Research Article
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The compatibility between optical coherence tomography and fundus fluorescein angiography in the detection of macular edema involving the fovea

Abstract

Objective: To investigate the compatibility between optical coherence tomography (OCT) and fundus fluorescein angiography (FFA) in the detection of macular edema (ME) excluding subretinal fluid (SRF) involving the fovea.

Materials and methods: In this retrospective study in the Ophthalmology Department at our university hospital, interpretation of OCT and FFA images was performed for 200 eyes that underwent simultaneous FFA and OCT to rule out ME. The cases having SRF were excluded from the study.

Results: Of 200 eyes, 193 eyes (96.5%) had the finding of ME confirmed by both techniques. There were 2 eyes (1%) for which FFA revealed ME involving fovea with hyperfluorescence in the macula while OCT demonstrated no intraretinal edema or subretinal fluid in the macula. For 5 eyes in the study (2.5%), OCT revealed intraretinal edema in the fovea, while these were not detected by FFA.

Conclusion: This study suggests that FFA and OCT are highly sensitive techniques for the detection of ME and they correlate with each other. The little discrepancy between OCT and FFA for determining ME may be due to intracellular or extracellular edema and fast or slower development of retinal edema.

Keywords: macular edema, intracellular, extracellular, optical coherence tomography, fundus fluorescein angiography, discrepancy, compatibility

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Introduction

Macular edema (ME) arises from fluid accumulation in the retinal layers in the macula. If it involves the fovea, ME causes significant visual loss. In most cases, ME is associated with the breakdown of the blood-retinal barrier (BRB). ME may occur in a range of ocular diseases such as ocular inflammatory diseases (uveitis), ocular trauma or intraocular surgery (Irvine-Gass syndrome), retinal vascular disorders (hypertensive retinopathy, diabetic retinopathy (DRP), retinal vein occlusion (RVO), retinal artery macroaneurysm (RAM), radiation retinopathy (RR)), vitreomacular interface disorders, choroidal tumors, panretinal photocoagulation, hereditary dystrophies (retinitis pigmentosa (RP), foveoschisis), drugs (epinephrine, latanoprost, nicotinic acid) and age-related macular degeneration (ARMD).[1–15]

In ME, the fluid accumulates in the outer plexiform (Henle's), inner nuclear and plexiform layers of the retina. Accumulated fluid may be in an intracellular or extracellular location. Intracellular edema (ICE) (cytotoxic edema) rarely occurs and the retinal cells are swollen by the alteration of the ionic distribution in the cells in the presence of an intact BRB. In turn, sodium ions (Na^+) excessively accumulate inside the cells in ICE. ICE may be caused by ischemia, trauma, or toxic cell damage. On the other hand, extracellular edema (ECE) is more frequent and it arises from an open BRB or the breakdown of the inner or outer BRB (IBRB or OBRB). The retina thickens due to the accumulation in the retinal extracellular space**.** The fluorescein leakage in fundus fluorescein angiography (FFA) is an indicator of the breakdown of the BRB.[1,5] Currently, optical coherence tomography (OCT) and FFA have been largely used to evaluate ME**.** Theoretically, FFA reveals the IBRB breakdown while OCT demonstrates the OBRB breakdown.[11,16–21] In this study, we aimed to investigate the compatibility between OCT and FFA in the detection of the ME excluding SRF involving the fovea.

Material and methods

This study was designed as an observational retrospective study in the Ophthalmology Department at the university hospital. The patients who had simultaneously undergone both FFA and OCT on the same day were included in the study. Two hundred eyes were performed simultaneously FFA and OCT to rule out ME. The study was designed according to the Helsinki Declaration. Results of two hundred good-quality/signal ratio OCT and FFA for patients by a single retina specialist were reviewed to diagnose or suspected ME due to different causes. The patients having poor quality images and inconsistency and also subretinal fluid (SRF) were excluded from the study because SRF may be detected only by OCT.

OCT scanning and analysis

OCT examinations were performed using spectral OCT (Cirrus HD 5000 OCT, Zeiss, Germany). OCT scanning of the maculae was performed by a single technician. Acquired OCT images were evaluated by the same ophthalmologist (BT).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 (Chicago, IL, USA). Results were given as the means ± standard deviations. The chi-square test was used to compare categorical variables in the study groups, respectively. A P value less than 0.05 was considered statistically significant.

Results

Of 200 eyes, 193 eyes (96.5%) had the finding of ME confirmed by both techniques. There were 2 eyes (1%) for which FFA revealed ME involving fovea with hyperfluorescence in the macula while OCT demonstrated no intraretinal edema in the macula. For 5 eyes in the study (2.5%), OCT revealed intraretinal edema in the fovea, while these were not detected by FFA. Table 1 presents the distribution of subjects according to diagnoses and Table 2 shows the values of the detection of ME by FFA and OCT.

Table 1 Distribution of subjects according to diagnoses

Diagnoses	No (Percent)
DRP	106 (53%)
ARMD	36 (18%)
RVO	38 (19%)
CSCR	12(6%)
Uveitis	8 (4%)
Total	200 100.0 %

DRP, diabetic retinopathy; ARMD, age related macular degeneration; RVO, retinal vein occlusion; CSCR, central serous chorioretinopathy

Table 2 Detection of ME by FFA and OCT

	Negative for ME by FFA		Negative for ME by OCT		Positive for ME by both	
Detection of ME	**No.**	**%**	**No.**	**%**	**No.**	**%**
	2	1%	5	2.50%	193	96.50%

ME, macular edema; FFA, fundus fluorescein angiography; OCT, optical coherence tomography

Discussion

Outer and inner BRB breakdown and vascular leakage leading to ME may be mediated by locally released cytokines, chemokines, growth factors including prostaglandins, interleukins and vascular endothelial growth factor, and inflammatory cells. At the physiological conditions, the dryness of retinal interstitial spaces is obtained via the limitation in the fluid transport into the retina from the vitreous by the intraocular pressure (IOP), retinal osmotic and hydrostatic forces, the strong choroidal osmotic pressure absorbing SRF and active RPE pump sending fluid out of the subretinal space towards the choroid. BRBs prohibit entering the proteins into the retina. The IBRB is formed by the tight junctions between the retinal capillary endothelial cells while OBRB is formed by the tight junctions between the RPE cells. At the pathological conditions causing BRB breakdown, proteins enter the retina, and fluid accumulates in the retina secondary to osmosis and eventually, ME develops.[1–5]

ICE develops when the cell membrane transport systems are damaged. These systems are responsible for maintaining the delicate ion-water movement across the cell membrane. This leads to the release of various excitotoxins and free radicals, and eventually to the BRB breakdown. There are many studies on the compatibility between OCT and FFA detection of macular edema in various diseases in the literature. Jittpoonkuson et al reported that cystoid ME associated with RVO, ARMD, and DRP were not detected by FA in approximately 18-33% of cases and that SD-OCT has greater sensitivity than FA in detecting ME in these patients.[16] In a recent study on diagnosing macular edema, Kozak et al reported that the sensitivity of FFA and OCT was 98.7% and 96.1%, respectively and they found that FFA showed the leakage in the macular area, but OCT showed normal foveal contour in 3.86% of eyes. They also reported that OCT detected both intraretinal and SRF in 1.17% of eyes, while FFA failed to detect any fluid. They reported that the largest number of discrepancies was in diabetic ME, and FA was more sensitive than OCT for this condition.[17]

The discrepancy between FFA and OCT is not uncommon in the eyes of patients with diabetes. Barteselli et al.[18] reported a high discrepancy rate (18.12%) between both modalities in eyes with diabetic ME. FFA appeared to be more sensitive than OCT in detecting ME (1.00 vs 0.79).[18] In another study of 252 eyes, Saleem et al demonstrated that ME was confirmed by both OCT and FFA in 92.1% of the eyes. There were 8 eyes (3%) for which FFA showed leakage in the macular area and OCT showed normal foveal contour without intraretinal edema. For 12 eyes in their study (5%), OCT showed intraretinal and SRF, which was not detected by FFA.[19]

In uveitis patients, Kempen et al.[20] showed that macular thickening can be present with or without leakage on FFA. In their study, macular FFA leakage was present in 40% of cases without macular thickening, whereas macular thickening was present in 34% of cases without macular FFA leakage.[20]

Antycliff et al.[21] found that the sensitivity and specificity of OCT for detecting cystoid ME in uveitic eyes were 96% (including SRF) and 100%, respectively compared to FFA.[21] Yeung et al demonstrated that the outer retina was the predominant location of fluid in diabetic ME and that a positive correlation between the severity of retinal edema on OCT and the severity of leakage on FFA.[22] Pseudo-cystoid ME (non-angiographic, non-leaking cystoid ME) is probably caused by the accumulation of intracellular fluid (ICE), but not by extracellular as developed in the true retinal edema, along with toxicity in the Müller cells and subclinical extracellular leakage. It may occur in conditions such as X-linked foveoschisis, myopic foveal schisis, Goldman Favre disease, the pseudo-hole with an epiretinal membrane, nicotinic acid maculopathy, some forms of RP, vitreomacular traction syndrome, hydroxychloroquine, and taxane maculopathy.[23–26] This ME can be detected only by OCT. In FFA, the amount of leakage depends on the amount of dysfunctional retinal vascular endothelium.[14,27]

Conclusion

In conclusion, our study suggests that FFA and OCT are highly sensitive techniques for the detection of ME. Theoretically, it has been considered that FFA reveals the IBRB breakdown and OCT indicates the OBRB breakdown in the retina. The discrepancy between both imaging modalities for determining ME may be due to ICE or ECE and fast or slower development of retinal edema.

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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