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Macular changes obtained with optical coherence tomography angiography in children with type 1 diabetes mellitus: literature review

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Abstract

Background. Type 1 diabetes mellitus is a disease in which relative or absolute insulin deficiency leads to the development of hyperglycaemia, which can cause microvascular complications such as diabetic retinopathy. Type 1 diabetes is the most common type of diabetes in children and adolescents worldwide. Diabetic retinopathy is a complication of diabetes, caused by hyperglycemia damaging small blood vessels of the retina, it can lead to blindness, which is why it is so important to diagnose the disease and to correct its risk factors such as hypertension, poor glycaemic control and obesity. Optical coherence tomography angiography is a new method of retinal imaging that can non-invasively diagnose the changes specific to diabetic retinopathy.

Methodology. Four scientific publications were selected from the „PubMed“ and „Science Direct“ databases based on keywords and inclusion and exclusion criteria.

Results. Four studies were analysed where children with type 1 diabetes mellitus and healthy children were examined using optical coherence tomography angiography. Statistically significant correlations were observed when comparing retinal capillary plexuses vessel densities between the study groups. Statistically significant correlations were also found between retinal capillary plexuses vessel densities and duration of the disease and glycated haemoglobin values.

Conclusions. The study found presence of microvascular changes in macula in children with type 1 diabetes mellitus and significant associations with both diabetes duration and glycated haemoglobin. Optical coherence tomography angiography can be used for the early detection of diabetic retinopathy in children.

Keywords: type 1 diabetes mellitus, macula, optical coherence tomography angiography, diabetic retinopathy.

1. Introduction

Type 1 diabetes mellitus (T1DM) is a disease characterised by elevated blood glucose levels due to relative or absolute insulin deficiency caused by autoimmune destruction of pancreatic β-cells or genetic factors (1). The International Diabetes Federation (IDF) has estimated that in 2021, the approximate number of children and adolescents with T1DM worldwide was 1.2 million, with around 149 500 new cases diagnosed each year (2). T1DM can lead to microvascular complications, including diabetic retinopathy (DR), in which persistent hyperglycaemia damages the small blood vessels of the retina and can lead to blindness (1,3). DR can be divided into two stages: non-proliferative and proliferative. The first signs of non-proliferative DR are microaneurysms, retinal haemorrhages and hard exudates. Proliferative DR is a stage of advanced DR that develops as retinal ischaemia progresses, resulting in the formation of new pathological blood vessels (neovascularisation) that can cause haemorrhages or retinal detachment. At any stage of DR, diabetic macular edema may occur, characterised by increased vascular permeability and the accumulation of fluid in the retina (4). Children and adolescents with T1DM may be at risk of developing DR at a young age due to a long duration of T1DM, poor glycaemic control, hypertension, hyperlipidaemia, obesity, and a family history of T1DM or its complications (5,6). The American Academy of Ophthalmology (AAO) guidelines recommend annual DR screening for all patients with T1DM 5 years after the diagnosis of diabetes mellitus, and the American Academy of Paediatrics (AAP) guidelines recommend annual DR screening 3 – 5 years after the diagnosis of diabetes mellitus, or at 9 years of age, whichever is later. However, the prevalence of DR in children is not well established and there is a lack of information in the literature on its manifestation, which is why it is very important to diagnose the disease in time to prevent visual impairment in the future (7,8).

One of the branches of the ophthalmic artery is the central retinal artery, which divides and forms different retinal capillary plexuses that cover the entire retina except for the foveal avascular zone (FAZ) of the macula and the periphery (9). The number of retinal capillary plexuses depends on the eccentricity and varies from one to four: radial peripapillary capillary plexus, superficial capillary plexus (SCP), intermediate capillary plexus, and deep capillary plexus (DCP) (10).

Optical coherence tomography angiography (OCTA) is a new, fast, non-invasive imaging technique based on optical coherence tomography technology that captures images of retinal and choroidal layers capillary blood flow within a few seconds and allows quantitatively measure the density of capillary plexuses, assess enlargement of the FAZ, identify microaneurysms, retinal perfusion impairment, degree of neovascularisation (11,12). FAZ is a region of the macula that has no blood flow and is supplied by choroidal choriocapillaries. The analysis of the FAZ is very important as its changes are directly related to a number of important clinical conditions, such as the severity of the disease and visual acuity in patients with DR (13).One of the main advantages of OCTA is the ability to examine different retinal vascular layers and to separate SCP and DCP, allowing precise identification of the damaged area (14).

2. Materials and Methods

The literature search was done in the „PubMed“ and „Science Direct“ databases using the following keywords: type 1 diabetes mellitus in children, optical coherence tomography angiography, foveal avascular zone, retinal capillary plexus. Studies were included if they met the following criteria:

studies with participants younger than 18 years diagnosed with T1DM, studies published within the past 10 years, and written in English. Articles not written in English were excluded. Studies that did not use OCTA for imaging the retina were also excluded.

3. Results

Four articles were included in the study: Gołębiewska J. et al. 2017 (15), Mameli C. et al. 2019 (16), Inanc M. et al. 2019 (3), Wysocka – Mincewicz M. et al. 2021 (17). In all included studies, the eyes of subjects (diabetic (DM+)) and controls (non-diabetic (DM–)) were examined by OCTA, and the duration of the T1DM and the glycated haemoglobin (HbA1c) value of the study group were reported (Table 1).

Table 1. Characteristics of the study and control group

Authors	Study group (DM+)		Control group (DM–)		Age of children (years)		Duration of T1DM (years)	HbA1c (%)
	Participants	Eyes	Participants	Eyes	DM+	DM–		
Gołębiewska J. et al. (2017)	94	188	36	60	15.3 ± 2.1*	13.6 ± 1.8*	6.4 ± 3.3*	8.1 ± 1.1*
Mameli C. et al. (2019)	53	106	48	96	15.5 (12.4-19.4)**	13.7 (11.8-18.9)**	6.0 (3.3-10.3)**	7.6 (6.9-8.1)**
Inanc M. et al. (2019)	60	60	57	57	13.81 ± 3.06*	14.12 ± 2.80*	6.54 ± 3.86*	6.42 ± 1.12*
Wysocka – Mincewicz M. et al. (2021)	50	50	21	21	16.92 ± 1.6*	16,2 ± 3*	6.88 ± 4.34*	8.43 ± 1.38*

**mean ± standart deviation (SD); ** median (min-max)*

Gołębiewska J. et al. did a study in Poland that involved 130 children (94 in the study group and 36 in the control group). FAZ, foveal SCP vessel density, DCP vessel density, parafoveal SCP and DCP vessel densities were assessed by OCTA. The mean duration of T1DM in the study group was 6.4 (± SD = 3.3) years, and the mean HbA1c was 8.1 (± SD = 1.1) %. The authors did not determine statistically significant difference between SCP, DCP vessel densities and FAZ region in children with T1DM compared with the control group. On the other hand, a statistically significant negative correlation was observed between an increased HbA1c and decreased parafoveal SCP vessel density in the study group (r = -0.17, p = 0.039), whereas parafoveal DCP vessel density decreased when T1DM duration increased (p = 0.014) (15).

Mameli C. et al. did a study in Italy and used OCTA to examine both eyes of 53 children with T1DM and both eyes of 48 healthy children. Fovea SCP and DCP vessel densities, parafoveal SCP vessel density, parafoveal temporal superficial capillary plexus (TSCP) vessel density, parafoveal superior superficial capillary plexus (SSCP) vessel density, parafoveal nasal superficial capillary plexus (NSCP) vessel density, parafoveal inferior superficial capillary plexus (ISCP) vessel density, parafoveal DCP vessel density, parafoveal temporal deep capillary plexus (TDCP) vessel density, parafoveal superior deep capillary plexus (SDCP) vessel

density, parafoveal nasal deep capillary plexus (NDCP) vessel density, parafoveal inferior deep capillary plexus (IDCP) vessel density was assessed and compared between the two groups. The authors did not find any significant changes while comparing these parameters. The FAZ zone was not assessed in the study. The most significant difference among the two groups was observed between parafoveal TSCP vessel density ($p = < 0.001$), parafoveal SSCP vessel density ($p = 0.0028$) and parafoveal TDCP vessel density ($p = <0.001$). These parameters were significantly lower in the T1DM group. The median duration of T1DM in the study group was 6.0 (3.3; 10.3) years, and the median HbA1c value was 7.6 (6.9; 8.1) %, but no correlation was observed between these parameters and vessel densities of retinal capillary plexuses (16).

Inanc M et al. did a study in Turkey in which 57 healthy children and 60 children with T1DM were examined using OCTA. The authors assessed the patients' FAZ, foveal SCP and DCP vessel densities as well as parafoveal SCP, TSCP, SSCP, NSCP, ISCP, DCP, TDCP, SDCP, NDCP, and IDCP vessel densities and found a statistically significant decrease in the parafoveal TDCP ($p = 0.015$) and parafoveal SDCP ($p = 0.005$) vessel densities in the study group while comparing with the control group. Inanc M et al. did not find a significant correlation between the mean duration of T1DM (6.54 (± SD = 3.86) years), mean HbA1c (6.42 (± SD = 1.12) %), and FAZ as well as capillary plexuses vessel densities of the study group (3).

The study by Wysocka-Mincewicz M et al. in Poland included 71 children: 50 in the study group and 21 in the control group. Patients were examined using OCTA. FAZ, foveal, as well as parafoveal SCP and DCP vessel densities were assessed. A statistically significant correlation among the two groups was found between parafoveal SCP vessel densities ($p = <0.005$); it was lower in the T1DM group. Also, the authors found a correlation between the duration of T1DM (6.88 (± SD = 4.34) years) and FAZ ($r = 0.29$, $p < 0.05$). No significant correlation was found when comparing FAZ and capillary plexuses vessel densities with mean HbA1c in children with T1DM (17).

After analysing 4 studies, it was found that Mameli C. et al. and Inanc M. et al. determined a statistically significant decrease in vessel density in the parafoveal TDCP area, while Mameli C. et al. and Wysocka-Mincewicz M. et al. determined a statistically significant decrease in vessel density in the parafoveal SCP area when comparing the study group with the control group. Only Wysocka-Mincewicz M. et al. found a significant positive correlation between FAZ and the duration of the disease in the study group. Gołębiewska J. et al. observed a significant negative correlation of the parafoveal DCP vessel density with the mean duration of T1DM as well as a statistically significant negative correlation between the parafoveal SCP vessel density and the mean value of HbA1c.

4. Conclusions

In conclusion, the study found presence of microvascular changes in macula in children with T1DM and significant associations with both diabetes duration and HbA1c. OCTA can be used for the early detection of DR in children.

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