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EVALUATION OF THE ROLE OF FUNDUS FLUORESCEIN ANGIOGRAPHY IN NON PROLIFERATIVE DIABETIC RETINOPATHY.

Ophthalmology

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ABSTRACT

Introduction: Diabetic retinopthy (DR) can be broadly classified as non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) with or without diabetic macular edema (DME). Management of all stages of DR are drastically different and early and accurate diagnose will make a lot of difference in final outcome for that patient. Fundus fluorescein angiography (FFA) is a useful tool which can diagnose early changes which clinical fundus examination might miss.

Materials And Methods: This is a cross sectional observational study with sample size of 96 eyes of 48 patients. After thorough history taking and examination, diabetic profile, serum lipid profile and renal function tests were carried out. This was followed by FFA under anaesthetist observation. Patients were managed accordingly. Data was entered in Microsoft Excel sheet for statistical analysis.

Results: In maximum patients duration of diabetes fell in range of 5-10 years and 15-20 years. 58.33% patients had associated hypertension. In patients with uncontrolled hyperglycemia, the incidence of PDR was 38.46%. Whereas in patients having good glycemic control, incidence of PDR was 14.28%. FFA could identify mild NPDR in 3 eyes where clinical fundus examination was normal. FFA diagnosed 11 more eyes with DME and 10 more eyes with PDR which was missed on fundus examination.

Conclusion: FFA helps in accurate diagnosis which can be missed on clinical ophthalmoscopic examination if subtle. Early treatment can prevent irreversible vision loss hence FFA should always be used especially in doubtful conditions such as pre-proliferative DR where the management changes drastically.

KEYWORDS

Fundus fluorescein angiography, Diabetic retinopathy, Non proliferative diabetic retinopathy, Proliferative diabetic retinopathy, Diabetic macular edema.

INTRODUCTION

Diabetic Retinopathy is the most common microvascular complication of diabetes and is the leading cause of blindness globally. India has second most number of diabetics in the world after China. It is the most common vascular retinopathy encountered by ophthalmologist.

Incidence is higher in IDDM but due to higher prevalence of type II, greater percentage of cases occurs in type II. Duration of diabetes is the most important determining factor in the occurrence of retinopathy. It has also got genetic predisposition. Diabetic retinopathy is also correlated with glycemic control , nephropathy, insulin usage, smoking and physiological conditions like pregnancy. There is less agreement on the influence of age at onset, gender, associated hypertension, cardiovascular disease, serum cholesterol, HDL and serum triglycerides.

Diabetes can be broadly classified as –Non proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR)

The NPDR without macular edema needs no local treatment, only regular follow-ups and good glycemic control along with control of associated systemic conditions such as hypertension are advised. Regular follow up can be key to early detection and treatment of proliferative changes and treatable

maculopathies. On the other hand, proliferative diabetic retinopathy needs urgent treatment by means of photocoagulation , anti VEGF injections and vitrectomies. As the management of both the conditions are very different, accurate diagnosis and early detection of PDR is very important. This can prevent irreversible vision loss due to advanced diabetic eye disease.

Fundus Fluorescein angiography (FFA) provides a means by which early changes inthe retina can be detected even when these changes are not detected

Ophthalmoscopically. Unlike, fundus photography, which is purely documentary, FFA is a diagnostic test yieldinginformation about the patient's ocular health otherwise unavailable to theophthalmologist. This can act as a baseline investigation and it can also help in evaluating response to treatment.

Diabetic macular edema (DME) if subtle, can be missed by clinical fundus examination which is also treatable and chronic edema can eventually lead to photoreceptor loss which can ultimately lead to irreversible visual impairment. NPDR in seemingly normal eyes can be detected by FFA which can guide patient management in terms of regular follow-up and management of systemic conditions which might prevent progression of NPDR into more severe forms and can thus help the patient.

This study is meant to determine the role of FFA in patients of NPDR. Early detection and accurate diagnosis of higher stages of DR compared to ophthalmological detection can make a huge difference in treatment guidelines and in overall patient management.

MATERIALAND METHODOLOGY

Ethical measures were adhered to throughout all phases of the research. The study was conducted among patients above the age of 30 years, attending our tertiary healthcare referral centre, who were diagnosed with NPDR with or without macular involvement on clinical examination of posterior segment and were willing to participate in the study. The duration of the study was from August 2019 to January 2020. Patients with type 1 DM, clinically diagnosed PDR, in whom any prior intervention for DR had been done,those with any co-existing retinal disease, those with any known uncontrolled systemic illness apart from diabetes which is likely to have effect on retina including hypertension, known drug sensitivity or allergy ,those having contradictions for FFA and those with any media opacity precluding posterior segment examination were excluded from the study.

Ours is a cross sectional observational study with sample size of 96 eyes of 48 patients. Informed consent was obtained from all the respondents before enrolling into study.

After thorough history, detailed examination was done followed by investigations. Ocular examination comprised of best corrected visual acuity (BCVA), slit lamp examination including intraocular pressure (IOP) measurement followed by posterior segment examination with help of slit lamp biomicroscopy using 90 dioptre lens and indirect ophthalmoscopy. We uniformly used combination eye drop having tropicamide 0.8% w/v with phenylephrine 5% w/v for fundus examination .Systemic investigations included diabetic profile, serum lipid profile and renal function test. A physician's opinion was sought for patient's fitness for FFA whenever required. Patient was given appointment for FFA with 4 hours fasting. Any history of drug reaction or allergy was excluded and patients were explained about the procedure and purpose of FFA and were warned against the possible side effects. Procedure was carried out as an outpatient department procedure under in house anaesthetist observation. Colour fundus photography and red free photography was done followed by injection of the fluorescein dye (10%) in to the antecubital vein and serial photographs were captured with both exciter and barrier filters ON for 15 minutes. Whenever needed Injection pheniramine (2 ml ampoule) was used to combat any minor drug reaction caused by dye injection. All through the procedure the patient's pulse and general condition were monitored by an assistant and any reaction attended to and noted. Digital fundus camera with built- in FFA by Carl Zeiss was used in all the patients. After the procedure the patient were observed for 30 minutes. They were explained about the change in urine colour and skin. The findings were recorded and patient was managed accordingly.

We have followed Early treatment diabetic retinopathy study (ETDRS) classification of diabetic retinopathy for classifying stages of the DR in all our patients. We have tried our best to differentiate changes of hypertensive retinopathy from changes of DR and to focus mainly on changes of DR, we have excluded those patients with any known uncontrolled systemic illness apart from diabetes which is likely to have effect on retina including hypertension and not taken changes of hypertensive retinopathy into account while doing statistical analysis.

The data was entered into Microsoft Excel sheet for statistical analysis. Percentage values were calculated whenever applicable.

RESULTS:

The study included 48 patients out of which 30 (62.50%) were males and rest 18 (37.50%) were females. Age of the patients was in the range of 40 to 65 years. Maximum duration of diabetes in these patients was 28 years and minimum was 3 years. In maximum patients duration of diabetes fell in range of 5-10 years (29.16% patients) and 15-20 years (25% patients).Out of 48 patients, 26 (54%) patients had family history of diabetes.In our study, 28 (58.33%) patients had associated hypertension which was most common systemic association found followed by hyperlipidaemia (9 patients- 18.75%).

Majority 38 (79.16%) patients were on oral hypoglycaemic drugs. 7 (14.58%) patients were on insulin injection and rest 3 (6.25%) patients were using both. Overall long term glycemic control and associated systemic conditions was asked and hence this was a subjective finding. Among 13 patients with history of irregular treatment, 5 patients had changes of proliferative diabetic retinopathy (PDR) on FFA which is 38.46%. From rest 35 patients with tight glycemic control, only 5 patients were diagnosed as PDR on FFA which is 14.28%. This proves direct relation of severity of retinopathy with level of glycemic control. The ophthalmoscopic findings of both eyes of each patient were compared with FFA findings. A total of 96 eyes of 48 patients were examined, findings of which are summarised in the table below. (Table 1, 2)

Table 1: Comparison Of Interpretation Of Background Retinopathy By Ophthalmoscopic Examination And FFA

Interpretation	Number of eyes detected by ophthalmologic examination	Number of eyes detected by FFA examination
Normal fundus/ No DR	4 (4.16%)	1(1.04%)
Very mild NPDR	8(8.33%)	4(4.16%)
Mild NPDR	21(21.87%)	18(18.75%)
Moderate NPDR	27(28.12%)	21(21.87%)
Severe NPDR	24(25%)	25(26.04%)
Very severe NPDR	12(12.50%)	17(17.70%)
Mild to moderate PDR	Exclusion criteria	10(10.41%)
High-risk PDR	Exclusion criteria	0
Advanced diabetic eye disease	Exclusion criteria	0
Total	96 (100%)	96 (100%)

Table 2: Comparison Of Interpretation Of Diabetic Macular Edema (DME) By Ophthalmoscopic Examination And FFA

Interpretation	Number of eyes detected by ophthalmologic examination	Number of eyes detected by FFA examination
DME without background DR	6(6.25%)	8(8.33%)
Any stage of NPDR with DME	25(26.04%)	32(33.33%)
Any stage of PDR with DME	Exclusion criteria	2(2.08%)

Ophthalmoscopically 4 (4.16%) eyes were coined as normal but on FFA examination only one eye turned out to be normal and rest 3 eyes were actually NPDR which were missed on clinical examination. In our study, 10 (10.41%) eyes were actually PDR but misdiagnosed as NPDR ophthalmoscopically which were eventually picked up on FFA. This completely changes the management of disease and early diagnosis could prevent irreversible vision loss in the patient. On ophthalmological examination only 31 (32.29%) eyes were diagnosed as having DME, whereas FFA could pick up 42 (43.75%) eyes with DME, which were managed accordingly. (Table 3)

Table 3: Conclusive Table Regarding Comparison Of Ophthalmological Examination And FFA

Diagnosis	Number of eyes detected by ophthalmologic examination	Number of eyes detected by FFA examination
Normal Fundus	4(4.16%)	1(1.04%)
NPDR	92(95.83%)	85 (88.54%)
PDR	Exclusion criteria	10(10.41%)
DME	31 (32.29%)	42(43.75%)

In our study, no patient suffered from any serious side effects of fluroscein dye.

DISCUSSION:

In cases of posterior segment pathologies sometimes the clinical examination alone is not sufficient for diagnosis and management. Fluorescein angiography was invented in 1961 by Dr. Novotny and Dr. Alvis. This investigative modality has enhanced the diagnostic accuracy of ophthalmic examination. [1]

Purpose of the present study is to determine practical value of fluorescein angiography with regards to its role as a diagnostic, confirmatory and prognostic indicator.

Wykes et al in their study in 1991 on 330 patients concluded that "treatment could have proceeded without FA only in 24% of diabetic patients".[2] Barta et al in their study on 124 patients stated that "microaneurysm of size 10-30µ can be detected by FA while ophthalmoscopy can see microaneurysm above size of 30 µ only". [3]

Jain IS et al in their study at PGI, Chandigarh on 44 pateints stated that "major contribution of FA is differentiate new vessels from collaterals. Presence of non perfusion areas and broken foveal arcades can be demonstrated on FA". [4]

Kimmel AS et al evaluated diabetics under the age of 20 years by FA. This study emphasized the importance of having prepubescent and teenage diabetics examined for presence of maculopathy. [5]

In our study we have examined 96 eyes of 48 patients in whom both FFA and clinical ophthalmoscopy was done for detection of retinopathy changes. We found that micro aneurysms are seen and defined much better and can easily be differentiated from dot and blot haemorrhages and thrombosed capillaries on FFA. FFA is useful to recognize early diabetic changes in the retina where small microaneurysms are easily picked up where ophthalmological examination can miss it and misdiagnose it as 'normal fundus'. The number and degree to which microaneurysms leak can be assessed and is important to grade NPDR as mild, moderate or severe. The appearance and disappearance of microaneurysm indicates the activity of retinopathy. FFA was

helpful in locating ischaemic areas and leaking new vessels especially when the new vessels are small in area and the location is peripheral where it is not very obviously detected using ophthalmoscope. It can also be used in cases post panretinal photocoagulation where ophthalmological examination can easily miss residual CNP areas and newly developed small vessels.FFA is also useful in ruling out diabetic maculopathy especially the ischaemic type which is not easily recognized by ophthalmoscope.

In our study 5 patients showed areas of non perfusion in the retina of which 3 were involving the macula. FFA showed leakage in 5 cases in periphery from early subtle neovascularisation which was missed on clinical fundus examination. These patients underwent laser therapy eventually. DME was picked up in 11 more patients on FFA compared to ophthalmoscopic examination which underwent anti- VEGF injections.This shows how drastically the management was changed for these patients.

FFA is a relatively safe procedure to perform but utmost precautionsis to be taken to deal with the emergencies which can be fatal.

CONCLUSION

Fundus flourescein angiography helps to a great extent in evaluating diabetic retinopathy for diagnosis, classification and treatment. It is also useful for post laser evaluation & decision for further treatment & prognosis of the eyes. Considering early and accurate diagnostic power of FFA combined with low rate of complications of the procedure, FFA can be very useful tool for guiding and monitoring the therapy in cases of DR. This becomes extremely valuable when the patients are likely to be lost on follow up in a setting like us.

There is a definite indication for use of FFA in diabetic patients, especially in doubtful early proliferative diabetic retinopathy, suspected maculopathies & assessment post laser treatment . Every retinal physician should make most of this very useful investigation which is sadly taking relatively backstage in array of newer investigations in the current scenario.

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