Is Intraocular Pressure in Myotonic Dystrophy Patients Spuriously Low?

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Abstract

Background: Ocular hypotony is a common unexplained feature of myotonic dystrophy type 1. Spuriously low applanation tonometric readings can be caused by thin corneas, flat corneal curvature and corneal edema.

Objectives: To determine whether structure abnormalities of the cornea cause spuriously low readings in applanation tonometry.

Methods: We utilized a TMS-2N corneal topographer, a NonconRobo SP-6000 Specular microscope and a Corneo-Gage Plus 1A Pachymeter to examine seven patients with DM1 and eight healthy controls. Intraocular pressure, central corneal thickness, and endothelial cell density were measured, and simulated keratometry readings were made. Cornea guttata and irregularity of corneal topography patterns were also sought.

Results: The mean intraocular pressure was 9.86 ± 1.29 mmHg for all patients (intraocular operated and non-operated eyes) and 12.88 ± 1.89 mmHg for the controls ($P = 0.000021$, two-tailed t-test). Central corneal thickness was 530.57 ± 35.30 micron for all patients and 535.00 ± 39.62 micron for the controls ($P = 0.75$, two-tailed t-test). Endothelial cell density was 3164 ± 761 cells/mm^2 for all patients and 3148 ± 395 cells/mm^2 for the controls ($P = 0.94$, two-tailed t-test). Simulated keratometry readings were similar in both groups when the operated eyes were excluded. Cornea guttata and irregularity of corneal topography patterns were also noted in the study group.

Conclusions: Corneal thickness, corneal curvature and corneal hydration were within normal limits and thus were not the cause for the low applanation tonometry reading in DM1. The presence of cornea guttata and irregularity of corneal topography patterns in DM1 warrants further investigation.

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Myotonic dystrophy is the most common adult form of muscular dystrophy that begins in adulthood. It is characterized by autosomal dominant inheritance, muscular dystrophy, myotonia and multisystem involvement [1]. The two types of myotonic dystrophy are designated type 1 and type 2. The clinical features of type 2 myotonic dystrophy tend to be milder than those of type 1, and the two types are caused by mutations in different genes. Four decades ago, Brand [2] was one of the first investigators to report ocular hypotony in patients with myotonic dystrophy type 1. Ocular hypotony is a common, unexplained feature of DM1 [3]. Extremely low intraocular pressure is one of a constellation of clinical signs that sometimes accompany this disorder. Previous studies investigated the inflow and outflow of aqueous in order to explain this phenomenon [3,4]. They showed that the rate of aqueous humor flow is reduced by approximately 9% and that the rate of inward leakage of light-scattering proteins is increased by approximately 37% in well-established DM1 with ocular hypotony. These findings imply that the rate of aqueous fluid flow into the eye is lower, thus contributing to a lower hydrostatic pressure in the eye. Another proposed mechanism for explaining the presence of ocular hypotony is based on atrophy of the ciliary muscle, a condition that increases fluid exchange between the anterior chamber and the anterior uvea with consequent enhancement of uveoscleral outflow of fluids from the eye [4]. Facilitating outflow changes the equilibrium towards a lower hydrostatic pressure in the eye.

Central corneal thickness was found to be a powerful predictor for the development of primary open-angle glaucoma, independent of IOP as measured by applanation tonometry [5]. The extent of pachymetry-measured central corneal thickness has a significant effect on the clinical management of patients with glaucoma and suspected glaucoma, in as many as 20% of the patients [6].

While tonometry accurately measures tension of the eyeball, tonometric readings do not always reflect true IOP values. Measured applanation tonometry deviates when corneal thickness, curvature, or biomechanical properties vary from normal values [7]. There is a positive correlation between tonometric readings and corneal curvature: the flatter the curvature, the lower the reading on the scale of the tonometer [8]. Corneal edema, caused by primary or secondary endothelial cell dysfunction and largely manifest by abnormal specular microscopy, can alter applanation tonometry readings, yielding a lower measured value compared to the real manometric value [9].

There are no data on corneal thickness, corneal curvature and corneal endothelial cell density in DM1 patients. The present study was designed to measure corneal thickness and curvature and to perform specular microscopy to determine whether structural abnormalities of the cornea cause spuriously low readings in applanation tonometry in this population.

DM1 = myotonic dystrophy type 1

IOP = intraocular pressure

Patients and Methods

Patients diagnosed as having DM1 based on neurological examination and electromyographic findings that were confirmed by genetic studies were selected for this study. The controls were recruited from apparently healthy hospital staff members visiting our ophthalmology outpatient clinic. Corneal-simulated keratometry was recorded using the TMS-2N corneal topographer (Tomey, Erlangen-Tennenlohe, Germany). Non-contact specular microscopy was performed with the NonconRobo SP-6000 Specular microscope (Konan Medical Inc, Mishinomiya, Japan). Ultrasound measurement of central corneal thickness was by the Corneo-Gage Plus 1A Pachymeter (Sonogage, Cleveland, USA). Slit-lamp examination, including applanation tonometry, was performed on a 900 series slit-lamp and applanation monometer (Haag Streit, Bern, Switzerland). The testing sequence was corneal topography followed by specular microscopy, slit-lamp examination, tonometry and pachymetry.

Statistical analysis

Data analysis was performed with the SPSS statistical package version 11, utilizing independent samples t-test for the numeric parameters. Fisher's exact test was applied for the descriptive parameters.

Results

We studied seven patients (one female, six males) with DM1 and eight healthy controls (five females, three males) (comparing between groups $P = 0.011$, Fisher's exact test). The study group's age (mean ± SD) was 46 ± 13.66 years and the control group's 39.37 ± 17.47 years ($P = 0.26$, t-test). Both eyes of each subject were examined. Each eye was included independently in the statistical analysis.

IOP was 9.86 ± 1.29 mmHg in the study group and 12.88 ± 1.89 mmHg in the control group ($P = 0.000021$, two-tailed t-test).

Cataract surgery had been performed on 5/14 study eyes but not on any control eye ($P = 0.014$, Fisher's exact test). Another study eye had cataract, yielding a total of 6/14 with cataract ($P = 0.005$, Fisher's exact test). After excluding the 5 operated eyes, we observed guttata (signifying corneal endothelial dystrophy) in 2 of the remaining 9 study eyes and none in any of the 16 control eyes ($P = 0.12$, Fisher's exact test).

Central corneal thickness was 530.57 ± 35.30 microns for the 14 eyes in the study group and 535.00 ± 39.62 for the 16 control eyes ($P = 0.75$, two-tailed t-test). After excluding the operated eyes in the study group, central corneal thickness in the remaining 9 eyes was 526.22 ± 40.45 micron, still not different from the control group ($P = 0.61$, two-tailed t-test).

Endothelial cell density was 3164 ± 761 cells/mm^2 for the 14 eyes in the study group and 3148 ± 395 cells/mm^2 for the 16 control eyes ($P = 0.94$, two-tailed t-test). Endothelial cell density was 3342 ± 379 cells/mm^2 in the 9 non-operated study eyes, not different from the control group ($P = 0.24$, two-tailed t-test).

Simulated keratometry readings are affected by surgical scars in the corneal periphery. When comparing the study group (without the eyes that had undergone cataract surgery) to the control group, simulated keratometry readings were similar. We performed the same comparison without excluding the eyes that had undergone cataract surgery. Two of the parameters that were compared (the curvature of the flat orthogonal axis, and the curvature of the flattest axis) were significantly lower (flatter) in the study group than in the control group. Review of the dataset revealed that these two parameters were considerably lower in both eyes of one of two patients who had undergone cataract surgery. We attribute these results to the effect of the cataract surgical scar and thus prefer the results calculated from the data obtained from non-operated eyes, as reported above and in Table 1.

The best spectacle-corrected visual acuity was 0.66 ± 0.28 in the study group (20/30) and 0.99 ± 0.03 in the control group (20/20) ($P = 0.000514$, two-tailed t-test). After excluding the operated eyes, the visual acuity for the 9 remaining eyes in the study group was 0.72 ± 0.27 (20/28), still significantly different from the control group ($P = 0.016$, two-tailed t-test). After also excluding the eye with non-operated cataract, the BCVA in the 8 remaining eyes in the study group was 0.8015 ± 0.14025 (20/25), again significantly different from the control group ($P = 0.006$, two-tailed t-test).

Funduscopy revealed tilted disks in both eyes of one DM1 patient and none in the control eyes ($P = 0.209$, Fisher's exact test).

Color vision disorder was found in four eyes of two DM1 patients, and not in the control group ($P = 0.037$, Fisher's exact

BCVA = best spectacle-corrected visual acuity

Table 1. Simulated keratometry obtained by the TMS-2N videokeratoscope (eyes that had undergone surgery were not included)

	A: Study group	(all eyes)	B: Study group	(non-operated eyes)	C: Control group		P* (A-C)	P* (B-C)
	N#	Mean (SD)†	N#	Mean (SD)†	N#	Mean (SD)†		
Steep axis (diopters)	14	45.99 (1.28)	9	46.06 (1.59)	16	46.21 (0.75)	0.58	0.79
Steep axis (degrees)	14	89.14 (48.40)	9	90.11 (22.65)	14	84.93 (25.12)	0.78	0.61
Flat axis (diopters)	14	44.29 (1.08)	9	44.43 (1.34)	16	45.18 (0.88)	0.02	0.16
Flat axis (degrees)	14	102.00 (65.94)	9	100.11 (78.76)	16	110.64 (75.66)	0.75	0.16
Minimal curvature (diopters)	14	44.22 (1.05)	9	44.35 (1.31)	16	45.09 (0.89)	0.02	0.16
Minimal curvature (degrees)	14	101.86 (96.57)	9	118.00 (73.23)	14	96.57 (78.30)	0.85	0.51

Some data were not generated by the software when the cornea had no cylindrical power.

* Independent samples t-test, two-tailed (equal variances not assumed).

Number of eyes included in the analysis.

† Curvature at the steep axis of simulated keratometry, curvature at the flat axis of simulated keratometry and curvature of the flattest axis, as well as their axes, were similar in both groups.

test). Each eye of one patient of these two patients scored 6/10, and each eye of the other patient scored 0/10. All the control eyes had normal color vision.

Blepharitis was detected in 4/14 study eyes, and in none of the 16 control eyes ($P = 0.037$, Fisher's exact test). Ptosis was present in 2/14 study eyes only (none of them operated eyes) and not in any control eye ($P = 0.12$, Fisher's exact test).

Discussion

DM1 is a multisystem disorder that affects skeletal and smooth muscle, as well as the eye, heart, endocrine system, and central nervous system [1]. Classical DM1 is characterized by slowly progressive muscle weakness and wasting, myotonia, cataract, testicular atrophy, frontal balding and often by cardiac conduction defects [1]. Adults become physically disabled and may have a shortened life span. The most severe form is congenital DM1, where babies present with hypotony and severe generalized weakness at birth, often with respiratory insufficiency and early death. Survivors tend to have delayed motor development, and mental retardation is common.

The most common ocular abnormality of classical DM1 is presenile cataract, specifically, with posterior subcapsular stellate ("Christmas tree") opacities. Bilateral iridescent lens opacities and posterior cortical lens opacities are highly specific for DM1 and useful for establishing a clinical diagnosis of DM1 [10]. Bilateral ptosis, exposure keratitis, pigmentary retinopathy, pupillary changes in the form of light near dissociation and weakness of the orbicularis oculi muscles [6,8] can also be present. Low IOP is another well-described phenomenon in some patients with DM1 [9].

IOP is determined by the rate of aqueous production by the ciliary body epithelium and the resistance to outflow of aqueous from the eye. Active secretion accounts for approximately 80% of aqueous production. The aqueous is secreted by the non-pigmented epithelium via an active metabolic process that is dependent upon a number of enzymatic systems. Passive secretion accounts for the remaining 20%. Here, aqueous is produced by passive processes, such as ultrafiltration and diffusion, which are dependent on the level of blood pressure in the ciliary capillaries, the plasma oncotic pressure and the level of the IOP [8]. The normal IOP varies between 10 and 21 mmHg (mean 16 mmHg). Fluctuation of IOP occurs with the time of the day, heartbeat, blood pressure level and respiration.

Focal signs of retino-uveal affection were present in 9/33 patients examined by Raitta and Karli [11]. Clinically, they appeared as acquired lesions affecting the retina, pigment epithelium, and choroid. One patient was found to have an outburnt panuveitis [11].

Our study patients shared some of the previously known characteristics of DM1 eyes such as ocular hypotony and the tendency to have cataracts as well as ptosis and blepharitis. They also demonstrated a significant reduction in BCVA independent of either the presence of cataract or of a history of cataract surgery. Another significant feature was the presence of color vision disorder in the eyes of DM1 patients. We believe that these findings are symptoms of uveoretinal damage secondary to the primary disease.

The main purpose of the study was to examine the effect of corneal parameters on IOP as measured by applanation tonometry. The values of all three known parameters – corneal thickness, corneal curvature and endothelial cell density – were within normal limits among our patients with DM1, and not different from those of normal control eyes. These findings negate the hypothesis that tonometry readings are spuriously low.

The eyes of some of our DM1 patients did, however, display several abnormal features that did not reach a level of significance. Cornea guttata in the absence of clinical edema (corneal endothelial dystrophy) were observed in two eyes of one DM1 patient, but not in any of the control eyes. Corneal endothelial dystrophy that does not reach endothelial failure is not a rare condition, but it takes on greater interest when it appears concomitantly with DM1. Another abnormality was an irregularity of the corneal topography, which was not expressed in the keratometry readings.

In conclusion, IOP in MD1 is significantly lower than normal levels. Factors that might spuriously lower IOP values, such as thin corneas, flat corneal curvature and corneal edema, failed to do so among our DM1 patients. The presence of cornea guttata and irregularity of corneal topography patterns in DM1 warrant further study.

References

1. Adams RD, Victor M, Ropper HL. Principles of Neurology. 6th edn. New York: McGraw-Hill,1997:1423–6.
2. Brand I. Intraokulare hypotonie bei myotonikern. *Ophthalmologica* 1955;129:81–8.
3. Dreyer RF. Ocular hypotony in myotonic dystrophy. *Int Ophthalmol* 1983;6:221–3.
4. Khan AR, Brubaker RF. Aqueous humor flow and flare in patients with myotonic dystrophy. *Invest Ophthalmol Vis Sci* 1993;34:3131–9.
5. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:714–20.
6. Shih CY, Graff Zivin JS, Trokel SL, Tsai JC. Clinical significance of central corneal thickness in the management of glaucoma. *Arch Ophthalmol* 2004;122:1270–5.
7. Liu J, Roberts CJ. Influence of corneal biomechanical properties on intraocular pressure measurement: quantitative analysis. *J Cataract Refract Surg* 2005;31:146–55.
8. Mark HH, Mark TL. Corneal astigmatism in applanation tonometry. *Eye* 2003;17:617–18.
9. Dueker D. Tonometry, tonography, and aqueous fluorophotometry. In: Duane's Clinical Ophthalmology 2003 CD-ROM Edition, Clinical Volume 3, Chapter 46.
10. Ashizawa T, Hejtmancik JF, Liu J, Perryman MB, Epstein HF, Koch DD. Diagnostic value of ophthalmologic findings in myotonic dystrophy: comparison with risks calculated by haplotype analysis of closely linked restriction fragment length polymorphisms. *Am J Med Genet* 1992;42:55–60.
11. Raitta C, Karli P. Ocular findings in myotonic dystrophy. *Ann Ophthalmol* 1982;4:647–50.

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