecond laser technology was introduced to create intracorneal channels for ICRS implantation.There are several advantages over the mechanical method, including that femtosecond channel creation is minimally invasive, creates more uniform dissection, gives more consistent results, causes less patient discomfort, provides faster visual recovery, and allows more accurate ICRS placement.[26] A combination of these modalities (CXL, ICRS, and femtosecond laser) should yield better results because the procedures complement one another. However, the ideal sequence of intervention is still unknown.

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