Progression of Keratoconus in Turkish Adult Patients

Türk Erişkin Popülasyonunda Keratokonus Progresyonu

Shahin NOVRUZLU,[a]
Erdem YÜKSEL,[a]
Kamil BİLGİHAN[a]

[a]Department of Ophthalmology, Gazi University Faculty of Medicine, Ankara

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Yazışma Adresi/*Correspondence:*
Erdem YÜKSEL
Gazi University Faculty of Medicine, Department of Ophthalmology, Ankara, TÜRKİYE/TURKEY
rdmyksl@yahoo.com

ABSTRACT Objective: To evaluate progression of keratoconus in adult patients diagnosed as keratoconus and to compare it with the disease progression in pediatric patients reported in the literature. **Material and Methods:** Five hundred and forty-seven patients diagnosed as keratoconus were reviewed retrospectively and 143 eyes of 106 adult patients were included into the study. The patients were assigned into two groups: Group I was aged 18-24 years and Group II was aged over 24 years. Data about age, best corrected visual acuity (BCVA) with glasses, spherical equivalents (SE), corneal thickness, simulated mean kerotometry (SimK) and follow-up periods were collected. The patients having progression in keratoconus were recommended a treatment with corneal collagen cross-linking. **Results:** The mean age of the patients was 21.34±1.75 years and 30.26±5.10 years in Group I and Group II respectively. The mean follow-up period was 11.96±7.24 months in Group I and 15.44±12.6 months in Group II. The rate of the progression was 25.6% and 23.1% in Group I and Group II respectively, though there was not a significant difference (p=0.549). The rate of the progression was 24.4% in the adults recently diagnosed as keratoconus at the end of a mean follow-up period of 12.74±10.60 months. **Conclusion:** About one fourth of the adult patients required cross-linking therapy during a one-year follow-up and 75% of the adult patients with keratoconus did not have disease progression at the end of a one-year follow-up. Before adults recently diagnosed as keratoconus are advised to have cross-linking therapy, they should be given an anti-allergic treatment and followed for the disease progression.

Key Words: Keratoconus; corneal surgery, laser

ÖZET Amaç: Keratokonus tanısı konulan erişkin hastalarda keratokonus progresyonunu değerlendirmek ve literatürde bildirilen çocuk hastalarla karşılaştırmak. **Gereç ve Yöntemler:** Keratokonus tanısı alan 547 hasta retrospektif olarak incelendi, 106 hastanın 143 gözü çalışmaya dahil edildi. Çalışmada hastalar iki gruba ayrıldı. 1. grup 18-24 yaş, 2. grup 24 yaş üzeri olacak şekilde oluşturuldu. Hastaların dosyalarından, yaş, gözlükle en iyi görme keskinliği (EİDGK), sferik eşdeğer (SE), korneal kalınlık, ortalama simüle keratometri (SimK) ve takip süreleri not edildi. Keratokonusta progresyon görülen hastalara korneal çapraz bağlama tedavisi yapıldı. **Bulgular:** Hastaların ortalama yaşı, Grup 1 ve Grup 2'de sırasıyla 21,34±1,75 yıl ve 30,26±5,10 yıl idi. Grup 1'de takip süresi 11,96±7,24 ay, Grup 2'de 12,74±10,60 ay idi. Progresyon oranı, Grup 1 ve Grup 2'de sırasıyla %25,6 ve %23,1 idi (p=0,549). Erişkinlerde ortalama 12,74±10,60 ay sonunda progresyon oranı %24,4 idi. **Sonuç:** Ortalama 1 yıl sonunda tüm erişkinlerin 1/4'ünde korneal çapraz-bağlama tedavisi ihtiyacı olmaktadır ve 3/4'ünde keratakonus progresyonu izlenmemektedir. Keratokonus tanısı konulan erişkin hastalarda, korneal çapraz bağlanma endikasyonu konulmadan önce, anti-alerjik tedavi verilmeli ve hastalığın progresyonunun görülmesi gerekmektedir.

Anahtar Kelimeler: Keratokonus; kornea cerrahisi, lazer

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Keratoconus is a disease characterized by progressive thinning in the corneal stroma. Although etiopathogenesis of keratoconus is not known well, it is thought to be multifactorial and genetic and envi-

ronmental factors (e.g. microtraumas and oxidative stress) are most frequently incriminated.[1-5] Microtraumas which cause chronic irritation like using rigid contact lenses and rubbing eyes are the most important predisposing factors leading to progression of the disease.[6,7]

As keratoconus progresses, the corneal stroma becomes thinner and the cornea changes into a more conical shape. The resultant irregular astigmatism and high myopia reduce vision.[8] Keratoconus is usually bilateral and often has an asymmetric onset and progression.[9] Li et al. in their study on patients with unilateral keratoconus reported that 50% of the normal eyes developed keratoconus during a 16-year follow-up.[10]

Keratoconus is a progressive disease which usually affects young people. Wollensak et al. suggested using collagen cross-linking with ultra viole A (UVA) and riboflavin, a photosensitizer, to stop the disease progression.[11] There have been many studies showing that the treatment suggested by Wollensak et al. was effective in stopping progression of keratoconus.[12-15] It is recommended that corneal collagen cross-linking therapy should be implemented before the onset of progression of keratoconus in children (<14 years old) and adolescents (14-18 years), while it should be initiated after progression of the disease is monitored in adults (>18 years old). Although keratoconus has been reported to show progression especially in children and adolescents, little is known about clinical features and progression of keratoconus in adults.

Therefore, the aim of this study was to investigate progression of keratoconus in Turkish adult patients diagnosed as keratoconus and to compare it with the disease progression in pediatric patients reported in the literature.

MATERIAL AND METHODS

Records of 547 patients diagnosed as keratoconus were retrospectively reviewed and 143 eyes of 106 adult patients recently diagnosed as keratoconus were included into the study. Progression rates in these adult patients were documented and compared with those in pediatric groups reported in the literature. The adult patients included in the study were divided into two groups; i.e. those aged 18-24 years into Group I and those aged over 24 years into Group II. This study was approved by the local ethics committees of Gazi University Medical School. The tenets of the Declaration of Helsinki were followed throughout the study. Written informed consent was obtained from all the patients.

The disease was staged according to Amsler-Krumeich classification. Data about age, best corrected visual acuity (BCVA) with glasses, spherical equivalents (SE), corneal thickness, simulated mean kerotometry (SimK) and follow-up periods were collected. Exclusion criteria were having forme fruste and stage 3-4 keratoconus, pregnancy during the follow-up period, taking estrogen, having prior surgery and having a corneal scar.

Keratometry values and corneal thickness were evaluated with Scheimpflug camera and Placido disk based topography (Sirius, CSO, Scandicci Firenze -Italy) and the same topographic device was used during the follow-up period. The measurements with centralization and coverage percentages of over 90% were taken into consideration.

Treatment with topical anti-allergic agents and preservative-free artificial tear drops was initiated and the patients were told to avoid scratching and rubbing likely to cause progression of the disease.

The criterion for the progression was an increase in maximum K (Kmax) by more than 1D, in the mean K (Kort) by more than 1D or manifest refractive spherical equivalent (MRSE) by more than 0.5D. The patients having progression of keratoconus were recommended a treatment with corneal collagen cross-linking.

RESULTS

A hundred and forty-three eyes of 106 adults recently diagnosed as keratoconus (55 females and 51 males) were retrospectively reviewed. They were divided into two groups: Group I included 74 eyes (44 eyes with stage 1 disease and 30 eyes with stage 2

disease) and Group II included 69 eyes (33 eyes with stage 1 disease and 36 eyes with stage 2 disease). The mean age of the patients was 21.34±1.75 years in Group I and 30.26±5.10 years in Group II. The mean follow-up period was 11.96±7,24 months in Group I and 15.44±12.6 months in Group II (Table 1).

The mean visual acuity corrected manually with glasses (CVA), spherical equivalents (SE), corneal thickness and the simulated mean keratometry (SimK) values in Group I and Group II were not significantly different (Table 2).

The rate of the progression was 25.6% in Group I and 23.1% in Group II, without a significant difference (p=0,549).

The rate of the progression was 24.4% in adults and 82.1% in pediatric patients recently diagnosed as keratoconus at the end of a mean follow-up period of 12.74±10.60 and 12.32±9.80 months respectively (p=0.002).

DISCUSSION

Keratoconus is a disease which starts in puberty and has a progressive course until the age of 30-40 years. Although it is usually an isolated condition, it is known to accompany various systemic and ocular diseases such as Down syndrome, Leber's congenital amaurosis, connective tissue disorders, Turner syndrome and retinitis pigmentosa.[16,17]

As the disease progresses, the thickness of the cornea may decrease by 1/5. Although thinning mostly appears in the apex, it may be seen in the inferior and the inferior temporal regions. Cases of keratoconus located in the superior region have rarely been reported.[18] It is thought that apical thinning depends on a decrease in the number of lamellae rather than on the total corneal thinning process. The early stage of the disease can be asymptomatic. As the disease progresses, the symptoms arise. The visual acuity deceases and stromal

TABLE 1: The general characteristics of the patients.

Characteristics	Group 1	Group 2	P
Number of Patients	52	54	
Number of Eyes	74	69	
Mean Age (yrs	21.34±1.75	30.26±5.10	0.0001¥
Duration of Follow-up (mo)	11.96±7.24	15.44±12.6	0.024**
Stage 1 disease*	44	33	0.387†
Stage 2 disease*	30	36	0.688†
Number of eyes with progressive disease	19	16	0.549†

* Amsler-Krumeich classification; ¥ Independent Samples T-test; ** Mann-Whitney U test, p>0.05; † Chi-Square test, p>0.05.

TABLE 2: Clinical features of patients.

Clinical features	Group 1	Group 2	P
First BCVA (logMAR)	0.21±0.18	0.23±0.20	0.794†
Last BCVA (logMAR)	0.22±0.20	0.23±0.21	
First SEq (D)	-4.23±2.53	-4.50±2.91	0.060*
Last SEq (D)	-4.51±2.61	-4.65±3.05	
First CT (m)	474.66±33.21	447.64±34.19	0.814†
Last CT(m)	472.55±39.89	444.45±33.86	
First SimKmean (D)	46.82±2.49	47.48±2.09	0.147*
Last SimKmean (D)	47.62±2.88	48.23±2.47	

First: In the First Follow-up Visit; Last: In the Last Follow-up Visit; BCVA: Best Corrected Visual Acuity with Glasses; SEq: Spherical Equivalent; CT: Corneal Thickness at the Apex; SimKmean: Mean Keratometric Value; D: Diopter.

† Mann-Whitney U test, p>0.05.

* Independent Samples T-test.

thinning, Vogt lines, a Fleischer ring, corneal scar and hydrops can develop.

The incidence of keratoconus varies with populations. It is 50/100.000 in the general population, 2/100.000 in the United States, 1.3/100.000 in Denmark, 20/100.000 in Saudi Arabia and 7.6/100.000 in Japan.[8,16,19-21] To our knowledge, there have not been any studies on the incidence of keratoconus in Turkey.

Keratoconus more frequently appears in the young population. In a study by Lass et al. on 417 patients with keratoconus, 70% of the patients were aged 21-40 years and 10% of the patients were aged over 50 years.[22] Zadnik et al. reported that out of 1579 patients with keratoconus, 4% were younger than 20 years, 59% were aged with 20-40 years, 33% were aged 40-60 years and 4% were aged over 60 years.[23]

There has been conflicting evidence in the literature about the rate of progression in keratoconus. Choi and Kim. evaluated 94 eyes of 85 patients with keratoconus and found that keratoconus showed progression in 25 eyes (26.5%) at the end of a follow-up period of 8 years.[24] They also reported that the mean age of the patients with the disease progression was 21.5±4.5 years. Consistent with the results reported by Choi et al., in the present study, the mean age of the patients was 21.34±1.75 years in Group I and the rate of the disease progression was 25.9% in this group at the end of a one-year follow-up period. However, Kennedy et al. reported that of 64 patients with keratoconus living in a state, only nine required penetrating keratoplasty due to progression of keratoconus at the end of a 48-year follow-up period.[25] Kim and Joo evaluated 56 eyes of 35 adults with keratoconus in Korea (18-35 years) and observed progression of the disease in 30 eyes (53,5%) during a 3-year follow-up.[26] The reason for this high rate of the disease progression might have resulted from a longer period of follow-up and different criteria used to determine the disease progression.

In the study performed by Kim and Joo, 52.9% of the patients were female and 47.1% of the patients were male. In the present study, 51.9% of the patients were female and 48.1% of the patients were male. Consistent with the literature, the results of the present study suggest that the disease progression is not associated with gender or laterality.

Chatzis and Hafezi in a study on children and adolescents (9-19 years) found that the rate of the disease progression was 88% in 59 eyes of 42 patients at the end of a follow-up period of 26 months.[27] Also, in the present study, the progression rate of keratoconus was 82.1% in pediatric patients at the end of 12.32±9.80 months. It has been reported in the literature that progression of keratoconus is related to age and microtraumas, but not related to gender, laterality or familial history.[6,7,28]

There have been differences in the criteria used to determine the progression of keratoconus in the literature. O'Brart et al. recommended cross-linking therapy when there was a one-unit regression in corrected and uncorrected visual acuity, an increase in refractive and corneal astigmatism and an increase in keratometry and conical apex strength by 0.75D in 12-24 months.[29] Choi and Kim. considered an increase of 1.5D in central K on the first examination as a sign of the disease progression [24]. Kim and Joo thought that an increase of >0.5 D in keratometric values in 6 months was sufficient to suggest the disease progression.[26] In the present study, the criterion used to determine the disease progression was an increase in maximum K (Kmax) by more than 1D, in the mean K (Kort) by more than 1D or in manifest refractive spherical equivalent (MRSE) by higher than 0.5D. Presence of one of the above mentioned criteria was considered as a sign of the disease progression. Gore et al. in their review of contemporary studies determined the presence of one of the following parameters as a criterion for the disease progression: maximum K (Kmax) of >1D, a difference of >1D between maximum and minumum K values (Kmax-Kmin), corneal apex power of >1D, the mean K of >0.75D, an increase in MRSE by >0.5D or a decrease in the central corneal thickness by >2%.[30]

This is the first study to show progression of keratoconus in adults in Turkey, where vernal keratoconjunctivitis and keratoconus are common.

However, further multicenter studies which have large patient series are needed for population studies in Turkey.

In conclusion, the rate of the progression of keratoconus detected in the adult patients in the present study was lower than that reported in the pediatric age group in the literature. Thanks to appropriate recommendations and an anti-allergic topical therapy, about one fourth of the adult patients required cross-linking therapy during a one-year follow-up. About 75% of the adult patients with keratoconus were not observed to have a disease progression in about a one-year follow-up. Before recommending cross-linking therapy to adults recently diagnosed as keratoconus, they should be offered an anti-allergic treatment and followed for the disease progression.

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