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Sweet hyperopia: Refractive changes in acute hyperglycemia

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PURPOSE. *A prospective study was performed to evaluate refractive and ocular biometric changes in acute hyperglycemic status in patients with diabetes mellitus.*
METHODS. *From January to August 2002, 48 eyes of 24 patients with persistent diabetes and a plasma glucose level 17 mmol/L or HbA1c 10.0% on admission were enrolled in this prospective study. Upon admission to Tri-Service General Hospital in Taipei, Taiwan, these patients underwent intensive glycemic control. The basic ophthalmic examinations, including visual acuity, intraocular pressure measurement, slit lamp, and fundus examinations, were conducted. The ocular parameters including refraction, anterior chamber depth, lens thickness, axial length, mean keratometry, and thinnest corneal thickness were evaluated by A-mode scan and Orbscan II. Each patient underwent clinical follow-up visits at 1, 2, and 4 weeks after the acute hyperglycemic episode.*
RESULTS. *Of the 24 patients, 18 were male and 6 were female. The mean age of the patients was 55 years (range: 38 to 69). Comparing the refractive status on admission and at week 4, the authors found that 8 cases (16 eyes, 33%) showed hyperopia during hyperglycemia (+1.9±0.8 D), but in the other 16 cases (32 eyes, 67%), there were no significant changes. In addition, there were also no significant changes in anterior chamber depth, lens thickness, axial length, thinnest corneal thickness, or mean keratometry in the follow-up period.*
CONCLUSIONS. *Transitory hyperglycemia produces hyperopia. The alteration in refractive index in the lens may contribute to the hyperopic change, but no change of ocular biometrics in lens or cornea is observed. (Eur J Ophthalmol 2006; 16: 663-6)*

KEY WORDS. *Diabetes mellitus, Hyperglycemia, Myopia, Refraction, Refractive index, Sweet hyperopia*

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INTRODUCTION

Myopia associated with hyperglycemia and hyperopia with hypoglycemia has been reported to develop in diabetic patients. While an early study suggested that decreased plasma glucose causes hyperopia (1), others cite increased blood sugar as its cause (2-6). Sweet hyperopia is a term first coined by Roxburgh in 2000 (7). Our study examines the mechanism of hyperglycemia and hyperopia. The refractive power of the eyes depends on the anterior and posterior curvature of the lens, the axial length of the eye, and the refractive index of the cornea, aqueous, lens, and vitreous. The biologic basis of refractive changes in the eyes of diabetic patients has not yet been established, and the underlying mechanism is unknown.

We conducted a prospective study of 48 eyes of 24 diabetic patients who were hospitalized for acute, severe hyperglycemia then underwent glycemic control to make an objective evaluation of changes in refraction and ocular biometrics. Mean keratometry, anterior chamber depth, and thinnest corneal thickness measurements were obtained with Orbscan II®.

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METHODS

A total of 24 patients with diabetes mellitus admitted to Tri-Service General Hospital in Taipei, Taiwan, between January and August 2002 were enrolled in this study. Exclusion criteria from the study were diabetes mellitus-related ocular conditions, such as cataracts or vitreoretinal disease and ocular surgery.

The study protocol and consent forms were accepted on November 15, 2001, according to the regulation rules of the Investigational Review Board of the National Defense Medical Center, Taipei, Taiwan. Informed consent was obtained from all patients participating in the study. The study group consisted of 16 males and 8 females; the mean age was 55 ± 12 years. All patients had a plasma glucose level 17mmol/L or HgbA1C of 10% on admission.

All patients had been diagnosed with diabetes mellitus for more than 2 years and had been placed on medical treatment. However, due to poor control of plasma glucose, acute hyperglycemia was noted before admission. The mean plasma glucose concentration on admission was 19 mmol/L (SD = 5, range = 16.7 to 25.8), and the mean HbA1C value was 10.9% (SD = 1.2, range = 10 to 14).

The basic ophthalmologic examinations including assessment of visual acuity and intraocular pressure, slit lamp microscopic examination, and funduscopy were conducted after admission but before sugar level control.

Week 0 was defined as the date of enrollment. After topical instillation of 1% cyclopentolate hydrochloride and 0.5% tropicamide, refraction under cycloplegia was measured by automatic refractokeratometer (ARK-2000, Nidek Co Ltd., Gamagori, Aichi, Japan). From the onset of refractive change, the ocular parameters including refraction, anterior chamber depth, lens thickness, axial length, mean keratometry, and thinnest corneal thickness were evaluated by A-mode scan (US-1600, Nidek Co Ltd., Gamagori, Aichi, Japan) and Orbscan® II (Bausch & Lomb, Inc., Rochester, NY, USA). Ultrasonic biometry was performed for anterior chamber depth, lens thickness, and axial length using A-mode scan. The same examiner performed the A-mode ultrasonography five times in each eye at each examination to measure the lens thickness, anterior chamber depth, and axial length. The mean value of the five measurements was used for analysis of each biometric parameter. Mean corneal curvatures were measured using Orbscan® II; thinnest corneal thickness and anterior chamber depth were estimated through this device as well. Each patient underwent clinical follow-up visits at 1, 2, and 4 weeks after the acute hyperglycemia episode. Refractive change more than 0.5 diopters over the period was regarded as a significant change.

Statistical analysis

A commercially available statistical software program (SPSS 11.5, SYSTAT Inc., Chicago, IL, USA) was used for analyzing the patients' data, presented as mean ± standard deviation. The paired t-test or Wilcoxon signed rank test was used to compare differences in continuous variables between week 0 and week 1, week 0 and week 2, and week 0 and week 4. The level of statistical significance was set at p0.05.

TABLE I - OCULAR BIOMETRICS AND REFRACTIVE CHANGE IN HYPEROPIC SHIFT PATIENTS

	Week 0 Week 1[a]	Week 2[b] Week 4[c]		
ACD/Orb	2.4 ± 0.4	2.4 ± 0.4 (0.016*)	2.4 ± 0.3 (0.175)	2.4 ±0.3 (0.520)
ACD	3.1 ± 0.2	3.1 ± 0.3 (0.190)	3.1 ± 0.2 (0.251)	3.1 ±0.3 (0.056)
TCT	544.6 ±16.3	544.5 ±15.7 (0.932)	547.4 ±17.1 (0.064)	545.9 ±14.8 (0.410)
MK	44.0 ± 1.8	43.9 ± 1.9 (0.627)	43.9 ± 1.9 (0.233)	43.9 ±1.9 (0.714)
AL	23.6 ± 1.4	23.6 ± 1.3 (0.453)	23.6 ± 1.3 (0.261)	23.6 ±1.3 (0.543)
LT	4.5 ± 0.2	4.5 ± 0.2 (0.347)	4.5 ± 0.2 (0.804)	4.4 ±0.2 (0.190)
Refraction	1.9 ± 0.8	1.4 ± 0.5 (0.002*)	0.8 ± 0.4 (0.002*)	0.4 ±0.2 (0.000*)

Values are mean ± SD (p value). Statistical method: paired Student t test
[a]Compared at week 0 and week 1
[b]Compared at week 0 and week 2
[c]Compared at week 0 and week 4
*Statistical significance: p 0.05
ACD = Anterior chamber depth; TCT = Thinnest corneal thickness; MK = Mean keratometry; AL = Axial length; LT = Lens thickness

RESULTS

Comparing the refractive status on admission and at week 4, we found that 8 cases (16 eyes, 33%) showed significant hyperopia (>0.5 diopters) at hyperglycemic status. Of those patients with resultant hyperopia, the mean refraction was +1.9±0.8 diopter at week 0 and +0.4±0.2 diopter at week 4. Some residual hyperopia remained at week 4. A statistically significant change in refraction occurred from week 0 to week 1, as well as from week 0 to weeks 2 and 4 (p 0.05) (Tab. I). This study showed hyperopia in a hyperglycemic condition, and the change subsided when blood sugar level returned to normal following control with medication. In the remaining 16 cases (32 eyes, 67%), there were no significant changes.

The anterior chamber depth measured with Orbscan® II produced a significant change only from week 0 to week 1 (p=0.016). Sonography did not produce a significant change for the same period. Further measurement of anterior chamber depth from week 0 to week 2 and week 0 to week 4 showed no significant change with either sonography or Orbscan® II (Tab. I). Additionally, there was no statistically significant measurable change in lens thickness, axial length, thinnest corneal thickness, or mean keratometry during the follow-up period (Tab. I).

The Orbscan® II produced consistently smaller measurements of the anterior chamber depth as compared to those produced by A-mode sonography. This is because sonography measures anterior chamber depth from the anterior surface of the cornea to the lens, while the Orbscan® II measures anterior chamber depth from the posterior surface of the cornea to the lens.

DISCUSSION

As early as 1925, it has been recognized that the refractive power of the eye varies with blood sugar, with hyperopia developing in those patients with decreased blood sugar and myopia in those patients with increased sugar (1). Other studies cite the occurrence of hyperopia following insulin therapy (8, 9). Conversely, several reports in the literature claim that hyperglycemia produces hyperopia (3-6). In a study by Riordan et al, 12 patients with hyperglycemia developed hyperopia ranging from 1.00 to 3.25 diopters (2). In 2000, Okamoto et al presented a study of 14 patients with diabetes in whom transient hyperopia occurred after hyperglycemia (6).

Other studies of patients with diabetes mellitus have investigated possible anatomic changes as the source of refractive changes. Okamoto et al report that there was no evidence of a change in lens or corneal curvature, lens thickness, or axial length of the eye in diabetic patients during intensive glycemic control. They conclude that a change in refractive index of the lens is responsible for the refractive changes (6).

In Gwinup and Villarreal's study measuring the change in refraction post-intravenous injection of a 50% glucose solution, the vision of diabetic patients with phakia became more myopic or less hyperopic, whereas aphakic eyes showed a slight hyperopic change (9). The difference in the eyes with or without a lens indicates that the change in refraction associated with a change in blood glucose levels is primarily related to the lens. In the patients of this study (before sugar level control), acute hyperglycemia followed meal consumption and resulted in sweet hyperopia. When the blood glucose level increased, an osmotic imbalance was created by the high concentrations of sorbitol and fructose in the lenses relative to their concentrations in the aqueous. The difference in osmotic pressure results in the influx of water from the aqueous humor into the lens, causing lenticular swelling with hyperopic refractive changes.

In the present study, ultrasonographic biometry did not show any significant changes of anterior chamber depth and lens thickness. A change in refractive index must be considered as a more effective contributing factor to the refractive change. This refractive change might be due to the osmotic change generated from the glucose concentration change and is likely reversible.

The refractive power of a lens is determined by its thickness, anterior and posterior surface curvature, refractive index, and the refractive index of the aqueous humor and vitreous body directly in contact with the lens.

In a study by Saito et al, an increased lens thickness was shown by photography and sonography, while photography showed a decreased anterior chamber depth (11). Their study did not produce a change in axial length or corneal curvature. Saito et al showed both hyperopia and lens swelling on photography and sonography. This is suggestive that lens curvature steepened by swelling may produce myopia. However, Saito et al proposed that the refractive index change of the lens following the influx of water caused the hyperopic change.

Conversely, a study by Okamato et al showed no change in lens thickness upon sonography (6). Further-

more, no changes in the anterior chamber depth, axial length, or anterior corneal curvature were noted. Their study further showed transient hyperopia without lens swelling (6). A reduction in the refractive index of the lens, rather an alteration of the lens size, appears to be responsible for this hyperopic change. It appears that the refractive index in the anterior portion of the lens may have produced the hyperopia, since aldose reductase is located in the lens epithelium and cortex.

This finding is further confirmed by slit lamp photography in a study by Planten (10). This study concludes that if areas with different refractive indices develop, a plane between these areas will become visible. Planten states that changes in refraction are due to a change in the refractive index of the layers of the lens.

The lens refractive index is a variable rather than a constant factor (although under normal conditions, it is a constant). In hyperglycemia, a decrease in refractive index due to lens hydration will produce index hyperopia up to 3.5 diopters. Conversely, in cases of cataracts in young adults, an increase in refractive index due to lens dehydration will produce myopia up to –10 diopters. However, this needs to be proved with further study. Over time, we know hyperglycemia can cause cataracts. If this result shares the same mechanism of action as that presented in this study, in the future we may be able to prevent cataracts with medication designed to control this mechanism. Whether lens refractive index variation can be applied to the correction of refractive error requires further investigation.

Future study of a larger study population would confirm the findings presented in this report. Additionally, further technologic advances in ophthalmology may allow for more definitive results than those produced by the latest technology presented here, the Orbscan II®.

From this study, it seems that refractive change could be resultant primarily from the refractive index within the lens, instead of other causes within the lens (for example, the curvature or thickness of the lens) or outside of the lens (for example, the corneal or anterior chamber).

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