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CLINICAL STUDY

Corneal topographic response to intraocular pressure reduction in patients with vernal keratoconjunctivitis and steroid-induced glaucoma

T Dada[1], V Konkal[1], R Tandon[2], R Singh[3] and R Sihota[1]

Abstract

***Purpose*: To study the corneal topographic response to IOP reduction in vernal keratoconjunctivitis (VKC) with steroid-induced glaucoma.**

***Methods*: A total of 42 eyes of 21 patients with VKC and steroid-induced glaucoma (Group I) and 66 eyes of 33 patients with VKC without glaucoma (Group II) underwent an evaluation by Orbscan topography. In eyes with glaucoma, the IOP was controlled medically and the corneal topography was repeated at 3 months to evaluate effect on corneal parameters.**

***Results*: The mean baseline IOP was 36.40 ± 13.08 mmHg in Group I, 14.67 ± 4.62 mmHg in Group II ($P < 0.0001$). The IOP after treatment at 3 months follow-up was 15.00 ± 5.41 mmHg in Group I ($P < 0.0001$). In Group I, the mean maximum Sim K decreased from 44.86 ± 3.21 D to 43.87 ± 2.62 D ($P = 0.031$) and mean posterior corneal elevation decreased from 64.9 ± 22.36 μm to 35.7 ± 28.91 μm at 3 months after reduction of IOP ($P = 0.001$). There was a significant positive correlation between the reduction in the IOP and the decrease in the posterior corneal elevation ($r = 0.664$, $P = 0.001$).**

***Conclusion*: Eyes with VKC with and without glaucoma have similar corneal topography. Increased IOP associated with steroid-induced glaucoma and VKC may contribute to an increase in the corneal curvature and posterior corneal elevation. These changes may be reversed by a reduction in the IOP with medical therapy.**

[1]Glaucoma Research Facility, Dr Rajendra Prasad Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

[2]Cornea and Refractive Surgery Services, Dr Rajendra Prasad Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

[3]Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India

Correspondence: T Dada, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi-110029, India.
Tel: +91 11 2658 9695; Fax: +91 11 2658 8919.
E-mail: tanujdada@hotmail.com

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Introduction

Vernal keratoconjunctivitis (VKC) is a seasonal or perennial allergic ocular surface disease that affects mainly young males aged 6–21 years.[1–4] Many of these patients are treated with topical corticosteroids and can develop secondary open angle glaucoma.[5,6] Visual morbidity due to this disease is considerable as the glaucoma leads to a gross diminution of vision before patients are aware of the problem.

Although corneal changes in VKC are well documented,[7–11] there has been no study on corneal changes in patients with steroid-induced glaucoma and VKC using a slit scan topography system. This study was designed to study the corneal topographic changes associated with steroid-induced glaucoma in eyes with VKC and the effect of reduction in intraocular pressure on the corneal variables.

Materials and methods

A prospective study of consecutive patients seen over 1 year, suffering from VKC was carried out. The study had been approved by our institutional review board and all participants gave informed consent in accordance with the Declaration of Helsinki.

Patients with VKC and a history of steroid usage, who had at least two of the following

three criteria, were recruited for the study as Group I—applanation intraocular pressure more than 21 mmHg on more than two occasions, glaucomatous optic nerve head changes or glaucomatous visual field defects on Humphrey 30–2 full threshold test. Those with VKC who did not meet these criteria were recruited as Group II. Patients with pre-existing glaucoma (prior to steroid use) or a history of ocular trauma or surgery were excluded from the study. A detailed history was taken for dose and duration of the steroid use, the reason for steroid use and any family history of glaucoma. Baseline examination included best-corrected visual acuity, slit lamp biomicroscopy, fundus examination, applanation tonometry, gonioscopy, Humphrey 30–2 full threshold perimetry, and Orbscan topography. In addition, 32 age matched healthy controls with a refractive error within ± 1 D were taken for comparison.

The Orbscan II corneal topography system was used for the assessment of the corneal topography, anterior chamber depth, and pachymetry. The measurements were performed by one senior technician with more than 2 years experience with the Orbscan.

All steroids were stopped at presentation. Patients with an intraocular pressure of less than 40 mmHg were given acetazolamide for 3 days and simultaneously started on topical antiglaucoma treatment −0.2% brimonidine, 0.5% timolol, or 0.005% latanoprost. If the intraocular pressure was >40 mmHg at presentation, syrup glycerol was given in addition to maintain an intraocular pressure of less than 20 mmHg. During follow-up, some patients had an exacerbation of their VKC for which lotepred eye drops 0.5% were used sparingly.

Patients were reviewed at 2 weeks, 4 weeks, and 3 months. They were asked to stop systemic acetazolamide and/or glycerol 3 days prior to each visit to allow measurement of IOP on topical medications alone. During each visit Goldmann applanation tonometry, best-corrected visual acuity and fundus examinations were carried out. Corneal topography with Orbscan II was measured at the time of induction into the study and then 3 months after the IOP was controlled medically.

Patients who achieved their individualized target intraocular pressure, on medication, had their drug therapy tapered until the intraocular pressure were controlled without medication, and were then monitored till the end of the study.

Statistical analysis

Statistical Analysis was performed using descriptive statistics that is mean and standard deviation, for the continuous variables, whereas frequency distribution and percentages were calculated for categorical variables. Astigmatism and its axis were calculated using double angle formula method. To look for significant differences at particular points of time for continuous variables, Student's *t*-test (unpaired) was applied. χ^2 test was used to find associations between the categorical variables. Trend analyses within variables were assessed using two-way ANOVA for both the groups separately. A *P*-value of <0.05 has been considered statistically significant. SAS 8.0 statistical software has been used for these statistical analyses.

Results

A total of 42 eyes of 21 patients with VKC and steroid-induced glaucoma (Group I) and 66 eyes of 33 patients with VKC without glaucoma (Group II) and 32 eyes of 18 normal controls were included in the present study. There were 18 males and three females in Group I, 23 males and 10 females in Group II, and 10 males and eight females among the controls. The mean age of patients in Group I was 18.8 ± 4.6 years (range 12–35 years) as compared to 11.7 ± 5.1 years (range 4–22 years) in Group II ($P < 0.0001$). The mean age of the controls was 18.2 ± 3.3 years.

The mean duration of the disease was 5.0 ± 2.73 year in Group I and 2.56 ± 2.21 year in Group II ($P < 0.0001$). The mean baseline IOP was 36.40 ± 13.08 mmHg in Group I, 14.67 ± 4.62 mmHg in Group II ($P < 0.0001$), and 15.2 ± 3.82 mmHg in the controls. The IOP after treatment at 3 months follow-up was 15.00 ± 5.41 mmHg in Group I ($P < 0.0001$). Historically topical dexamethasone (0.1%) was the most common type (78.5%) of steroid used followed by betamethasone (0.1%) in 16.6% and hydrocortisone ointment in 4.7% of cases in Group I, while fluoromethalone (0.1%) was the most commonly (63.6%) used steroid in Group II, followed by dexamethosone in 28.7% cases.

Mixed form of VKC was the most common form of VKC in Group I (22 eyes) followed by limbal (12 eyes) and palpebral (eight eyes) forms. Palpebral form (28 eyes) was the most common form in Group II followed by mixed (26 eyes) and limbal (12 eyes) forms.

Corneal parameters

The mean maximum Sim K was 43.80 ± 2.73 D in Group I and 44.06 ± 3.47 D in Group II ($P = 0.86$). The mean minimum Sim K was 41.90 ± 1.74 D in Group I and 42.34 ± 3.39 D in Group II ($P = 0.066$). The mean astigmatism was 1.90 ± 2.12 D in Group I and 1.72 ± 1.34 D in Group II ($P = 0.049$).

The mean central anterior elevation above the mean best fit sphere (BFS) was 11.43 ± 13.88 μm in Group I (mean BFS $= 40.2 \pm 4.2$ D) and 13.87 ± 22.86 μm in Group

II (mean BFS = 41.1 ± 3.7 D) ($P = 0.099$). The mean central posterior elevation above the BFS was 27.57 ± 17.44 μm in Group I (mean BFS = 51.2 ± 5.1 D) and 31.22 ± 13.03 μm in Group II (mean BFS = 50.9 ± 4.8 D) ($P = 0.123$).

The maximum anterior elevation above BFS was 26.86 ± 21.72 μm in Group I (mean BFS = 39.4 ± 3.9 D) and 35.61 ± 38.99 μm in Group II (mean BFS = 40.1 ± 4.3 D) ($P = 0.215$). The mean of the maximum posterior elevation above BFS was 64.9 ± 32.36 μm in Group I (mean BFS = 51.2 ± 3.7 D) and 54.87 ± 22.66 μm in Group II (mean BFS = 50.8 ± 4.6 D) ($P = 0.059$).

The mean central pachymetry was 576.71 ± 72.15 μm in Group I and 552.61 ± 38.11 μm in Group II ($P = 0.117$). The mean thinnest pachymetry values were 567.57 ± 80.54 μm in Group I and 527.57 ± 50.01 μm in Group II ($P = 0.078$). The mean pachymetry values in the midperiphery at the 5 mm optic zone are as shown in Figure 1. There was a significant difference between the inferior pachymetric values in the two groups ($P = 0.046$) (Table 1).

Eight eyes (19.04%) in Group I and 11 eyes (15.15%) in Group II had suspicious clinical findings on corneal examination suggestive of keratoconus, which were then evaluated according to the Rabinowitz criteria.[10] The corneal curvature was measured at 3 mm from the centre at the 30, 60, 90, 120, and 150° in the superior half of the topography and compared with corresponding points on the inferior half of the topography chart. The mean keratomery in the superior part of the cornea at 3 mm from the centre was 46.33 ± 0.89 D as compared to 47.37 ± 2.16 D in the inferior part of the cornea in Group I ($P = 0.03$). In Group II, the mean keratometry in the superior part of the cornea at 3 mm from the centre was 48.95 ± 1.65 D as compared to 50.73 ± 5.12 D in the inferior part of the cornea ($P < 0.01$). In both groups keratoconus was seen most commonly in the mixed form of VKC.

In the control group, the mean maximum Sim K was 42.73 ± 1.96 D, the mean minimum Sim K was 41.97 ± 2.07 D. The mean central anterior elevation above the BFS was 7.78 ± 2.66 μm and the mean central posterior elevation above the BFS was 15.08 ± 9.90 μm. The maximum anterior elevation was 11.83 ± 3.80 μm (significantly different from Group II, $P = 0.014$). The mean of the maximum posterior elevation was 20.28 ± 5.28 μm (lower than both Groups I&II, $P < 0.001$). In the controls, the mean central pachymetry was 559.33 ± 35.76 μm, the mean thinnest pachymetry was 552.61 ± 37.94 μm (Table 1).

Table 1 Comparison of corneal variables in Group I, II, and controls

Corneal parameter	*Group*	*Mean ± SD*
Maximum Sim K	I	43.80 ± 2.73 D
	II	44.06 ± 3.47 D
	C	42.73 ± 1.96 D
Minimum Sim K	I	41.90 ± 1.74 D
	II	42.34 ± 3.39 D
	C	41.97 ± 2.07 D
Astigmatism	I	1.90 ± 2.12 D
	II	1.72 ± 1.34 D
	C	0.83 ± 0.38 D
Central pachymetry	I	576.71 ± 72.15 μm
	II	552.61 ± 38.11 μm
	C	559.33 ± 35.76 μm
Thinnest pachymetry	I	567.57 ± 80.54 μm
	II	527.57 ± 50.01 μm
	C	552.61 ± 37.94 μm
Maximum anterior corneal elevation	I	26.86 ± 21.72 μm
	II	35.61 ± 38.99 μm
	C	11.83 ± 3.80 μm
Maximum posterior corneal elevation	I	64.9 ± 32.36 μm
	II	54.87 ± 22.66 μm
	C	20.28 ± 5.28 μm

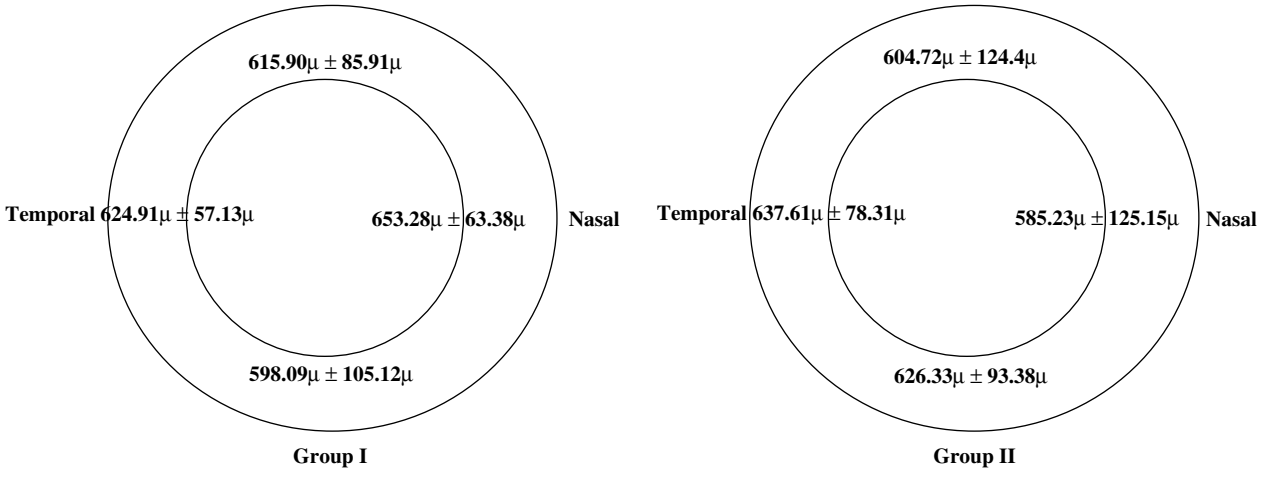

Figure 1 Corneal pachymetry at 5 mm zone in Group I and Group II.

Effect of IOP on corneal variables

The corneal parameters at 3 months after control of IOP were compared to the baseline corneal variables in Group I. The baselines mean IOP was 36.42 ± 13.54 mmHg and at the end of 3 months it was 15.0 ± 5.41 mmHg ($P < 0.0001$).

The baseline mean maximum Sim K was 44.86 ± 3.21 D and after 3 months of control of IOP it was 43.87 ± 2.62 D ($P = 0.031$). The baseline mean minimum Sim K was 42.74 ± 2.28 D and after 3 months of control of IOP it was 42.00 ± 1.71 D ($P = 0.033$). The baseline mean central pachymetry was $524.17 \pm 68.30\,\mu$m and after 3 months it was $539.81 \pm 66.82\,\mu$m ($P = 0.019$). The baseline mean thinnest pachymetry values before and after IOP control were $500.94 \pm 93.42\,\mu$m and $511.83 \pm 92.43\,\mu$m repectively ($P = 0.626$). The baseline mean posterior corneal elevation values in steroid-induced glaucoma with VKC were $64.9 \pm 22.36\,\mu$m and after 3 months the value was $35.7 \pm 28.91\,\mu$m ($P = 0.001$) (Figures 2 and 3). There was a significant positive correlation between the reduction in the IOP and the decrease in the posterior corneal elevation ($r = 0.664$, $P = 0.001$) (Table 2).

Discussion

Steroid-induced glaucoma is iatrogenic secondary open angle glaucoma, with decreased trabecular outflow causing a rise of intraocular pressure. In VKC steroid-induced glaucoma is a common complication as patients require long-term therapy and steroids are often used to provide early relief of symptoms. Bonini *et al*[1] in a long-term review of VKC recorded a 2% incidence of steroid-induced glaucoma.

Our study showed that the mixed form of VKC was most commonly associated with steroid-induced glaucoma, followed by the limbal, least with palpebral variety, while the palpebral form was the most common variety in VKC eyes without steroid-induced glaucoma. The palpebral form has been the most frequently reported form of VKC in previous studies. In a case series of 195 patients with long-term follow-up by Bonini *et al*,[1] the palpebral form (83.6%) of VKC was the most common followed by mixed form (8.7%) and limbal form (7.5%). In another study by Cameroon *et al*[8] out of 61 patients with VKC, there were 29 patients (47.54%) with palpebral form, 14 (22.95%) with limbal VKC and 18 (29.51%) with mixed form of vernal conjunctivitis.

A male preponderance was noted in patients of steroid-induced glaucoma in our study, this was seen both groups of patients having VKC which is consistent with previous studies on VKC. In a study by Neumann *et al*,[2] 400 cases of VKC were reviewed in which 72.5% were males, while Khan *et al*[7] reported a male preponderance of 83.3% in 530 cases of VKC.

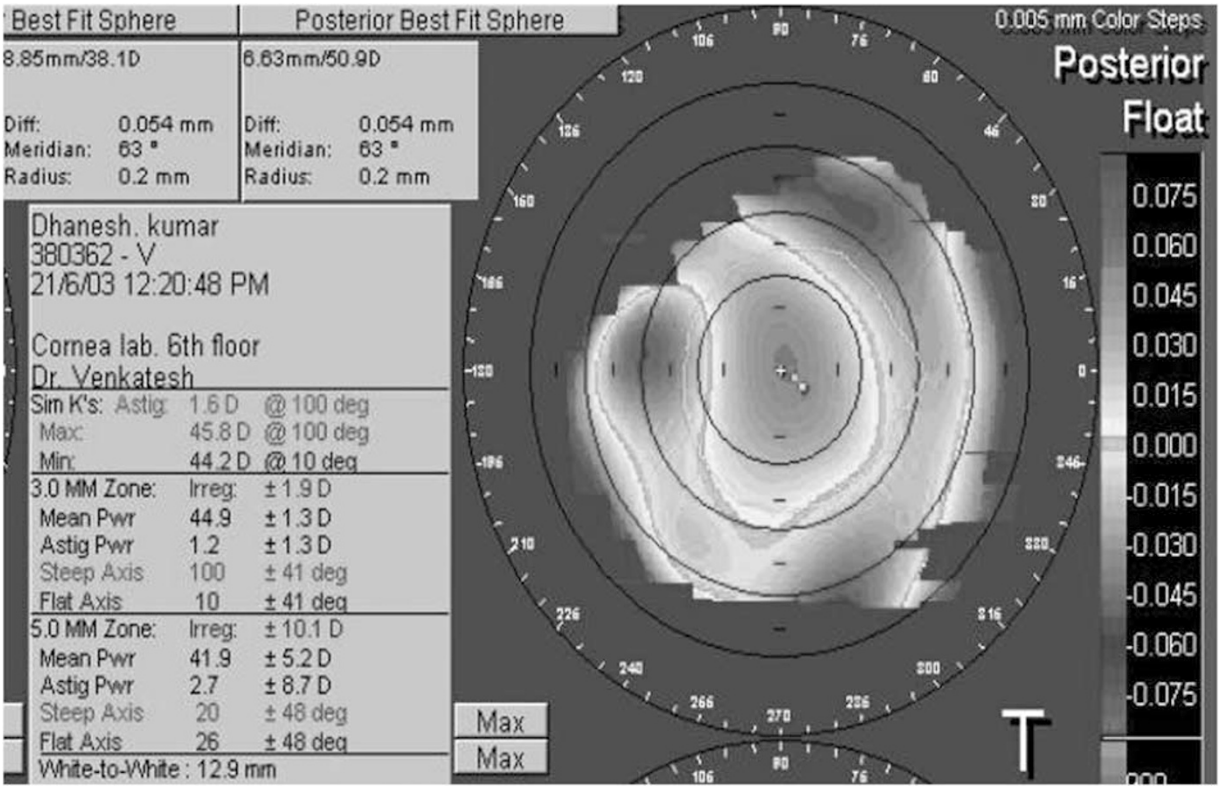

Figure 2 Posterior elevation (0.054 mm) with high intra ocular pressure (IOP 50 mmHg).

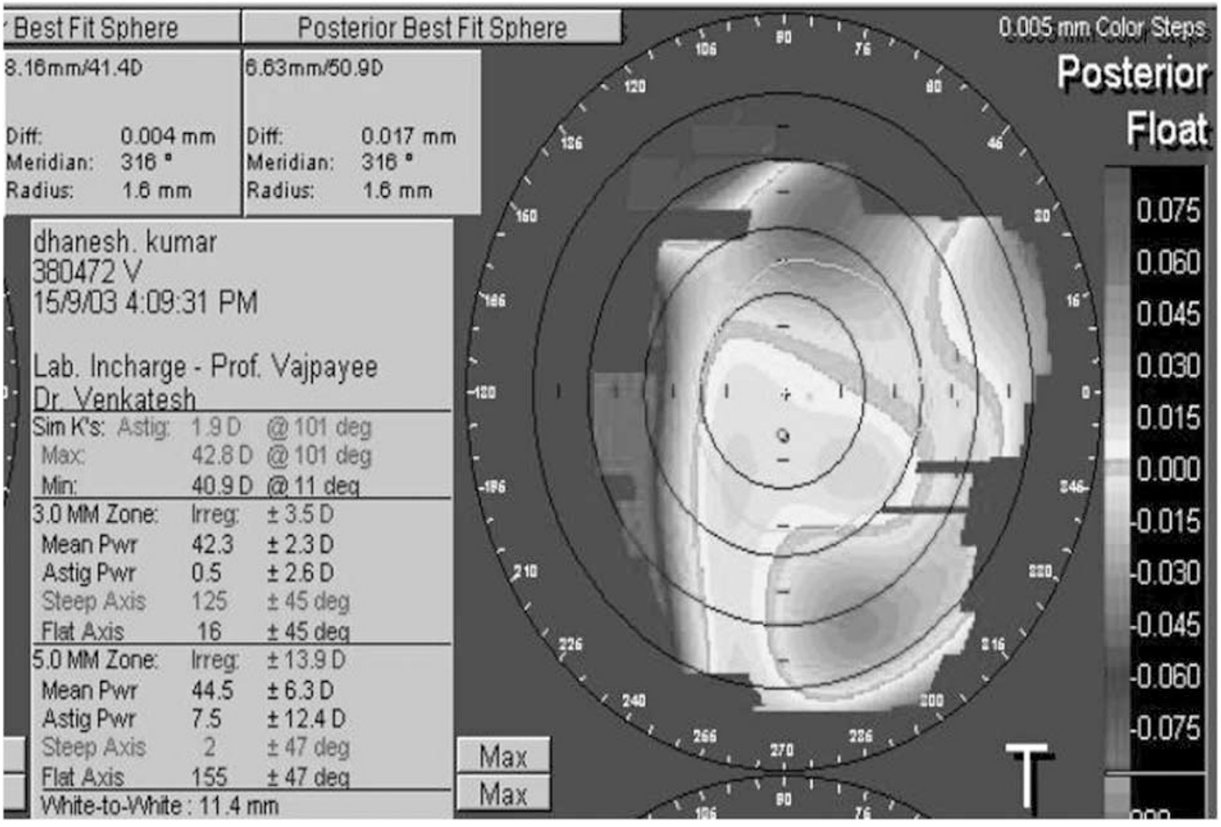

Figure 3 Reduction of posterior elevation (0.017 mm) after reduction of intraocular pressure (IOP = 14 mmHg).

Table 2 Effect of IOP reduction on corneal variables

Corneal parameter	*Baseline*	*After IOP control*	P-*value*
IOP (mmHg)	36.42 ± 13.54	15.00 ± 5.41	**0.000**
Maximum Sim K	44.86 ± 3.21 D	43.87 ± 2.62 D	**0.031**
Minimum Sim K	42.74 ± 2.28 D	42.00 ± 1.71 D	**0.033**
Astigmatism	2.21 ± 2.39 D	1.88 ± 2.01 D	0.540
Central corneal thickness	524.17 ± 68.30 μm	539.81 ± 66.82 μm	**0.019**
Thinnest pachymetry	500.94 ± 93.42 μm	511.83 ± 92.43 μm	0.626
Maximum posterior corneal elevation	64.9 ± 32.36 μm	35.7 ± 28.91 μm	**0.001**

Bold values indicate that *P*-values are <0.05 (i.e. statistically significant).

The mean age distribution in our study, was 18.8 ± 4.6 years in VKC with glaucoma and 11.7 ± 5.1 years in VKC without glaucoma. Neumann *et al*[2] reported that 80% of cases with VKC were less than 15 years, while Khan *et al*[7] mentioned that 68.9% of cases were under 20 years. The three groups were not age and sex matched and this is one of the limitations of the present study which could have affected the results.

In our study, the maximum corneal power 43.80 ± 2.73 D in Group I and 44.06 ± 3.47 D in Group II ($P = 0.86$) as compared to 42.73 ± 1.96 D in controls. In a study by Gortzak *et al*,[9] 40 patients with vernal catarrh and 36 controls were studied and the maximum corneal power in vernal catarrh group was 44.9 ± 5.1 D and in the control group it was 42.9 ± 1.9 D.

In this study the incidence of keratoconus was 19% in steroid-induced glaucoma with VKC and 15% in VKC alone. In a study by Khan *et al*,[7] the incidence of keratoconus was 7%, while Totan *et al*[11] reported keratoconus in 26% of their cases. We found mixed form of VKC to be most commonly associated with keratoconus.

Until now there have been no reports of posterior corneal elevation in VKC patients. In our study, there was higher posterior corneal elevation in both VKC groups (64.9 ± 32.36 μm in Group I and 54.87 ± 22.66 μm

in Group II) as compared to the controls. With the reduction of IOP there was a flattening of the corneal curvature and a significant reduction in the posterior corneal elevation (from $64.9 \pm 32.36\,\mu$m to $35.7 \pm 28.91\,\mu$m). There was also a positive correlation between the IOP reduction and the change in the corneal elevation. This may indicate that in addition to an inherent corneal pathology which leads to corneal ectasia in VKC, in eyes with VKC and steroid-induced glaucoma, the IOP may play an additional role in producing corneal steepening and increasing the posterior corneal elevation. An increase in the IOP may accentuate the posterior corneal elevation and lead to an aggravation of the corneal ectasia. Hence, in addition to the permanent structural changes in the corneal stroma which produce corneal topographic changes in VKC with steroid-induced glaucoma, there may be an element of IOP related reversible change which can be reduced by controlling the IOP. The importance of posterior corneal elevation has been highlighted by Rao *et al*[12] who evaluated 60 eyes with suspicious videokeratography using Orbscan II. They reported that a posterior corneal elevation of $40\,\mu$m should be taken as the screening threshold for patients who want to undergo refractive surgery.

After reduction of the IOP there was a slight increase in the central corneal pachymetry from $524.17 \pm 68.30\,\mu$m to $539.81 \pm 66.82\,\mu$m in the present study. The increased IOP results in surface tension causing the globe including the cornea to expand with an increase in anterior/posterior elevation and a decrease in thickness.[13] The high IOP may lead to a mechanical compression of corneal stromal lamellae and this may also contribute to an apparently lower pachymetric reading. With the reduction of the IOP, the corneal thickness is restored to normal levels and this may be responsible for the apparent increase in the central corneal pachymetry.

In conclusion, high IOP associated with steroid-induced glaucoma and VKC may lead to an increase in the corneal curvature, a significantly increased posterior corneal elevation and a reduction in the central corneal pachymetry and these changes may be reversed by a reduction in the IOP with medical therapy. Further long-term studies are required to study the effect of intraocular pressure on the corneal topography in VKC patients.

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