

Research Article

Role of fundus fluorescein angiography in macular disorders

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Abstract

Objectives: To assess and evaluate the role of fluorescein angiography as an important tool in diagnosis of macular disorders.

Methods: A hospital based prospective randomized study was done which included 50 patients who attended the OPD during study period. Detailed history was taken from the patient and a thorough ocular and systemic examination was done. All patients were examined by conventional methods of ophthalmoscopy (direct, indirect and slit lamp examination with +90 D lens) followed by a fluorescein angiography. Patients were advised necessary ocular and systemic treatment.

Results: 50 cases were analyzed and sub-divided into 5 categories of AMD, Diabetic maculopathy, vascular occlusive disorders, macular dystrophy and CSCR. FFA altered the diagnosis in 40% cases and categorized the lesions in all cases. 6% of patients experienced adverse reactions. On statistical analysis, using binomial test FFA proved to be a far superior diagnostic modality than clinical examination (ophthalmoscopy).

Conclusions: FFA has played major role in diagnosing wet AMD, especially in diagnosing CNVM. It is a superior diagnostic modality in differentiating macular edema and macular ischemia in vascular disorders and hence guides in further management. It provides definitive diagnosis in CSCR and detects exact leakage points. It is of immense value in diagnosing new vessels, planning for further treatment. FFA has a limited role in evaluation of macular dystrophy.

Keywords: Altered, Categorized, Macular disorders; Retinal diseases; Side effects

1. Introduction

The human central retina, "the macula", is the anatomical structure responsible for fine detailed vision and when subjected to disease causes irreversible blindness. Retinal disorders are the largest cause of legal blindness in the age group of 20 to 65 years.¹ Annually, 18 million people in India have severely impaired vision due to retinal diseases.² Studies in developing countries have reported retinal diseases constituting between 8.1–12.5% of patients presenting to outpatient department of eye units.³ Retinal disease was the primary cause in 12.7% of blindness in a population based surveys in India.⁴

Macular disorders (MD) were the most frequent constituting 35.6% of all posterior segment diseases. Age related macular degeneration (AMD) constituted 38.6% of all macular disorders; other macular diseases were macular scars (34.8%), macular holes (18%), drug induced maculopathy (3.4%) and nonspecific pigmentary maculopathy (43.8%).

Retinal vascular occlusions were central retinal vein occlusions (CRVO) in 9%, branch retinal vein occlusions (BRVO) in 4% and central retinal artery occlusions (CRAO) in 2%.⁵

AMD leads to blindness in 18% of the population in the age group 65-75 years and in 30% of persons aged above 75 years.⁶ Even in developing nations, AMD is gaining attention due to increased life expectancy and improved visual care facilities. In an Indian study, prevalence of AMD in a clinic-based population above the age of 50 years was noted to be 4.8%.⁷ Prevalence of AMD above 60 years ranges from 0.6% to 1.1% in India.²

Diabetic maculopathy (DM) causes gradual and largely irreversible loss of central vision. Diabetic macular edema (DME) will develop in up to 10% of all diabetics. DME affects central fovea in 4% of cases and up to 30% of patients develop moderate visual loss (MVL).⁸

FFA is most useful and practical for tracing the lesions in retina, including macular lesions and it is conclusive in 80% of cases.⁹ It allows to examine the structures beyond the reach of clinical examination. A modern angiogram consists of a series of high contrast black and white transparencies taken at speeds of 0.6 sec interval.

The blood-retinal barriers are at Retinal Pigment Epithelium (RPE), Bruch's membrane and retinal vasculature. FFA findings are analyzed in relation to these barriers.¹⁰ A positive fluorescein angiographic finding is a frequent occurrence in ophthalmoscopically invisible lesions.

Macular disorders in the eye can be potentially grievous and should be treated at the earliest. FFA leads to an alteration in treatment of AMD, DM, CSCR, vascular occlusions etc. Thus FFA helps in early diagnosis and treatment of macular disorders and helps in prevention of irreversible blinding conditions and therefore the study is essential.

2. Material and Methodology

The present study was carried out on 50 patients attending the outpatient department of ophthalmology at JJM Medical College, Davangere from August 2013 to July 2014. It was carried out after obtaining permission from ethical committee of the Institution and consent from the study participants.

Patients with retinal disorders with suspected AMD, Diabetic maculopathy, vascular occlusive disorders, macular dystrophy and CSCR were included in the study. Retinal disorders other than the above mentioned, viz., very old, uncompliant patients, pregnant women, and immunocompromised status patients, patients with hypersensitivity to fluorescein dye, renal insufficiency or cardiovascular diseases were excluded.

Using a preformed proforma, detailed history was obtained from each patient. Patients underwent a detailed clinical examination that included unaided visual acuity and best corrected visual acuity with snellen's chart and near vision; pupil size and reactions; anterior segment examination and slit lamp biomicroscopy; measuring IOP using Goldmann applanation tonometer. A thorough, careful and detailed examination of the fundus was done initially by a direct ophthalmoscope and subsequently with an indirect ophthalmoscope and slit lamp examination with +90 D lens and +78D lens giving special attention to macula.

A written informed consent was taken from the participants after explaining condition of the eye, the procedure, purpose and possible side effects of FFA. Patients were evaluated and investigated by physician to note the presence of any systemic diseases especially to rule out renal failure and fitness for the above procedure was taken.

Procedure: Patient's pupils were dilated with a combination of 5% phenylephrine and 1% tropicamide 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 dye was injected. Procedure was conducted under supervision of standby anaesthetist. Using a Zeiss fundus camera Colour fundus photographs, Monochromatic fundus photographs (red free) were taken prior to performing FFA. 3ml of 25% fluorescein dye was injected in the antecubital vein. Pictures were taken after 10sec at an interval of 1.5-2sec approx. 6 photographs were taken in succession. Patient was monitored for one hour after procedure. On analysis of findings, patient was advised general and specific ocular treatment according to the disease.

Binomial test was created with FFA confirmed and FFA altered diagnosis and declared $p < 0.001$ as statistically significant. With the above mentioned background this study was conducted to assess and evaluate the role of fluorescein angiography as an important tool in diagnosis of macular disorders.

3. Results

50 cases were analyzed and sub-divided into 5 categories of AMD, Diabetic maculopathy, vascular occlusive disorders, macular dystrophy and CSCR.

Of the 50 cases 18 cases of AMD (36%), 17 cases of diabetic maculopathy (34%), 7 cases of vascular occlusions (14%), 4 cases of macular dystrophies (8%) and 4 cases of CSCR (8%) were studied. (Table 1)

Table 1: Diagnosis of patients studied

Diagnosis	Number of patients (n = 50)	Percentage
AMD	18	36.0
Diabetic Maculopathy	17	34.0
Vascular Occlusions	7	14.0
Macular Dystrophy	4	8.0
CSCR	4	8.0

On analysis out of 18 cases of AMD, 13 cases were of Dry AMD (72.2%) and 5 cases were of Wet AMD (27.7%).

Table 2: Distribution of wet AMD by FFA

Disease	FFA confirmed	FFA Altered
Wet AMD	1	4
Types of WET ARMD		
PED	1 (5.55%)	1 (5.55%)
CNVM	0	2 (11.11%)
Disciform scar	0	1 (5.55%)

On analysis of 5 cases of wet AMD (10%), 50% cases of PED were diagnosed by clinical examination and 50% by FFA. And 100% of CNVM by FFA and 100% of DS by FFA. (Table 2)

Table 3: Role of FFA in AMD

Disease	Number of cases	Percentage
ARMD	18	100
FFA Confirmed Diagnosis	12	66.6
FFA Altered	6	33.3

FFA confirmed the diagnosis in 66.6% of AMD cases, altered the diagnosis in 33.3% cases. (Table 3). In analysis of wet AMD by FFA 1 case (20%) was confirmed by FFA and 4 cases (80%) were altered by FFA.

On analysis out of 17 cases of Diabetic maculopathy, 5 cases were of CSME (29.4%), 3 cases were focal maculopathy (17.6%), 4 cases were diffuse maculopathy (23.52%) and 5 cases were found to be of ischemic maculopathy (29.4%).

Table 4: Role of FFA in Diabetic Maculopathy

Disease	Number of cases	Percentage
Diabetic maculopathy	17	
FFA confirmed diagnosis	4	23.53
FFA altered diagnosis	13	76.47

In this study, out of 17 cases of diabetic maculopathy, FFA has confirmed type of diabetic maculopathy only in 4 cases and has altered diagnosis in 13 cases. (Table 4)

On analysis out of 7 cases of vascular occlusions, 3 cases were found to have macular edema (42.8%) and 4 cases were found to have macular ischemia (57.2%).

Table 5: Role of FFA in Vascular Occlusions

Disease	Number of cases	Percentage
Vascular occlusions	7	
FFA Confirmed Diagnosis	4	57.4
FFA Altered Diagnosis	3	42.85

On analyzing vascular occlusions, FFA has confirmed diagnosis in 4 cases (57.14%) and has altered its diagnosis in 3 cases (42.85%). (Table 5)

Table 6: Role of FFA in Macular Dystrophy

Disease	Number of cases	Percentage
Macular dystrophy	4	
FFA confirmed diagnosis	4	100
FFA altered diagnosis	0	0

In the analysis of macular dystrophy, FFA has confirmed diagnosis in all cases. (Table 6). Out of 4 cases of macular dystrophy studied, 3 were found to be stargadt's disease (75%) and 1 was fundus flavimaculatus (25%).

Out of 4 cases of CSCR studied, 3 cases showed single leak point on FFA (75%) and 1 case showed multiple leak point on FFA (25%).

Table 7: Distribution of appearance of FFA in CSCR

DISEASE	Ink blot appearance	Smoke stack appearance
FFA appearance in CSCR	2	2

On analysis of FFA appearance in CSCR 50% showed inkblot appearance and 50% showed smoke stack appearance. (Table 7)

Table 8: Efficacy of FFA diagnosis in relation to Clinical evaluation of macular disorders in patients studied

Role of FFA	Number of patients (n=50)	%	P value
FFA Confirmed(A)	30	60.0	46.18-72.39
FFA altered (B)	20	40.0	27.61-53.82
Total	50	100.0	-
Inference	FFA altered diagnosis significant with $P < 0.001^{**}$		

For total sample size (n = 50), between A & B according to binomial test $p < 0.001$, is Significant. (Table 8) In this present study, FFA has proved to be a far superior diagnostic modality as compared to ophthalmoscopy.

On careful analysis

- 60% of cases detected positive by ophthalmoscopy were confirmed positive by FFA.
- On the contrary, a 40% of cases diagnosed by ophthalmoscopy were altered in their diagnosis by FFA indicating low negative predictive value.
- A very high percentage of cases although diagnosed positive by ophthalmoscopy are categorized into subtypes by FFA.

Thus we deduce that, CO has a high positive predictive value but a low negative predictive value. Hence, FFA is a superior diagnostic tool and is a necessity for evaluating clinically negative fundus disorders when in doubt.

Incidence of side effects was 6% (3 out of 50 cases). Nausea was the most common side effect seen in 66.6% of cases (2 out of 3 cases) and vomiting seen in 33.3% of cases (1 out of 3 cases). FFA is a safe procedure in our study.

4. Discussion

Macular diseases are the most frequent constituting 35.6% of all posterior segment diseases⁵. In this study, we have examined 50 patients in whom FFA and clinical examination was done for detection of macular disorders. For analysis, they have been divided into following sub groups- AMD, Diabetic maculopathy, vascular occlusive disorders, macular dystrophy and CSCR.

In this study out of 18 cases of AMD, 72.2 % were found to be of dry type and 27.8 % were of wet type. In this study 84.61% of dry AMD cases was diagnosed by clinical ophthalmoscopy and confirmed by FFA. FFA confirmed diagnosis in 20% of wet AMD cases and altered diagnosis in 80 % cases of wet AMD. Talks J et al in their retrospective study showed that 81% cases of wet AMD could be diagnosed only by FFA.¹¹ In this study FFA confirmed diagnosis in 66.66% cases of AMD and altered diagnosis in 33.33% cases of AMD and played an important tool in diagnosing wet AMD. In present study, 11.11% of CNVM, 5.5% of PED and 5.5% of disciform scarring could be diagnosed only by FFA. 11.11% of CNVM cases diagnosed were found to be subfoveal type. Talks J et al in their cross sectional study FFA was performed on 111 patients and had provided following diagnoses: predominantly classic CNV (19.8%), serous pigment epithelial detachment (7%), disciform scar (8.1%), occult CNV (40.5%), dry AMD (13.5%).¹¹

In present study out of 17 cases of Diabetic maculopathy, 29.4% were of CSME, 17.6% cases were focal maculopathy, 23.52 %cases were diffuse maculopathy and 29.4% cases were found to be of ischemic maculopathy. Syed et al in their interventional study on diabetic retinopathy found following angiographic patterns of diabetic maculopathy by FFA: diffuse maculopathy-59.24%, focal maculopathy - 17.69%, ischemic maculopathy-11.55%.¹² In this study FFA has confirmed type of diabetic maculopathy only in 23.53% cases which was diagnosed ophthalmoscopically and has altered diagnosis in 76.47% cases and played important tool in categorizing type of diabetic maculopathy and helped in further management and predicting prognosis.

Wykes et al showed in their study that FFA confirmed diagnosis in only 40% cases of diabetic maculopathy.⁹ In present study, we found that all cases of ischaemic maculopathy were diagnosed by FFA with areas of capillary non-perfusion which are not easily recognised by ophthalmoscopy.

In present study FFA showed vascular occlusions associated with macular ischemia in 42.85 % cases and confirmed presence of macular edema in all cases. Wykes et al showed in their study that FFA showed vascular occlusions associated with macular ischemia in 15% cases and that with macular edema in 84%cases.⁹ SS Hayreh in his landmark study in 1994 concluded that "In FFA, the extent of capillary non- perfusion is a reliable criterion to differentiate the two types of CRVO".¹³

In present study, macular dystrophies form 8% of macular disorders. All were diagnosed clinically and confirmed by FFA. Wykes et al showed in their study that FFA confirmed 100% cases of hereditary macular degeneration which was diagnosed by clinical examination.¹⁴ Present study is consistent with the above mentioned study.

In present study four cases of CSCR which were diagnosed by clinical examination, and confirmed by FFA. Single leak point was seen in 75% cases and multiple leak point in 25% cases with ink blot appearance in 50% cases and smoke stack appearance in 50% cases.

Siddiqui et al in their hospital based study on CSCR showed that ink blot appearance was seen in 67.64% and smoke stack appearance was seen in 30.35%.¹⁵ Present study shows similar findings to the above mentioned study.

In present study, incidence of side effects was 6% (3 out of 50 patients). Side effects like nausea (4%), vomiting (2%) were noted. Thus FFA is a relatively safe procedure.

Kwan AS et al in their study on 898 patients concluded that "FFA is a relatively safe procedure and comparable to other intravenous radio contrast media angiography. Prophylactic treatment, fluorescein desensitization or oral FFA can be considered in high risk patients".

On applying binomial-test, analysis of comparison between ocular examination and FFA was found to be significant. Thus, proving FFA to be a superior investigative modality.

In present FFA altered the diagnosis in 40% of cases and more importantly, categorized the lesion in most macular disorders.

FFA proved to be a superior modality of diagnosis and categorization of lesions in macular disorders. Without doubt, the single largest factor in the evaluation of macular disease in recent years has been the development of the technique of fundus fluorescein angiography.

5. Conclusion

In the study of ARMD: Most of dry ARMD cases was diagnosed by clinical examination (ophthalmoscopy) and confirmed by FFA. It played a vital role in diagnosing wet ARMD.

In the study of diabetic maculopathy: FFA was very useful in categorizing types of diabetic maculopathy, is a valuable tool in diagnosis of ischaemic maculopathy leading to an increased foveal avascular zone being the predominant type of diabetic maculopathy.

In the study on vascular occlusive disorder: FFA was useful in differentiating ischaemic or non-ischaemic type of lesions. These factors were important in the treatment and prognosis of these conditions.

In the study on macular dystrophies: FFA categorized the lesions into specific entities although all of them were diagnosed accurately by clinical examination.

In cases of CSCR: FFA was helpful in providing a definitive diagnosis, delineating the extent of edema, characteristic angiographic appearances, and the number of leak points and in detecting the exact site of leakage which is of value in laser photocoagulation.

Side effects

In this study, FFA was found to be a relatively safe procedure with minor side effects.

Limitations of the study

Small sample size, broad spectrum of disease and lack of non invasive imaging techniques.

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