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Comparison of amplitude of accommodation in type 1 and type 2 diabetes mellitus

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Abstract

Background: The prevalence of diabetes is increasing exponentially due to increasing obesity and reduced physical activity levels. Diabetes affects all structures of the eye; the optics and biometry of the eye are also affected in diabetic patients.

Purpose: To compare the amplitude of accommodation (AA) in type 1 and 2 diabetic patients with the age-matched controls.

Methods: One hundred individuals under the age of 40 years were examined. There were 22 subjects with type 1, 43 with type 2 diabetes and 35 age-matched controls. The AA was measured using the subjective push-up with the RAF rule (Royal Air Force rule). Descriptive statistics and regression analysis were used to analyse the data.

Results: The mean AA was 3.92±0.93, 4.93±1.05 and 7.26±1.30 dioptres (D) in type 1, type 2 and healthy subjects, respectively. There was a significant difference between the mean AA of all diabetic patients and the control subjects, $p \leq 0.01$. The t-test showed that there was significant difference between the AA measurements in type 1 and type 2, $p \leq 0.01$.

Conclusion: The results of this study indicate that diabetes mellitus type 1 may have a major impact on the lens biometry and the AA measurements. The differences may indicate a fundamental difference in pathogenesis of reduced AA.

Keywords: amplitude of accommodation, beta cells, diabetes, hyperglycaemia, insulin, pancreas

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Introduction

Diabetes mellitus (DM) is a complex and heterogeneous group of metabolic diseases characterised by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action or both.[1-6] The chronic hyperglycaemia of diabetes is associated with long-term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels. DM is classified based on aetiology into four main groups: type 1, type 2, gestational and other types.[2-10]

The human crystalline lens continues to grow throughout life.[11-17] New cell fibres continually form and wrap around older cells without any of the cells being discarded. As a result, the lens becomes thicker and more convex with age. The normal increase in convexity of the lens with age could be expected to result in an increase in lens power and thus the tendency towards myopia. However,

in healthy eyes no such tendency is observed, but rather, the eyes change in the direction of hyperopia by an average of about 2 dioptres between the ages of 30 and 60 years. This is called the lens paradox.[14] This lens paradox is due to a decrease in the refractive index of the lens with age, which compensates for the more convex shape of the lens with age. The amplitude of accommodation (AA) normally decreases with age, leading to presbyopia.

From an optical perspective, the optics and biometry of the eye are affected or altered in people with diabetes. The diabetic eye acts like an older normal eye, and with increasing age the changes seem to be exacerbated in diabetes. In patients with diabetes, the optics and biometry of the crystalline lens is disturbed. DM causes an early loss of AA.

Several studies have reported a greater reduced AA in people with diabetes when compared with healthy age-matched controls.[18-21] The purpose of this study was to investigate the influence of DM type 1 and type 2 on the AA on pre-presbyopic diabetic and control subjects.

Methods

This study was carried out in the Department of Ophthalmology, Steve Biko Academic Hospital in Pretoria. The study comprised subjects under 40 years of age. There were 65 subjects with diabetes and 35 age-matched control subjects.

Informed consent was obtained in all subjects involved in the study in accordance with the Declaration of Helsinki, and confidentiality was maintained. Inclusion criteria for the diabetic group were individuals aged between 30 and 40 years (as detected by an endocrinologist) with no diabetic retinopathy on fundus examination. Inclusion criteria for the control group were healthy individuals in the same age range without signs or symptoms of diabetes. Exclusion criteria were subjects with cataract, uveitis, glaucoma, prior ocular surgical or previous history of ocular trauma, evidence of diabetic retinopathy, hypertension and other endocrine disorders. Subjects using systemic medications with known accommodative effects were excluded from both groups. Also subjects with manifest presbyopia were excluded.

Detailed ocular examination including case history, best corrected visual acuity for distance, intraocular pressure (slit-lamp), biomicroscopy and fundus examinations were performed on both groups. The AA was measured using the RAF rule push-up method.

Procedure

Subjects initially looked at N5 line of the RAF rule at a distance of approximately 40 cm while wearing their habitual prescriptions in the trial frame.[22] Subjects were instructed to look at the target and keep it as clear as possible. Once this was achieved, the target was moved slowly toward the subjects in a smooth manner along the rule and the subject asked to report when it first became blurred. The endpoint was the first slight sustained blur, which was considered to be the point when the target could not be cleared after 2 or 3 seconds of blink and attempts to focus. The average speed of the target was 4 cm/s. It took approximately 30 seconds to complete the measurement per subject.

Statistical analysis

Data collected was analysed using the statistical software, IBM Statistical Package for Social Sciences (SPSS), version 24 (SPSS Inc., Chicago, IL). The normality of data was determined using the Shapiro-Wilk test. Statistical significance was set at p-values < 0.05 for all tests and a 95% confidence interval was used as a measure of precision. An independent sample t-test was applied to determine the difference between two independent means. Correlation between age and AA was established using the Pearson correlation coefficient (r).

Results

The duration of diabetes overall ranged from 1 to 25 years, with a mean of 7.6±6.6 years. There were 38 females and 27 males in the diabetic group while the control group had 22 females and 13 males. *Table I* shows the demographics of both the diabetic and control groups for AA measurements. The mean AA in the diabetic group was 4.52±1.20 and 4.68±0.99 D for females and males, respectively. In the control group, the mean AA was 7.43±1.34 D for females while it was 6.92±1.18 D for males.

Figures 1 to 4 show the box plots for the distribution of the AA measurements in diabetic and control subjects, and in the type of diabetes, respectively. In *Figure 1*, the diabetic group had a wide distribution of the AA when compared with the controls. However, both measurements

Table I. Descriptive statistics (mean ± standard deviation) for the diabetes and control subjects

Variable	Diabetes			Control	*p*-value
	Type 1	Type 2	All		
Number of subjects	22	43	65	35	
Age (mean±SD) years	34.23±3.35	35.70±3.31	35.2±3.37	34.69±3.38	0.09
Sex: F/M	13/9	25/18	38/27	22/13	0.91
Corrected visual acuity	6/6	6/6	6/6	6/6	
Amplitude of accommodation	3.92±0.93	4.93±1.05	4.95±1.16	7.26±1.30	
Mean duration of diabetes in years	15.46±4.48	3.58±2.30	7.6±6.6		0.00
Capillary blood glucose	8.95±2.08	9.81±2.63	9.51±2.5		0.22
Medication:					
– Insulin	22/22 (100%)	25/43 (58%)	47/65 (72%)		
– Oral agents	0	18/43 (42%)	18/65 (28%)		
– Diet	0	0	0		

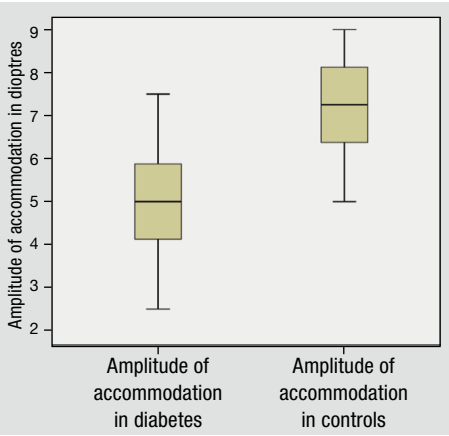

Figure 1. Box plots of measurements of the amplitude of accommodation in diabetic and control subjects. The diabetic subjects had a wider distribution. The average mean difference was –2.23 D.

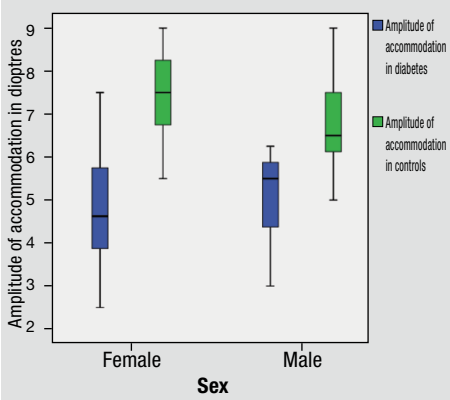

Figure 2. Box plots showing the distributions of amplitude of accommodation in females and males in both diabetic and control subjects, respectively. The distributions of both females and males in the control group were skewed, one negative and the other positive.

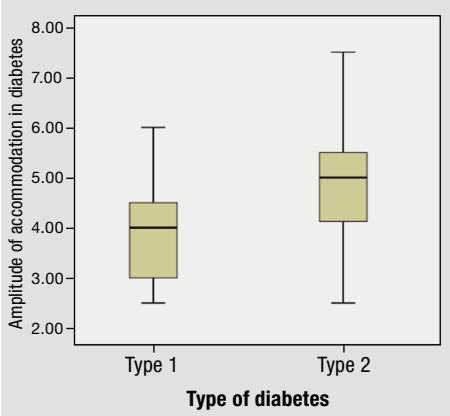

Figure 3. Box plots of the distributions of the amplitude of accommodation in type 1 and type 2 diabetics. The distribution of the amplitude of accommodation in the type 2 diabetics was wider.

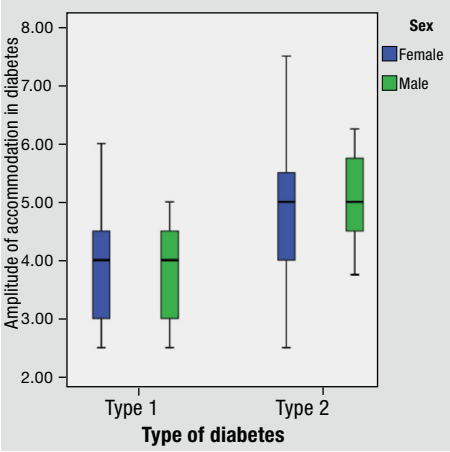

Figure 4. Box plots according to the type of diabetes in female and males

were normally distributed when compared to the Gaussian normal distribution curve. The mean difference between subject with diabetes and the controls was −2.30±1.83 D. On average, AA measurements in the control group were 2.23 D higher than the measurements in diabetics.

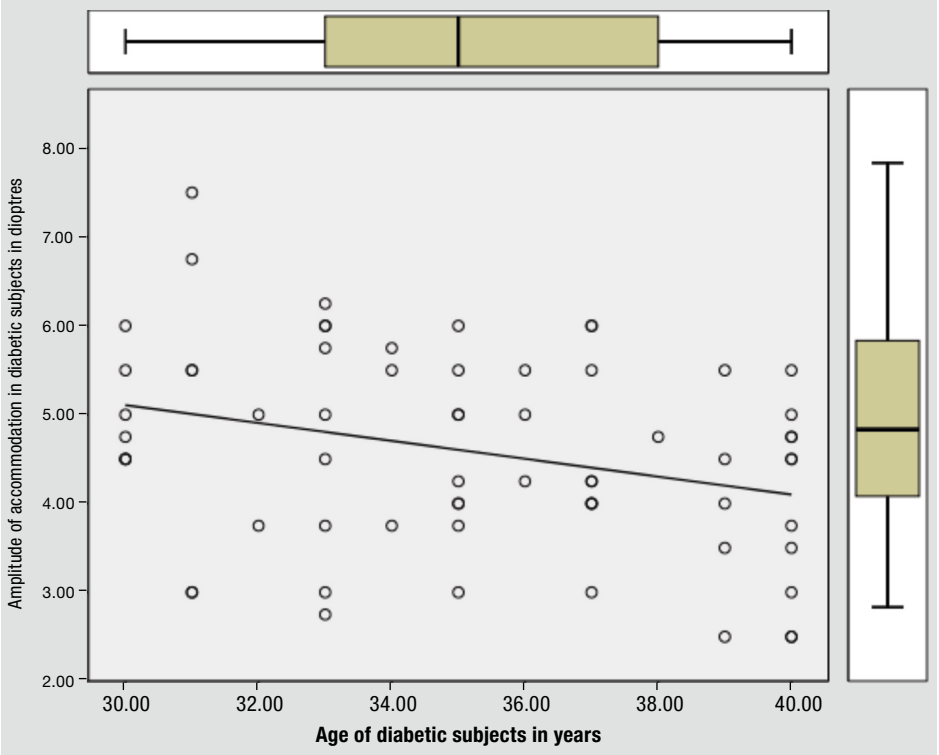

Figure 5. Change in amplitude of accommodation with age in the diabetic subjects, y=8.13−0.1 (age). As the age increases, the amplitude of accommodation decreases, r=−0.3. There does appear to be some weak negative relationship.

Figure 3 shows the distribution of the measurements of the AA between type 1 and type 2 diabetics. The mean AA in type 1 was 3.92±0.93 D while in type 2 diabetics was 4.93±1.05 D. The Levene's test for equality of variances showed that there was a significant difference between the measurements of AA in type 1 and type 2 diabetic subjects. The mean difference was −1.00 D with a 95% confidence interval of between −1.54 and −1.52 D, $p<0.05$. However, there was no statistically significant difference between the AA measurements in females and males. The means were 4.52±1.20 and 4.68±1.00 D for females and males, respectively ($p=0.356$).

Regression analysis was performed. *Figures 5 and 6* show the association between the AA and age in both the study and control groups. There is a

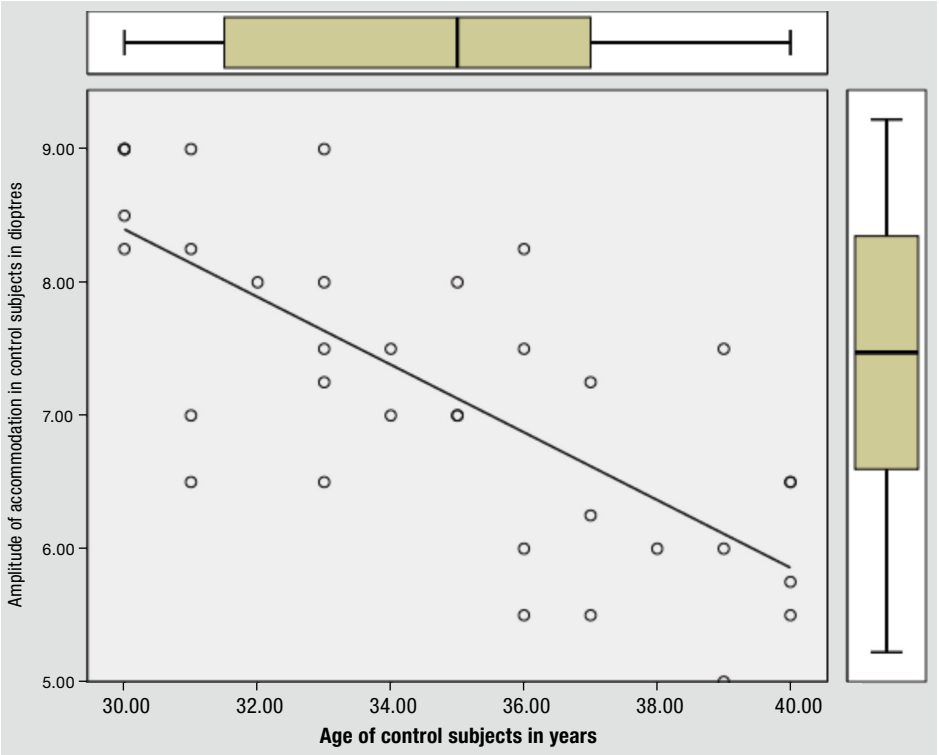

Figure 6. Change in amplitude of accommodation with age in the control group, r=−0.7

weak negative linear relationship (r=−0.3) between AA and age in diabetic group, p=0.00. Some younger diabetic subjects had more reduced AA. There was a significant linear relationship (r=−0.7) between AA and age in the control group, p=0.00. The duration slopes indicate the effect of diabetic duration on the AA.

Discussion

DM is a group of heterogeneous metabolic disorders characterised by chronic hyperglycaemia.[1] It has many complications, with premature morbidity and mortality. DM affects the optics and biometry of the eye, and blurriness of vision is often reported as one of the first signs of its presence.[16] The results of this study showed that subjects with type 1 DM had AAs that were lower than those with type 2 and control subjects. Many studies have reported reduced AA with diabetes when compared with healthy controls.[18-21,23-25] The results of this study showed that type 1 DM is having a profound effect on the AA measurements when compared with type 2 DM subjects. The substantial differences between type 1 and type 2 DM may indicate a fundamental difference in effects on lens optics and biometry related to the aetiology of diabetes.

In diabetic patients, the crystalline lens has been reported to become significantly thicker and more convex with age when compared with those of non-diabetic controls. The origin of the profound increase in the dimension of the lens in DM has not yet been explained. Sparrow *et al.*[15,16] found that the increase in lens biometry in patients with DM type 1 is a result of an increase in both the cortex and the nucleus of the lens, which is less apparent in patients with type 2 DM. The causes of thicker and more convex lenses in diabetics could be the increase in cell membrane permeability, deficiency in ionic membrane pump, abnormality in the lens growth, greater cortical thickness or osmotic swelling.[26-32]

The cause of the reduced AA measurements noted in this study in type 1 DM remains unclear. It is possible that there is an enhanced production rate of individual lens fibres stimulated by the use of insulin. However, it is also possible that the increased thickening of the diabetic lens is the result of cellular or extracellular over-hydration, which could have been caused by an increase in the osmotic pressure within the lens due to the accumulation of glucose and its metabolic products within the lens.[20] Insulin has been reported to produce a hypertrophic cellular response in an epithelial tissue, leading to extracellular over-hydration or increased growth of individual lens fibres of the crystalline lens in type 1 diabetics.[16,26-32]

Type 1 diabetes is an autoimmune disorder characterised by the destruction of the insulin-producing pancreatic beta cells without apparent pathological alterations of other Langerhans cells.[22,26-29] However, the cause is still unknown since it shows heterogeneity in terms of age of onset, severity of autoimmune response and efficacy of therapy. Our study subjects with type 1 diabetes, who are likely to have absolute insulin deficiency, had an average disease duration of 15.5 years. The duration of diabetes is of paramount importance in the reduction of the AA. Individuals at risk of type 2 DM (obese and first-degree relatives) display an initial state of insulin resistance compensated by beta-cell hypersecretion of insulin (hyperinsulinaemia). Over time the pancreatic functional reserve is no longer associated with compensatory hyperinsulinaemia, resulting in an increased blood glucose concentration, called hyperglycaemic hyperinsulinaemia.[26-29] By the time DM is diagnosed, beta cells are no longer able to secrete enough insulin (hyperglycaemic hypoinsulinaemia). However, patients with type 2 DM are not ketosis prone and do not require insulin therapy to prevent ketoacidosis, which is a hallmark feature of type 1 diabetes.[33] The subjects with type 2 diabetes had a disease duration of 3.6 years and thus would be expected to still have residual beta-cell activity due to replacement of insulin.

In contrast to type 1 DM, the duration of diabetes had no significant effect on the AA measurements in the type 2 DM. This may be due to the fact that the onset of disease is insidious and hence, the duration of DM in type 2 is often unknown. The duration of type 2 DM is generally underestimated. All patients with type 1 and 58% of type 2 diabetic patients used insulin. The AA measurements did not change with the duration of the diabetes. The effect of the duration of DM on the AA measurements was the same between females and males in both type 1 and type 2 DM.

Conclusion

The human crystalline lens continues to grow throughout life, and it may become more convex and thicker with age because of the addition of new fibres. In diabetic patients the lens becomes even thicker and more convex with age compared with the lens in healthy subjects. The increase in the dimensions of the diabetic lens may be due to an abnormality in the growth or a swelling of the lens.

The results of this study indicate that the group with type 1 diabetes may have a greater impact on the lens biometry, neural factors and changes in curvature of lenticular surfaces and the measurements of AA. This substantial difference may indicate a fundamental difference in pathogenesis. The crystalline lens of the human eye is affected by DM in a number of different and important ways. Hence, eyes of individuals with DM appear to function as more aged than those of age-matched controls without diabetes. Further research is needed to clarify how the AA of thediabetic patient differs from that of a healthy non-diabetic individual of the same age.

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