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Childhood Keratoconus

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Abstract

The present research represents a theoretical, retrospective and cross-sectional study, 50 clinical histories were analyzed, of patients between 4 and 18 years old, who attended the Consultation at the Ophthalmologist of Santa Lucia during the period from March 2012 to March 2013, evaluating a total of 100 eyes, from which were taken as study objectives age and sex, refraction, referred symptoms and clinical signs to biomicroscopy, keratometry values, pachymetry and corneal topography indices. In the results It was observed that the female sex represented 58% and the age from 7 to 9 years 30% of the sample, in a large majority (64%) ocular pruritus was associated, the keratometry altered slightly I represent 47%, 34% presented minor corneal thinning 555 microns, 42% presented associated myopic astigmatism and the oval and asymmetric topographic pattern was predominant, the topographic indices of SRI, SK and KC were those studied for patients with suspicion of this pathology. Finally, it is concluded that, the female sex and the ages between 7 and 9 years were those that predominated in this study. Clinical findings of ocular pruritus, Vogt stretch marks and Fleischer rings were reported in our patients, as well as keratometry with slightly altered values and pachymetries below 555 microns. The associated predominant refractive defect was Myopic Astigmatism. The topographic patterns found in our patients were round, oval and asymmetric, the latter 2 being the most frequent. The topographic parameters of SRI, SK and KC, were very useful in the diagnosis of patients with a clinic suggestive of keratoconus.

Keywords: *Parameters for the Diagnosis; Keratoconus; Ophthalmology*

Introduction

Keratoconus (KC) has been known since 1748, when German professor Burchard Mauchart (1696 - 1751) described the eye disease now known as KC. It is a pathology of the ectatic cornea that causes it to take the form of a cone. There is no medical treatment, but the application of riboflavin/UVA- has become a standard method to stop the progression of the disease (Wollensak., *et al*. 2003). With a prevalence of 1: 1200 (Nielsen., *et al*. 2007) it is one of the most frequent causes of penetrating keratoplasty and anterior lamellar keratoplasty. The diagnosis of patients in the KC terminal phase for corneal transplantation is simple, but the diagnosis of the early stages is more difficult. A genetic diagnostic tool, based on the growing knowledge of corneal dystrophies (Weiss., *et al*. 2008), is desirable [1].

Apical keratoconus is the most common thinning, affecting the paracentral region of the cornea. Atopy, hard contact lenses and eye rubbing are often observed in KC patients, although their direct causality is not yet proven. Most cases of KC seem sporadic, but genetic factors may be involved because certain families show an apparent autosomal dominant pattern of inheritance, there is a higher

prevalence of KC in families with an affected individual (Wang., *et al*. 2000) and Concordance is high among monozygotic twins (reviewed in Weed., *et al*. 2006) [2].

The smaller amount of the extracellular matrix (ECM) indicates an alteration of homeostasis that may be caused by reduced synthesis or increased degradation. Proteases and their inhibitors are implicated in the latter. Likewise, the distribution of keratocytes is decisive. This is demonstrated in the study Corneal keratocytes: the organization of contractile proteins of the cytoskeleton in situ and *in vitro* [3].

They describe that recent studies on the healing of corneal wounds suggest that the activation of corneal keratocytes they develop myofibroblastic characteristics that include a contractile apparatus composed, in part, of a group of intracellular microfilaments (e.g. stress fibers) containing f-actin, myosin and α-actinine; extracellular fibronectin fibrils; and surface membrane fibronectin receptors (integrin α_5 β_1). The purpose of the study was to determine the exposure and organization of specific components of the normal contractile apparatus and inactive corneal keratocytes in situ; compare the organization in situ with those that are active and also compare tissue cultures of corneal keratocytes *in vitro* that can mimic fibroblast healing [3].

The method used was cat corneal tissue, obtained immediately after being sacrificed and prepared for in situ studies or cultured in a culture medium supplemented with 10% fetal calf serum for *in vitro* studies. Keratocytes (in situ and *in vitro*) were stained with: phalloidin, is a mycotoxin specifically linked to f-actin; Rabbit antibovin aortic myosin; anti-human monoclonal α-actinin; anti-human monoclonal vimentin; integrin α_5 β_1 rabbit antihuman; anti-human monoclonal α_5 integrin; connexin 43 monoclonal antihuman; and goat antihuman fibronectin. Cytoskeleton organization and colocalization were evaluated using an epifluorescent and confocal microscope. The results obtained describe that normal and resting corneal keratocytes were distributed within the cornea as a lattice network, interconnected widely by cellular processes extended from the body of a flattened cell. The distribution of f-actin of the kerocytes in situ was predominantly cortical and appears to be closely associated with the plasma membrane. Additionally, certain areas that appear to be related to the adhesion sites were identified. These areas in particular seemed to stain with antibodies to α_5 β_1 but not to α_5. These data suggest that the receiver of fibronectin, integrin α_5 β_1 is not present in normal corneal keratocytes. Based on the colocalization studies, the traces of rabbit aortic myosin, anti-rabbit and monoclonal anti-α-actinin had a distribution quite similar to FITC phalloidin. The interconnections between keratocytes also showed traces of connexin 43, which indicated the presence of intercellular junctions. In contrast, *in vitro* activated keratocyte cultures showed an FITC staining pattern of phalloidin located primarily along intracellular stress fibers that was not detected in normal and inactive keratocytes. The myosin and α-actinin traces had similar distributions in the stress fibers, arranged in alternate bands, which suggests a sarcomeric distribution. Traces of anti-α_5 β_1 and anti-α_5 were associated with stress fibers, which indicated the presence of local adhesion. These studies show that there are large structural differences in the organization of contractile cytoskeleton proteins between normal, resting (in situ) and active (*in vitro*) keratocytes. In situ, contractile proteins appear to be associated with the cortical f-actin network, probably related to the maintenance of the cellular form and its interconnectivity. On the other hand, activated keratocytes were characterized by the presence of a putative contractile apparatus composed of f-actin, myosin and α-actinin organized in sarcomeric muscle bundles (stress fibers) associated with focal contacts containing integrin α_5 β_1. This information suggests that the activation of keratocytes, such as the transformation of myofibroblasts, should involve the reorganization of contractile cytoplasmic proteins as well as the exposure of integrin α_5 β_1 and the formation of focal contacts [3].

Several functional candidate genes for KC have been proposed on the basis of, for example, histological observations, as well as biochemical studies and include those encoding components of collagens, proteinases, proteinase inhibitors, members of the homeobox family (for example VSX1 gene) and the antioxidant SOD1 gene. The concentration of the components of the ECM and the many different proteases were extensively investigated from the mid-1990s until the first five years of the 21st century. Most studies demonstrated statistically significant alterations, but no real progress was achieved. A general problem of controlling ECM homeostasis in KC is that the disease takes 10 - 30 years to develop, which suggests rather small changes in balance. It is not clear if these small changes are

measurable. Protease degradation monitoring is further complicated by the lack of correlation between activity and concentration; some proteases require activation (of other proteases), overlapping substrate activity between proteases and the presence of potential inhibitors. Extracellular matrix proteins create different families of proteins that play a very important role during tissue maturation, wound healing and structural tissue maintenance. Recent studies show that there are variations of specific tissue types. MEC proteins work by complexing with each other and also interacting with their receptor cells, called integrins. Integrins are heterodimeric glycoprotein membranes that are, in part, a type of cell in human tissue. Like other stratified epithelia, the integrins found in the corneal epithelium are α_2 β_1, α_3 β_1, α_6 β_1 [4] and α_v β_1 that mediate at the basement membrane junction and inter cellular interaction [4].

Knowledge of the pathological mechanism of corneal disease is important for diagnostic purposes and for the development of a medical treatment other than cross-linking. (Crosslinking) Several linkage studies and a few association studies have been performed to elucidate the genetics of KC [2].

These results will be discussed in this review along with the results of gene expression studies and animal studies. An example of this is found in the study identification and functional characterization of two type VI collagen receptors, integrin α_3 β_1 and ng2, during the development of the corneal stroma in birds [5].

They describe in their results that on the sixth day of the embryo the receptors α_3 β_1 and NG2 were present in a diffuse pattern in cells found in the corneal and juxta corneal regions, indicating a migratory phenotype. On the fourteenth day, when the stroma is clearly differentiated, α_3 and NG2 were placed in a dotted pattern in a subset of the corneal fibroblasts, while β_1 was in a more general way. The location of NG2 and type VI collagen indicated that the collagen was present and its organization was associated with NG2 positive cells. Immunochemical analyzes performed on the fifth and fourteenth day revealed that α_3 has 155Da and that β_1 has 120Da and showed that these subunits interacted to form a heterodimer. NG2 was present with a central protein of 330Da and an intact proteoglycan of approximately 600Da; and stromal lysate analysis indicated a proteoglycan containing chondroitin sulfate [5].

Matrix-receptor binding demonstrated an interaction of β_1 and NG2 in periocular mesenchymal cells and corneal fibroblasts with type VI collagen, while only a subset of cells revealed the presence of α_3 and indicated the presence of another integrin β_1. No changes were observed in the results of *in vivo* and *in vitro* analyzes of α_3β_1 and NG2. So they conclude that two type VI collagen receptors. α_3 β_1 and NG2, are present during the development of the corneal stroma with an interaction between both receptors. These interactions can play a very important role in corneal cell migration and in the development and maintenance of the corneal structure [5].

Likewise, the important role of integrins in corneal physiology is demonstrated in studies conducted in rabbits where their distribution is evaluated after corneal abrasion. In this summary, the integrin complex α_6 β_4 is a component of the hemidesmosome [6].

In the healthy cornea both subunits of the integrin are found in the basement membrane laminin, but the α_6 subunit is also found between the basal cells. While it was already known that epithelial cell migration is performed without hemidesmosomes, the distribution of α_6β_4 during epithelial recovery was investigated. A 7.5mm diameter abrasion was performed mechanically in the epithelium. The rabbits were sacrificed between 1 and 24 hours or 2, 3 or 7 days later. Monoclonal antibodies against α_6β_4 and against laminin A were used to detect their distributions through immunohistochemistry analysis. Positive immunostaining for laminin A on the surface of the stroma without epithelium indicated that the basement membrane was intact after epithelial abrasion. 3 hours after the wound in the cornea α_6 was detectable around the entire cell to the front edge of the epithelium that migrated. In the peripheral wound, α_6 was quite present around the basal and suprabasal cells only being negative in the superficial layers of the cell. The β_4 subunit showed a different distribution, it was not detectable at the underlying front edge. After 1 hour of immunoreaction for the β_4 subunit, 15 to 20 microns had disappeared at the periphery of the wound. Thereafter, the subepithelial band was reassembled into segments, starting from the

periphery until reaching the central area of the wound. 1 week after the epithelial wound was performed, the examination performed on both subunits of the integrins was indistinguishable from those of the control corneas. These results indicate that in addition to the β_4 in the rabbit cornea, the α_6 subunit binds to other β subunits during the epithelial healing process.

The results also suggest that the basal cells of 15 to 20 microns peripheral to the margin of the wound dismantle their hemidemosomes before the migration process [6].

There are also studies where the dynamism of the integrins is evidenced during the corneal aging process, where it describes in confocal image the integrin subunits α_6 and β_4 in the human aged cornea. The purpose of this study was to examine the changes in the distribution of the integrin subunits α_6 and β_4 in the human aged cornea [7].

As a method they used 30 normal corneas were examined and divided into 3 groups; corneas of children up to 2 years of age, corneas of adults aged between 29 and 70 years of age and corneas of adults 70 years and older. The corneas were frozen and the sections were cut, doubly stained with monoclonal antibodies to the aforementioned integrin subunits and visualized with Texas red (sulfodamine 101 acid chloride) or fluorescein using a scanning confocal laser microscope. Computerized images were made to determine differences. In their results they obtained that the α_6 subunit was generally located along the basal and lateral surfaces of the basal epithelial cells and projected towards the Bowman membrane. The β_4 subunit was present only along the basal surface. In general, the greatest difference related to age was the continuous loss of the α_6 and β_4 subunits along the basal surface of the basal epithelial cells. At the time of reconstructing the images made to the corneas taken from individuals over 70 years old they were optically sectioned in layers, the α_6 subunit appeared discontinuous. If the same optical image had been made of corneas of young people, it would have been appreciated that the trail was continuous. The number and distribution of Hemidesmosomes along the basal lamina did not change with age in the corneas examined. Therefore, they conclude that using computerized images made with a scanning confocal laser microscope, it has been shown that there is a change in the location of the α_6 and β_4 subunits related to age [7].

From all these investigations it is concluded that there is a multifactor mechanism in the etiology of keratoconus, which are still under study, where the genetic component is interrelated with the environmental factor, due to which the early diagnosis in the child population and its timely treatment It represents a great challenge to the specialist [8].

Reason why the optimal treatment for this age group is also in the research phases, where the use of contact lenses is described as ineffective due to poor adherence to the treatment [9].

In this order of ideas, collagen fiber crosslinking therapy and lamellar or penetrating keratoplasty are described as another treatment option, however the possibility of rejection or primary failure is a frequent complication [10].

Objectives of the Study

General objective

To evaluate parameters for the diagnosis of keratoconus in a population between 4 and 18 years of age who attended the Santa Lucia Ophthalmological consultation during the period March 2012- March 2013.

Specific objectives

1. Identify gender and age of affected population.
2. Describe symptoms, clinical signs and complementary tests for diagnosis of keratoconus.
3. Identify associated predominant refractive defect.

4. Describe topographic pattern of patients with suspected keratoconus.
5. Analyze topographic parameters of patients with suspected keratoconus.

The problem and its justification

Keratoconus as an ectatic disease of the cornea, which is characterized by the tuning of the progressive corneal stroma, which can cause irregular astigmatism and therefore a decrease in visual acuity. Normally, it begins at puberty and progresses to averaged 30 years, when the progression slows down and sometimes stops. It can start in one eye, but it usually affects both and one eye can be more affected than the other.

It is widely described in literature of both general ophthalmology and specialized books in the area, such as those made by Rabinowitz or Duke-Elder S, however the physical supports referring to this pathology in children and adolescents are scarce, for this reason it is taken as a reference the study by Dr. Harb of the Ophthalmological Institute of Castroviejo, Madrid. Spain. Published in 2012.

Motivated to the fact that keratoconus is described as appearing in elderly adults and taking into account the high number of childhood patients who go to the pediatric office every day at the Ophthalmological Center of Santa Lucia with suspicion of this diagnosis, during the period of time included Between March 2012 and March 2013, the present work of review of medical records is carried out, with the purpose of evaluating criteria barely described in children in order to unify parameters for the creation of public policies in the country that describe diagnostic protocols, treatment and prevention that guide the correct management of keratoconus in a population so important that it represents the future of our society.

Operationalization of the variables

Theoretical framework

Research Background

This chapter presents existing studies that report diverse information related to Keratoconus in children and youth ages. Based on these, the comparison of the results obtained will be carried out. Likewise, the theoretical and legal bases on which research is based. This chapter presents existing studies that report diverse information related to Keratoconus in children and youth ages. Based on these, the comparison of the results obtained will be carried out. Likewise, the theoretical and legal bases on which research is based.

At the National Reference Center for Keratoconus in France, a retrospective 10-year study (2,000 to 2010) of keratoconus patients diagnosed before age 15 has been carried out. Age, sex, reason for consultation, ethnicity, personal and family history, allergic history, eye rubbing, optic and surgical treatment and academic and professional training were identified. Forty-nine children were studied. Most of the patients were white. Children were more frequently male ($p = 0.0386$) and eye rubbing was found in 91.84% of children. In total, 12.24% of the children had a family history of keratoconus [2].

A retrospective monocentric study was carried out at the National Reference Center for keratoconus, Bordeaux (France), between October 2009 and November 2010. 216 patients were studied, aged ≤ 15 and 167 patients (77.3%) with ages ≥ 27 years at the time of diagnosis, which were seen within 2 years of diagnosis. The severity at the time of diagnosis was assessed by Krumeich classification. The results obtained were that keratoconus in children was significantly more severe at the time of diagnosis, with 27.8%, compared to 7.8% of adults ($p <0.0001$). In addition, ophthalmoscopic signs were more frequent in children (42.9% vs. 29.5%, $p = 0.05$). After diagnosis, keratoconus did not evolve more frequently in children. However, in the case of progression, it evolved faster in children, with significant differences in spherical equivalent and maximum and minimum keratometry ($P = 0.03$, $P = 0.02$, $P = 0.04$, respectively) [11].

Dr. Tamara Harb conducted in 2010 a descriptive, prospective study where corneal topography and refraction study is performed on 100 patients under 16 years. The topographic indices used were to:

a. Simulated keratometry 1 and 2 (-K1 and -K2).

b. Corneal Surface Regularity Index (SRI). (13)

The results obtained were: Distribution by age Taking into account the 2003 Zadnik study [13].

1. Children under 6 years (37 children).
2. Between 6-8 years (34 children).
3. Over 8 years (29 children).

The frequency distribution of the sex variable in boys shows a slight predominance of males: 52 boys (52%), 48 girls (48%). The mean value of K1 is 45.03 (± 1.81) in girls and 44.24 (± 1.64) in boys. There are no significant changes in K1 with age when the two sexes are analyzed together, but when analyzing each sex separately, K1 increases with age in girls and does not change in boys. The value of K2 in girls is 43.71 (± 1.84) and in boys 42.99 (± 1.45.) This value increases slightly with age, if we study the two sexes together, it increases with age in girls and does not It changes in children. The average SRI value is 0.46 ± 0.18 in girls and 0.42 ± 0.21 in boys. With an average of 0.44 and there are no changes with statistical significance between the two sexes. The predominant refractive defect was myopic astigmatism (66%), which increases with age [12].

At the Federico Gómez Children's Hospital of Mexico, the following work was carried out, which included all patients undergoing QPP during the period from March 2006 to March 2011 who were under 16 years of age at the time of transplant. 49 penetrating keratoplasties were performed in 39 patients The most frequent cause of QPP was keratoconus in 63.83% [14].

A retrospective review of all patients between the ages of 6 and 25 years, enrolled in the Bank of Corneas of the Hernán Henríquez Aravena Hospital of Temuco-Chile between the years 2008 to 2013 was carried out. Visual acuity, prognosis, was evaluated. Age, sex, surgical indication. The infectious cause was the most frequent both on the waiting list and patients undergoing penetrating keratoplasty and there are no statistically significant differences in terms of sex [15].

The La Trinidad Teaching Medical Center, in May 2014, held a conference entitled "Keratoconus in children", where it presents results of a prospective study conducted between February 2012 to August 2013, with a universe of 152 children with ocular atopy symptoms and 51 children between 4 and 18 years old were included in a protocol for the study of keratoconus, performing a complete ophthalmological examination and corneal topography every 6 months, for presenting suggestive refractions of the same (cyl difference of 1.50 between one eye and another). The main objective studied was corneal biomechanics and its association with keratoconus.

The results obtained were: average age of presentation, 9 years, without prevalence by gender. Central corneal pachymetry decreased in 45% cases, Keratometry averages K1 45 and K2 46.

Average of cil-4.00. Associated with myopia. It is concluded that the main prevention for this pathology must be to avoid manipulating the eyes with the knuckles of the hands [16].

In the Military Hospital "Dr. Carlos Arvelo "carried out a descriptive, prospective work, entitled" Incidence of astigmatism in pediatric ages from January to July 2010. "The population was represented by 250 pediatric patients and the sample was 60 patients between 5 and 18 years old; To those who underwent an atopy and hereditary background research questionnaire, visual symptomatology and subsequently the complete ophthalmological examination with respective post-cycloplegic refraction. The proposed objectives are

related to the main risk factor, incidence by sex and age group, the type of astigmatism and degree of severity and finally visual acuity and its relation to astigmatism according to its meridians. The results reported were that the main risk factor was inheritance, the incidence by sex was represented by the same proportion in both sexes, with the ages of 05 to 10 years having the highest proportion. The most frequent astigmatism was the hypermetropic (44.66%), mild type, (76.6%) and the type in favor of the rule presented better visual acuity, represented by 65% [17].

Theoretical bases

Keratoconus is a non-inflammatory pathology of the cornea that is characterized by the tuning of the progressive corneal stroma, which can cause irregular astigmatism and therefore a decrease in visual acuity. Normally, it begins at puberty and progresses to averaged 30 years, when the progression slows down and sometimes stops. It can start in one eye, but it usually affects both and one eye can be more affected than the other. Loss of vision is a consequence first of irregular astigmatism and myopia and secondly of corneal scar. Between 12 and 20% of affected patients may need cornea transplant at a relatively early age. The main objective of the treatment of keratoconus has been changing in recent years, before it focused on improving visual acuity, the new treatment modalities try to prevent the progression of the pathology [2].

The patient begins with a cornea that is spherical or has common astigmatism. The progression is characterized in its beginnings by a thinning of the tissue of the central corneal stroma, apical protrusion with the consequence of bending of the corneal curvature, as well as various degrees of scarring. The thinner apex shifts down, resulting in irregular astigmatism, characteristic of the condition, which results in a slight to marked disability in the quality of vision is primarily an isolated condition, despite various information that appears together with other conditions, such as Down syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, mitral valve prolapse and patients with atopic diseases. It can also develop from forms of eye trauma such as wearing contact lenses or rubbing the eye. It is possible to make an initial diagnosis of keratoconus during youth or until the mid-thirties of the patient. Symptoms include lack of clear or definite vision, particularly with low lighting (e.g. when driving or watching television in a dark room) [10,17].

The following is a list of symptoms and associated signs in the diagnosis of keratoconus:

- Slight or marked reduction of the high and low contrast visual accuracy corrected with glasses for both near and far vision
- Change in vision that occurs from puberty (eg, until thirty or forty of the patient, but late onset is also possible)
- Monocular diplopia and phantom image
- Abnormal contrast sensitivity

Historia del frotamiento ocular.

History of atopic conditions [19].

The following is a list of biomicroscopic signs that identify the disease.

Prominent corneal nerves

Change in the cylinder axis of the initial astigmatism correction, followed by a change in the amount of the cylinder.

Myopia and irregular astigmatism (in general, with the ruler or oblique) for keratoconus.

Tendency to hyperopia and irregular astigmatism against the Rule. These signs can take place at the beginning of the disease progression and help in the early diagnosis [10,20].

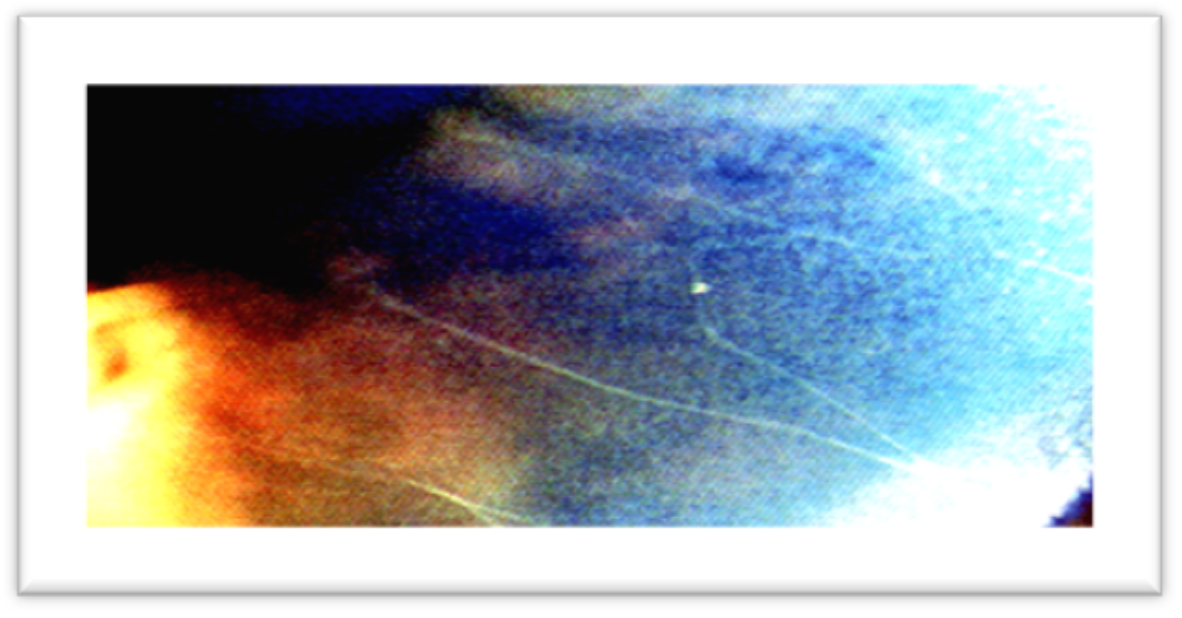

Figure 1: *Vogt striae: tension lines in the posterior stroma or in Descemet, which disappear temporarily before digital pressure.*

Figure 2: *The Fleischer ring (or the iron ring) that takes place in the conjunction of the thinner corneal sector and the thick unaffected area.*

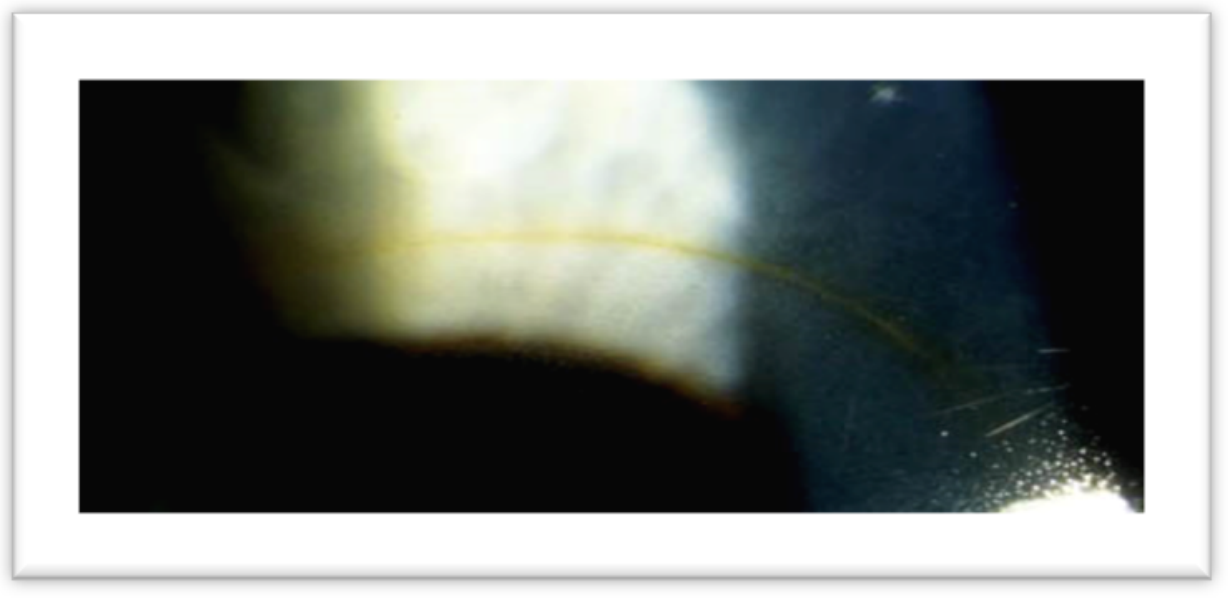

Figure 3: *Apical epithelial or subepithelial apical scars.*

Figure 4: *Munson sign, lower eyelid shift when looking down.*

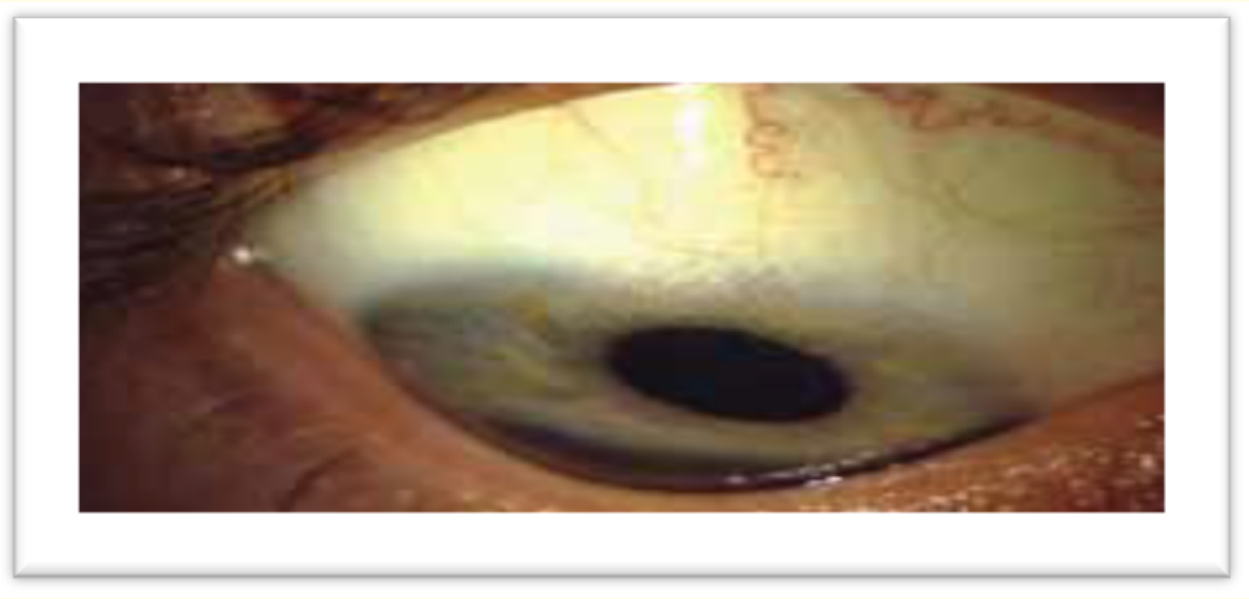

Figure 5: *Corneal hydrops (last stages), abnormal endothelial function that causes severe epithelial corneal edema with posterior scars.*

Figure 6: *Visualization of the cone in the red reflection inside the pupil area (Charleaux oil drop sign).*

Figure 7: *Irregularity or flickering of scissors of the retinoscopic reflex.*

Diagnostic exams

One of the most important tools in the detection and treatment of keratoconus is videokeratography (VKE). A common deficiency in the ability to detect keratoconus has been the use of an axial radius of curvature (sagittal) instead of instantaneous (tangential or local). Sagittal scales specifically look at optics in terms of corneal vision, while tangential scales assess the physical shape of the cornea. The use of axial radius in videokeratography distorts the apparent position and power of an apex that is located in the peripheral cornea, since its reference is the axis of the VKE [12,21].

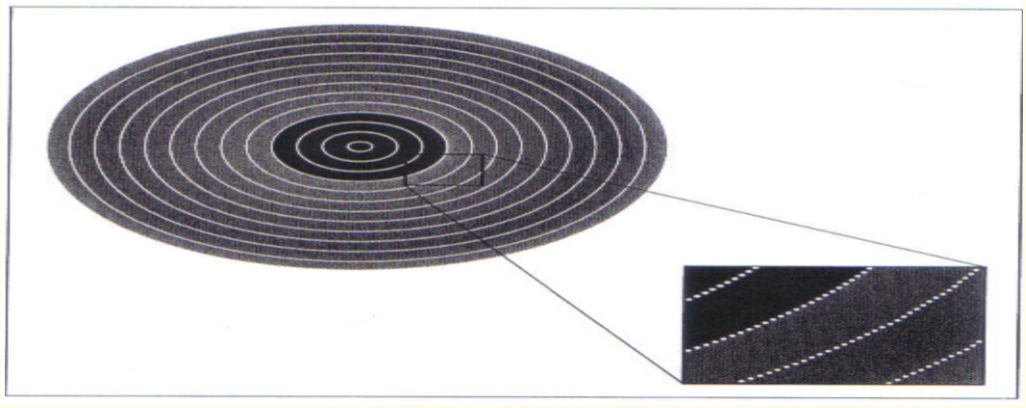

Figure 8

This distortion is exaggerated even more in the keratoconus, in which the more closed regions outside the center of the map are underestimated in its radius and the flatter regions of the periphery are overestimated. The use of the tangential map helps in a more accurate representation of the position and size of the cone due to the recalculation of the axial readings, now referenced to each adjacent ring rather than the axis [12].

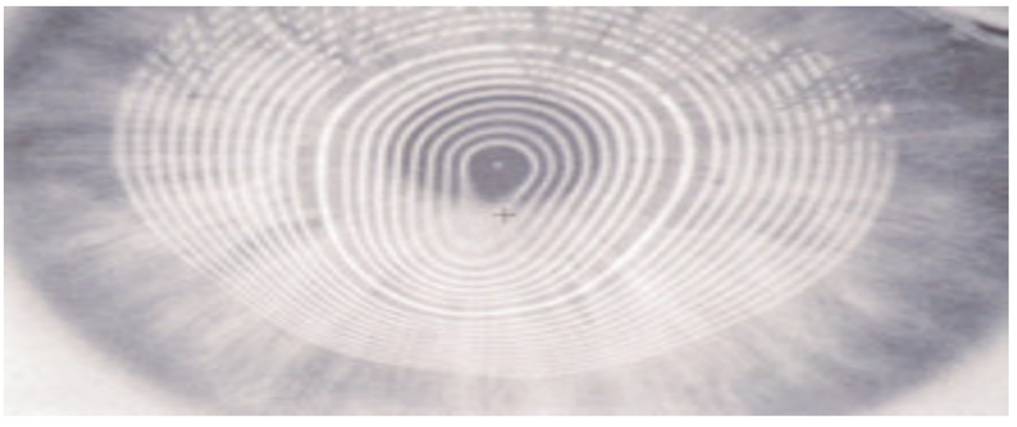

Figure 9

The use of elevation maps clearly indicates the presence and location of the cone but, without a radius of curvature, it is not so useful for adapting contact lenses [22].

Corneal topography can help identify the severity and type or shape of the keratoconus cone. The classification of keratoconus can be based on the severity of the curvature of the corneal cone, that is, the central averaged simulated keratometric readings provided by the corneal surveyor. A common estimate of severity is as follows [17,22].

If this average is less than 50.00 (6.75 mm), the cone is considered to be in its incipient stage; if it is from 50.00 to 56.00D (6.75 to 6.03 mm), the cone has advanced and after 56.00D (6.03 mm), it is considered in a severe state [12].

Secondly, the location or shape of the commonly identified cone, for example of the nipple or central type, oval, inferior temporal or nasal type and keratoglobo or generalized type (Figures 1, 2 and 3). Another condition or variation of keratoconus is marginal Pellucid degeneration (PMD), in which the thinning and cone occurs inferiorly, closer to the limbus than with the oval-shaped keratoconus, thus inducing astigmatism against the rule, a characteristic in the diagnosis of this variant [2].

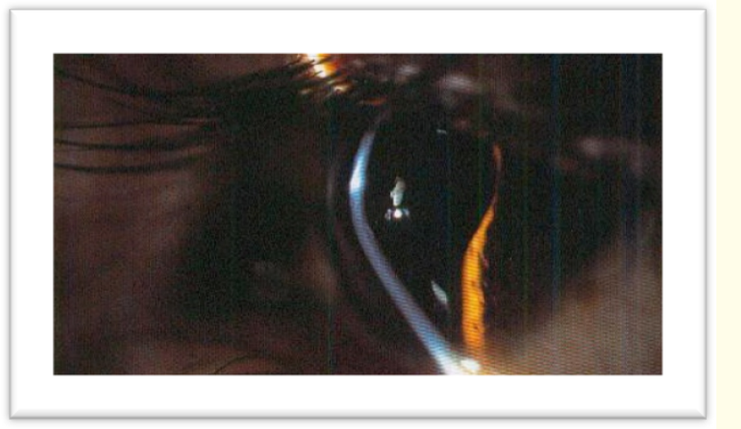

Figure 10

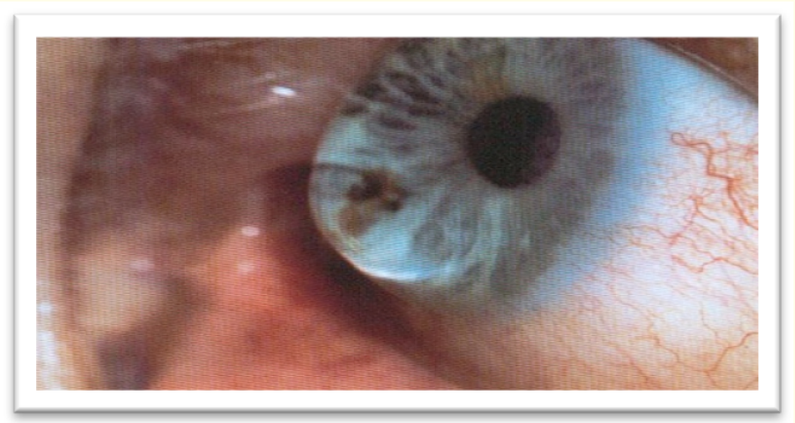

Figure 11

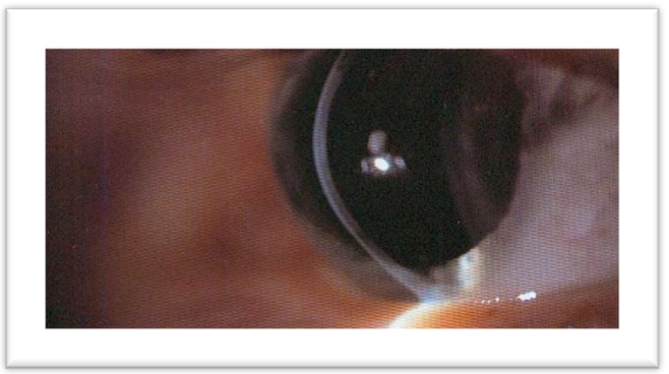

Figure 12

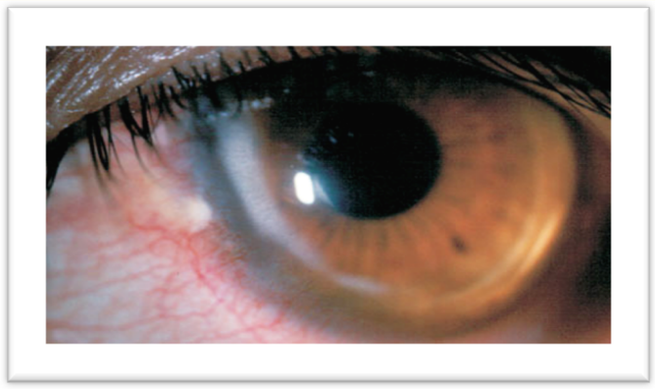

Figure 13

The topographic thickness measurement allows careful control of the progression of the condition, since it is possible to measure the same points and locations over time. The more advanced high-definition OCT spectral domains improve the resolution of these images, so that it is possible to more accurately measure the total epithelial and corneal thickness. Although there is no specific means of classifying the severity of keratoconus according to corneal thickness, there are significant differences between normal eyes and those with keratoconus with respect to thickness (all types and levels of gravity combined). It is generally accepted that corneal thicknesses of less than 300µm should be considered to be referred to a corneal surgeon for evaluation [22,23].

Obtaining topographic maps of the corneal surface: where the computer recomposes the thousands of points and measurements of corneal curvature and the data thus obtained turned over to the computer screen in the form of topographic maps [23,24].

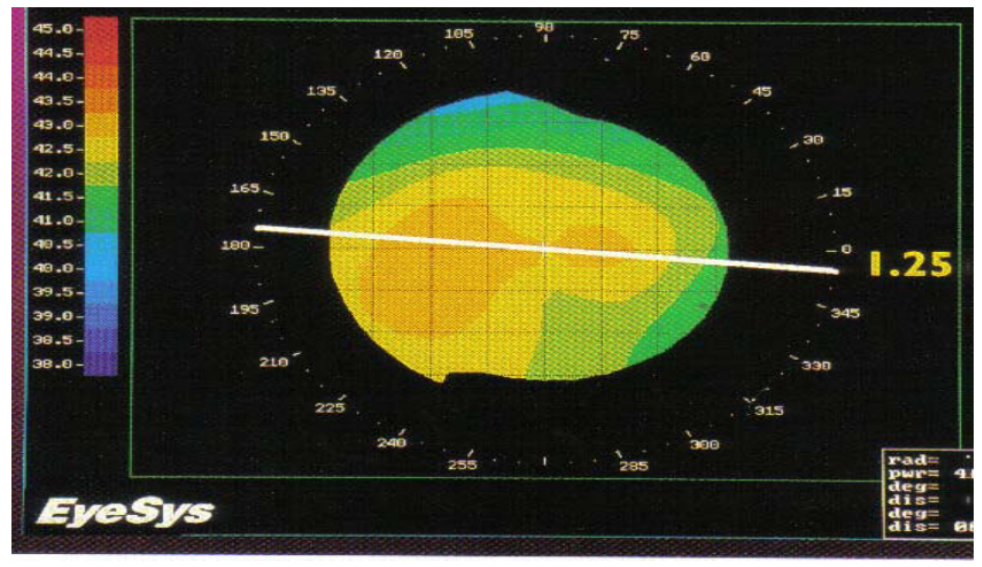

Figure 14: *Topographic Map.*

Presentation of topographic information

The data used to generate the color-coded maps must be reliable, if it is desired that said resulting map have significant clinical value. When instruments based on Placido discs are used, it is important to examine the image of the videokeratoscope together with the topographic map of colors. In this way the clinician can assess whether the map is based on a reliable image, which was properly processed [20].

In 1988, Klyce introduced the concept of color code maps as a method to make this information obtained with the surveyor, more useful and more sensitive for the examiner. Each color on the map is assigned to define a range of measures: information in the form translated into diopters [21,24].

The final objective of the corneal topography is to obtain details, correct data of the corneal surface and transform it into a clinical format. The interpretation of the map has to be with some basic ones to study the changes and diagnose the pathologies [24].

The accuracy of computerized topographic information depends on the proper acquisition of good images. Poor focus, decentration and shadows can negatively affect the image.

There are several calculations that can be obtained with the surveyor, such as the height, curvature and power of the cornea and it is transformed into numbers, colors and scales [24,25].

Color code map

The colors of the color scale that are recorded in the corneal topography maps correspond to the following [12].

Cold colors: (violet and blue): Low powers. They correspond to flat curvatures, low diopters.

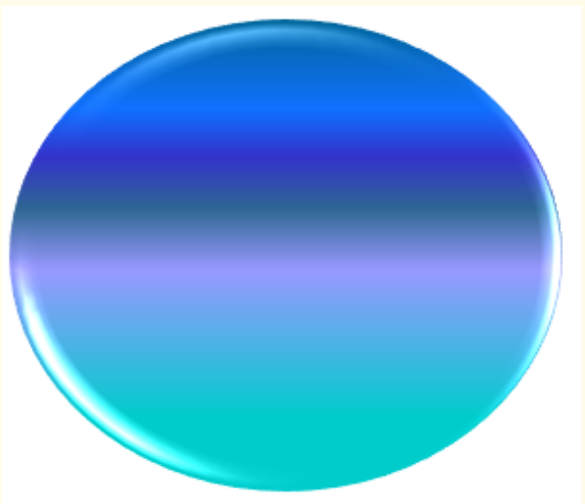

Figure 15

Green and yellow colors: Colors applied to the normal corneas of medium powers.

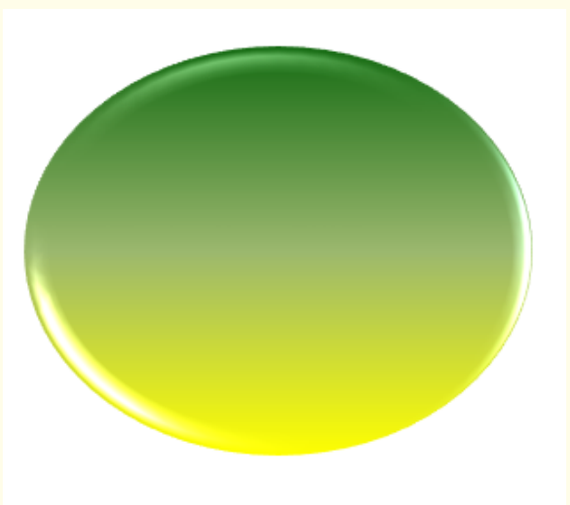

Figure 16

Warm or warm colors: (orange and red): High powers. They correspond to sheer curvature, high diopters.

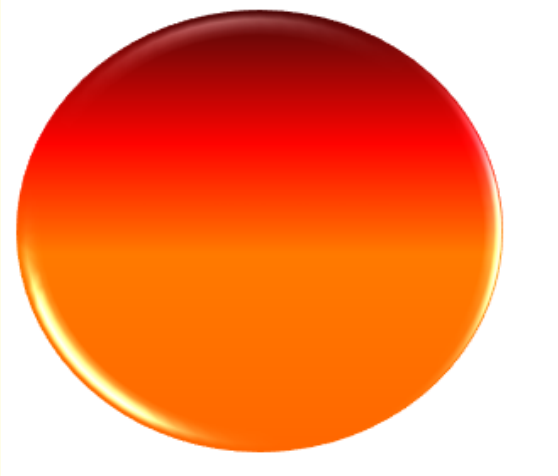

Figure 17

Color code

The colors are shown in the vertical bar next to the topographic map. The computer transmits the image to the video screen, reproducing it in colors and numbers. The video image on the computer screen provides a relative color scale to one side, which is enlarged or reduced depending on the range of corneal curvatures being measured. For example, the flattest area of a specific cornea is 37 diopters and the most curved area of 45 diopters, the relative scale of colors assigned by the computer would be dark blue for the areas of 37 diopters and dark red for the areas of 45 diopters. The intermediate colors are distributed between these two parameters [12,26].

Also on the height maps, where the high areas are presented with warm colors and the low areas with cold colors. It is very important to check the color scale on each map studied, because there are differences depending on the type of scale used. For example, in the case of keratoconus, the red zone on the height map is the highest point, which it is the apex of the cone, but the same point on the curvature map is the most curved area, which is located on the lower side of the cone [12].

In corneal topography, color differences are not always synonymous with differences in measurement values (diopters or radii), but may be synonymous with a voluntary change in the color scale by the explorer. Most surveyors programs allow you to increase the size of an image to see certain details. The realization of a corneal topography prior to the intervention is essential in candidates for refractive surgery, in order to identify possible corneal ectasias or keratoconos that could, if the intervention is performed, lead to failure [27].

Essentially, the map provides an estimate of the shape and refractive power of the cornea. This information is used to calculate the amount of ablation needed in each area, but remember that the information obtained is not perfect. When interpreting color maps, it should be observed particularly if the pattern is irregular enough to cause concern about the reliability of the map and to determine the Pupil position in relation to the curvature pattern shown on the map. The only way to obtain agility in reading and evaluating maps is through study and practice [27].

Interpretation of the correct topography

The correct interpretation of topographic maps requires knowledge and clinical experience in the most frequent patterns by the explorer.

To show surface power at different points of the cornea, modern surveyors rely on the color code of the Louisiana State University [25].

Clinicians prefer power values (measured in diopters) to radio values (measured in millimeters), although all surveyors can present cornea maps at both values. When the browser modifies the values and sets new parameters, the color scales are also modified [28].

The projection-based topography systems adopted a similar color scale to represent their height maps. High, elevated areas are represented in warm colors, while low, depressed areas are represented in cold colors [25,28].

Colors do not always represent an elevation map; correspond to curvature values. Therefore, the cornea is more curved or raised in the center (green) and flattened towards the periphery (blue). The nasal side turns blue faster, indicating that physiologically the nasal cornea is flatter than the temporal one [12,25].

Each map has a color scale and assigns a particular color to a certain keratometric dioptric range. You should never base an interpretation on color alone. The value in keratometric diopters is crucial in the clinical interpretation of maps and has to be examined when interpreting all maps [12,25].

Normal corneal topography

Normal corneal topography can have many topographic patterns, because no human cornea shows the regularity of a surveyor's calibration spheres.

Several authors carried out works to achieve a qualification that would simplify the different topographic patterns of normality, Rabinowitz., *et al*. [29] and Naufal., *et al*. [30], defending five classification patterns of the normal cornea:

a. **Round (spherical):** It occurs in 20 - 23% of cases. In this type of pattern the changes of dioptric power in the topographic map are made gradually and not significantly from the most central area to the periphery [29,30].

b. **Oval:** It occurs in 21 - 25% of cases. It is a variation of the previous one where changes in dioptric power are more pronounced in the longitudinal axis than in the transversal one. There are no differences between this pattern and the previous one in terms of refraction and keratometry [30,31].

c. **Symmetric astigmatism:** It occurs in 18-20% of cases, where the axis with greater dioptric power is symmetrical with each other and in turn, perpendicular to the axis of lower dioptric power (symmetric bow tie) [29,30].

d. **Asymmetric astigmatism:** It occurs in 32% of cases, as in the previous one, except that, in the axis of greater dioptric power there is no symmetry between the two hemimeridians (asymmetric bow tie) [30,31].

e. **Irregular:** It occurs in 6 - 7% of cases, consisting of a series of topographic patterns that cannot be classified by specific characteristics [29,30].

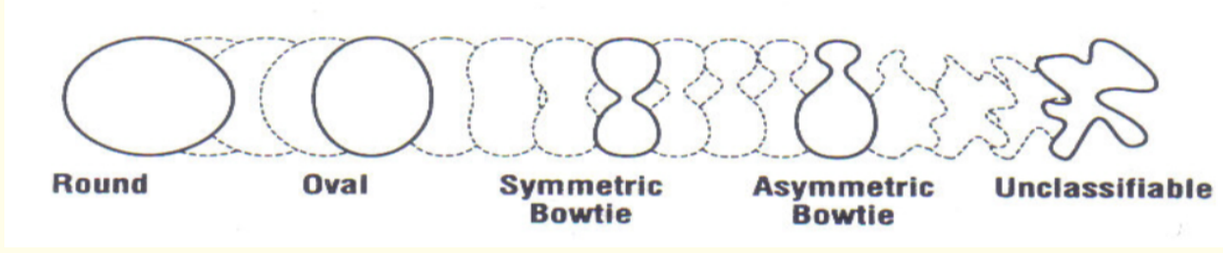

Figure 18

At certain stages of the condition, contact lenses become necessary in almost all cases of keratoconus, to provide optimal vision and approximately 10% to 26% of patients eventually need to undergo corneal surgery [31].

It is possible that the use of contact lenses in the keratoconic eye may lead to the appearance of corneal scars; However, reasonable evidence indicates that the cornea may suffer scars with or without the use of contact lenses [32].

The prognosis of this condition is unpredictable and its progression is variable; Eye exams are recommended every one year or less. The disease does not cause blindness, but it can compromise the quality of life, although keratoconic patients can still usually drive and read in the course of most of the progress of the condition. Most keratoconic patients (74% of the eyes) can be treated without surgery, with treatments that include crosslinking, while the remaining percentage (26%) is treated with intrastromal rings or keratoplasty [33].

The treatment depends on the progression of the pathology, in a first stage, the use of lenses is an option, especially for patients with a 20/40 vision with glasses. However, in case of irregular astigmatism the glasses do not work and the rigid gas permeable lenses provide a better correction. In 90% of cases, contact lenses are chosen. At the beginning of the pathology, soft contact lenses with toric design are suitable for correcting myopia and irregular astigmatism. As the disease progresses, rigid gas permeable lenses are used. Patients who prefer to undergo keratoplasty should also use lenses after surgery to achieve a better corrected visual acuity. It is important to understand that many patients with keratoconus depend on contact lenses for most of their daily activities. The selection of the appropriate lenses that best suit each case can delay the need for a more definitive treatment such as corneal transplantation [34].

A relatively new treatment option is crosslinking or cross-linking of collagen (CXL). The procedure consisting in the application of drops of riboflavin and exposure to ultraviolet rays A at 370 nm, for approximately 30 minutes [35].

Studies on the use of CXL have not reported significant adverse effects caused by this procedure. At present, CXL is used in many parts of the world for the treatment of progressive keratoconus. Although it provides a less invasive method to stop the progression of keratoconus, the long-term results and their safety must still be evaluated [36].

The intracorneal rings are, in principle, approved by the FDA and the European Community for the treatment of myopia and astigmatism. Recent studies have reported its effective use in the treatment of keratoconus, to stabilize ectasia, by surgery keratorefractive Such treatment does not eliminate the progression of keratoconus, but may delay corneal transplantation. There are three models of intracorneal rings for the correction of myopia: 1) Ferrara intracorneal ring (Brazil), 2) Bisantis segments (Italy) and 3) Intacts (USA), the latter being the most used. Patients with a clear central cornea, with a thickness of ≥400 μm at the insertion point of the stromal segment, are suitable for this treatment. The channels for the insertion of the rings or segments can be created mechanically or with the help of a femtosecond laser. This tool reduces the possibility of complications because it is much more accurate [37].

Although a combination of Intacs with CXL could be used, to achieve stability in cases of progressive keratoconus, further studies are needed to validate the long-term results of the combined treatment [35,37].

Recently, the successful use of both toric and phakic intraocular lenses has been reported in patients with keratoconus [38].

The main drawback with the use of phakic intraocular lenses is that these patients probably require another procedure if they develop cataracts in the future [38].

The use of special intraocular lenses in patients with non-progressive keratoconus is new and research results with carefully selected participants and long-term follow-up should be expected [38].

Rose K contact lens placed on keratoconical cornea [39].

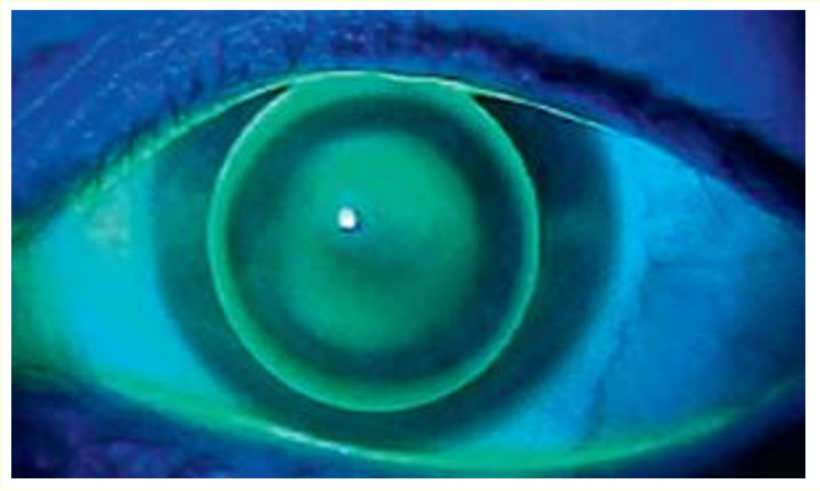

Figure 19

Conclusion

The keratoconus has been worrying cornea specialists for a long time, raising doubts regarding the genetics, progression and treatments of this pathology. Modern technology has undoubtedly served to better understand the pathophysiology and diagnosis of keratoconus. In many cases a conservative method, with contact lenses can make the patient's life easier. Surgical alternatives have been advancing with the availability of new femtosecond laser tools and equipment. The change from traditional treatment with penetrating keratoplasty to para-surgical therapeutic alternatives has tried to change the paradigm. Therapies such as crosslinking or corneal cross-linking could contain the key to stop the progression of keratoconus in the future [40,41].

Legal Basis

This work has its legal bases in the following constitutional articles and in the law on donation and transplantation of organs, tissues and cells in humans.

Art. 83: Health is a fundamental right, an obligation of the State, that will guarantee it as part of the right to life, collective well-being and access to services. All persons have the right to health protection, as well as the duty to participate actively in its promotion and defense and to comply with sanitary and sanitation measures established by law, in accordance with international treaties and conventions. signed and ratified by the Republic [42].

Art. 84: To guarantee the right to health, the State shall create, exercise the rectory and manage a national public health system, of an intersectoral, decentralized and participatory nature, integrated into the social security system, governed by the principles of gratuity, universality, integrality, equity, social integration and solidarity. The public health system will give priority to health promotion and disease prevention, guaranteeing opportunity treatment and quality rehabilitation. Public health services goods are owned by the State and cannot be privatized. The organized community has the right and the duty to participate in decision-making on the planning, execution and control of the specific policy in public health institutions [42].

Law on Donation and Transplantation of Organs, Fabrics and Cells in Beings Human.

Article 27

Presumptive Donation: Any person of legal age, who has been diagnosed with death, will be presumed to donate organs, tissues and cells for therapeutic purposes, unless there is a manifestation of will to the contrary.

Methodology

This chapter describes the type and level of research, design, population and bioethical aspects, sources from which information, procedures and techniques for data collection and information analysis were obtained, in order to respond to the problem of investigation.

Kind of investigation

This research is part of the modality of a retrospective - quantitative and cross-sectional theoretical study. In it, 50 medical records were analyzed, evaluating a total of 100 eyes, from which data on age and sex, refraction, referral symptoms and clinical signs to biomicroscopy, keratometry values, pachymetry and corneal topography were taken.

Feasible project

The present investigation has characteristic aspects of a feasible project for its execution, since it shows parameters for the diagnosis of keratoconus in children and adolescents, which constitutes an important tool for generating responses to the treatment of patients with suggestive symptoms of this disease

Population

The Universe of this study is represented by patients, who correspond to the total pediatric cases treated by consultation at the Santa Lucia Ophthalmologist during the period from March 2012 to March 2013.

Sample

The sample is represented by 50 patients, between 4 and 18 years of age, corresponding to the analysis of clinical and paraclinical parameters in 100 eyes.

Inclusion criteria

All those patients aged between 4 and 18 years of age, with a clinical suggestive of keratoconus, represented by signs typical of ophthalmological evaluation, those with refractive differences of cyl-1.50 between one eye and another or with refractive instability were included. with topographic surveys suspected of keratoconus.

Exclusion criteria

Those patients with ages over 18 years and those patients whose clinical records did not record all the necessary data to investigate were excluded from this study.

Data collection techniques

The main techniques for collecting data from this study were clinical records of 50 patients between 4 and 18 years of age with visual symptoms suggestive of keratoconus.

Data processing

Among the instruments to be used are records, lists, statistical tables. An HP Model dvd6 brand computer with a 32-bit Windows 7 operating system was used to process the information. Digital writing and graphic interfaces were made with the Microsoft Word program. Absolute frequencies and percentage distributions were taken as a means of summary. The results obtained were represented in simple and double-entry statistical tables with Microsoft Excel links, this facilitated the analysis and understanding.

Data analysis plan

Once the information was obtained according to the collection techniques, the data was analyzed and interpreted, during its development the methods of quantitative and qualitative analysis were used, depending on the category and the variables used.

For the quantitative analysis, tables and graphs with absolute numerical expressions or percentage fractions were used, which allowed comparisons to be made and the exact calculation of a given situation easily appreciated by the reader.

Finally, the analyzes were integrated with all the data source associated with bibliographies, the author's own criteria and academic study groups.

Bioethical considerations

Results and conclusions were objectively sought that give answers and solutions to the problem posed, which has an impact on the entire national population.

The fundamental social right to health was taken into account as part of the right to life, social inclusion and the highest respect for all other human rights when their institutions and vital processes are submitted to research that modifies their health, quality of life and well-being in general. When conducting a retrospective study and, therefore, not directly investigating in humans, the informed consent modality was not used.

Results

In this chapter the results were identified and the analysis of data obtained by the instrument used, as well as the experience of the researcher, was carried out in order to meet the specific objectives of this work, which contributed to propose an evaluation of parameters for Keratoconus diagnoses in children.

Gender	Male	Female
N°	21	29
%	42	58

Table 1: *Sample distribution by sex.*
Source: Clinical History.

In our study a slight predominance of the female sex is observed, represented by 58%, which does not determine a prevalence by gender, coincides with the study carried out in CMDLT and in the military hospital "Dr. Carlos Arvelo "and differs from research carried out in the Reference Center for Keratoconus in France and in that carried out by Dr. Tamara Harb, of the Castroviejo Ophthalmological Institute in Madrid, Spain, where they report female sex as a predominant gender.

Years	4 - 6	7 - 9	10 - 12	13 - 15	16 - 18
N°	9	15	12	8	6
%	18	30	24	16	12

Table 2: *Age distribution of the sample studied.*
Source: Clinical History.

In our study the predominant ages are between 7 - 9 years (30%) and between 10-12 years (24%). This coincides with the studies carried out at the CMDLT and the Military Hospital "Dr. Carlos Arvelo "and does not coincide with that made by Dr. Harb, where the majority report for those children under 6 years. It is worth highlighting the coincidence of results regarding gender and age in studies conducted in this country, which differ from those presented in the European continent.

Symptoms/Signs	Eye pruritus	Vhog Streaks	Fleisher ring
N°	32	5	2
%	64	5	2

Table 3: *Classification according to clinical symptomatology.*
Source: Clinical History.

In our study, ocular pruritus was the most frequent symptomatology reported, (64%), which coincides with what is widely described in the literature and in the studies carried out at the CMDLT, at the Castroviejo Ophthalmological Institute of Madrid and in the center of reference for keratoconus from France. The symptoms found are reported only in 5 and 2 percent of cases because they occur already in advanced cases of the disease, with which we do not make a comparison because in the background studies they were not research objectives.

Keratometric classification	Low	Moderate	Severe	S/A
N°	47	26	3	24
%	47	26	3	24

Table 4: *Classification according to complementary tests: Keratometry.*
Source: Clinical History.

In our study the alteration of the keratometry in a mild way, that is to say less than 48Dp, is the most frequent found, which represents 47% and coincides with the investigations carried out by Dr. Harb and Dr. Spaggarino of the CMDLT. Severe type alteration is only reported in 3% in this study.

Normal Thickness	Corneal thinning
66 (66%)	34 (34%)

Table 5: *Classification according to complementary exams: pachymetry.*
Source: Clinical History.

In our study, 34 of the cases presented decreased corneal thickness. Below 555. However, CMDLT has reported 45% of its sample with decreased central pachymetry.

Pathology	Myopic astigmatism	Astigmatism Hyperopia	Simple astigmatism
N°	42	26	32
%	42	26	32

Table 6: *Classification according to refractive defect.*
Source: Clinical History.

In our study, the predominant refractive defect was myopic astigmatism (42%), followed by simple astigmatism (32%). This coincides with what is described in the literature and with the study of Dr. Harb. It differs from that performed by Dr. Delgado of the Military Hospital "Dr. Carlos Arvelo", since in this case he reports hypermetropic Astigmatism. In our opinion this is due to the fact that this study is based on epidemiological aspects of the incidence of astigmatism in children in general, unlike the other investigations where cases with a clinical suggestive of keratoconus were included.

Topographic map	Asymmetric	Oval	Redondo
N°	39	44	17
%	39	44	17

Table 7: *Classification according to topographic map.*
Source: Clinical History.

In this study, the oval topographic pattern was the most frequent, (44%), followed by that of an asymmetric bow tie or bowtie, represented by 39%, which does not represent a significant difference between both types. This coincides with the study conducted by Dr. Tamara Harb, of the Castroviejo Ophthalmological Institute in Madrid.

SRI	SK	KC
80	72	5
(80%)	(72%)	(5%)

Table 8: *Classification according to topographic parameters.*
Source: Clinical History.

In our study we observed that a great majority of cases presented alterations in the superficial regularity index of the cornea, (80%), also a high percentage is associated with the Suspect Keratoconus index, (72%), however the diagnosis of Keratoconus performed by the Surveyor Software, only reported 5 cases, which coincides with those in which clinical signs characteristic of this disease are already observed. Since, since no report of data related to the preceding analysis is found, it is impossible to compare the results obtained.

Conclusion

1. The female sex and the ages between 7 and 9 years were those that predominated in this study.
2. Clinical findings of ocular pruritus, Vogt stretch marks and Fleischer rings were reported in our patients, as well as keratometries with slightly altered values and pachymetries below 555 microns.

3. The associated predominant refractive defect was Myopic Astigmatism.
4. The topographic patterns found in our patients were round, oval and asymmetric, the latter 2 being the most frequent.
5. The topographic parameters of SRI, SK and KC, were very useful in the diagnosis of patients with a clinic suggestive of keratoconus.

Recommendations

1. In principle any irregular congenital astigmatism should enter into differential diagnosis of a premature keratoconus and should be studied in detail.
2. The number of patients who have had a cornea suspected of keratoconus has been high. We do not have enough parameters to rule out that in the future they have a keratoconus.
3. Carry out prospective, multicentric studies that allow to conclude with all those cases that this pathology is suspected and based on this define criteria for a protocol of diagnosis, treatment and prevention of keratoconus in pediatric ages.
4. Due to the high relationship between ocular manipulation due to local allergy symptoms and keratoconus, it is recommended to carry out preventive work, informing and educating parents and patients about the need to avoid this type of maneuver.

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