Review Article

Keratoconus: Latest Approaches to Treatment

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Abstract

Background: Keratoconus is a degenerative disease entity characterized by conical shape ectasia of the cornea. The progressive conical deformation of the cornea leads to substantial astigmatism. Patients who are at an advanced stage of ectasia are often led to corneal transplant or other treatments, which essentially aim at correcting the refractive error and not in treating the ectasia. Lately, the corneal collagen interface is
Objectives: The purpose of this review is to investigate the parameters of the disease, namely the pathogenesis, causes and treatments so far and the analysis of the new therapy aimed to treat the disease.
Methods: An advanced search in the literature was carried out using the Pubmed database, Scopus and Google scholar, from 2009 until today. Keywords and combinations of Keratoconus, cross linking, riboflavin, collagen, corneal topography, UVA were used.
Results: The cuckold in early stages is treated conservatively by wearing contact lenses, which are designed to flatten the cornea and hamper further development. In advanced stages of keratoconus a surgical treatment is recommended, with corneal transplantation being the main choice. A newer approach to the treatment of the disease is corneal collagen interface using riboflavin and ultraviolet light, aimed to the stability and rigidity of the cornea. The nurse plays a key role in the treatment of keratoconus in all stages of treatment. The main nursing interventions include medical history, ocular examination by the review, psychosocial assessment, preoperative and postoperative care and teaching the patient the treatment parameters.
Conclusion: The keratoplasty and collagen interface are the main approaches to treatment of extensive disease of the cornea.

Key words: Keratoconus, cross linking, riboflavin, collagen, corneal topography, UVA

Introduction

Keratoconus is a disease entity of the optical system, characterized by a conical corneal ectasia. The ectasia consists in abnormal thinning of central and paracentral regions of the cornea, as well as progressive central deformation resulting in significant irregular astigmatism. The top of the protruding cone that corneal configuration may be close to the visual axis or below and nasal of that. The disease manifests during adolescence, followed by slow progressive course, although it is possible to stabilize anytime. In 85% of cases both eyes are affected, but the severity of the attack can present significant asymmetry (Kanski, 2004). Often in keratoconus a positive family history is present, and in some patients the inheritance appears to play an important role, but the character in which the disease is inherited is yet to be clarified. The disease has been described in conjunction with a variety of systemic diseases are mainly atopic diseases (atopic dermatitis), endocrine disorders, Down's syndrome, Marfan syndrome and ocular diseases such as vernal conjunctivitis, retinitis pigmentosa, congenital amaurosis of Lieber and ectopic lens (Leitmam et al, 1987). Bearing hard

contact lenses and rubbing the eyes have been proposed as potential predisposing factors (Vander and Gault, 1999).

It is difficult to estimate the incidence of keratoconus, because the diagnosis is easy to mistake, especially in the early stages (Snell and Lemp, 2006). The reported frequencies ranging from 400-600 to 100,000. It seems that there is no predisposition related to sex. Some studies report female predominance, while other studies report prevalence of the male sex. There is no known predisposition for race (Gore et al, 2013; Roe et al, 2008).

Eye and vision

The eye is located within the corresponding orbit, from which it is protected from the top, bottom, back and sides. The wall consists of three tunics, the fibrous, the vascular and retina. The forward fibrous sheath is transparent and is called cornea while the back is opaque and called the sclera. The cornea is the anterior portion of the fibrous tunic. It has round shape, diameter about 11 mm with transparent tissue and consists of five layers (epithelium, Bowman's membrane and the anterior aphoristic petal, substance or layer, the Descemet membrane or rear aphoristic petal and endothelium) (Kanski, 2004).

Descriptively, it exhibits two surfaces, the front which is convex and the back which is concave condenser len with power of 42 to 45 diopters. The cornea plays the main role in the refractive eye system. The thickness of the cornea is not the same in its entirety. They are thinner in the center, about 0.5 mm, while in the region increases to approximately 0.70 mm. Normally, the cornea lacks blood vessels. Its feeding is provided by the vessels of the limbus in the region of the aqueous humor of the anterior chamber, which wets the posterior surface of the cornea and from the tears that wet the front surface (Smith, 1984). The cornea, despite having no blood vessels, is nourished from the sources mentioned above and normally contains 65% H_2O. The anatomical conditions ensuring transparency of the cornea is the absence of blood vessels, the parallel arrangement of collagen fibrils and lamellae, the absence of the myelin sheath nerve grids and the limited number of corneocytes in the layer. The main functions of the cornea are the light refraction, the light transmission and the protection of the bulb. More important are considered the first two. The cornea is the major refracting portion of the ocular diopter with refractive power of 43 - 48D of the 60 - 65D total refractive power of the eye (Koo et al, 2011).

Etiology of keratoconus

The cause of keratoconus is unknown. Several biochemical abnormalities have been reported in corneas with keratoconus including defective collagen content, less or modified sulfate keratin molecules, reduced total protein and increased amount of non hydro protein material, and increased collagenolytic and gelatinolytic activity correlated with a decreased level of inhibitor of matrix metalloproteinase. Various studies have shown that the enzyme abnormalities and the proteinase inhibitor is more pronounced in the epithelial layer of the cornea, suggesting that the basic fault in keratoconus may occurs in the epithelium and interacts with the layer. The eye rubbing has been implicated as the cause of keratoconus. Patients with Keratoconus often admit excessive rubbing of their eyes (Tuft et al, 1994; Haddad et al, 2012).

By keratometry, keratoconus is categorized as mild (≤48 D), moderate (48-54 W) and severe (> 54 D) (Table 1). In mild forms the morphology of the cone is not specified.

Clinical keratoconus

Early points: The primary symptom for the patient is the reduction of vision (contralateral) due to irregular astigmatism. But as the disease progresses, visual impairment occur on the other eye too. The patient may indicate the need for frequent changes to correct omatogyalion or a decreased tolerance to contact lenses' strength. The ophthalmoscope shows a reflection like a drop of oil. In Javal optometry characteristic weakness of congruent mirror images is observed, which is an early and objective characteristic finding of keratoconus (Filippello et al, 2012).

Abnormal astigmatism can also be established by skiaskopia (irregular reflection), and with the Placibo disk (distortion of the concentric rings of the disk projected on the cornea). These tests are useful for early diagnosis of keratoconus, when there is no apparent deformation of the cornea and the disease is still limited in one eye, when the other is free of overt clinical astigmatism. The earliest signs of keratoconus when considering the slit lamp is thinning the top and bulging, usually located below the pupil center.

As keratoconus progresses, the thinning and ectasia become more pronounced with the development of the peak scarring. This begins in the anterior layer and is then displayed in the deeper layers of the mattress. Thin straight streaks are visible deep in the mattress, just in front of the Descemet's membrane, usually in the direction vertical or oblique. It is believed to represent stress lines in the rear layer, known as the Vogt lines (Rebenitsch et al, 2011).

Sequelae points: In this phase the cornea is deformed even longer, the irregular astigmatism is further increased and, additionally, myopia occurs. The conical prominent deformation presses the lower eyelid when the gaze is downward and imparts a V morphology shape. The slit lamp corneal thinning becomes readily apparent. In cases of long established keratoconus, haemosiderin deposits are observed to be deposited by the tears around the base of the cone into the epithelium and Bowman's membrane. Another finding in the slit lamp is scars from ruptures of the membrane of Bowman, which results in the clouding of the cornea (Vander and Gault, 1999). A serious complication that occurs in advanced forms of keratoconus is acute hydrops. Ruptures in Deskemeteio membrane allow the aqueous to enter the corneal stroma, resulting in a marked thickening and clouding of the cornea that is usually limited to the cone. The layer suffers no pronounced thickening with large cracks filled liquid, supernatant epithelial edema and blistering. Rarely a syringiodis diode can be formed, which causes leakage of aqueous humor through the full layer of fluid and epithelium on the corneal surface.

The corneal swelling gradually resolves over weeks or months, as the adjacent to the rupture of the membrane Deskemeteio endothelial cells grow and migrate across the lesion, creating new Deskemeteio membrane. In healing, the scarring tends to flatten the cornea, thereby facilitating the possibility of contact lenses use. Some corneas with acid hydrops tend to develop stromal neovascularization, which increases the potential risk of graft rejection, in the case of a corneal transplant. Acute hydrops is most common in patients with Down syndrome and vernal keratoconjunctivitis, possibly associated with the recurring injury from eye rubbing in these patients. Most cases of acid hydrops automatically are resolved, requiring supportive care with local hyperosmolar agents such as sodium chloride drops 5% and / or ointment to promote apooidimatopoiisi cornea. [3] Some patients with acute hydrops complain of severe photophobia and have the benefit from the use of topical steroids. In addition, topical steroids should be administered to patients with corneal neovascularization hints. Once the hydrops are resolved, the patient can try to continue the use of contact lenses, if the central cornea has scarred badly. Otherwise, the only alternative is the corneal transplant (Vander and Gault, 1999).

Keratoconus and contact lenses

The association between the use of contact lenses and keratoconus is contradictory. Opportunistic evidence suggests that the use of contact lenses can lead to the creation of keratoconus, particularly in the case of long use of hard contact lenses. Such patients tend to appear keratoconus later in life and have corneal curvature flatter than typical patients with keratoconus. Additionally, contact lens-induced cones tend to be located more centrally in the cornea of the most characteristic keratoconus, which is eccentrically localized downwardly (Kymes et al, 2008).

In the contact lens warpage syndrome, the wear of contact lens causes uneven staining without the typical signs of keratoconus in the slit lamp. The interruption of the use of lenses for weeks or months eliminates astigmatism and allows the cornea to recover its normal shape, while in the induced by contact lenses keratoconus, the changes are permanent and they do not resolve when the use of contact lenses is discontinued.

Some contact lens fitters find that the lenses can be used to flatten the cornea, and to reverse or at least delay, further progression of keratoconus. However, the flattening of the cornea induced by contact lens to patients with keratoconus are temporary and the cornea returns to its original shape, which it had before the application of the contact lens, when the use of the lens is stopped.

Conventional soft contact lenses can be successfully used in mild cases of keratoconus with little overt astigmatism. Local soft lenses can also be used in some patients without excessive amounts of irregular astigmatism. The vast majority of patients with keratoconus are treated with rigid gas-permeable contact lenses. The application of such lenses in an

irregular cornea extensional is difficult. Large lens designs are available for application to patients with keratoconus, including varying diameters of the spherical lenses, spherical lenses, local lenses and lenses with multiple curvatures of the rear surface, such as conical lens Soper. The Soper cone lenses have more convex central curvature to align with the more normal peripheral cornea. The computer topography is used by some contact lens fitters to assist implementation in these difficult patients (Caporossi et al, 2010).

Treating keratoconus

Surgical intervention is reserved for patients with keratoconus in which the contact lens is unsuccessful or for those who fail to obtain satisfactory vision with contact lenses. The atopic patients with keratoconus tend to go for surgery more often than non-allergic patients because the allergic disposition tends to interfere with the tolerance of contact lenses (Snibson, 2010; Kanellopoulos, 2012). The most common surgical interventions are:

- The transparent keratoplasty (transplant corneal overall t hick). It is the most common surgical technique for patients with keratoconus. The surgery procedure requires standard full of cone, often defined from the dachtylio of Fleisher. The cone extends near at limbus (usually downwards) requires large corneal graft. Usually the graft is centered over the pupil, but when the cone is eccentric, eccentric graft is used to surround the entire cone, while attention must be paid in allowing the optical zone free of stitches. Increased graft size that adjacents to the blood vessels of limbus reduces " immune privilege " of the normally avascular cornea, increasing thereby the risk of immunologic reaction**.**
- The surface (partial thickness) keratoplasty may be applied to patients with keratoconus, although the process is technically difficult and in the hands of most surgeons achieves a slightly poorer visual effect than the total thickness procedure. However, a partial thickness graft has the advantage of extraocular procedure that avoids the risk of endothelial rejection. Most cases of partial thickness keratoplasty performed as tectonic processes for large cones where the thinning extends to the limbus. If no satisfactory visual effect is achieved, a smaller central corneal transplantation total thickness can be performed afterwards, within the range of partial thickness graft, avoiding in this way an increased risk of immune rejection is a large total thickness keratic explants.
- Epikeratofakia is a type of partial thickness keratoplasty, using a frozen and dried donor cornea, stapled over the cornea apepithiliopoiimeno receiver. The purpose of this process is to flatten the cornea with the hope of improved - aidedr with glasses - visual acuity and / or better implement contact lens. [5] After the initial enthusiasm in the late 80s, the procedure was abandoned by most surgeons because of complications and poor visual effects. However, in selected cases, in which a full thickness corneal transplantation is contraindicated the partial thickness procedures, such as horseshoe-shaped grafts or epikeratofakia worth considering. Cases like these are patients with Down syndrome who are aggressively rubbing their eyes and generate a full-thickness wound, or in patients at risk for immune rejection (ie. failed transplants the other eye).
- Thermoplastic is a technique in which the cornea is heated at 19-120o C to provoke shrinkage of the fiber of the collagen corneal, which leads to eveling of the cornea. This procedure has been abandoned by most clinicians because of the unexpected results of scarring generation and the probability of appearance of erosions of corneal due to damage at the basic membrane of the epithelium.

Some patients with keratoconus develop over stimulated epoepithiliaki scar on the top of the cone as a result of chronic irritation of the peak by the use of contact lenses. Crush of the corneal epithelium can occur above the scar, thereby

interfering with the use of contact lenses. These scars can be removed by hand with a blade or by laser excimer, which permits the use of contact lenses once again (Mazzotta et al, 2007; Wollensak et al, 2007).

Latest approaches to treatment of keratoconus

The corneal collagen linkage using riboflavin and ultraviolet - A (UVA) constitutes the most recent method of treatment of keratoconus. The interconnect technique is a common tissue stabilization process. [4] Corneal Collagen Cross-linking (CXL) using riboflavin and ultraviolet A (UVA) is a new therapeutic method, which stops or slows the progressive thinning of the stratum corneum, as well as increasing industrial stability of tissue (Mazzotta et al, 2007; Wollensak et al, 2007).

Ultraviolet radiation is electromagnetic radiation with a wavelength between that of visible light and X-rays. The range of UV radiation is divided into UVA (315-380nm), UVB (280-315nm) and UVC (<280nm). Cross linking of the collagen of the cornea (CXL) is achieved with the help UVA of 365nm wavelength. UVA is produced by a specific device, which is suitable for clinical use. Before use, it is necessary to regulate it by using a radiation UVA meter (Wollensak et al, 2007).

Riboflavin or vitamin B_2 photosensitiser, shows an absorption maximum at 365nm and plays an important role in maintaining human health. Riboflavin is difficult to dissolve and thus the therapy is used CXL riboflavin phosphate, which is more expensive but more soluble form of riboflavin. When CXL is used, riboflavin permeate the corneal layer and meets the anterior and posterior chamber of the eye and the vitreous. This is best achieved when preceded by apoepithiliopoiisi of the cornea, which enables the macromolecule riboflavin to penetrate more easily (Kelly et al, 2011; Snibson,2010).

Riboflavin under the effect of UVA sensitized, i.e. absorbed protons and it induces. Immediately after irradiation, growth in industrial rigidity of the cornea is observed by about 300% along with growth of the resistance to the action of enzymes. This rigidity is due to the creation of additional bonds between the fibrils of type I collagen, that is the collagen which confers tissue durability (Kelly et al, 2011; Wollensak et al,2007; Gkika et al, 2011).

Table 1. Types of keratoconus

Type of keratoconus	Size	Characteristics
Cones like nipple	**<5mm**	Sharp curvature. The top of the central region of the cone usually located in the center or off-center and are displaced downward and nasally.
oval cones	**5- 6mm**	Ellipsoidal Displaced downwardly temporally.
Cones like a bullet	**> 6mm**	Concern more than 75% of cornea

Nursing interventions

The nurse collects information from the patient to determine if the problems of the eyes or vision impact on everyday life. The patient gives an accurate history that includes any visual disorder and the visual process and the ocular structure are assessed. Questions about diabetes, hypertensive disease and systemic medical problems that could affect the vision are asked and lifestyle, type of work and family history are evaluated. The review checks the head tilt and

actions suggest compensatory positions evaluated to achieve pure vision. The symmetry in the appearance of the eyes, the placement of the eyes in the orbit and the symmetry of their movements are also assessed (Ignatavicius and Workmann, 2008).

The psychosocial assessment is also particularly important for patients with changes of normal visual function, as anxiety or fear of possible loss of vision can be present. The feeling of dependence caused by impaired vision can affect self-esteem. The nurse discuss the concerns of the patient with family members to determine if there is support (Wang and Tian , 2015; Stevens, 1994).

When the conservative treatment is chosen, the nurse enhances the patient's ability to use his remaining sight. When administered medication, the nurse plays a key role in teaching the patient or relatives the best practice to instill eye drops and hand disinfection.

Preoperatively, the nurse informs the patient of the process of surgery and discusses his expectations and he/she examines the eyes for signs of infection. Postoperative care mainly involves administering antibiotic treatment, change of eye patches, measurements to prevent the increase of intraocular pressure, evaluation of pain and administration of mild analgesics as well as promoting patient comfort and space orientation (Ignatavicius Workmann and, 2008; Wang and Tian , 2015).

Conclusions

New therapeutic developments for the treatment of keratoconus are an encouraging message for the patients. The CXL treatment is a promising technique that aims at halting the pathogenetic mechanism of the underlying ectasia and delays or even interrupts the progression of keratoconus and the possible need for keratoplasty. Furthermore, it presents small learning curve since, in contrast to other treatments, is technically simpler and less invasive. The international literature shows that to some extent there is a regression in 50% of patients in the years to follow. This regression is of 2-3 D, and could be attributed to the post-operative wound healing process. The health practitioner who knows the details of addressing keratoconus and the newer approaches of this therapeutic solution, he will be able to provide the best health care in the patient.

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