ARTICLE

Corneal thickness in Fuchs' dystrophy with and without epithelial oedema

KEAN T. OH, LESLIE J. WEIL, DAWN M. OH, WILLIAM D. MATHERS

Abstract

Purpose **To investigate whether the occurrence of epithelial oedema in Fuchs' endothelial dystrophy is associated with a particular corneal thickness or the extent of central corneal guttae.**

Methods **Sixty-seven patients, aged 52–90 years, presenting in our clinic with Fuchs' dystrophy were divided on the basis of the presence or absence of epithelial oedema as determined by slit lamp examination. After exclusion of extreme cases, the 56 cases without oedema were compared with the 10 cases with oedema with respect to corneal thickness, measured by ultrasound pachymetry and corneal guttae diameter, obtained from the slit lamp examination.**

Results **Mean corneal thickness was significantly higher ($p = 0.002$) in the oedematous group (mean = 0.682 mm) than in the group without epithelial oedema (mean = 0.624 mm). A corneal thickness greater than 0.650 mm was associated with a greater than 85% probability of oedema occurrence. Corneal guttae diameter did not differ significantly ($p = 0.941$) between the two groups and was not significantly correlated with corneal thickness ($p = 0.269$).**

Conclusion **There is a demonstrable association between epithelial oedema and the measured thickness of the cornea.**

Key words Fuchs' dystrophy, Guttae, Corneal oedema, Epithelium, Endothelium

K.T. Oh ✉
L.J. Weil
W.D. Mathers
D.M. Oh
Department of Ophthalmology
University of Iowa Hospitals and Clinics
200 Hawkins Drive
Iowa City
IA 52242-1091
USA
Tel: +1 (319) 356-2861
Fax: +1 (319) 356-0363

Fuchs' endothelial dystrophy is a progressive corneal dystrophy associated with decreased numbers of endothelial cells and the development of corneal guttae. It becomes apparent after 40 years of age with a noticeably decreased visual acuity due to swelling of the stromal layer and subsequent corneal epithelial oedema. As the disease progresses, further visual loss and potential epithelial bullous disease require penetrating keratoplasty for their management.[1,2]

Guttae seen in this disease are localised excrescences of Descemet's membrane resulting from the abnormal production of collagen by endothelial cells and are believed to be associated with endothelial dysfunction.[1–4] The corneal endothelium plays a key role in vision by maintaining corneal deturgescence. It serves as a passive barrier to fluid movement and also actively pumps fluid out of the corneal stroma.[2,5–9] In Fuchs' dystrophy the initial defect appears to be in the barrier function served by the endothelium, resulting in progressively increasing corneal swelling.[10–12] Ultrastructural studies of the endothelium in Fuchs' dystrophy have demonstrated loosening and drop-out of tight junctions due to stretching of a decreasing number of endothelial cells over the corneal area.[3,7,9] Influx of fluid is initially balanced by adaptive up-regulation of the Na/K-ATPase pump that maintains corneal thickness and clarity. Ultimately the loss of pump function results in epithelial swelling and decreased visual acuity in the late stages of disease.[5,6,9,12,13]

Prediction of the development of epithelial oedema in patients with Fuchs' dystrophy would assist in the management of their disease. In this study, we examined several parameters of Fuchs' dystrophy, specifically the degree of central corneal guttae and corneal thickness, in order to establish a predictive relationship with epithelial oedema.

Materials and methods

Sixty-seven patients with Fuchs' dystrophy were recruited from our corneal clinic. Fuchs' dystrophy was defined as the presence of moderate to severe corneal guttae bilaterally. All patients underwent a complete ocular history and physical examination using a slit lamp and Goldmann tonometry upon entry into the study. The first eye to be examined was enrolled, except for the 6 patients who had one eye with and one without oedema. In these patients the eye with oedema was enrolled in the study. Eyes with previous surgery or any

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other ocular disease, except cataracts, were not considered eligible for the study.

Fifty-six enrolled eyes did not have epithelial oedema, while 11 presented with oedema. The patients ranged in age from 52 and 90 years; 52 were female, 15 were male. All eyes included in the study had an intraocular pressure of less than or equal to 22 mmHg. No patients were using any ocular medications, except artificial tears.

The area covered by dense corneal guttae was measured across its horizontal diameter by a slit beam in 55 patients. Another 12 patients had corneal guttae qualitatively estimated on a scale from 1+ (dense guttae in the central 3 mm) to 4+ (dense guttae in the central 7 mm). Fluress (fluorescein and benoxinate) or a moistened fluorescein strip was used to detect and demarcate epithelial oedema. The horizontal diameter of the area of epithelial oedema was measured with a slit beam. Any eye with epithelial oedema greater than 5 mm was considered to have advanced oedema and was subsequently excluded from the study. Following slit lamp examination, the patients underwent pachymetry with an ultrasonic pachymeter (Pachsonic, Teknar, St Louis, MO) performed by one of two experienced pachymetry technicians. The measurements were made with the patient sitting in an upright position looking straight ahead and focusing on a distant target. The probe was positioned perpendicular to the central cornea and gently applied to obtain the reading. At least three measurements were taken and the mode of the measurements was recorded for the study. Time of day was not noted in the study, but all measurements were made between 0900 and 1600 hours.

Results

Corneal thickness and guttae diameter measurements were evaluated for normality assumptions using the Wilk–Shapiro statistic calculated by SAS (SAS, Cary, NC). Corneal guttae diameter was found not to be normally distributed ($p = 0.0001$), and the oedema/non-oedema groups were subsequently compared for differences in guttae diameter using a non-parametric Wilcoxon rank-sum test. The test showed no significant differences between the two groups with respect to guttae diameter ($p = 0.9414$). Guttae diameter was then tested for correlation with corneal thickness; the Spearman rank correlation coefficient was 0.153, demonstrating no significant correlation ($p = 0.2694$).

Corneal thickness was found to be distributed normally. A two-sample t-test found the mean thickness of the oedema group (0.682) to be significantly higher than that of the non-oedema group (0.624) with $p = 0.0024$. A stem-and-leaf plot of the thickness measurements from the two groups (Fig. 1) shows the highest concentration of oedema occurring in eyes with a corneal thickness greater than 0.650 mm. Probit analysis suggests that a corneal thickness greater than 0.650 mm yields a greater than 85% probability of epithelial oedema occurrence.

Discussion

Fuchs' dystrophy is a common endothelial dystrophy causing visual loss due to endothelial dysfunction and stromal swelling.[1-3] This process is thought to occur as a result of a breakdown in the function of the endothelium as a passive barrier against fluid movement, leading to

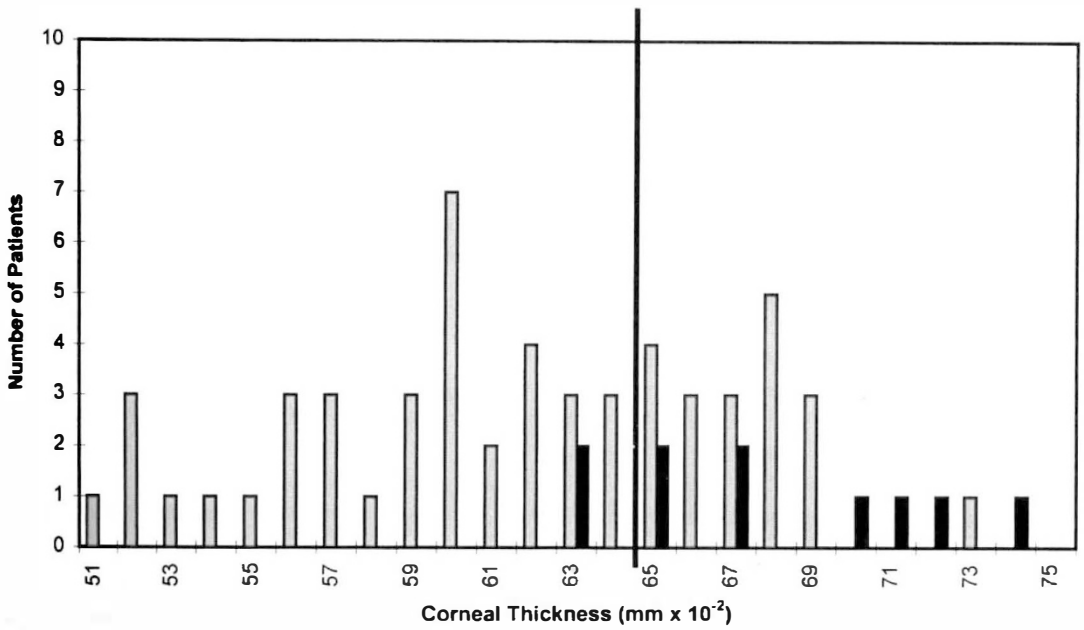

Fig. 1. *Stem-and-leaf plot of the patient population. Patient distribution demonstrates normal distribution of Fuchs' dystrophy patients with regard to corneal thickness. Black columns represent patients with epithelial oedema while grey columns represent patients without epithelial oedema. The vertical line at 0.65 mm marks the point at which there is an 85% probability of epithelial oedema.*

further deterioration of endothelial function and subsequent stromal swelling.[10–12] Fluid from stromal oedema collects below the epithelial basement membrane and, eventually, within the epithelium itself causing an irregular surface. Normally, the microvilli of the surface epithelium create an optically smooth surface but the presence of epithelial oedema results in large irregularities in tear film causing subsequent decreased visual acuity. Ultimately, patients develop microcystic epithelial changes and subepithelial bullae secondary to corneal swelling.

This study examined the association between the area of the cornea involved with guttae and the development of epithelial oedema. In an attempt to define an easily applied clinical parameter associated with epithelial oedema, we measured the horizontal diameter of guttae involving the central cornea without taking into consideration the density of guttae. The results failed to demonstrate a correlation between the diameter of corneal guttae and corneal thickness or epithelial oedema. Previous studies have suggested such a relationship between guttae area and the progression of Fuchs' dystrophy. However, those studies evaluated the guttae utilising a specular microscope, thus providing a more reliable but clinically more cumbersome measurement of guttae by considering their density within the affected region of the cornea. Furthermore, the association between guttae and endothelial dysfunction has been well documented clinically and by laboratory investigations.

Evaluation of corneal thickness by pachymetry demonstrated a significantly higher average corneal thickness in patients with epithelial oedema. Oedema occurred more frequently in eyes where the corneal thickness exceeded 0.650 mm (Fig. 1). A corneal thickness of 0.650 mm was associated with a greater than 85% probability of the presence of epithelial oedema. Consequently, a thickness of 0.650 mm can be considered as a possible demarcation point between a low and high probability of developing epithelial oedema.

Mandell *et al.*[13,14] suggested that the potential variations in corneal thickness are partly due to rates of evaporation from the corneal surface and concluded that an arbitrary corneal thickness by itself could not adequately gauge the progression of Fuchs' dystrophy. Consequently, diurnal timing of measurements may introduce bias into the study. This effect is important but there is still a basic relationship between endothelial function in Fuchs' dystrophy and corneal thickening.[10–12] The mean corneal thickness will be higher in Fuchs' dystrophy patients than normal controls even though individual variability will be considerable.[11]

In a clinical setting, corneal thickness may provide a simple clinical means of assessing the severity of Fuchs' dystrophy and assessing the risk of visual loss from epithelial oedema. It can provide additional information in the therapeutic management of patients with regard to future cataract surgery and penetrating keratoplasty.

References

1. Waring GO, Rordrigues MM, Laibson PR. Endothelial dystrophies. Surv Ophthalmol 1978;23:147–68.
2. Irvine ARJ. Pathology of corneal endothelium. In: King JH, McTigue JW, editors. Proceedings of the Corneal World Congress, Baltimore, Md. London: Butterworth, 1965:230–4.
3. Bourne WM, Johnson DH, Campbell RJ. The ultrastructure of Descemet's membrane. III. Fuchs' dystrophy. Arch Ophthalmol 1982;100:1952–5.
4. Schnitzer JI, Krachmer JH. A specular microscopic study of families with endothelial dystrophy. Br J Ophthalmol 1981;65:366–400.
5. Geroski DH, Matsuda M, Yee RW, Edelhauser HF. Pump function of the human corneal endothelium. Ophthalmology 1985;92:759–63.
6. McCartney MD, Wood TO, McLaughlin BL. Moderate Fuchs' dystrophy. ATPase pump site density. Invest Ophthalmol Vis Sci 1989;30:1560–4.
7. Sasaki Y, Tuberville AW, Wood YO, McLaughlin BL. Freeze fracture study of human corneal endothelial dysfunction. Invest Ophthalmol Vis Sci 1986;27:480–5.
8. Tuberville AW, Wood RL, McLaughlin BL. Cytochrome oxidase activity of Fuchs' endothelial dystrophy. Curr Eye Res 1986;5:939–47.
9. McCartney MD, Robertson DP, Wood TO, McLaughlin BL. ATPase pump site density in human dysfunctional corneal endothelium. Invest Ophthalmol Vis Sci 1987;28:1955–62.
10. Burns RR, Bourne WM, Brubaker RF. Endothelial function in patients with cornea guttae. Invest Ophthalmol Vis Sci 1979;18S:37.
11. Wilson SE, Bourne WM, O'Brien PC, Brubaker RF. Endothelial function and aqueous humor flow rates in patients with Fuchs' dystrophy. Am J Ophthalmol 1988;106:270–8.
12. Rodrigues MM, Krachmer JH, Hackett J, Gaskins R, Halkias A. Fuchs' corneal dystrophy: a clinicopathologic study of the variation in corneal edema. Ophthalmology 1986;93:789–96.
13. Mandell RB, Polse KA, Brand RJ, Vasine D, Dermartini D, Flam R. Corneal hydration control in Fuchs' dystrophy. Invest Ophthalmol Vis Sci 1989;30:845–52.
14. Polse KA, Brand RJ, Mandell RB, Vastine D, Demartini D, Flam R. Age differences in corneal hydration control. Invest Ophthalmol Vis Sci 1989;30:392–9.