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CLINICAL STUDY

Relationship of diabetic macular oedema with glycosylated haemoglobin

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Abstract

Purpose **To evaluate the correlation between glycosylated haemoglobin (HbA1c) and central foveal thickness as measured by optical coherence tomography (OCT) in patients with diabetes.**

Methods **Retrospectively review of medical records of central foveal thickness as measured by OCT and laboratory data of glycosylated haemoglobin. HbA1c was compared with foveal thickness measured by OCT within the preceding 3 months. Clinically significant macular oedema (CSME) was diagnosed if central foveal retinal thickness was greater than 325 μm in OCT.**

Results **One hundred and two eyes of 102 patients were included in this cross-sectional study. Univariate analysis revealed that the CSME diagnosed by OCT in diabetes was not statistically significant with sex, right or left eye, DM duration over 10 years or not, and AC sugar level (over 140 or not). The HbA1C level (8 or over) and age (50 or less) showed a significant ($P = 0.005$ and 0.006, respectively) and positive association with macular thickness in OCT. A trend towards higher risk was seen for factors of age $\leqslant$50 and HbA1c $\geqslant$8%.**

Conclusions **Patients with HbA1c of 8 or above had an increase in macular thickness in type 2 diabetic eyes and there was a statistical significant correlation between younger age, shorter DM duration and thicker macular thickness. Strict sugar control decreased the risk of diabetic macular retinopathy, and OCT could be an excellent detector of early diabetic macular oedema.**

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Keywords: diabetic macular oedema; glycosylated haemoglobin; optical coherence tomography

Introduction

Diabetic retinopathy (DR) is one of the complications of diabetes mellitus (DM) that causes most suffering. It is the leading cause of blindness in working-age adults. Diabetic macular oedema (DME), characterized by increased vascular permeability and deposition of hard exudates at the central retina, can occur at any stage of DR. DME is the main cause of poor visual acuity in patients with diabetes. In the past, DME was diagnosed by ophthalmoscope as clinical significance macular oedema. Fluorescein angiography is indicated in guiding treatment of macular oedema.[1] With the help of optical coherence tomography (OCT), it is now possible to measure the macular thickness objectively and to follow the progression of DME quantitatively.[2] Periodic glycosylated haemoglobin (HbA1c) measurements can reflect the long-term control of hyperglycaemia. Intensive glycemic control had been proved to be effective in decreasing incidence rate of development and progression of DR in type 1 and type 2 diabetic mellitus as demonstrated by the diabetes control and complications trials[3] and the United Kingdom Prospective Diabetes Study.[4]

To our knowledge, no published study at present has evaluated the relationship between macular thickness (measured by OCT) and long-term glycemic control (demonstrated by glycosylated haemoglobin). The purpose of this study is to evaluate the correlation between HbA1c and central foveal thickness measured by OCT in patients with diabetes.

Materials and methods

This study is a retrospective review of medical records. Patients who were examined between December 2004 and July 2007 and had diagnoses of type 2 diabetes and pre-proliferative DR were identified through medical records. Eligible subjects had to meet all of the following criteria: (1) received complete ophthalmic evaluation; (2) had HbA1c measured by specific high-pressure liquid chromatography methods; and (3) received OCT examination (Stratus OCT 3, Carl Zeiss Meditec, Dublin, CA, USA) within 3 months preceding HbA1c measurement. OCT was performed in both eyes, but the eye with thicker macular oedema was used for statistical analysis. Exclusion criteria included patients who received intraocular surgery (cataract surgery, pars plana vitrectomy, intravitreal injection of triamicinolone or Bevacizumab), subtenon injection, or photocoagulation therapy within 1 year of evaluation and severe vitreous haemorrhage or vitreous opacity that would interfere with the OCT examination. Clinically significant macular oedema (CSME) was diagnosed according to central macular retinal thickness greater than 325 μm in OCT.[5] This study was approved by Chang Gung Memorial Hospital Institutional Review Board. All research procedures followed the tenets of the Declaration of Helsinki.

Statistical analysis

Data were analysed using χ^2 test or Fisher's exact test (if the expected value was under 5) for the univariate analysis of factors associated with CSME. Probability values of $P<0.05$ were considered statistically significant. In addition, logistic regression was used to estimate odds ratios and 95% confidence intervals for further independent variables. Variables that were significant at the $P\leqslant 0.2$ level in the univariate analysis were included in backward logistic regression analysis to select the final list of independent variables. All analyses were computed using SPSS software (v10.0, SPSS Inc., Chicago, IL, USA).

Results

One hundred and two eyes of 102 patients were included in this cross-sectional study. Sixty three patients were male and 39 were female. The mean age ± SD was 62.3 ± 8.1 years (range, 40–77 years). The mean DM duration was 11.2 ± 5.5 years (range, 1–30 years). The mean value of HbA1c was 7.8 ± 1.4% (range, 5.1–12.1%). The mean central retinal thickness was 257.1 ± 79.3 μm (range, 151–526 μm).

Table 1 shows the distribution of possible risk factors for CSME diagnosed by OCT among patients with

Table 1 Univariate and multivariate logistic regression analysis of factors associated with OCT-based CSME in diabetic eyes

Factor	*Definition*	*No CSME (OCT <325 μm) No. (%)*	*CSME (OCT ⩾325 μm) No. (%)*	*Univariate analysis*		*Multivariate analysis*	
				OR (95% CI)	*P-value*	*OR (95% CI)*	*P-value*
Age	>50	81 (95.3)	12 (70.6)	1.0	0.006*	1.0	0.008*
	⩽50	4 (4.7)	5 (29.4)	8.4 (1.9–35.7)		8.2 (1.7–38.8)	
Sex	Male	52 (61.2)	11 (64.7)	1.0	0.78		
	Female	33 (38.8)	6 (35.3)	0.9 (0.3–2.5)			
Laterality	Left	49 (57.6)	11 (64.7)	1.0	0.59		
	Right	36 (42.4)	6 (35.3)	0.7 (0.2–2.1)			
DM duration (years)	<10	26 (30.6)	8 (47.1)	1.0	0.18	1.0	0.166
	⩾10	59 (69.4)	9 (52.9)	0.5 (0.2–1.4)		0.92 (0.8–1.0)	
AC sugar (mg/100 ml)	<140	28 (40.6)	4 (26.7)	1.0	0.315		
	⩾140	41 (59.4)	11 (73.3)	1.9 (0.5–6.4)			
HbA1c (8%)	<8	56 (65.9)	5 (29.4)	1.0	0.005*	1.0	0.013*
	⩾8	29 (34.1)	12 (70.6)	4.6 (1.5–14.9)		4.5 (1.4–15.1)	

Abbreviations: DM, diabetic mellitus. HbA1c, hemoglobin A1c.
For age, 0 indicates >50 years and 1 indicates ⩽50 years. For sex, 0 indicates male and 1 indicates female. For laterality, 0 indicates left and 1 indicates right. For DM duration, 0 indicates <10 years and 1 indicates ⩾10 years. For AC sugar, 0 indicates <140 mg/100 ml and 1 indicates ⩾140 mg/100 ml; For HbA1c, 0 indicates <8 and 1 indicates ⩾8.
*Indicates statistically significant ($P<0.05$).

diabetes and results of the univariate and multivariate analysis.

Univariate analysis revealed that the CSME diagnosed by OCT in diabetes was not statistically significant with sex ($P=0.78$), right or left eye ($P=0.59$), DM duration over 10 years or over ($P=0.18$), and AC sugar level (over 140 or not) ($P=0.315$). The HbA1C level (8 or over) and age (50 or less) showed a significant ($P=0.005$ and 0.006, respectively) and positive association with macular thickness in OCT.

A trend towards higher risk was seen for factors of age $\leqslant 50$, DM duration <10 years, and HbA1c $\geqslant 8\%$ ($P\leqslant 0.2$). These three variables were included in multivariate analysis. Two variables including age $\leqslant 50$ and HbA1c $\geqslant 8\%$ were independently associated with CSME in diabetic eyes. HbA1c of 8 or over was associated with an increased risk of CSME in diabetic eyes (adjusted odds ratio, 4.5; 95% confidence interval, 1.4–15.1, $P=0.013$). Age of 50 or less was associated with increased risk of CSME in diabetic eyes (adjusted odds ratio, 8.2; 95% confidence interval, 1.7–38.8, $P=0.008$).

Discussion

The incidence of type 1 diabetes is highly variable among different ethnic populations.[6] It is especially lower in Chinese. The overall age-adjusted incidence of type 1 diabetes is 0.1–4.6/100 000 per year in China.[7] In our study, there were two type 1 diabetes patients in 104 eligible subjects. To prevent from statistical bias, only type 2 diabetes patients were included in our study.

In the Wisconsin epidemiologic study of DR, the incidence of macular oedema over the 10-year period was associated with higher levels of glycosylated haemoglobin and more severe retinopathy in both younger- and older-onset groups.[8] In our study, only mild-to-moderate DR was included, as severe cases were treated either by grid laser or intravitreal injection of triamicinolone or bevacizumab. It may explain that the shorter DM duration (<10 years) is associated with macular oedema in our study.

Intensive glycemic control is associated with the development and progression of DM retinopathy. HbA1c of 8 or above increased the risk of macular oedema. Moreira *et al*[9] also found that HbA1c was the only variable that showed a significant association with macular oedema.

Periodic HbA1c measurements could be of value in understanding the long-term glycemic control. OCT is a sensitive noninvasive diagnostic tool in the evaluation of macular oedema. OCT examination within 3 months preceding HbA1c measurement may provide enough information about dynamic state of macular oedema and transitory glycemic control.

In our study, there is no significant linear correlation between the values of macular thickness and HbA1c. Hee *et al*[10] also found that OCT values of foveal thickness between 200 and 325 μm often disagreed with slit-lamp examination results of CSME. Therefore, CSME was diagnosed when central macular retinal thickness was greater than 325 μm of OCT values in our study.

Diabetic macular oedema is associated with increased vascular permeability and vitreous traction. Although fluorescein angiography provides a qualitative assessment of vascular leakage and could help to distinguish the aetiology of macular oedema, actual macular thickness is the greatest contributing factor to best-corrected visual acuity.[11]

Other reported risk factors of DME, including increased diastolic blood pressure, insulin use, nephropathy, cataract surgery, and panretinal photocoagulation, were not analysed in our study. Further prospective study may be indicated for evaluation.

In conclusion, patients with HbA1c of 8 or above had an increase in macular thickness as measured by OCT in diabetic eyes and there was a statistical significant correlation between younger age, shorter DM duration, and thicker macular thickness. Strict sugar control decreased the risk of diabetic macular retinopathy, and OCT could be an excellent detector of early DME.

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