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ORIGINAL ARTICLE

Accommodative disorders in non-presbyopic subjects with type 1 diabetes without retinopathy: A comparative, cross-sectional study

María-Carmen Silva-Viguera | **María-José Bautista-Llamas**

Department of Physics of Condensed Matter, Optics Area, Vision Research Group (CIVIUS), University of Seville, Seville, Spain

Correspondence
María-José Bautista-Llamas, Physics Faculty, University of Seville, Reina Mercedes Street, Seville, Spain.
Email: mbautista5@us.es

Abstract

Purpose: The purpose of this study was to assess accommodative function in non-presbyopic individuals diagnosed with type 1 diabetes (T1D) without any signs of retinopathy, to determine the existence of possible accommodative disorders related to this disease, and to determine the influence of T1D duration and glycosylated haemoglobin values on accommodative function.

Methods: This comparative, cross-sectional study included 60 participants between 11 and 39 years old, 30 with T1D and 30 controls, with no previous eye surgery, ocular disease or medication that could affect the results of the visual examination. Amplitude of accommodation (AA), negative and positive relative accommodation (NRA and PRA), accommodative response (AR) and accommodative facility (AF) were assessed using the tests that showed the highest repeatability. Participants were classified based on normative values into 'insufficiency, excess or normal results', and a diagnosis of accommodative disorders (accommodative insufficiency, accommodative infacility and accommodative excess) was made.

Results: Participants with T1D had statistically significant lower AA and AF and higher NRA values than the controls. Furthermore, AA was significantly and inversely correlated with age and the duration of diabetes; however, AF and NRA were only correlated with disease duration. In the classification by accommodative variables, a higher percentage of 'insufficiency values' was observed in the T1D group (50%) than in the control group (6%; $p < 0.001$). In terms of accommodative disorders, accommodative infacility was the most prevalent (15%), followed by accommodative insufficiency (10%).

Conclusions: Our findings indicate that T1D affects most accommodative parameters, with accommodative insufficiency being associated with this disease.

KEYWORDS
accommodation, accommodative anomalies, diabetes mellitus, diabetic complications, type 1 diabetes, visual disorders

INTRODUCTION

Diabetes mellitus is a chronic, systemic disease with variable degrees of hereditary predisposition. It is characterised by chronic hyperglycaemia due to a deficiency in insulin production or action, affecting the metabolism of carbohydrates, proteins and fats. There are different types of this condition, and in type 1 diabetes (T1D), there is destruction of β cells in the pancreas, which leads to absolute insulin insufficiency in the blood.[1]

At the ocular level, diabetes can affect practically all ocular structures. In the posterior segment, patients with diabetes can experience diabetic retinopathy, neuropathy, glaucoma and macular oedema.[2,3] In the anterior segment, complications include corneal dysfunctions, such as abnormal sensitivity, late corneal re-epithelialisation, diabetic keratopathy, progressive decrease in density and/or alteration of the corneal nerve and clouding of the lens at an early age.[4]

Changes can also become manifest at a functional level. Most authors suggest that a large increase in glucose can lead to changes in the refractive index within the ocular media, increasing refractive power and causing temporary myopia.[5] Others have noted the existence of hypermetropic variations with plasma glucose levels, mainly due to the crystalline lens, regardless of whether these levels increase or decrease.[6] With regard to accommodation in individuals with diabetes, as a product of hyperglycaemia the proteins of the lens are lost, leading to a decline in elasticity and the ability to focus on near objects. Therefore, some authors have suggested that these subjects have decreased accommodative power for their age compared with patients without diabetes,[7–10] and in some cases, these changes are related to glycaemic control, with contradictory results in this regard.[11–13]

Variations within the crystalline lens could lead to accommodative disorders, that is, visual disturbances that affect the subject's binocular vision and visual performance, particularly when performing near-vision tasks. The most frequent symptoms are headache, blurred vision, difficulty focusing at different distances and eye pain, amongst others.[14]

To the authors' knowledge, a detailed analysis of complete accommodative function has not been performed in persons with T1D. This would require identifying the presence of accommodative disorders in this population. This is crucial due to the possible effect of these disorders on the patient's everyday quality of life. This study aims to address that gap in the scientific evidence.

Therefore, the aim of this research was to comprehensively assess accommodative function in non-presbyopic individuals diagnosed with T1D without retinopathy compared with controls by studying accommodative amplitude (AA), negative and positive relative accommodation (NRA and PRA), accommodative response (AR) and monocular and binocular accommodative facility (AF), and to identify the existence of possible accommodative disorders related to this disease. In addition, the investigation determined the influence of T1D duration and capillary glycosylated haemoglobin (HbA1c) negative values on accommodative function.

Key points

- Although the amplitude of accommodation has been studied in subjects with type 1 diabetes, a comprehensive evaluation of all clinical accommodative parameters has not previously been performed nor a diagnosis of accommodative disorders.
- Subjects with type 1 diabetes showed a lower ability to accommodate and reduced accommodative facility compared with controls, as well as higher negative relative accommodation.
- A higher percentage of accommodative disorders was observed in the type 1 diabetes group than in the control group, all related to accommodative insufficiency.

METHODS

Study design and ethics

A prospective, comparative, cross-sectional study was carried out in the Optometry Facilities of the Faculty of Pharmacy of the University of Seville, between May 2021 and October 2021. The study was approved by the Ethics Committee of the Regional Government of Andalusia (code 0997-M1-18) and was conducted according to the ethical principles for medical research set out in the Declaration of Helsinki. Adults signed an informed consent form after an explanation of the nature and consequences of the study, and minors under 18 years of age gave verbal consent while informed consent was signed by their parents or legal guardians.

Subjects

For the selection of participants with T1D, a proposal for participation in the study was sent by email to the Association of Diabetics of Seville (ANADIS). Control participants were selected from the university community of the Faculty of Pharmacy of Seville.

The inclusion and exclusion criteria were the same for all participants: (1) between 11 and 40 years of age; (2) having monocular corrected distance visual acuity (VA) <0.10 logMAR; (3) absence of systemic, ocular disease or visual impairment that could affect the results of the visual examination (implying that participants could not have suppression); (4) no medication that could affect the results of the visual examination and (5) no previous eye surgery. Participants with T1D, who controlled their DM with insulin injections, were required to have been diagnosed by a diabetes physician specialist at least 3 years earlier and could not have any signs of retinopathy on fundus imaging, according to the Early Treatment of Diabetic Retinopathy Study.[15] Control participants must have an HbA1c concentration ≤5.6%.[16]

The participant selection process for this study is shown in Figure 1. The sample population was composed of 60 subjects, 30 with T1D and 30 controls. The descriptive characteristics of the participants by study group are presented in Table 1.

Examination procedure

A data collection sheet was used for each participant, which included personal data, medical history (last visual examination and whether they had an optical correction, symptoms, pharmacological treatment and family history of ocular problems) and optometric data.

Preliminary measurements

Non-mydriatic fundus photography (CSO Nonmydriatic Fundus Camera Cobra HD, Italy, csoitalia.it) was performed to rule out signs of diabetic retinopathy. Intraocular pressure was measured using a non-contact tonometer (Topcon CT-800, Japan, topconhealthcare.eu). The anterior segment was evaluated with a slit lamp biomicroscope (Topcon SL-6E, Japan, topconhealthcare.eu), to rule out the presence of cataracts and to check that the cornea and conjunctiva were healthy.

Distance VA was measured using an Early Treatment of Diabetic Retinopathy Study (ETDRS) chart in a backlit light box (85.0 cd/m^2) at 4 m. Near VA was measured with an ETDRS chart (Optometric Promotion, promocionoptometrica.com) at 40 cm. To prevent participants from memorising the letters, they were asked to read the lines from left to right for the right eye measurement, from right to left for the left eye and from right to left again for both eyes.[17] The VA was recorded in logMAR.[18] Objective refraction was performed by static retinoscopy (Welch Allyn retinoscope, welchallynstore.com), followed by subjective refraction using an Essilor MPH100E S/N 000104 phoropter (essilorpro.com) to obtain the refractive error of each eye, along with the corrected VA. For data analysis, the spherical equivalent refractive error was calculated as the algebraic sum of the sphere and half of the cylinder power. Unilateral and alternating cover tests at far and near fixation distances were performed to detect heterophoria or heterotropia. The Worth four-dot test was used to assess fusion while moving the flashlight from 33 cm to 6.0 m.[19] To quantify the glycaemic control of each participant, the HbA1c percentage was determined using the Cobas b-101 analyser (Roche Diagnostic, diagnostics.roche.com). Once it was confirmed that subjects met the established inclusion criteria, then accommodation was evaluated.

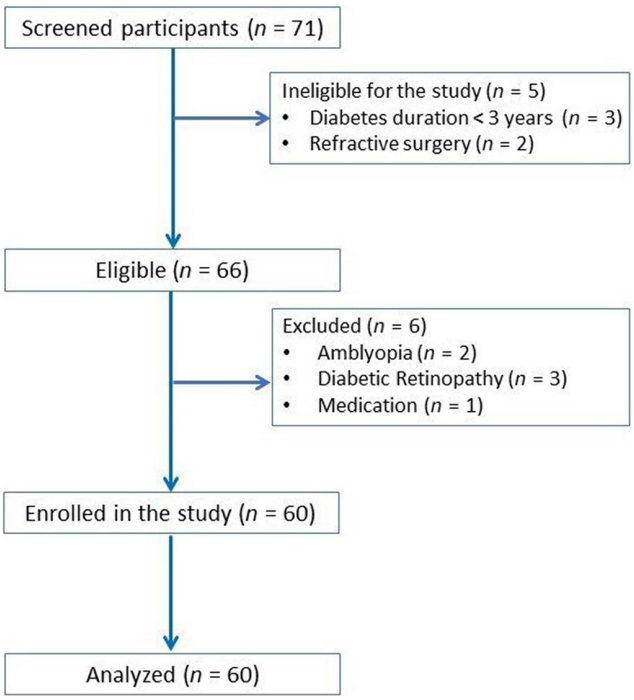

FIGURE 1 Flow chart of the study selection process.

Accommodative examinations

The following accommodative parameters were evaluated: monocular AA, AR, monocular and binocular AF, NRA and PRA.

Amplitude of accommodation was determined monocularly using the minus lens method (Sheard method). Minus lenses were added in the phoropter in −0.25 D steps until the subject reported sustained blur of a printed ETDRS optotype at 40 cm. The AA was measured firstly from the right eye and then from the left eye. The minus lens method was used because it was the most repeatable.[20–22]

The AR was determined by Nott dynamic retinoscopy using the streak retinoscope under binocular conditions. A card on the near-vision rod of the phoropter was positioned at a distance of 40 cm and used as a fixation target.[23] The target contained several lines of high-contrast black-on-white letters and the subject viewed a 0.0 logMAR line with both eyes. This method was chosen because it presented the highest repeatability.[24]

Accommodative facility was measured using ±2.00 D flipper lenses and a near-vision card at 40 cm, first monocularly and then binocularly.[25] The test was carried out for 1 min and the total number of cycles (clearing both the plus and minus lenses) was recorded.[26] We also noted whether the subject had difficulty clearing either the plus or minus lenses (or both) to differentiate between insufficiency, excess and infacility.

Negative and positive relative accommodation were assessed using a near-vision card positioned at a viewing distance of 40 cm. NRA represents the ability to relax accommodation by adding plus lenses. PRA represents the ability to stimulate accommodation by adding minus lenses. NRA was measured first. While subjects fixated the horizontal 0.0 logMAR line, the examiner added spherical lenses in 0.25 D steps binocularly, at the rate of one step every 2 s until the subject reported the first sustained blur.[27]

All measurements were performed with the subjects' best refractive correction in the phoropter (AA, AR, NRA and PRA) or in a trial frame (AF), in the same room under photopic conditions, with the same materials, order of testing and by the same optometrist. All subjects were advised not to wear contact lenses for 24 h prior to measurements.

TABLE 1 Comparison of demographic data and clinical characteristics between participants in each study group (T1D and control).

Variable (units)	T1D group ($n=30$), mean ± SD (range)	Control group ($n=30$), mean ± SD (range)	p Value
Age (years)	22.90 ± 9.56 (11 to 39)	23.67 ± 7.31 (11 to 39)	0.57
Male, *n* (%)	12 (40)	11 (37)	0.79
Female, *n* (%)	18 (60)	19 (63)	
HbA1c (%)	7.41 ± 0.85 (5.9 to 9.4)	5.00 ± 0.25 (4.6 to 5.4)	<0.001*
T1D duration (years)	10.8 ± 7.2 (3 to 26)	–	–
Spherical equivalent, RE (dioptres)	−0.25 ± 1.86 (−5.50 to 4.25)	−0.84 ± 1.79 (−6.50 to 3.25)	0.07
Spherical equivalent change, RE (dioptres)	−0.04 ± 0.25 (−0.50 to 0.50)	−0.04 ± 0.28 (−0.75 to 0.50)	0.95
Spherical equivalent, LE (dioptres)	−0.40 ± 1.92 (−7.00 to 4.00)	−0.82 ± 1.84 (−6.75 to 3.50)	0.27
Spherical equivalent change, LE (dioptres)	−0.03 ± 0.22 (−0.50 to 0.50)	−0.04 ± 0.27 (−0.50 to 0.75)	0.39
Distance VA, RE (logMAR)	−0.07 ± 0.05 (0.04 to −0.18)	−0.06 ± 0.07 (0.10 to −0.20)	0.77
Distance VA, LE (logMAR)	−0.08 ± 0.07 (0.04 to −0.24)	−0.07 ± 0.07 (0.04 to −0.20)	0.39
Distance VA, BE (logMAR)	−0.12 ± 0.06 (0.00 to −0.24)	−0.12 ± 0.06 (0.00 to −0.24)	0.70
Near VA, RE (logMAR)	−0.07 ± 0.05 (0.06 to −0.10)	−0.08 ± 0.05 (0.00 to −0.18)	0.09
Near VA, LE (logMAR)	−0.06 ± 0.05 (0.06 to −0.14)	−0.08 ± 0.05 (0.00 to −0.16)	0.07
Near VA, BE (logMAR)	−0.09 ± 0.03 (0.00 to −0.18)	−0.10 ± 0.04 (0.00 to −0.18)	0.05
Intraocular pressure, RE (mmHg)	15.8 ± 1.9 (11 to 19)	15.8 ± 1.8 (13 to 19)	0.84
Intraocular pressure, LE (mmHg)	15.6 ± 2.0 (11 to 19)	15.8 ± 2.0 (13 to 19)	0.80

Abbreviations: BE, both eyes; HbA1c, capillary glycosylated haemoglobin; LE, left eye; RE, right eye; SD, standard deviation; SE, spherical equivalent; T1D, type 1 diabetes; VA, visual acuity.

*Statistically different by Student's *t*-test.

TABLE 2 Normative values for each accommodative variable and values classified as insufficiency and excess.

Variables (units)	Normative values	Values considered as insufficiency	Values considered as excess
AA (D)	Hofstetter's AA 18 – (0.3 × age) – 2.00 ± 2.00	Min Hofstetter's AA 15 – (0.25 × age) – 4.00	Max Hofstetter's AA[a] 25 – (0.40 × age) + 2.00
AR (D)	+0.50 ± 0.25	≥+1.00	<+0.25
PRA (D)	−2.37 ± 1.00	≤−1.25	≥−3.25
NRA (D)	+2.00 ± 0.50	≥+2.75	≤+1.50
MAF (cpm)	8–12 years: 5 ± 2.5 13–34 years: 11 ± 5	8–12 years: ≤2 13–34 years: ≤6 Fails with −2.00 D	8–12 years: ≤2 13–34 years: ≤6 Fails with +2.00 D
BAF (cpm)	8–12 years: 5 ± 2.5 13–34 years: 10 ± 5	8–12 years: ≤2 13–34 years: ≤3 Fails with −2.00 D	8–12 years: ≤2 13–34 years: ≤3 Fails with +2.00 D

Abbreviations: AA, amplitude of accommodation; AR, accommodative response; BAF, binocular accommodative facility; cpm, cycles per minute; D, dioptres; MAF, monocular accommodative facility; Max, maximum; Min, minimum; NRA, negative relative accommodation; PRA, positive relative accommodation.

[a]This value does not correspond to an accommodative excess but refers to a value higher than that considered normal.

Diagnosis of accommodative disorders

From the accommodative measurements, a new variable was determined, namely 'insufficiency-normal-excess values', to describe the global state of the accommodative function. This was based on the Scheiman and Wick[28] criteria and following the study of Sanchez-Gonzalez et al.[17] The classification into 'excess, insufficiency and normal values' was made by grouping the accommodative variables into a set of specific tests, whether they assessed the same function directly or indirectly, and identifying excess or insufficiency values according to the tests and grouping of the results.[17] Table 2 shows the normative values for each accommodative variable and those classified as 'insufficiency' and 'excess'. For normative values, we relied on the work of Scheiman and Wick.[29] In addition, a diagnosis of the following accommodative disorders was performed: accommodative insufficiency, accommodative excess and accommodative infacility, using the criteria presented by Lara et al.[30] (Table 3).

Statistical analysis

Statistical analysis of the data was performed using IBM SPSS® Statistics 26 (ibm.com). Descriptive analysis was carried out using the number and percentage in each group for qualitative variables. These quantitative variables were described by the mean (standard deviation, SD) and range (minimum to maximum). The normality of the data was analysed using the Shapiro–Wilk test. Differences between the two groups were analysed using the Student's *t*-test for independent samples or the Mann–Whitney *U*-test. When the variables were qualitative, the chi-squared test or Fisher's exact test was used. The relationship between the variables was assessed using the Pearson or Spearman correlation test with simple and multiple linear regression analysis. The level of significance was set at 95% ($p < 0.05$).

The sample size was assessed with the EPIDAT® 4.2 software (Department of Health, Government of Galicia, Spain; https://www.sergas.es/Saude-publica/EPIDAT) with AA as the main study variable. Using an alpha of 0.05 and a beta of 0.2 in a two-sided test, 19 subjects were necessary in each group to identify a difference in AA ≥2 D as statistically significant. The common SD for AA was assumed to be 2.37 and 1.88 for the T1D and control groups, respectively, based on the results from a previous pilot study with 30 participants (15 with T1D and 15 controls) by the same researchers.

RESULTS

Demographics and clinical characteristics

Table 1 shows the comparison between the two study groups. The T1D and control groups were similar with respect to age, sex, refraction, VA and intraocular pressure. The only statistically significant difference between the two groups was in the percentage of HbA1c ($t = 9.96$, $p < 0.001$).

Accommodative test results

Table 4 shows the values of the accommodative variables and statistical significance (*p*-value) obtained in the comparison between the two groups, as well as the classification of the participants in each group as accommodative insufficiency, excess or normal based on the normative values.[28]

The T1D group exhibited significantly lower values than the control group for AA (right eye, $t = 3.92$, $p < 0.001$; left eye, $t = 3.63$, $p < 0.001$), monocular AF (right eye, $t = 3.55$, $p = 0.001$; left eye, $t = 2.94$, $p = 0.005$) and binocular AF ($t = 3.87$, $p < 0.001$). In addition, the T1D group showed significantly higher NRA ($U = 2.12$, $p = 0.03$) than the controls (Figure 2).

Diagnosis of accommodative disorders

Using the classification of accommodative variables as 'insufficiency, excess or normal results', a higher percentage of insufficiency values was found in the T1D group (compared with the controls) for all of the examined accommodative variables except NRA (Table 4). This between-group comparison was significant ($p = 0.001$), with a higher percentage of insufficiency values in the T1D (50%) compared with the control group (6%).

In addition, with regard to the diagnosis of accommodative disorders using the criteria presented by Lara et al.,[30] of the 60 subjects examined, 27% had an accommodative disorder, with 23% coming from the T1DM group. Accommodative infacility (15%) was the most prevalent disorder, followed by accommodative insufficiency (10%), with the latter being present only in the T1D group. Only one subject had accommodative excess (1.7%; Table 5).

TABLE 3 Diagnostic criteria for accommodative disorders used.[30]

Accommodative disorder	Fundamental sign	Complementary sign[a]
Accommodative insufficiency	AA < 4 D[b] of Hofstetter's minimum AA (15–0.25 × age) MAF (± 2.00 D) ≤ 6 cpm (fails with −2.00 D)	BAF ≤ 3 cpm (fails with −2.00 D) AR > +0.75 D PRA ≤ −1.25 D
Accommodative excess	Variable VA findings Variable refraction MAF (± 2.00 D) ≤ 6 cpm (Difficulty clearing +2.00 D)	BAF ≤3 cpm (difficulty clearing +2.00 D) AR < +0.25 D NRA ≤ +1.50 D
Accommodative infacility	MAF (± 2.00 D) ≤ 6 cpm BAF (± 2.00 D) ≤ 3 cpm NRA ≤ +1.50 D PRA ≤ −1.25 D	

Note: Diagnostic criteria presented by Lara et al.[30]

Abbreviations: AA, amplitude of accommodation; AR, accommodative response; BAF, binocular accommodative facility; cpm, cycles per minute; D, dioptres; MAF, monocular accommodative facility; NRA, negative relative accommodation; PRA, positive relative accommodation; VA, visual acuity.

[a]Need to be present two of the three signs.

[b]Instead of <2 D due to the use of the minus lens method for AA measurements.

Correlation analysis of age, HbA1c and diabetes duration with accommodative tests

In examining the relationship between the variables, in view of the strong correlation between the findings obtained in each eye, only the right eye values were used. Age was significantly correlated with AA ($\rho = -0.687$, $p < 0.001$). Comparison of AA with age for each group is shown in Figure 3.

No significant correlation of HbA1c with any of the accommodative variables was found in either the whole sample or just the T1D group. A significant inverse correlation was observed between the duration of diabetes and AA ($\rho = -0.571$, $p = 0.001$) and between the duration of diabetes and both monocular AF ($\rho = -0.322$, $p = 0.01$) and binocular AF ($\rho = -0.375$, $p = 0.003$). Furthermore, the duration of diabetes was positively correlated with NRA ($\rho = 0.327$, $p = 0.01$).

However, when analysis was restricted to the T1D group, the correlation between the duration of diabetes and accommodative parameters was only significant for AA ($\rho = -0.533$, $p = 0.002$). Based on these results, a multiple regression analysis was conducted for AA using the duration of diabetes and age as predictive variables for the complete set of subjects ($n = 60$). Both factors contributed significantly, adjusting to the equation: $y = 14.337\ (\pm 0.61) - 0.166\ (\pm 0.29)$* duration of T1D $- 0.207\ (\pm 0.25)$* age ($R^2 = 0.69$, adjusted $R^2 = 0.68$, $F = 63.12$, $p < 0.001$).

DISCUSSION

This study fully assessed accommodative function in non-presbyopic individuals diagnosed with T1D without retinopathy and in a control group. AA and FA were significantly lower and NRA was significantly higher in the T1D group than in the control group. In addition, T1D subjects showed a higher percentage of insufficiency values. Regarding accommodative disorders, accommodative infacility was the most prevalent, followed by accommodative insufficiency, with the latter only being present in the T1D group.

Of the accommodative variables analysed in previous investigations, AA has been the most studied.[7–13,31,32] This work corroborates the results of previous studies that noted a lower AA in T1D subjects with respect to the expected values based on age[32] or a control group,[7–11,13,31] regardless of the method of measurement. In the present study, the mean AA in the T1D group was approximately 2.50 D less than the control group, which can be considered a clinically significant difference. Regarding the method used to assess AA, most prior studies used the push-up method, which provides higher AA values than the minus lens technique. The decreased finding with the minus lens method is due to the reduction in image size induced by the minus lens, which increases the subject's ability to detect defocus earlier, resulting in a lower AA measurement.[20] However, the minus lens method has been shown to have the best repeatability, thus minimising intra-measurement errors.[20,33,34] In a linear regression analysis, AA was significantly associated with age and the duration of diabetes, corroborating the results of previous studies.[7,8,11,13,32] Some previous investigations have observed both fasting plasma glucose and HbA1c to be inversely correlated with AA.[10–12] However, in the present study, this association was not found, consistent with Braun et al.[32] and Sirakaya et al.[13] In a longitudinal study by Abokyi et al.,[12] a dynamic relationship was observed between blood glucose concentration and the AA in subjects with T1D, with a higher blood glucose concentration (>7 mmol/L) being associated with a lower AA. This possible relationship between blood glucose and accommodation needs to be confirmed in other longitudinal studies.

Our results agree with others showing a significantly lower monocular[9,10] and binocular AF[31] in subjects with T1D. The difference in AF between the groups was around 4 cpm, which could be clinically relevant. Nabovati et al.[10] reported a significant negative correlation between monocular AF and HbA1c, although this association was not found in the present investigation. Additionally, a significant negative correlation was seen between both monocular and binocular AF and the duration of diabetes, confirming that T1D does affect AF.

The results of the present study disagree with previous findings with regard to NRA and PRA, since we observed higher mean values for NRA in the T1D group, versus the control group, with a significant difference of 0.25 D. Other authors did not find statistically significant differences between the two groups,[9,31] although the magnitude of this difference cannot be considered clinically significant. A possible cause of this finding could be the lower AA present in the T1D group, which might imply better acceptance of additional plus lenses than for the control subjects. On the other hand, Etezad et al.[31] found significantly higher PRA in a T1D group compared with controls, whereas here, similar values were found in the two groups, consistent with Srihard and Ramachandra.[9] It should also be noted that there were significant differences in age between the two groups of participants in Etezad et al.[31] However, as NRA and PRA are measured under binocular conditions, they are tests of both the accommodative and vergence system, and therefore should only be considered as supplementary tests in the diagnosis of accommodative disorders.

The AR results also differ from previous research. While other studies have reported a significantly larger accommodative lag in T1D subjects,[10–12] in this study, the results were similar in the two groups. This may be due to the method used, with MEM retinoscopy being used in other investigations compared with Nott retinoscopy in this study. Cacho et al.[35] noted a linear relationship between the two methods, although the result with Nott retinoscopy was approximately one-half of the value found using MEM retinoscopy.

Comparison between the accommodative parameters is of interest to analyse the effect of diabetes on particular aspects of accommodation, but it should be noted that these parameters are isolated clinical signs. For an accurate assessment of accommodative function, several of these signs must be taken into account.[17] In the present study, we

TABLE 4 Comparison between participants' accommodative variables by group (type 1 diabetes [T1D] and control) and classification of subjects based on normative values as 'insufficiency, excess or normal values' by accommodative variable and group.

Variables (units)	T1D group mean ± SD (range)	Control group mean ± SD (range)	*p* Value	Classification of subjects according to normative values, *n* (%)						
				Type 1 diabetes group (*n* = 30)			Control group (*n* = 30)			
				Insuffic	Normal	Excess	Insuffic	Normal	Excess	*p* Value
RE AA (D)	7.33 ± 2.63 (3.25 to 12.00)	9.90 ± 2.45 (4.50 to 14.00)	<0.001*	11 (37)	19 (63)	0 (0)	1 (3)	29 (97)	0 (0)	0.001***
LE AA (D)	7.65 ± 2.64 (3.50 to 12.00)	9.97 ± 2.28 (4.50 to 14.00)	0.001*	9 (30)	21 (70)	0 (0)	1 (3)	29 (97)	0 (0)	0.006***
RE AR (D)	0.61 ± 0.23 (0.25 to 1.25)	0.63 ± 0.17 (0.28 to 0.96)	0.77	5 (17)	23 (77)	2 (7)	2 (7)	27 (90)	1 (3)	0.38
LE AR (D)	0.56 ± 0.20 (0.23 to 0.96)	0.61 ± 0.17 (0.12 to 0.91)	0.45	4 (13)	23 (77)	3 (10)	2 (7)	26 (87)	2 (7)	0.59
RE AF (cpm)	7.05 ± 4.92 (0 to 18)	11.13 ± 3.93 (3.50 to 20)	0.001*	14 (47)	16 (53)	0 (0)	2 (6)	27 (90)	1 (3)	0.002***
LE AF (cpm)	7.52 ± 5.16 (0 to 18)	11.07 ± 4.14 (3.5 to 23)	0.005*	14 (47)	16 (53)	0 (0)	3 (10)	26 (87)	1 (3)	0.005***
BE AF (cpm)	7.00 ± 3.91 (0 to 12.5)	10.75 ± 3.59 (1.50 to 20)	<0.001*	8 (27)	22 (73)	0 (0)	2 (6)	27 (90)	1 (3)	0.08
NRA (D)	2.44 ± 0.47 (1.50 to 3.50)	2.21 ± 0.33 (1.75 to 3.00)	0.03**	11 (37)	17 (57)	2 (7)	3 (10)	26 (87)	1 (3)	0.03
PRA (D)	−2.51 ± 1.49 (−0.75 to −6.50)	−2.39 ± 0.95 (−1.00 to −5.75)	0.55	5 (17)	19 (63)	6 (20)	3 (10)	24 (80)	3 (10)	0.35
Total number of subjects with normal/insufficiency/excess accommodative values				15 (50)	15 (50)	0 (0)	2 (6)	27 (91)	1 (3)	0.001***

Abbreviations: AA, amplitude of accommodation; AF, accommodative facility; AR, accommodative response; BE, both eyes; cpm, cycles per minutes; D, dioptres; Insuffic., insufficiency; LE, left eye; NRA, negative relative accommodation; PRA, positive relative accommodation; RE, right eye; SD, standard deviation.

*Statistically different by Student's *t*-test; **Statistically different by Mann–Whitney *U*-test; ***Statistically different by Fisher's exact test.

detected accommodative anomalies using the system developed by Scheiman and Wick (integrative analysis),[28] which is commonly adopted as a reference for the classification, diagnosis and treatment of accommodative disorders,[17,24,36,37] as well as the methodology followed in the study by Sánchez-González et al.[17] When applying this classification system, subjects who present with normal values of accommodative function, considering isolated clinical signs, may also show differences in other signs, so they will be added to the group

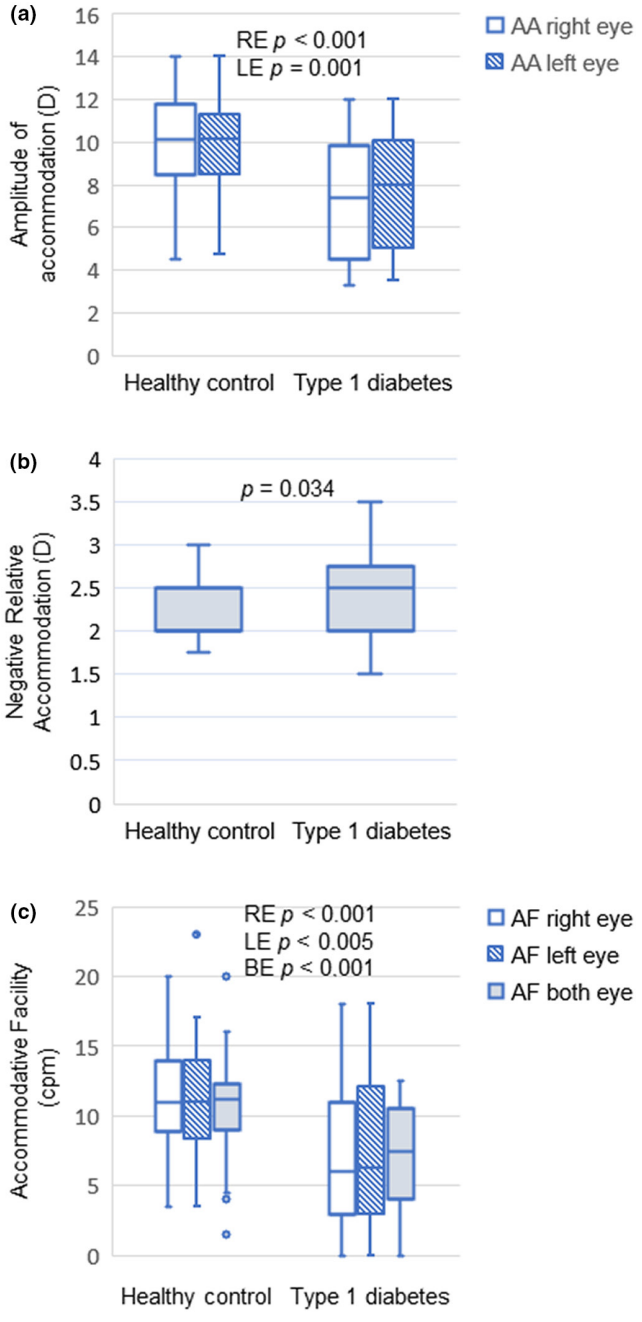

FIGURE 2 Comparison of accommodative variables showing a significant difference between the type 1 diabetes and control groups. (a) Amplitude of accommodation (AA) measured in dioptres (D). (b) Negative relative accommodation (NRA) measured in dioptres. (c) Accommodative facility (AF) measured in cycles per minute (cpm). BE, both eyes; LE, left eyes; RE, right eyes.

classified with global values of accommodative excess or insufficiency. For example, when evaluating AR in the left eye of the T1D group, 3, 4 and 23 exhibited excess, insufficiency and normal values, respectively. However, of these 23 subjects with normal values, some also showed differences in other signs and therefore became part of the global group of insufficiency or excess. Accordingly, in the global variable determined using the Scheiman and Wick criterion,[28] there should only be 15 T1D subjects with normal values, 15 with insufficiency and none with excess. Of the 17 participants with insufficiency (considering the global variable), 15 had T1D and two were controls, while only two participants with T1D and four control subjects had insufficiency when considering the left eye AR alone. This is due to 'normal' subjects with this isolated sign being added to the insufficiency group for the global variable. The results obtained in the global variable are the most relevant, since this truly shows whether the subject has excess or insufficiency.[17] Furthermore, in the diagnosis of accommodative disorders, a higher percentage of these dysfunctions was observed in the T1D group than in the control group, in terms of both the ability to accommodate (i.e., accommodative insufficiency) and reduced AF (i.e., accommodative infacility). However, the very small number of subjects in each group must be noted.

Therefore, the results of this work and others both demonstrate decreased accommodation in subjects with T1D causing an increase in accommodative disorders.[7–13,31] Fischer et al.[38] pointed out that the lens lost more elasticity in diabetic patients, while Pierro et al.[39] observed that the thickness of the lens was greater in proportion to the duration of diabetes.

The main contribution of this study is to note that AA is not the only parameter affected, as both AF and NRA were also altered significantly. Furthermore, from a clinical point of view, the results verify the association of T1D with accommodative insufficiency. AA and monocular AF are clinical diagnostic criteria for accommodative insufficiency.[34,40] In addition, to our knowledge, this is the only study of similar characteristics where participants were not selected from a hospital but from the general community, and the HbA1c value was determined not only in subjects with diabetes but also in control subjects.

The relationship between hyperglycaemic levels and loss of AA has not yet been demonstrated since these levels

TABLE 5 Classification of subjects with accommodative dysfunctions by group.

Accommodative disorder	T1D group	Control group	*p* Value
Accommodative insufficiency, *n* (%)	6 (20)	0 (0)	0.02*
Accommodative excess, *n* (%)	0 (0)	1 (3.3)	>0.90
Accommodative infacility, *n* (%)	8 (27)	1 (3.3)	0.03*
Total accommodative disorder	14 (47)	2 (6.7)	–

Note: The classifications were based on the diagnostic criteria presented by Lara et al.[30]

*Statistically different by Fisher's exact test.

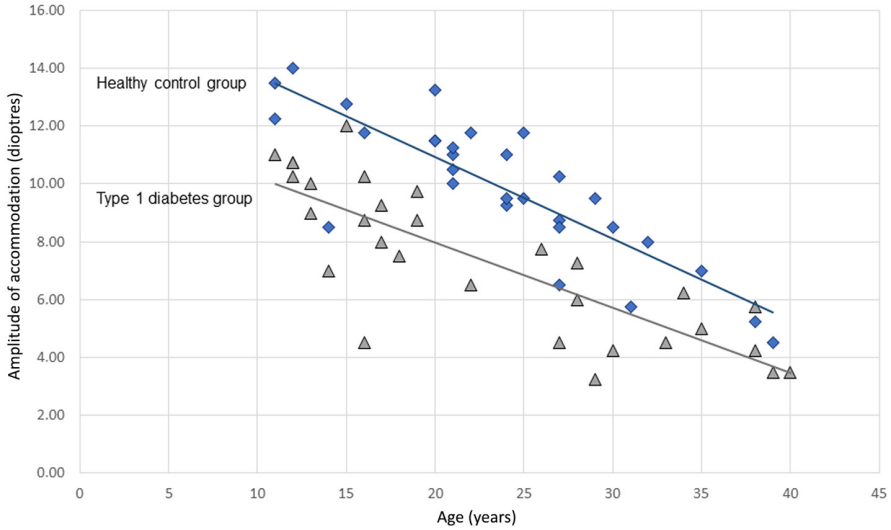

FIGURE 3 Scatter plot of the change in the amplitude of accommodation (dioptres) with age (years) in the type 1 diabetes and control groups.

in monitored subjects are not usually maintained over time. Reactive oxygen species increase because of auto-oxidation, so their metabolism promotes the accumulation of metabolites, such as fructose, sorbitol and triose phosphate. The latter generates reactive α-oxoaldehydes with a high capacity to bind to proteins and generate oxidative stress. The accumulation of sorbitol due to its inability to diffuse easily to the outside, leads to an increase in osmotic stress in the cells, and this is especially important to explain the damage at the crystalline lens.[41]

A limitation of this study was that the examiner was not masked as to the type of patient due to the initial anamnesis. Furthermore, a cross-sectional study was performed, and therefore it was not possible to establish a relationship between T1D and accommodative anomalies, since only a single measurement in time was recorded. Therefore, these results should be considered with caution. In addition, we also consider the sample size a limitation. With a greater number of participants, stratification of the sample into different age groups could have been carried out to observe whether the behaviour varied with age. Future longitudinal studies will be necessary to corroborate these results and to determine whether other binocular functions are also affected by T1D as well as the relationship with glycaemia.

CONCLUSION

These findings indicate that T1D affects most of the parameters which assess accommodative function. The AA and AF were significantly reduced while NRA was higher in the T1D population than in the control group. More accommodation insufficiency was seen in the T1D group than in the control subjects. In addition, there was a relationship between the duration of diabetes and AA, AF and NRA, but such a relationship was not seen for the glycosylated haemoglobin values.

AUTHOR CONTRIBUTIONS

María-Carmen Silva-Viguera: Conceptualization (equal); data curation (equal); formal analysis (lead); investigation (equal); methodology (equal); resources (equal); supervision (equal); validation (equal); visualization (equal); writing – review and editing (equal). **María-José Bautista-Llamas:** Conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); supervision (equal); validation (equal); visualization (equal); writing – review and editing (equal).

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ORCID

María-Carmen Silva-Viguera https://orcid.org/0000-0002-2750-655X
María-José Bautista-Llamas https://orcid.org/0000-0001-8317-5014

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