FFA STUDY OF MACULAR LESIONS

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ABSTRACT

BACKGROUND

Macula is an important portion of retina that occupies the posterior pole of retina. Any disease that affects macula results in significant loss of central vision, form vision and colour vision to an extent. Macular lesions can be hereditary as well as acquired. Macular lesions occur in both younger and older individuals. Anatomically, a macular lesions can vary from a simple lesion like an RPF defect to a vision-threatening lesions like choroidal neovascular membrane.

Many screening tests that are sensitive and specific are available to assess the functioning of macula called as 'macular function test'. But, the greater understanding of the retinal vascular led to the usage of fluorescein angiogram in the detection and screening of macular, retinovascular and optic disc lesions. Through fundus fluorescein angiogram is a thirty-year-old procedure; it is still in vogue in almost all parts of the world. It has its own merits.

The aim of the study is to study the role of fluorescein angiography in the evaluation of macular lesions.

MATERIALS AND METHODS

A hospital-based prospective randomised study was done, which included 50 patients. Detailed patient history was taken and thorough ocular and systemic examination was done. All patients were examined by ophthalmoscopy (direct and indirect) and slit-lamp examination with 90D followed by fluorescein angiography. Ophthalmoscopic and fluorescein angiography findings were analysed and categorised. Patients were advised proper ocular and systemic treatment and follow up.

RESULTS

50 cases with macular lesions were analysed and categorised into conditions like ARMD, CSR, macular oedema, CME, degenerations and dystrophies and miscellaneous conditions. FFA altered the diagnosis in 8% cases and categorised the cases in all cases. 16% patients developed adverse reactions like allergy, vomiting and nausea. On statistical analysis, FFA proved to be cheap and superior diagnostic tool in confirming the lesions detected by ophthalmoscopy clinically.

CONCLUSION

FFA is a superior diagnostic tool even after four decades of its use in ophthalmology for evaluating, localising, confirming lesions involving macula, retinal vasculature and choroid.

KEYWORDS

Macula, Hyperfluorescence, Choroiditis.

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BACKGROUND

Macular disorders are common between the second and sixth decade,[1] which if left untreated can lead to profound visual loss, even blindness. FFA has wide usage in the diagnosis and monitoring the prognosis of treatment of various macular lesions like ARMD, diabetic macular oedema, CSR, choroiditis, etc. It helps in distinguishing between macular and choroidal lesions.

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Burke in 1910 used oral fluorescein for delineating retinal pathology. Kikai used intravenous fluorescein in animal models to study retinal vasculature in 1930. In 1940, IV use of fluorescein was used to study the aqueous circulation. The first use of IV fluorescein in ophthalmology was by Maclean and Maumenee who used it to confirm the diagnosis of choroidal haemangioma and to differentiate it from choroidal haemangioma,[2] but photographic documentation was not done.

MATERIALS AND METHODS

This study was carried on 50 patients attending the Ophthalmology Department of Government Chengalpattu Medical College with macular disorders from January 2015 to December 2016. Study was conducted after approval from the Ethical Clearance Committee of the Institute. Informed consent from all patients included in the study was taken after explaining about the procedure and possible side effects.

All patients with defective visions identified to have definite macular lesions by ophthalmoscopic examinations and patients found to have defective 'macular function test' were included in the study. Very old patients, pregnant women, immunocompromised and debilitated patients, patients with renal insufficiency and cardiovascular diseases, patients with history of hypersensitivity to dye were excluded from the study. Patients with moderate-to-severe lens changes, vitreous haemorrhage were excluded as visualisation of the fundus lesions become difficult, clarity and subsequent interpretation of angiogram was impaired. Patients with concomitant macular diseases such as myopia that might have to contribute to visual loss were excluded.

Clinical assessment of patient began with a thorough history taking, which took into account factors such as presence of diabetes, hypertension, family history of macular disease, prior treatment history like eye surgery and drug intake were verified. Patients who had similar episodes before were assessed. This was followed by other investigations like best corrected near and distant visual acuity, detailed examination of eye with slit lamp, the state of crystalline lens was specifically recorded, detailed fundus exam using direct and indirect ophthalmoscopy, posterior pole was observed using 90D and SLE biomicroscopy, ancillary macular functions tests like Amsler grid, colour vision, photo stress test was done after explaining to the patient. Patients having confirmed macular lesions with defective macular functions test were subjected to FFA.

Procedure of Fundus Fluorescein Angiography

Patient's pupils were dilated with combination of 5% phenylephrine and 1% tropicamide eye drops 30 minutes prior to the procedure. An intradermal test dose of the dye was given 10 minutes prior to the procedure. A 21-gauge scalp vein set was put in the antecubital vein. Patient was seated in front of the fundus camera and the eye was injected. Procedure was conducted under supervision of a standby anaesthetic. Monochromatic fundus photographs (red free) were taken prior to performing FFA. 3 mL of 25% fluorescein dye was injected in the antecubital vein. Pictures were taken after 10 secs. at an interval of 1.5-2 secs., approx. 6 photographs were taken in a succession. Novotny H.R. et al[3] also describes the method of photographing fluorescein in circulating blood in the human retina. Findings like hyperfluorescence, hypofluorescence, autofluorescence, blocked fluorescence, leak, window defect based on the structures affected and disease were recorded. Patient was monitored for one hour after procedure. On analysis of findings, patient was advised general and specific ocular treatment accordingly.

RESULTS

A total of 50 patients who presented to ophthalmic outpatient department with macular pathology were evaluated clinically by ophthalmoscopic examination and by fundus fluorescein angiography.

66 eyes of 50 cases with macular involvement were studied. Patients with macular involvement were identified as individuals with specific defects like pigment epithelial defect, macular oedema, retinal pigmental atrophy, drusen, cystoids macular oedema, etc.

Table 1 shows the characteristic of patient population, 38 male patients (76%) were having maculopathies and 12 female patients, 24% were having macular lesions. Males are mostly affected because they bear the maximum stress and strain in their process of earning their livelihood. They are the precipitating factor for systemic diseases like diabetes, hypertension, anxiety, neurosis, etc. Most of the Indian females are housewives, they stay indoors, so the chances of exposure to UV rays and stress are also minimal compared to males, which could be the cause for low incidence of maculopathy like ARMD and diabetes mellitus.

Table 2 shows the age distribution of the patient population. Age of the patient varied from 9 years to 82 years. The average age incidents was 45.5 years, maximum number of patients (22%) were in the age group of (40-49) years. At extremes of age, minimum numbers of cases were recorded 4% between 1-9 years and 2% between 80-89 years, but it is also a proof that macular lesions occur both younger and older individuals as early as first decade.

Sex	**Maculopathies**	
	Number of Patients	**Percentage**
Male	38	76%
Female	12	24%
Total	**50**	**100%**

Table 1. Sex Distribution in Patient Population

Table 3 shows the incidence of macular lesions out of 50 patients with macular lesion, 12 patients had ARMD, 7 cases of central serous retinopathy, 7 cases of diabetic maculopathy and 7 cases of macular degeneration were noted. Five cases of macular dystrophy, 4 cases of macular choroiditis, 3 cases of cystoid macular oedema and 3 cases of macular hole were noted. Two patients had Stargardt's disease at the time of study, 26 patients had unilateral involvement and 24 patients had bilateral involvement. The causes for bilateral involvement is mostly due to ARMD, diabetic maculopathy and macular dystrophy. Unilateral lesions contributed by CME in postoperative patients, CSR and macular hole. It is therefore important to observe other eye carefully at regular intervals for early signs of disease in patients who present with unilateral features. Some patients clinically had frank bilateral lesions. Some cases clinically had unilateral lesions, but FFA showed fellow eye also to be affected subclinically.

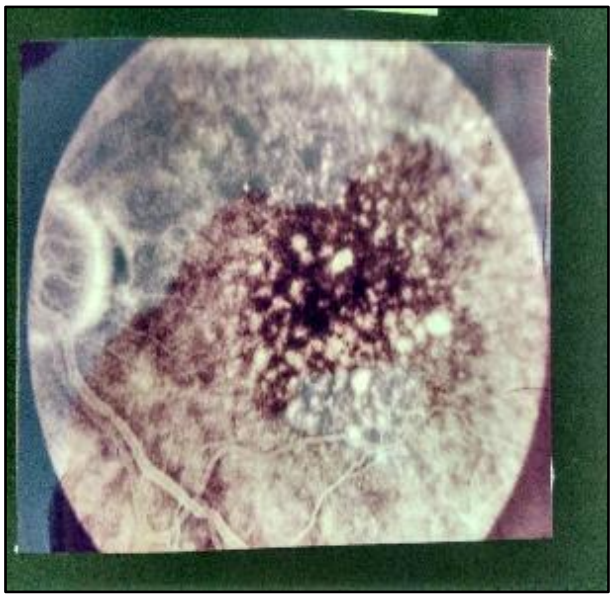

Figure 1. FFA Pictures in ARMD

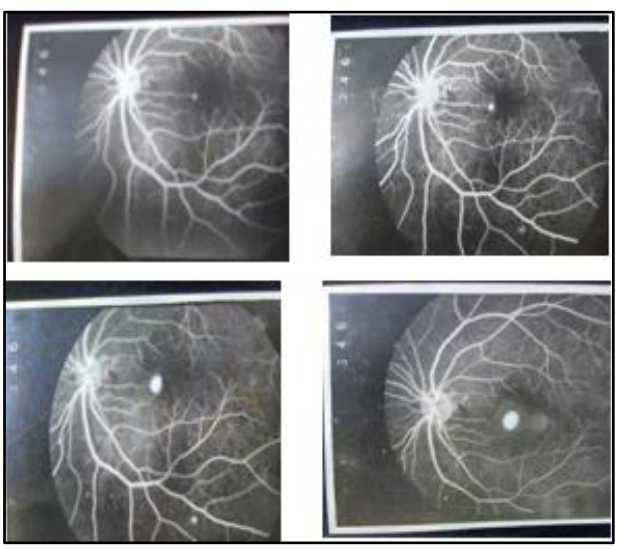

Figure 2. FFA Picture of CSR (Pinpoint Leak)

Age (Years)	Maculopathies	
	Number of Patients	Percentage
1-9	2	4%
10-19	1	2%
20-29	8	16%
30-39	7	14%
40-49	11	22%
50-59	9	18%
60-69	10	20%
70-79	1	2%
80-89	1	2%
Total	**50**	**100%**

Table 2. Age Distribution in Patient Population

Age Distribution

Table 4 shows the classification of diseases studied. The first common macular lesion was ARMD 30% was males and 8% was female. In Framingham eye study, males are more affected by ARMD. In another study by Hines et al reported women to have equal prevalence as men in ARMD. FFA helped to classify ARMD into dry ARMD and wet ARMD. It is also helped confirming the diagnosis. ARMD constituted 38% of the total cases.

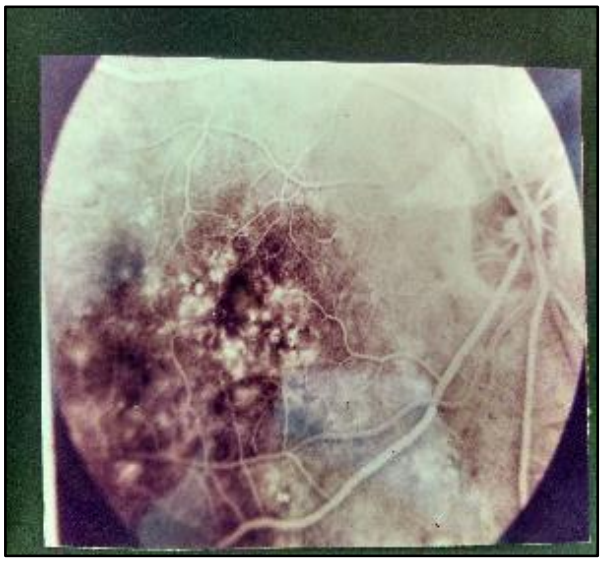

Figure 3. FFA Picture of Diabetic Maculopathy

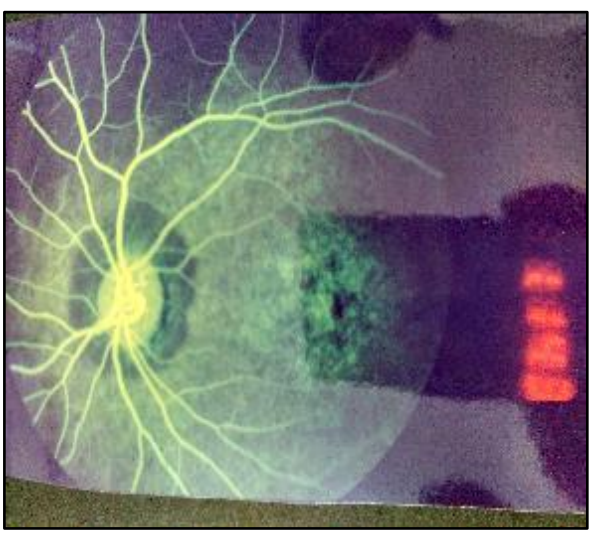

Figure 4. FFA Study of Stargardt's Disease (Bulls Eye Pattern)

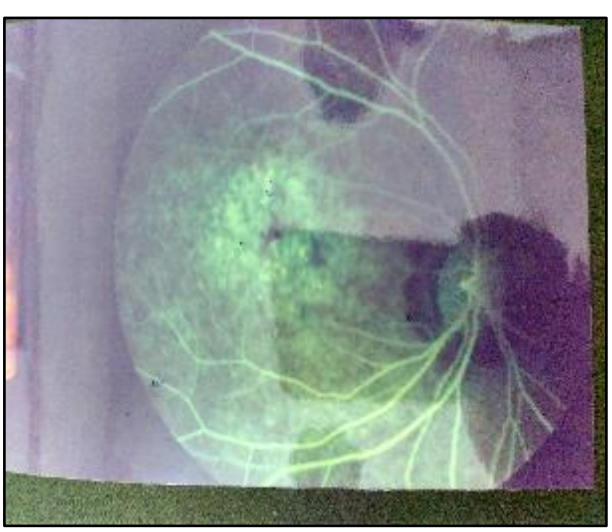

Figure 5. FFA Picture of SRNVM

Incidence of Macular Lesion

Sl. No.	Type of Macular Lesion	Number of Patients	Percentage	Number of Eyes affected at Time of Study	
				One Eye	Both Eyes
1.	ARMD	12	24%	7	5
2.	CSR	7	14%	7	-
3.	Diabetic maculopathy	7	14%	3	4
4.	Macular degeneration	7	14%	3	4
5.	Macular dystrophy	5	10%	-	5
6.	Macular choroiditis	4	8%	2	2
7.	CME	3	6%	3	-
8.	Macular hole	3	6%	1	2
9.	Stargardt's disease	2	4%	-	2
	Total	**50**	**100%**	**26**	**24**

Table 3. Characteristics of Macular Lesion

Disease Pattern

Sl. No.	Type of Maculopathy	Sex		Total
		Male	Female	
1.	ARMD	30%	8%	38%
2.	CSR	12%	3%	15%
3.	Diabetic maculopathy	12%	2%	14%
4.	Macular dystrophies	5%	8%	13%
5.	Inflammatory disorders	9%	2%	11%
6.	Macular hole	7%	2%	9%
Total		**75%**	**25%**	**100%**

Table 4. Classification of Cases

Second most common lesion was that of central serous chorioretinopathy. It was seen in 15% of the cases. Here also, males were commonly affected 12% and females 3%. FFA not only helped in confirming the diagnosis of CSR also helped in differentiating the types of leak like into ink blot appearance and smoke stack pattern.

In this study, diabetic maculopathy was the third common lesion accounted for 14% of the cases, males 12% and females 2% apart from classifying the case into PDR and NPDR. FFA helped in differentiating the macular oedema into clinically significant macular oedema, ischaemic, focal and diffuse type.

Next common lesion was macular dystrophy, which constituted 13% of the cases, males 5% and females 8%. FFA helped in distinguishing the different types of dystrophies. In Stargardt's disease, it helped in identifying the Bull's eye pattern.

Next, common macular lesion was inflammatory disorders. It accounted for 11%, males 9% and females 2%. FFA helped in classifying macular choroiditis into old and fresh lesions. Postoperative lesions like cystoid macular oedema showed flower petal pattern.

Macular hole was reported 9% of the cases, 7% males and 2% females.

Initial Diagnosis	No. of Cases	Confirmed	Revised
Disciform macular degeneration	5	3	2
Preretinal gliosis	2	0	2

Table 5. Revision of Diagnosis

Table 5 shows the number of cases in which FFA was useful in revising the diagnosis, out of 5 cases, which was clinically diagnosed as disciform macular degeneration, 3 cases had same diagnosis and 2 patients were found to have dystrophy. Two cases initially diagnosed as preretinal gliosis, initially were found to have macular degeneration.

Sl. No.	Nature of Symptoms	Number of Cases
1.	Nausea	4
2.	Vomiting	3
3.	Giddiness	1
4.	Urticaria	-
5.	Shock	-

Table 6. Incidence of Complications Following Fluorescein Injection

Table 6 shows the common complications following injection of fluorescein dye, the common complications were nausea 4 cases, vomiting 3 cases and giddiness noted in 1 patient. FFA is a safe procedure, but we have to be ready to face any complications arising.

DISCUSSION

Macular lesions have varied presentation depending upon the type of pathology varying from inflammation, degeneration, dystrophy and age-related changes. Because of the vast advancement in this field, many gadgets have flooded the market to achieve diagnostic accuracy and at the same time expensive. Fluorescein angiography is an emerging technique used to study the retinal vasculature, macula, choroid and disc.

Demography- In this study, the incidence of macular lesions was more common in males. The male:female ratio was 3:1. The lesions like ARMD, CSR and diabetic macular

oedema was more common in males. Since, the male members of the family bear the burden of earning, their livelihood, the role of stress, exposure to UV rays while working outdoors, modern youngsters strive hard to achieve their goals resulting in lot of stress and strain, which contributed to the macular lesions. The Framingham eye study[4] also reported males more commonly affected in ARMD.

Age Group- In this study, macular lesions were more commonly reported in the 5th and 6th decade and also in the 3rd decade. As proved by other studies, disease like ARMD, diabetic maculopathy was more common in the people belonging to the 5th and 6th decade. During this time, the age-related changes and maculopathy due to diabetic retinopathy tends to manifest. CSR was more common in the people belonging to the 3rd decade. This group of people is exposing to lot of stress and strain in their job and academic activity.

Classification of Lesions- In the study, the single most common macular lesions detected through FFA was that of ARMD 38%. The second most common macular disorders followed by CSR 15%, diabetic maculopathy 14%, macular dystrophy 13% and inflammatory disorders 11%, lastly macular hole 9%.

ARMD- 24% (12 cases), FFA helped in differentiating ARMD into dry ARMD and wet ARMD. Talks J. et al reported that 81% cases of wet ARMD were diagnosed only by FFA.[2] Most of the dry ARMD cases were detected clinically. FFA plays an important role in early detection and localisation of the site of CNVM in relation to foveal avascular zone. Figure 1 shows FFA picture of ARMD with drusen. Figure 5 shows FFA picture of SRNVM.

CSR- 14% (7 cases) were reported, which were detected clinically by ophthalmoscopy and confirmed by FFA. Single leak was seen in 80% cases and multiple leaks in 20% cases. Smoke stack appearance 60% and in blot appearance seen in 40% cases. Similar study by Suresha AR et al on role of FFA in macular disorders reported the same.[5] Siddique et al in their study reported that ink blot appearance and smoke stack appearance were seen in 67% and 33%, respectively.[6] FFA confirmed the diagnosis in 50% cases and 8% cases. It altered the diagnosis, 42% cases it categorised. Wykes et al in the study showed that FFA confirms the diagnosis in 40% cases.[7] FFA helped in pinpointing the site of leakage and helped in planning laser treatment. Figure 2 shows the pinpoint leak in CSR.

Diabetic maculopathy was the third most common macular lesion in this study when compared to the study by Kahn et al,[8] which reported this as the most common disorder and responsible for major cause of visual impairment. FFA in addition to differentiating PDR from NPDR also helped in identification of Clinically Significant Macular Oedema (CSME) and foveal avascular zone. Figure 3 shows diabetic maculopathy.

Macular Dystrophy- 10% (5 cases), FFA helped in categorisation of lesion in all these cases. Wykes et al reported that FFA confirmed the diagnosis in 100% cases of hereditary macular dystrophies.[7] Figure 4 shows Bulls eye pattern of Stargardt's disease.

Macular Choroiditis- 8% (4 cases), macular lesions was inflammatory in nature. 75% were choroiditis. FFA helped to differentiate between healed and active lesions and serve to assess the treatment and prognosis. It helps in planning the treatment early.

Adverse Reactions- With regard to adverse reactions, FFA didn't produce serious complications, except for nausea and vomiting, which was frequently complained by patients. Nausea 4 patients, vomiting 3 patients and giddiness 1 case. Kwan AS et al reported that "FFA is the safe procedure than compared to other intravenous radiocontrast media angiography.[9]" It is relatively safe procedure well tolerated by people of all age groups.

Revision of diagnosis- 5 cases suspected as disciform macular degeneration by ophthalmoscopy, out of which 2 cases turned out to be macular dystrophy. Similarly, 2 cases diagnosed clinically as preretinal gliosis turned out to be macular degeneration after fluorescein angiography. FFA was helpful in confirming and revision of diagnosis. Jain L.S. et al reports the same.[10]

CONCLUSION

Macular lesion was detected clinically by routine ophthalmoscopic examination and other macular function test. But, to assess the integrity and status of RPE, inner and outer retinal barrier, retinal vascular lesion, macula, FFA is a very useful procedure. Fundus fluorescein angiography played a very crucial role in the evaluation of macular lesions. FFA helped in diagnosis, classification and monitoring the treatment of macular lesions. FFA helped in early detection and classification of ARMD. In CSR, FFA helped in identifying the site of leakage and helped in planning laser treatment. In diabetic maculopathy, FFA helped in classifying maculopathy and differentiating ischaemic maculopathy, other maculopathies, because the laser treatment is contraindicated in ischaemic maculopathy, whereas other type laser is useful. FFA was useful in classification and treatment of inflammatory lesions. FFA is safe and cost effective. This can be made available at an affordable cost. Though it is a very old procedure still it is popular tool in ophthalmology.

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