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The Topographic Corneal Changes in Patients with Vernal Keratoconjunctivitis

Vernal Keratokonjonktivit Tanılı Hastalarda Korneal Topografik Değişimler

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ABSTRACT Objective: The aim of this study is to compare the topographic corneal changes in patients with Vernal keratoconjunctivitis, to a control group. **Material and Methods:** 41 patients (81 eyes) with active vernal keratoconjunctivitis and 41 control subjects (82 eyes) were included in this prospective study. The Corneal topography of subjects were examined with Pentacam (Oculus HR inc., Germany). **Results:** The eyes with vernal keratoconjunctivitis was palpebral in 32 eyes (39.5%), limbal in 24 eyes (29.6%), and mixed in 25 eyes (30.9%). There were no statistically significant differences between groups in K1, K2, Kaverage. On the other hand, the mean Kmaximum value was much higher in the patient group than the control group. There were statistically significant differences between the groups for the mean astigmatism, thickness at the thinnest location, thickness at the apex of the cornea, the difference in the thickness between the apex and the thinnest location, the mean anterior and posterior elevation peak and keratoconus index. According to our parameters, 7 of the 41 subjects (17.07%) were detected as keratoconus and 9 of the 41 subjects (21.95%) were detected as subclinic keratoconus in vernal keratoconjunctivitis group. The correlation between age and keratoconus parameters was not statistically significant in the group with keratoconus. In patients with subclinical keratoconus, the elevation of Kmaximum values was statistically significant as their ages progressed. There was no correlation between a set of factors that are the age, the gender, duration of the symptoms and types of vernal keratoconjunctivitis in patient group and development of keratoconus and subclinic keratoconus. **Conclusion:** In our study, in comparison to the control group, more topographic changes in favor of keratoconus and subclinical keratoconus were detected in patients with vernal keratoconjunctivitis. In patients with vernal keratoconjunctivitis, analysis of corneal topography is important for early diagnosis of keratoconus.

Keywords: Vernal keratoconjunctivitis; topography; keratoconus

ÖZET Amaç: Bu çalışmada, kliniğimizdeki vernal keratokonjonktivit tanılı hastaların korneal topografik değişimlerinin kontrol grubu ile karşılaştırılması amaçlanmıştır. **Gereç ve Yöntemler:** Bu prospektif çalışmaya; vernal keratokonjonktivit tanılı 41 hastanın 81 gözü ile 41 kontrol hastasının 82 gözü alındı. Korneal topografi, Pentacam (Oculus HR inc., Almanya) ile değerlendirildi. **Bulgular:** Vernal keratokonjonktivit tanısı konan gözlerin 32'si (%3,5) palpebral, 24'ü (%29,6) limbal, 25'i (%30,9) karışık tipteydi. Gruplar arasında K1, K2, Kortalama değerleri açısından anlamlı fark saptanmadı. Diğer taraftan, Ken yüksek ortalaması ise hasta grubunda kontrol grubuna göre anlamlı olarak yüksekti. Astigmat değeri ortalaması, kornea en ince noktası ile kornea apeksinin pakimetri değeri, kornea apeksi ile en ince noktası arasındaki pakimetri farkı, kornea ön ve arka yüzeyi elevasyon ortalaması ile keratokonus indeksi arasında gruplar arasındaki fark istatistiksel olarak anlamlı saptandı. Belirlenen kriterlere göre vernal keratokonjonktivit grubundaki 41 hastanın 7 tanesinde (%17,07) keratokonus, 9 tanesinde (%21,95) ise subklinik keratokonus saptandı. Keratokonus tanısı alan grupta, yaş ile keratokonus parametrelerinin korelasyonu istatistiksel olarak anlamlı değildi. Subklinik keratokonus tanılı hastalarda, yaşları ilerledikçe Ken yüksek değerindeki artış istatistiksel olarak anlamlıydı. Hasta grubunda yaş, cinsiyet, semptom süresi, vernal keratokonjonktivit tipi gibi faktörler ile keratokonus ve subklinik keratokonus gelişimi arasında korelasyon yoktu. **Sonuç:** Çalışmamızda, hasta grubunda, kontrol grubuna kıyasla daha fazla oranda keratokonus ve subklinik keratokonus lehine topografik değişimler görülmüştür. Bu nedenle vernal keratokonjonktivit tanılı hastaların takiplerinde keratokonusun erken teşhisi için topografik tetkiklerin analizi yararlı olacaktır.

Anahtar Kelimeler: Vernal keratokonjonktivit; topografi; keratokonus

Vernal keratoconjunctivitis (VKC) is a bilateral, chronic inflammatory disease of conjunctiva and of cornea showing inflammatory symptoms in a seasonal manner particularly in springtime. It generally affects children and young people living in hot and dry climates. The disease occurs more often in male patients below the age of 10 years old with a history of atopy. The disease may resolve completely at puberty or may ease off.[1-6]

Vernal keratoconjunctivitis has the potential of worsening the visual acuity. The severe and persistent forms of the disease might cause corneal ulcer, degeneration in corneal tissue hence might reduce visual acuity due to corneal ectasia. Ocular trauma caused by scratching, is an environmental factor in the development of keratoconus in the patients with a genetic predisposition, in particular those with palpebral or mixed forms. It has been showed that chronic epithelial defects result in changes in corneal topography by causing long term and slight oscillation in destructive enzymes.[3,7-9]

The studies conducted in previous years have shown the relation between keratoconus and VKC with clinical analysis.[9-11] Yet, with these methods, it cannot be proven the relationship between VKC and keratoconus in the patients with subclinical keratoconus. Quantitative analysis of anterior corneal surface by computerized corneal topography, topographic changes, subclinical and clinical keratoconus can be easily determined in the patients diagnosed with VKC.[12] In our study, we intended to evaluate VKC-keratoconus relationship (corneal topographic changes) with Pentacam which is an up-to-date method of analysis.

MATERIAL AND METHODS

This prospective study, between June 2012 and September 2012 at Istanbul University, Istanbul Faculty of Medicine, Department of Ophthalmology, enrolled 81 eyes of 41 patients with VKC who were under follow-up at least for one year in our clinic. One eye of the one patient was excluded from this study because of previously penetrating keratoplasty due to keratoconus. 82 eyes of 41 patients who do not have ocular and systemic pathology except refractive errors, were included in the control group. Two groups have been formed: control group and patient group.

Patients with additional ocular disease, using of contact lens, corneal scars and opacities, history of corneal surgery were excluded in the study.

Before beginning to study, we obtained the approval the Ethical Committee of Istanbul University Faculty of Medicine (dated 15.6.2012 and with 2012/972-1101 protocol number). Informed written consent was obtained from all patients and parents of patients (under 18 years old). Patients age, sex, the age that VKC symptoms develop, duration of symptoms and presence of additional atopic disease have been recorded. Vernal keratoconjunctivitis was diagnosed with the severe itchy eyes and giant papillary found in palpebral conjunctiva, limbal papillae and with the presence of Horner Trantas spot which are characteristic symptoms. Every patient underwent ophthalmologic examination. Visual acuities were measured according to Snellen and converted to logmar. We recorded the best corrected visual acuity according to logmar, spherical equivalent (SE), biomicroscopic evidence and fundus findings. We recorded the presence of punctate epithelial keratitis, pseudogerontoxon, shield ulcer, corneal vascularization 1mm past the limbus, Vogt's striae in keratoconus, corneal thinning, Munson's sign and, Fleischer ring. Vernal keratoconjunctivitis was clinically divided into three: palpebral, limbal and mixed.

An experienced technician operated corneal topography with Pentacam (oculus, HR inch, Germany). We obtained the values of anterior corneal surface K_1, K_2, $K_{average}$, K_{max}, sagittal curvature, rate of astigmatism, corneal apex and pachymetry rates of its thinnest point, anterior and posterior corneal elevation, keratoconus index (KI) by using topography. In order to diagnose the disease keratoconus and subclinical keratoconus we accepted the following five topographic criterias:

K_{max}
Anterior corneal elevation
Posterior corneal elevation
Pachymetry value of the thinnest corneal point
Keratoconus Index (KI)

The diagnosis of keratoconus was based on the fact that four of the five criteria above were pathologic, with at most one being suspicious in both eyes. In the subclinical keratoconus diagnosis, we placed a total of two pathological criterias, one of which was the most suspicious of the five criterias in both eyes.

STATISTICAL ANALYSIS

Whilst seizing upon the study findings, we used statistical package program. During data analysis. We used Kolmogorov-Smirnov test in order to analyze normal distribution along with descriptive statistical methods (Frequency, Percentage, Average, Standard deviation). Yet, we used Pearson's chi-squared test in comparison of qualitative data. In the comparison of quantitative data, in the case of two groups, we used Mann Whitney U test in the comparison of parameters that were not normally distributed. In order to multivariably analyze the factors contributing to kerataconus, we used binary logistic regression. In the analysis of Multivariate Binary Logistic Regression, variants were chosen with enter method and odds ratio was calculated by taking first categories as reference.

RESULTS

In this study, between June 2012-September 2012, 81 eyes of 41 patients, aged 6-30, were included in the patient group. 28 of patients (68%) men, 13 of patients (32%) women, median age was 14.073± 6.813 years. 82 eyes of 41 patients, aged 6-30, were included in the control group. 26 of patients (63%) men, 15 of patients (27%) women, median age was 13.878±6,698 years. Regarding age and sex, no significant differences were detected between these groups (p>0.05).

Patients diagnosed with VKC, median age of disease onset was 8.4±4.1 (3-20) years, median duration of symptoms was 5.6±4.9 (1-26 year). The distribution of clinical forms of VKC were as follows: 39.5% palpebral, 30.9% mixed, and 29.6% limbal types.

Spheric equivalent is determined as-0.564±2.016 D in the patients group and as-0.425±1.243 D in the control group. The difference between the groups was not statistically significant (p>0.05). According to logmar, best corrected visual acuity (BCVA) was 0.065±0.178 in the patients group. On the other hand, it was 0.000±0.000 in the control group. This shows that BCVA of the patients group was significantly higher than BCVA of the control group (p<0.01).

In the patients group, symptoms such as Munson sign, apical thinning, Vogt striae, and Fleischer rings which biomocroscopically support diagnosis of kerataconus, were detected in 6 eyes of 81 (7.4%). Yet, we did not detect any of them in the control group. This difference was found statistically significant (p<0.05).

The horizontal keratometry average of the patient group (K_1) is detected as 42.921±2.674 D, the vertical keratometry average is detected as (K_2) 44.333±3.113 D, $K_{average}$ is detected as 43.607±2.755 D. In the control group, the same rates were measured as 42.417±1.198 D, 43.423±1.263 D, 41.962±6.093 D, respectively. Amongst groups, any significant difference regarding K_1, K_2, $K_{average}$, was not detected (p>0.05). The highest keratometry K_{max} average was detected as 46.058±4.210 D in the patient group, and as 44.093±1.290 D in the control group. The difference between K_{max} average values of each group was statistically significant (p<0.05).

The average of sagittal curvature, in the patient group is found as 43.832±3.448 D, whereas in the control group it is found as 42.948±1.233 D. The difference between groups was not statistically significant (p>0.05). The median of rate of astigmatism was 1.660±1.339 D in the patient group, whereas it was 1.054 ±0.514 D in the control group. The difference between groups was found statistically significant (p<0.01).

Pachymetry value in the corneal thinnest point was measured as 556.889±46.782 μm in the patient group and 579.512±30.150 in the control group. Pachymetry value of corneal apex was found as 562.630±45.653 μm in the patient group and 582.915 ± 30.335 μm in the control group. The difference between corneal apex and the thinnest point is measured as 5.704±4.723 μm in the patient

group and 3.378±2.397 μm in the control group. The difference between these three parameters, which is about corneal thickness, was seen statistically significant (p<0.01).

Elevation average of anterior corneal surface was measured 4.284±5.573 in the patient group, and was measured 2.146±1.572 in the control group. Elevation of posterior corneal surface was found 4.938±10.257 in the patient group and it was found 1.463±2.932 in the control group. Regarding these two parameters, the difference between these groups, was statistically significant (p<0.01).

Average of kerataoconus index, is established 1.059±0.061 in the patient group and 1.019±0.020 in the control group. The difference between these groups, was statistically significant (p<0.01).

When keratometry values above 48 D are considered as pathological, in the VKC group, K_1 values of 2 eyes (2.5%), K_2 values of 5 eyes (6.2%), $K_{average}$ values of 3 eyes (3.7%), K_{max}. values of 14 eyes (17.3%) were detected higher than 48D. On the other hand, in the control group, no value was found over 48D in any eye. The ratio of K_2 and K_{max} values of VKC group were found significantly high compared to the control group (p<0.05).

Pachymetry value of the thinnest corneal point, in the control group, was found keratoconus suspect (470-500 μm) in 4 eyes (4.9%), in 6 eyes pathological (<470μm). In the control group, it was found keratoconus suspect in 1 eye 1 (1.2%). The difference between groups was statistically significant (p<0.05).

Anterior corneal elevation; was found normal (≤12) in 77 (95.1%) eyes, keratoconus suspect (13-15 μm) in 1 (1.2%) eye and pathological (>15 μm) in 3 eyes (3.7%). Whereas, in the control group, anterior elevation values in all eyes were normal. However, the difference between groups was not found statistically significant (p>0.05).

Posterior corneal elevation; in the patient group, was found normal (≤17μm) in 76 eyes (93.85), keratoconus suspect (18-20 μm), in 1 eye (1.2%) and pathological (>20 μm) in 4 eyes (4.9%). In the control group, all posterior values were normal and no difference between groups was found statistically significant (p>0.05).

Keratoconus index (KI); in the patient group, in 24 eyes (27.2%) was evaluated in favor of keratoconus (KI>1.07). In the control group, no value was found above 1.07. The difference between groups was statistically significant (p<0.01).

In reference to the criteria stated in the methodology, in 7 of 41 patients (17.07%) in the VKC group, keratoconus was detected and in 9 patients (21.95%) subclinical keratoconus was detected. Thirteen eyes of 7 patients (16.04% of all eyes) were diagnosed with keratoconus in the VKC group. Four of the seven patients (57.1%) were male and 3 (42.9%) were female. Ten of the thirteen (76.9%) eyes had palpebral, and 3 (23.1%) had mixed type VKC.

The difference in level of astigmatism of all the patients in VKC group and of the patients diagnosed with keratoconus and subclinical keratoconus was statistically significant (p=0.030<0.05). The level of astigmatism diagnosed with keratoconus was higher than those who were not diagnosed with keratoconus (Mann Whitney U=197.500; p=0.030<0,05). The effect of factors such as age, sex, duration of symptoms and type of VKC was not statistically significant to those who were diagnosed with keratoconus in the VKC group (p>0.05).

DISCUSSION

The severe and persistent forms of the VKC might reduce visual acuity due to corneal complications (ulcers, keratoconus etc). Vernal keratoconjunctivitis is one of the risk factors for corneal ectasia. Ocular trauma caused by eye rubbing accelerates the onset and progression of keratoconus. Routine corneal topography in patients with VKC allows early detection and management of subclinical and clinical keratoconus.[7-9]

Gautam and his friends conducted a study on VKC patients in Nepal. 28.7% of patients was diagnosed with palpebral, 14.8% of patients was diagnosed with limbal and 56.5% of patients was diagnosed with mixed VKC.[13] Whereas in the study of Totan and his friends, in 36 eyes (43.9%) was

found palpebral VKC, in 8 eyes (9.7%) limbal VKC, in 38 eyes (46.3%) mixed VKC.[14] All these studies like our studies support the fact that palpebral and mixed VKC is more often seen.

Best-corrected visual acuity of patients diagnosed with VKC, in our study, was detected as 0.065±0.178 in logmar. It has been thought that this significant difference compared to the control group, is related to corneal complications and topographic changes.

In the current study, findings biomicroscopically and topographically supporting kerataconus diagnosis was higher in patients group than the control group ($p<0.05$). In the study of Dantas and his friends which explored topographic changes in patients diagnosed with VKC, clinical diagnosis of keratoconus was determined 9.85% and topographic diagnosis of keratoconus was determined 22.5%. In the study of Totan which aimed to determine the incidence of keratoconus in patients diagnosed with VKC, biomicroscopic and topographic diagnosis of keratoconus was determined as 8.5% and 26.8%, respectively.[14] Likewise, in a similar study of Shoja and his friends, biomicroscopically determined diagnosis of keratoconus was found 14% and topographically diagnosis of keratoconus was determined 28%.[15] In the study of Caputo and his friends, the frequency of clinical and topographic diagnosis of keratoconus in at least 1 eye associated with VKC was 0.77%.[16] In this study, compared with previous reports in the literature, keratoconus prevalence is much lower. All these studies, except Caputo's study, show that patients diagnosed with VKC are at high risk of keratoconus.[12,14,15] These results suggest the necessity of topographic evaluation for all suspected patients.

In our study, between the control and patient group, no statistically significant difference was found in K_1, K_2, $K_{average}$ values whereas the difference of K_{max} values was found statistically significant ($p<0.05$). When values of keratometry above 48D are accepted as pathological, K_2 and K_{max} values' ratio of being above 48D was found significantly high compared to the control group ($p<0.05$). Wheras in the average of sagittal curvature, no statistical difference was detected between groups ($p>0.05$). However, when the values above 47D are accepted as pathological, 5 eyes of 81 were accepted as pathological. While in the study Barreto and his friends conducted, sagittal curvature came out significantly high compared to the control group. ($p<0.05$).[10] These data showed that keratometry values might increase in the patients diagnosed with VKC. This increase might be the result of microtrauma in corneal structure which occurs due to intense itching.

Regarding the pachymetry value of the corneal thinnest point, pachymetry value of corneal apex and the difference between corneal apex and the thinnest point, statistically significant difference was detected between the patient and the control group ($p<0.01$). In two studies from India and Nepal, central corneal thickness was significantly reduced in VKC subjects with suspected keratoconus like topography.[9,13] Whereas in the study of Barreto and his friends, the pachymetry value of the corneal thinnest point of the patients diagnosed with VKC was found statistically significantly lower than the control group.[10] These changes in the corneal thickness can be explained by the fact that corneal epithelial trauma due to severe eye itching and keratocyte apoptosis lead to corneal thinning in the upcoming years. For this reason, the findings obtained from thickness mappings might of help to the clinician whilst examining the development of keratoconus.

The study that Barreto and his friends did with Orbscan II, similar to our study, the anterior and posterior elevation difference between the groups was found statistically significant.[10] In the studies conducted, in keratoconus, anterior corneal surface and posterior corneal surface deformation was detected. Besides, posterior elevation became an important parameter in keratoconus evaluation because it was not influenced from irregular tear film and the use of artificial tears. It has been showed that attention should be paid to anterior and posterior elevation mappings regarding keratoconus development in the follow-up of patients diagnosed with VKC because the fact that we detected the average of anterior and posterior values higher than the control group. In our study, and the fact that, in the publications, it

was proved that these parameters played a major role in keratoconus detection.[17-20]

Two studies, similar to our study, proved the fact that keratoconus frequency is higher in palpebral and mixed type VKC.[14,21] In our study; the fact that sex, age and duration of symptom and the fact that VKC type does not affect keratoconus and subclinical keratoconus development might be explained with limited number of patients.

In conclusion, in the patients with VKC, while the evaluation of cornea with Pentacam reveals the topographic changes, in suspicious cases, thanks to regular topographic measurements, keratoconus and subclinical keratoconus will be able to be detected in the early phase.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *F. Nilüfer Alparslan;* ***Design:*** *F. Nilüfer Alparslan;* ***Control/Supervision:*** *F. Nilüfer Alparslan, Dilbade Yıldız Ekinci;* ***Data Collection and/or Processing:*** *Dilbade Yıldız Ekinci;* ***Analysis and/or Interpretation:*** *Dilbade Yıldız Ekinci;* ***Literature Review:*** *Dilbade Yıldız Ekinci;* ***Writing the Article:*** *Dilbade Yıldız Ekinci;* ***Critical Review:*** *F. Nilüfer Alparslan, Zafer Cebeci, Raziye Dönmez Gün;* ***References and Fundings:*** *F. Nilüfer Alparslan;* ***Materials:*** *Dilbade Yıldız Ekinci, Zafer Cebeci;* ***Çeviri:*** *Leyla Yavuz Sarıçay.*

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