· Original article ·

Effects of artificial tears on corneal thickness in adult myopia

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Abstract

• AIM: To study the effects of Sodium Hyaluronate (HA) and Bion Tears on corneal thickness in adult myopic patients.
• METHODS: A total of 38 cases (76 eyes) were involved in this study. Three consecutive corneal measurements (the thinnest point of the cornea, THN) were evaluated before and half an hour after the instillation of one drop of HA in one eye and Bion Tears in the other at random with the Orbscan Corneal Topography System II (Orbscan, Inc, Salt Lake City, UT, USA, Version 3.00E).
• RESULTS: There were no significant between-group differences in baseline variable ($t=0.264$). Thirty minutes after the instillation of HA and Bion tears, THN were significantly increased by $5.57 \pm 7.00\mu m$ ($t=4.906$, $P<0.01$) and $7.89 \pm 7.64\mu m$ ($t=6.369$, $P<0.01$) respectively. However, there were no between-group differences in THN changes ($t=1.381$, $P>0.05$). Increase in the corneal thickness were found in 32 eyes (84%) and 33 eyes (87%) for the HA and Bion tears group, respectively.
• CONCLUSION: Artificial tears including HA and Bion Tears can significantly increase the corneal thickness in a short period of time. Corneal thickness can be used as one of the objective indices for evaluating the quality and therapeutic role of artificial tears.
• KEYWORDS: artificial tears; corneal thickness; Orbscan Corneal Topography System II
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INTRODUCTION

Artificial tears are, to date, the mainstay of the therapy for dry eye syndrome. They have been designed with a focus on physical properties relating to wetting of the ocular surface. The ideal tear replacement should have a composition which is compatible with the maintenance of a normal ocular surface epithelium. Although different artificial tears have different properties that may be advantageous or disadvantageous in the management of the ocular surface disorders, the manufacturing standards for artificial tears were generally more rigorous than other ophthalmic drops[1].

Evaluations of the artificial tears mainly focus on its physiological index, its effect on symptomatic relief and examinations such as the Break-up Time (BUT). However, many of the above index are subjective, results being difficult to compare, and with great intra- and inter observer variations. The uses of surface regularity index (SRI), surface asymmetry index (SAI) and the potential visual acuity (PVA) after the application of artificial tears have also been studied in the literatures[2,3].

The cornea perhaps may have more sensitive reactions than we ever expected to its environmental alteration. The corneal thickness and its shape were confirmed to be affected by various factors such as 10g/L atropine sulphate ointment, topical anesthetic, complex tropicamide, saline solutions[4-6]. Although a wide variety of artificial tear products to treat moderate to severe dry eye are currently on the market in China, two of the leading products are 1g/L Sodium Hyaluronate (HA, Santen, Japan) and Bion Tears (1g/L Dextran 70 and 3g/L Hydroxypropyl Methylcellulose 2910, Alcon Laboratories, Inc, USA). This study was designed to investigate the effect of the artificial tear application on corneal thickness in adult myopia patients and to explore the role of corneal thickness as an index of evaluating ideal artificial tears.

MATERIALS AND METHODS

Materials The prospective study involved 38 adult (above 18 years old) myopic patients from April to October 2005. All the patients come from the Refractive Center of Yantai Yuhuangding Hospital. Eyes were chosen randomly into the HA or Bion artificial tears groups for each patient. The patients then underwent an ophthalmic examination including the best corrected visual acuity, manifest refraction, slit-lamp examination and non-contact applanation measurement. All the patients enrolled did not have any significant eye diseases and no other eye drops administration before the examination. Informed consents were obtained from all participating patients. All experiments were performed in compliance with the tenets of the Declaration of Helsinki. Approval was obtained from the Yantai Regional Medical Center Institutional Review Board for the prospective study.

Apparatue and Procedure The Orbscan II corneal topography system (Orbscan, Inc, Salt Lake City, UT, USA, Version 3.00E) was performed on each eye before and half an hour after the administration of one drop of HA or Bion Tears, respectively. After instillation of one drop of HA in one eye and Bion Tears in another at random by one investigator, Gao L, the patients were asked to keep both of their eyes closed

before the final examination.

The corneal thickness measurements were taken by using the non-contact Orbscan II system following the procedures recommended by the manufacturer. Each patient was asked to blink before the corneal thickness measurement to avoid any bias because of corneal drying. Three consecutive corneal measurements of each eye (right eyes first) were recorded respectively before and half an hour after the instillation of eye drops. The procedures were performed by the same investigator Tan LX, who was masked from the randomization. Pachymetry was determined by this Orbscan according the difference in elevation between the anterior and posterior surface of the cornea. The instrument could recognize the thinnest point of the cornea (THN) and marks its distance from the visual axial and its quadrant location. Acoustic factor for the Orbscan was set as 0.92 in all performances.

Non-cycloplegic refractive state was recorded with Canon RK-5 automated refractor (Canon INC, Japan). Myopia was defined as spherical equivalent refraction greater than -0.75D. Calibration and verification were performed weekly both for the Orbscan system and Canon RK-5 automated refractor to ensure their repeatability of readings.

Statistical Analysis Statistical data analysis was performed with SPSS for Windows, version 11.0 (SPSS Inc, Chicago, IL, USA) using Independent-samples and Paired-samples t test. P-value of less than 0.05 was considered statistically significant.

RESULTS

Thirty-eight healthy myopic patients (76 eyes) were recruited in the study. The age of patients ranged between 18 and 56 years with a mean age of 28.5 years. There were 20 males and 18 females with a mean refractive error of -4.37 diopter (D, range -0.75- -10.50D). The best spectacle-corrected visual acuity was equal to or better than 20/20.

The results of a normality test showed that the distributions of all variables before and after administration of eye drops were normal ($-1 <$ Skewness < 1). There was no difference in corneal thinnest values (THN) between two groups before instillation of the eye drops being tested ($t = 0.264$). The mean corneal thinnest values with their corresponding paired sample t test were presented in table 1. Following the HA and Bion Tears administration, the THN were significantly increased by $5.57 \pm 7.00\mu m$ ($t = 4.906$, $P < 0.01$) in HA group and $7.89 \pm 7.64\mu m$ ($t = 6.369$, $P < 0.01$) in Bion Tears group respectively. However, the differences in THN alteration between the two groups were not significant ($t = 1.381$, $P > 0.05$).

The maximum increase in THN within the half an hour for each groups were shown in table 2. Increase in the corneal thickness was found in 32 eyes (84%) and 33 eyes (87%) for the HA and Bion Tears group, respectively.

Table 1 Corneal thickness values observed between the first and the second Orbscan assessment

(Corneal thickness values $\bar{x} \pm s$, $n = 38$, μm)

Thickness values	HA group	Bion group
THN	542.77 ± 34.61	540.67 ± 34.74
THN	548.34 ± 36.26[a]	548.56 ± 35.00[b]

THN: corneal thickness at the thinnest point, [a] Data obtained from the second examination, t test: Paired sample t test

Table 2 Maximum and percentage of the increased observed with Orbscan ($n = 38$)

Variable	HA group	Bion group
Maximum increase (μm)	20.34	27.66
Increased ≥5μm(eyes,%)	21 (55.26)	22 (57.89)

DISCUSSION

With the aging population and the increasing access to video display terminals (VDTs), such as televisions and computers, the prevalence of dry eye syndrome is obviously increasing[1]. The prevalence of dry eye has been estimated to be approximately 10% to 20% of the adult population and may be more common in women and in the elderly[7-9]. Dry eye is a complex, multifactorial disease that has been proven difficult to show treatment success with medication. Causes of dry eye are varied and encompass one or all the components of the tear film (e.g., meibomian gland dysfunction, aqueous tear deficiency, or ocular surface disease). In view of the complex etiologies (some of which are even uncorrectable factors) of dry eye, and its relative diagnostic difficulties, the use of artificial tears for the relief of symptoms becomes an inevitable choice to most of the sufferers.

Artificial tears simulate normal human tears. It can increase humidity at the ocular surface, improve lubrication and produce hydrated mucous gel which covers the ocular surface for eye protection and vision improvement. As the roles of the artificial tears is to substitute the physiological tears, the more similar between their compositions the better. However, there is no single and readily available index for evaluating artificial tears which has a high degree of sensitivity and specificity, and that could be considered as a "gold standard"[1].

Corneal thickness has become an area of research interest due to the advancement of excimer laser corneal refractive surgery, particularly in laser *in situ* keratomileusis (LASIK). In our previous study, we confirmed that the thinnest pachymetry of the cornea were significantly increased 1.5 hours after administration of three drops of complex tropicamide ($23.36 \pm 15.01\mu m$, $t = -11.855$, $P < 0.01$) as well as 9g/L saline solutions ($7.13 \pm 8.11\mu m$, $t = -4.894$, $P < 0.01$)[5]. We suspected and believed that the microenvironmental differences in every aspect between eye drops and nature tear film could be the explanation for the changeable measurements of corneal thickness. Since the cornea is bathed with tears, corneal thickness could be served as an objective index for evaluating the quality of artificial tears as well as other eye drops based on the fact that eye drops being compatible with natural tears would have the minimal effects on the cornea.

Corneal thickness can be evaluated by a number of methods including ultrasonic pachymetry, optical slit lamp pachymetry, confocal microscopy, and optical coherence tomography[10]. Although ultrasound pachymetry has been used to measure corneal thickness worldwide, recent studies demonstrated that the Orbscan II pachymetry measurements correlated well with the ultrasound measurements in eyes with clear corneas for measuring corneal thickness[11,12]. It is a non-invasive and non-contact, well-controlled method of

excellent reproducibility both in clinical and research study[12,13]. Considering the fact that THN values were significantly increased 5 minutes after administration of one drops of Benoxil (Oxybuprocaine) 4g/L solution (Santen, Japan) to 98 patients (98 right eyes), it is not adaptive to measure the change of corneal thickness in such condition with ultrasound pachymetry.

Factors increasing the corneal thickness in the study may include: 1) Diurnal variations of the corneal thickness is believed to be related to eyelid closure and cornea metabolism[14,15]. It is reasonable to deduce that the increases of corneal thickness after the use of artificial tears may be due to the effect of closed eyelid. However, we have previously demonstrated that eyelid closure for 1.5 hours alone would not significantly affect the corneal thickness[6]. Therefore, eyelid closure for only half an hour would not, by the same theory, have a significant effect on the corneal thickness. 2) Preservatives of artificial tears, in particular benzalkonium chloride, were shown to cause emulsification of cell wall lipids with subsequent disruption of intercellular unions, leading to an increase in the corneal epithelial permeability[16]. HA contains preservatives of benzalkonium chloride, while Bion is sterile, unidose and preservative-free. However, there was no significant difference between their effects on corneal thickness. This may suggested that the effect of benzalkonium chloride on corneal thickness within half an hour is limited. 3) Artificial tears may directly lead to temporary thickening of precorneal tear film which may also be included in the corneal thickness measurement by using Orbscan system[10]. However, it is believed that 3g/L HA would be completely drained out from the ocular surface through the canaliculi half an hour after the instillation[17]. In addition, by using quantitative gamma scintigraphy to estimate the ocular surface residence times of different eye drops, Snibson *et al* [18] demonstrated that 2g/L sodium hyaluronate solution had a mean half-life on the ocular surface of 321seconds.

In conclusion, the perfect artificial tears could not be produced yet with the current understanding of the complex chemistry and regulation of natural human tears. Artificial tears can cause an increase in corneal thickness, and this finding could be served as an objective index for evaluating the quality of artificial tears as well as other eye drops, based on the fact that ideal eye drops should have minimal effect on the ocular surface function as well as the metabolism, and thus the effect on the corneal thickness.

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人工泪液对成年近视眼角膜厚度的影响

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摘要

目的:研究人工泪液爱丽和倍然对成年近视眼角膜厚度的影响。

方法:应用Orbscan II角膜地形图系统(Orbscan, Inc, Salt Lake City, UT, USA, Version 3.00E)对滴人工泪液爱丽或倍然0.5h后的最薄角膜厚度(THN)变化进行测量,38例(76眼)被随机分成爱丽组和倍然组,分别于滴药前和滴药后0.5h进行3次THN测量。

结果:两组THN在滴药前无差异($t=0.264$),但滴药0.5h后两组THN均显著增加(爱丽组5.57±7.00μm,$t=4.906$,$P<0.01$,倍然组7.89±7.64μm,$t=6.369$,$P<0.01$),两组之间的角膜厚度变化无显著性差异($t=1.381$,$P>0.05$);爱丽组共有32眼(84%)角膜厚度增加,而倍然组33眼(87%)角膜厚度增加。

结论:对生产工艺要求相对严格的人工泪液能短时间内显著增加近视眼角膜厚度,角膜厚度的变化可作为评估人工泪液等眼药制剂舒适度的客观指标之一。

关键词:人工泪液;角膜厚度;Orbscan II角膜地形图系统