

Tears Evaluation of One Sample of Keratoconus Patients in Kuala Lumpur

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SUMMARY

Objective: To evaluate tears of newly diagnosed keratoconus patients attending the Optometry clinic in Malaysia and to compare this with tears of normal myopic subjects. **Methods:** The ocular surface of newly diagnosed keratoconus patients were evaluated using tear break up time (TBUT) test, non invasive tear break up time test (NIBUT) and Schirmer test. Twenty keratoconus patients (40 eyes) and 40 normal subjects (80 eyes) participated in this study. **Results:** Significantly lower TBUT and NIBUT values were found in keratoconus patients than normal control subjects ($p < 0.05$). Mean TBUT and NIBUT for keratoconus patients were $3.99 \pm 1.69s$ and $7.03 \pm 3.48s$ and for normal subjects were $7.24 \pm 4.39s$ and $13.67 \pm 10.81s$ respectively. However, no significant difference was detected in Schirmer test values. Mean values of Schirmer tests I and II for keratoconus patients were $20.52 \pm 10.66mm$ and $10.71 \pm 10.43mm$ and for normals were $23.83 \pm 11.34mm$ and $13.27 \pm 8.28mm$ accordingly. **Conclusion:** It was concluded from this study that keratoconus patients have poor tear stability which need to be considered appropriately during management of the patients.

KEY WORDS:

Keratoconus, TBUT, NIBUT, Flourescein Staining, Schirmer Test

INTRODUCTION

Keratoconus is a non inflammatory disorder of the cornea that is characterised by progressive conical ectasia with a protrusion of the thinned stoma area¹. The typical manifestations are inferior corneal thinning and protrusion with increasing myopia and irregular astigmatism that leads to mild or marked visual impairment. The aetiology of the disease remains unknown, but there are evidences of genetic inheritance and possible linkage with systemic disease that may be associated with the disease^{2,3}. In studies of different ethnic population in UK, it was found that, compared with Caucasians Asians have a four- fold increase in incidence, are younger at presentation and require corneal grafting at an earlier age⁴.

Biochemical studies have pointed out that the defect of this disease may lie in the degradation processes of the macromolecules in the cornea. Distinct alterations in all corneal layers have been shown in some histopathology studies, depending on the progression of the disease⁵. However, the association between these alterations to tear

function changes in keratoconus is still controversial. Some authors suggested the possibility of abnormal tear circulation due to altered surface topography of the cornea in keratoconus patients⁶. Dogru *et al* (2003) found tear film disturbances among keratoconus patients that appear to evolve with the progression of the disease⁷. Results from recent works⁸ however showed insignificant difference in the ocular surface of keratoconus patients and the control group. The authors postulated that the changes in the ocular surface of keratoconus patients is not due to the abnormal cornea cones but may be caused by other factors such as contact lens wear⁸.

It is crucial for clinicians to know about changes in tear functions in keratoconus patients so that proper management can be initiated. To our knowledge there is no reported data available in the literature about the tear functions of keratoconus patients in Malaysia. To evaluate the tear functions of keratoconus patients, we conducted a cross sectional study using tear film breakup time analysis (TBUT), non invasive tear break up time (NIBUT) and Schirmer tests. Results of this study may increase our understanding in the alterations of the tear film of keratoconus patients in Malaysia and improve the management of the disease in this country.

MATERIALS AND METHODS

As the prevalence of keratoconus is very low (1 in 4,000), we use similar sample size as quoted in earlier works on keratoconus patients in Asia⁸. A total number of 20 keratoconus patients (13 males and 7 females) as well as 40 normal subjects (20 males and 20 females) from around Kuala Lumpur participated in this study. Informed consent was obtained from each subject and this study was approved by the Medical Ethics Committee of Universiti Kebangsaan Malaysia and followed the tenets of Declaration of Helsinki. Both groups were matched for age and sex. The standard ophthalmic examinations conducted consisted of best-corrected visual acuity measurements, slit-lamp examination and corneal topography. All the keratoconus subjects in this study were graded following the guidelines set by CLEK (Collaborative Longitudinal Evaluation of Keratoconus) study⁹. Only the results of the right eye (RE) are reported in this manuscript.

Tear functions were evaluated using TBUT, NIBUT and Schirmer tests. Both TBUT and NIBUT were performed using Tearscope (Keeler, United Kingdom). Measurements of NIBUT

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Table I: Demographic data

	Sample size (n)	Age (Mean \pm SD)	Female	Male	Keratometric reading (Mean \pm SD)
Keratoconus	20	25.2 \pm 6.54 years	7	13	54.46 \pm 3.92D
Control group	40	22.93 \pm 3.39 years	20	20	43.54 \pm 1.36D

Table II: TBUT, NIBUT and Schirmer Test I and II values

	TBUT	NIBUT	Schirmer test I	Schirmer test II
Keratoconus	3.99 \pm 1.69s*	7.03 \pm 3.48s*	20.52 \pm 10.66mm	10.71 \pm 10.43mm
Control group	7.24 \pm 4.39s	13.67 \pm 10.81s	23.83 \pm 11.34mm	13.27 \pm 8.28mm

*p<0.05 – significant difference

were performed before TBUT to avoid tears contamination and induce tears production due to the use of fluorescein. To measure TBUT, the subject's upper bulbar conjunctiva of the right eye was swiped with a saline wetted fluorescein strip (Haag-Streit International, Switzerland). Subject was told to close the eye for approximately 10 seconds, then to open the eye, blink twice and to keep the eye naturally opened and looking straight ahead (eye in primary position) into the Tearscope. The time from the last blink to the appearance of random dark spots or streaks in the tear film was taken as TBUT. Three readings were taken and the mean was recorded. Similar steps were taken to performed NIBUT, but without the use of fluorescein.

The Schirmer test is a measure of the aqueous volume of the tears. There are several variations of this test, but the one used in this study was Schirmer test I and II. Schirmer test I was conducted using Schirmer filter strip papers (Whatman 41, Coopervision, USA) without the use of topical anesthetics, while Schirmer test II was conducted using 0.5% proparacaine hydrochloride (Alcon, USA). To conduct the tests, the filter strip paper was folded at approximately 5 mm from the end of the paper. The subject was instructed to look up before the strip was inserted into the lower cull-de sac, placing the fold at the lid margin. Once the strip was in placed, the subject was asked to close his/her eyes gently. In Schirmer test II, the anesthetic was instilled prior to the insertion of the paper strip. The test was conducted for 5 minutes or until the strip was completely wet. At the end of the test, the strip was removed from the eye and the amount of wetting was measured using a ruler beginning at the folded notch. Three readings were taken and the mean was recorded.

RESULTS

Twenty keratoconus patients (20 eyes) and 40 control subjects (40 eyes) were involved in this study. Mean age of keratoconus patients and control subjects was 25.2 \pm 6.54 and 22.93 \pm 3.39 years respectively. Demographic data of subjects is shown in Table 1.0. The severity of the keratoconus disease was graded following CLEK guidelines⁹. Twenty five percent (25%) of the subjects were found to have mild/early keratoconus while the rest of the keratoconus patients (75%) were moderate cases.

Tears were evaluated using TBUT, NIBUT and Schirmer tests. Mean TBUT of keratoconus patient was 3.99 \pm 1.69s and for

control subjects was 7.24 \pm 4.39s. Statistical analysis using Mann Whitney U test showed significant difference between the two values (p<0.05). Mean NIBUT for keratoconus patients and control subjects were found to be 7.03 \pm 3.48s and 13.67 \pm 10.81s respectively. Statistical analysis also indicates significant difference between the two scores (p<0.05). Results are shown in Table 2.0.

Schirmer tests were used for measuring tear aqueous volume. Mean Schirmer test I and II values found for keratoconus patients were 20.52 \pm 10.66mm and 10.71 \pm 10.43mm respectively. Mean for the control subjects were 23.83 \pm 11.34mm and 13.27 \pm 8.28mm accordingly. Statistical analysis showed insignificant difference (p>0.05) of both test values between the two study groups.

DISCUSSION

The aetiology of keratoconus has been investigated frequently but is still largely unknown. Description of the tear film changes may help us to improve the management of this disease. Results from this study showed insignificant difference in Schirmer test values between keratoconus patients and controls. The present findings are similar to Dogru *et al*⁷ who evaluated tear functions and ocular surface changes in keratoconus patients in Turkey. Their results with Schirmer test showed an average value of 14.6 \pm 5.40 mm in patients with keratoconus vs. 16.6 \pm 5.1 mm in control subjects. No significant difference was noted between the Schirmer test values of both groups or among patients with mild, moderate and severe keratoconus (p<0.001). Based on their findings, the authors hypothesised that there is no aqueous deficient dry eye among the patients in their study. Our present results using Schirmer test I are slightly higher than the earlier findings. The averaged Schirmer test values were 20.52 \pm 10.66mm in keratoconus patients and 23.83 \pm 11.34mm in controls. The discrepancy in values was probably due to the difference in the distribution of subjects. Majority of the keratoconus patients in this study were in moderate stage of the disease. In the earlier study, around 32% of the eyes were in moderate stage and another 64% were in severe stage of keratoconus.

The results with TBUT and NIBUT however demonstrated different pattern between the two study groups. TBUT and NIBUT values of keratoconus patients were found to be significantly lower (p<0.05) than normal subjects. Almost

80% of the keratoconus patients have TBUT values lower than 10s. TBUT scores of less than 10s were considered as abnormal by earlier workers¹⁰. Our results with TBUT also supported earlier findings by Dogru *et al* who showed that almost 70% of the keratoconus subjects had poor TBUT scores, with mean TBUT of 6.80 ± 3.36 s compared to 14.5 ± 3.15 s in controls⁷.

Results from Dogru *et al* also demonstrated that TBUT is significantly lower in patients with moderate and severe keratoconus compared with mild keratoconus ($p < 0.001$)⁷. However their result is arguable as the number of subjects in each group of the study varies significantly with majority of them (64%) having severe keratoconus. We were unable to observe the trend in this study either as majority of our subjects (75%) were having moderate keratoconus. It was hypothesized that the decreased in TBUT scores was probably due to steepening of the cornea that alters the quality and/or quantity of the mucin secretion by the diseased corneal epithelium, reduction of goblet cell numbers or changes in the conjunctiva nongoblet epithelial cells^{7, 11, 12}. Tears of keratoconus patients were also found to have higher levels of Interleukin-6, TNF- α and MMP-9 which indicate involvement of chronic inflammatory events in the pathogenesis of the disease¹³ and may interfere with the stability of the tears.

Results from this study also showed lower TBUT values for normal subjects compared to the ones quoted for western population^{14, 15}. Ethnic differences have been quoted as one of the factors affecting TBUT values. Mean TBUT values for Asian eyes were found to be lower than ones quoted for Caucasians and needs to be taken into account when incorporated with other tests for diagnosis of dry eye^{16, 17}.

We were unable to compare the NIBUT scores in this study with earlier works as there were no data available in the literature. To our knowledge this is the first data on NIBUT scores of keratoconus patients reported. The NIBUT scores for normal subjects in Malaysia were found to be skewed toward lower values¹⁸. The mean value of NIBUT obtained was 15.8 ± 9.4 s, which was similar the one obtained for the control group in this study. There are other limitations in this study. The number of cases collected was rather small due to difficulties in getting patients. Therefore we were unable to compare tear functions between the severities of the disease. A large multi centre study is needed to provide more clues and information about tear function changes in keratoconus patients in this country. Future research should be initiated into this direction.

CONCLUSION

In this study the tears quality in keratoconus patients are affected mainly in TBUT and NIBUT but were normal in Schirmer test. Such condition need to be considered during management of keratoconus patients especially when treating them with contact lenses.

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