Relationship of Serum Glucose Concentration to Changes in Refraction

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SUMMARY

The effect of chronic changes in serum glucose concentration on refraction was studied by increasing the dose of insulin or chlorpropamide in 10 diabetic patients who initially had relatively high glucose concentrations. In every case when serum glucose concentration was reduced the vision became less myopic or more hyperopic.

To assess acute changes, 10 diabetics (including four with aphakic eyes) were given an intravenous injection of glucose. In patients with intact lenses the vision became more myopic or less hyperopic following the administration of glucose, but in the aphakic eyes hyperopia increased.

It is concluded from both the acute and chronic studies that higher levels of serum glucose concentration produce myopia and lower levels produce hyperopia. Furthermore, these changes are related to changes in the optical properties of the crystalline lens. DIABETES *25*:29-31, January, 1976.

In the 19th century it was recognized that the vision of diabetics is influenced by the changing concentrations of glucose in their blood.[1] In 1925 Duke-Elder refracted the eyes of two patients while they were in diabetic ketoacidosis and again after their blood glucose had returned toward the normal range. He concluded that hyperglycemia produced myopia and that lowering the blood sugar resulted in hyperopia.[2] Since that time, no systematic studies have been performed to further define the relationship of serum glucose to changes in refraction. However, differing opinions have been expressed about this relationship. For example, Eversman recently stated that with the onset of diabetes "there may be a change in the amount of myopia present, particularly a decrease, or an increase in hyperopia."[3] The present study was undertaken in an attempt to further define the effects of both acute and chronic changes in serum glucose concentration on the refractive properties of the eye.

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MATERIALS AND METHODS

All studies were performed in the diabetic outpatient clinic, where the results of the serum glucose determination were available within several minutes after the blood samples had been obtained.

The effect of chronic changes in serum glucose concentration on refraction was studied by choosing patients who were found to have relatively high serum glucose levels (above 150 mg./dl.) and who were receiving insulin or an oral agent that could be increased in dosage. The refractive error of both eyes was determined, and these patients were advised to increase their daily dose of either lente insulin or chlorpropamide. At the time of the next clinic visit, one to four weeks later, if the serum glucose concentration evidenced a reduction of more than 50 mg./dl., refraction was repeated. Ten patients met these criteria and were selected for study.

The acute studies were performed on six diabetics with relatively normal serum glucose concentrations (below 150 mg./dl.), all of whom were being controlled on diet alone. Immediately after the initial refraction of both eyes 50 cc. of 50 per cent glucose in water was administered intravenously over a five-minute period. The refractions were then repeated every 15 minutes for 90 minutes. Except for the initial level, serum glucose concentrations were not determined in this group. Four monocular-aphakic diabetic patients were similarly studied. Three were well controlled on chlorpropamide and the fourth was controlled on diet alone. Unfortunately, in none of the aphakic patients did the lens of the opposite eye permit refraction.

In both the acute and chronic studies, serum glucose was determined on the clinic's Technicon Auto-Analyzer using the O-toluidine reaction. Objective refraction was used to confirm subjective refraction in every case. Retinoscopy was performed with a streak retinoscope and subjective refraction was performed with a Stevens Photometer. In plotting the data, the prescription formula was converted into a spherical

dioptric equivalent by algebraically adding one half of the cylinder without consideration of the axis of astigmatism.

RESULTS

The data are presented graphically. The effect on refraction of chronic changes in serum glucose concentration is depicted in figure 1, in which it can be appreciated that as serum glucose changed from a greater to a lesser concentration the refractive error of both eyes of every patient (n=20) became more positive or less negative (vision became less myopic or more hyperopic). It can also be seen that generally a greater difference in serum glucose concentration was associated with a greater change in refraction, such that a change in serum glucose concentration of 100 mg. per deciliter produced a change in refraction of approximately ½ diopter.

The effect of an acute increase in serum glucose on refraction is depicted in figure 2. In every case the refraction in both eyes of the six diabetics (n = 12) promptly changed from the baseline condition to a more negative value (vision became more myopic, less hyperopic). This change was uniformly apparent within 15 minutes after the injection of glucose was completed. The maximum change was recorded at 45 minutes, at which time refraction began to return toward the baseline state. Surprisingly, in each of the very limited number of aphakic eyes studied (n = 4), within 15 minutes after the intravenous injection of glucose was completed, the refraction had become more positive (more hyperopic).

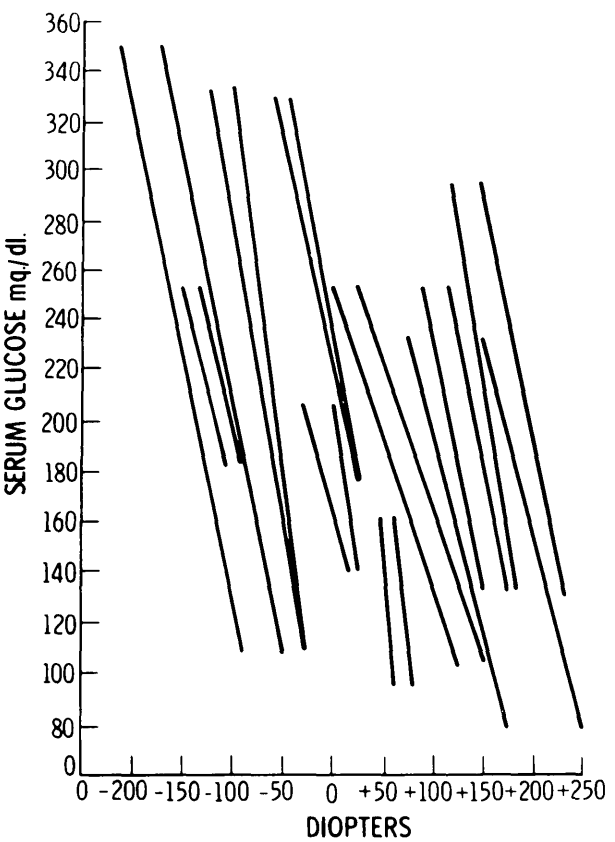

FIG. 1 Relationship of refractive error of the eyes of 10 diabetics (n=20) to initial serum glucose (top of each line) and subsequent serum glucose (bottom of each line) lowered by increasing the dose of insulin or chlorpropamide.

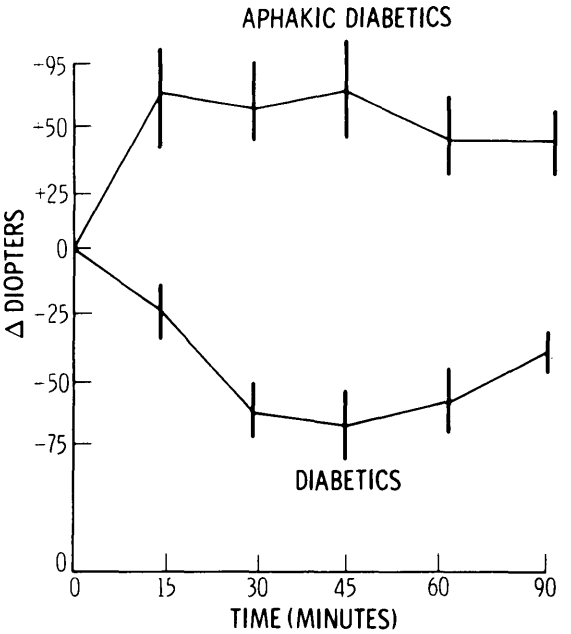

FIG. 2 Changes in refraction of the eyes of aphakic diabetics (n=4) and diabetics with intact lenses (n=12) following the intravenous injection of 25 gm. of glucose (mean ± S.D.).

DISCUSSION

Our studies suggest that an increase in serum glucose concentration, whether acute or chronic, is invariably associated with a more myopic or less hyperopic change in vision as long as the crystalline lens of the eye is intact. We found, however, that such changes do not occur in an eye from which the lens has been removed, which confirms Elschnig's observation that myopia was not produced by hyperglycemia in an aphakic.[4] The change in vision that accompanied chronic changes in serum glucose seemed to parallel the degree of change in glucose concentration, with a rise of 100 mg./dl. producing a refractive change of about ½ diopter. Since serum glucose measurements were not obtained in the acute studies, no relationship

between the degree of change in refraction and the degree of hyperglycemia produced can be determined. But since the intravenous injection of 25 gm. of glucose in mild adult diabetics produces a rather predictable rise of about 150 mg./dl. and a rather predictable fall over the next 90 minutes,[5] the relationship between the changes in refraction and serum glucose concentration would seem to be of the same order as those demonstrated in the chronic studies.

These results are compatible with reports by diabetic patients in which the discerning patient may relate that relatively small increases in this serum glucose concentration seem to be associated with changes in visual acuity. It should be noted that an increase in serum glucose may be associated with either decreased or increased visual acuity, depending upon the particular patient's baseline refractive error. For example, many older diabetic patients state that when their serum glucose level is higher they are better able to read the newspaper, while younger patients note that their visual acuity is diminished. It is perhaps this apparent discrepancy that has led to the different opinions regarding the effects of serum glucose on vision.

The mechanism responsible for the changes in refraction remains speculative; however, it is known that the extracellular space of the lens is freely permeable to glucose. Glucose enters the intracellular (lens fiber) space by "facilitated diffusion."[6] Penetration of glucose into the extracellular space of the lens would *not* cause lens swelling (no osmotic gradient across the capsule) and would have only a very small effect on the refraction index of the eye. Glucose accumulation intracellularly would lead to lens swelling and consequent myopia.

More recently the importance of the sorbitol pathway in metabolism of the crystalline lens has been emphasized.[7] Glucose entering the lens can be converted through the action of aldose reductase to sorbitol, which can in turn be converted through the action of sorbitol dehydrogenase to fructose. The accumulation of these sugar alcohols within the lens is paralleled by an accumulation of water, which produces lenticular swelling.[7]

The apparently paradoxic changes in refraction observed in the aphakic eye are more difficult to explain. Perhaps swelling occurs in the retina, slightly reducing the corneal-retinal surface distance.

Finally, the clinical implications of our findings of refractive changes with relatively small differences in serum glucose concentration serve only to reemphasize the proposition that the diabetic's eye should not be refracted for the prescription of glasses until his serum glucose concentration is adequately controlled.

REFERENCES

[1]Da Costa, J.: Medical Diagnosis, seventh edit. Philadelphia, J. B. Lippincott, 1890, p. 149.

[2]Duke-Elder, S.: Changes in refraction in diabetes mellitus. Br. J. Ophthalmol. *9*:167-87, June, 1925.

[3]Eversman, J.: Comprehensive approach to diabetes mellitus. Aud. Dig. Intern. Med. *18*:23, 1971.

[4]Elschnig, A.: Refraktionsanderungen bei Diabetes mellitus. Med. Klin. Berlin *19*:17, 1923.

[5]Amatuzio, D.S., Stutzman, F.L., et al.: Interpretation of the rapid intravenous glucose tolerance test in normal individuals and in mild diabetes mellitus. J. Clin. Invest. *32*:428-35, 1953.

[6]Patterson, J.: A review of glucose transport in the lens. Invest. Ophthalmol. *4*:667, Aug., 1965.

[7]Gabbay, K.H.: The sorbitol pathway and the complications of diabetes. N. Engl. J. Med. *288*:831-36, Apr., 1973.

[8]Kinoshita, J.H., Merola, L.O., et al.: Osmotic changes caused by the accumulation of dulcitol in the lenses of rats fed with galactose. Nature (Lond.) *194*:1085, June, 1962.