Research Article

Serum HbA1c level and Central Macular Thickness in Diabetic Cystoid Macular Edema

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(Received: August, 2016) (Accepted: January, 2017)

ABSTRACT

A randomized, prospective, interventional comparative study was conducted in 60 eyes of 30 diabetic patients with diabetic cystoid macular edema for 16 months. The eyes were categorized as Group A consisting 30 eyes of 15 patients and group B consisting 30 eyes of 15 patients. The purpose of the study was to compare the effect of serum HbA1c level in diabetic cystoid macular edema patients with and without serous macular detachment. Patients of group A were including patients had diabetic cystoid macular edema in both eyes but no serous macular detachment and in group B patients had diabetic cystoid macular edema in both eyes with serous macular detachment. The outcomes were different from baseline to 3 month, 6 month and 9 month follow up in mean HbA1c level and mean central macular thickness(CMT). Mean baseline serum HbA1c levels in percentage (%) were 7.91(SD 1.31) in group A and 11.42(SD 1.91) in group B. At 3 month of follow up the mean baseline HbA1c level in group A is 7.56(SD 1.04) and in group B is 10.32(SD 1.44). At 6 months, group A is 7.26(SD 0.97) and in group B is 9.44(SD 1.36) and After 9 months of follow up group A is 6.78(SD 0.75) and in group B is 8.32(SD 1.15). Mean baseline central macular thickness (CMT) in micron were 688.13(SD 50.05) in group A and in group B mean central macular thickness is 681.33(SD 59.76). After At 3 months the mean central macular thickness(CMT) of group A is 446.73(SD 80.85) and in group B is 568.86(SD 52.34). After 6 months, group A CMT is 375.93(SD 64.68) and group B CMT is 486.66(SD 60.71) . After 9 months of follow up ,in group A the CMT is 289.00(SD 70.56) and in group B is 376.60(SD 49.18). The significant reduction in mean serum/ HbA1c level also shows the reduction in the mean CMT.

KEY WORDS: central macular thickness; diabetic cystoid macular edema; serum HbA1c level

INTRODUCTION:

The World Health Organization (WHO) estimates that more than 180 million people worldwide have diabetes, and this number is expected to increase and to rise to epidemic proportions within the next 20 years[1]. Diabetic retinopathy, one of the most frequent complications of diabetes, remains a major public health problem with significant socioeconomic implications, affecting approximately 50% of diabetic subjects, and remains the leading cause of blindness in working-age populations of industrialized countries.

Macular oedema occurs when fluid and protein deposits collect within the macula, leading to thickening and swelling which distorts central vision.

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It is a common final pathway for many ocular diseases, including diabetic retinopathy, vascular occlusions, postsurgical conditions and uveitic diseases. The pathophysiological process is a breakdown of the blood-retinal barrier (BRB), which normally prevents water movement in the retina, thus allowing fluid to accumulate in the retinal tissue. Inflammatory processes and an increase in vascular permeability play a central role. Different mechanisms, complicated by ischaemic conditions, interact in a complex manner. Key factors are angiotensin II, prostaglandins and the vascular endothelial growth factor (VEGF).[2]

Cystoid macular oedema (CMO)[3] is characterised by intraretinal oedema contained in honeycomb-like (cystoid) spaces filled with clear fluid. The underlying cause is thought to be disruption to the BRB. Retinal cells are displaced by the cysts, so the fluid affects both cell function and cell architecture. Depending on the aetiology, CMO is usually self-limiting and spontaneously resolves within 3-4 months. Resolution may be helped via

medical or surgical options. If the oedema is chronic (more than 6-9 months) permanent damage to photoreceptors with retinal fibrosis can occur. CMO is a common 'endpoint' pathological response to a variety of insults to the macular area.

Serous macular detachment (SMD) may occur in conditions where retinal vascular leakage or Retinal pigment epithelium (RPE) dysfunction is seen, for example, in diabetic macular edema, branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), hypotonous maculopathy, retinal vasculitis and retinal macro-aneurysm. SMD associated with macular edema has been demonstrated in 15–46% of eyes with diabetic ME, 38–71% of eyes with BRVO, and 82% of eyes with CRVO. Although the exact mechanism of development of SMD is not known, it is probably due to excessive fluid flow from the abnormal retinal vessels, which overwhelms the RPE pump leading to serous retinal detachment.[4-11]

MATERIALS AND METHODS:

A total of 30 patients of either sex suffering from diabetes with cystoids macular edema were evaluated and randomly divided into two groups (group A and group B) were included in this study conducted in the Department of Ophthalmology, Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh, India over a period of 16 months from January 2015 to April 2016. The procedures followed were in accordance with the Ethical Standards Committee on Human Experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000. The necessary permission from the Ethical and Research Committee was obtained for the study.

Group 'A' included 30 eyes of 15 patients who had cystoids macular edema without SMD and group B included 30 eyes of 15 patients who had CME with SMD. CME was confirmed by the fundus fluorescein angiography and SMD was confirmed and documented by optical coherence tomography (OCT). The serum HbA1c levels were measured by liquid chromatography and the central macular thickness (CMT) were measured by OCT. Inclusion criteria comprised of all patients with diabetes having diabetic retinopathy, the presence of clinically significant macular oedema in the fundus examination, the presence of fluroscein angiographically confirmed diabetic macular oedema, the presence of CME and serous macular detachment documented by OCT . Exclusion criteria comprised of non diabetics with macular oedema, patients having undergone vitreo retinal surgery in past, eyes that had received previous grid laser photocoagulation,the presence of epiretinal membrane or vitreo-macular traction documented by OCT, the presence of dense media opacity or pre-retinal haemorrhage that might prevent OCT examination, eyes with previous intraocular surgery or vitreo-retinal pathology other than diabetic retinopathy, cataract, glaucoma, problem in follow-up or documentation.

The patients underwent complete ophthalmic examination, including best-corrected VA measurement were done as per logMAR, slitlamp biomicroscopy and fundus examination done with a 78/90 diopter noncontact lens and , OCT and FFA were done. OCT and FFA examinations and collection of venous blood samples were performed on the same day. The central macular thickness was measured automatically using the topography software built into the OCT device.

The patients were followed up for measuring HbA1c level, FFA, OCT for each eye at 3 month, 6 month, 9 month respectively. The patient's protocols were recorded in data collection form. Quantitative data were expressed as mean and qualitative variables were expressed using percentages. We applied t-test-two-sample assuming unequal variance, after calculating the variance of each data groups respectively. The p-value of < 0.05 for one - tailed hypothesis was considered statistically significant to reject the 'null hypothesis'. All statistical calculation/descriptive analysis were made with the help of data analysis tool of Microsoft Excel 2007.

RESULTS:

Majority of the patients 40% (12 patients) in the study group were >60 years of age in both groups (range 30 years to 70 years). The study included 11 males (73.33%) and 4 females (26.66%).and group B also had 11 males (73.33%) and 4 females (26.66%). The mean duration of diabetes in months in group A was 8.4(SD 2.94) and in group B the mean was 49.6(SD 24.36). The mean baseline visual acuity BCVA as per log MAR in group A was 0.7447(SD 0.23) and in group B was 1.0314 (SD 0.33).

The mean baseline HbA1c level in percentage (%) group A is 7.91(SD 1.31) and in group B mean baseline HbA1c level was 11.42 (SD 1.91) and p value comes out 2.07 indicating that there was no statistically significant difference in HbA1c level in two groups.

In our study the mean baseline central macular thickness (CMT) in micron was 688.13 ± 50.05 in

group A and in group B mean central macular thickness is 681.33±59.76 .The p value was 0.25 indicating that there was no statistically significant difference in mean baseline central macular thickness (CMT) in two groups.

After 3 months of follow up the mean baseline HbA1c level in group A is 7.56±1.04 and in group B was 10.32±1.44 and the p value is 1.3417 which is statistically not significant. At 6 months, the mean baseline HbA1c level in group A was 7.26±0.97 and in group B was 9.44±1.36 and the p value is 0.0012 which is statistically significant. After 9 months of follow up the mean HbA1c level of group A was 6.78±0.75 and in group B was 8.32±1.15 and the p value is 0.0010 which still showed statistically significant decreased.

Table 1: Age Distribution in study group.

Age group (years)	Number of patients	Percentage
31-40	01	3.33%
41-50	10	33.33%
51-60	07	23.33%
61-70	12	40%

Table 2: Gender Distribution in study group.

Sex	Group A	Group A %	Group B	Group B %
Males	11	73.33%	11	73.33%
Females	04	26.66%	04	26.66%

Table 3: Mean Duration of Diabetes in Months of Group A and Group B.

Duration of DM	Group A	Group B	p value
Mean	8.4	49.6	0.007
SD	±2.94	±24.36	

At 3 months the mean central macular thickness(CMT) of group A was 446.73±80.85 and in group B was 568.86±52.34 and the p value is 0.0026 which showed statistically significant. After 6 months, group A CMT was 375.93±64.68 and group B CMT was 486.66±60.71 and p-value is 0.0021 that is statistically significant. After 9 months of follow up, in group A the CMT was 289.00±70.56 and in group B was 376.60±49.18 and the p value comes out 0.0028 which also showed statistically significant.

DISCUSSION:

Diabetic retinopathy (DR), a major microvascular complication of diabetes,has a significant impact on the world's health systems. It is projected that number of people with DR worldwide will grow from 126.6 million in 2010 to 191.0 million by 2030, and the number with vision-threatening diabetic retinopathy (VTDR) is expected to increase from 37.3 million to 56.3million.[12] According to the latest World Health Organization (WHO) report, India has 31.7 million diabetic subjects, and the number is expected to increase to 79.4 million by 2030[13].

This study included total 22 males (73.33%) and 08 females (26.66%). Majority of subjects in the present study were more than 60 years. Our result were consistent with the finding of Burak Turgut, Fatih Cem Gul, Nevin Ilhan(2010)[14] showing in his study that the

Table 4: Mean Baseline Bcva (logmar) in two Groups.

BCVA (log MAR)	Group A	Group B
Mean baseline VA	0.7447	1.0314
SD	±0.2361	±0.3388

Table 5: Mean Baseline Hba1c Level in Percentage(%) in Both Groups.

Baseline (HbA1C level)	Group A	Group B	p value
Mean	7.91%	11.42%	2.07
SD	±1.310	±1.913	

Table 6: Mean Baseline CMT (in Micron) in Both Groups.

Mean baseline CMT in µm	Group A	Group B	p value
Mean	668.13	681.33	0.25
SD	±50.05	±59.76	

Table 7: Follow up of Mean Hba1c Level Baseline in Group A & B.

Follow up at	Mean HbA1C level in %		p value
	Group A	Group B	
3 Months	7.56±1.04	10.32±1.44	1.3417
6 Months	7.26±0.97	9.44±1.36	0.0012
9 Months	6.78±0.75	8.32±1.15	0.0010

Table 8: Follow up of Central Macular Thickness (cmt) in Group A & B.

Follow up at	Mean CMT in µm		p value
	Group A	Group B	
3 Months	446.73 ±80.85	568.86 ±52.34	0.0026
6 Months	375.93 ±64.68	486.66 ±60.71	0.0021
9 Months	289.00 ±70.56	376.60 ±49.18	0.0028

mean age was 62.9 ± 6.95 years (48–78) in group1 and 63.53 ± 6.04 years (52–73) in group 2. Our results were also consistent with the finding of Michael Larsen, Maria Wang et al, (2005)[15] did a prospective study of twelve eyes in 12 patients aged 39 to 78 years (mean age 57) with fovea-involving diabetic macular edema and 14 eyes in 7 healthy volunteers aged 30 to 70 years (mean age 57). Ling Yeung, Chi-Chin Sun, Wan-Chen Ku(2009)[16] had also found the mean age of diabetic patients is 62.2 years in his study.

Our study shows significant correlation between the reduction of HbA1c level and also decrease the CMT measured by OCT, that findings is consistent with Neil H. White, Wanjie Sun(2010)[17], clearly demonstrated in his study that the benefits of intensive diabetes therapy aimed at lowering blood glucose and HbA1c (A1C) as near to the normal range as safely possible. Ong Ming Jew, Mohammadreza Peyman, Tan Chen Chen, Subrayan Visvaraja (2012)[18] also demonstrate in his study that the HbA1c and total cholesterol are the two most important risk factors associated with CSME in patients with NPDR. Cho TH et al (2008)[19] also clearly showed in his study that the strict sugar control decreased the risk of diabetic macular retinopathy, and OCT could be an excellent detector of early diabetic macular oedema.

Studies have shown that the reduction of (CMT) by using various treatment modalities and the CMT finding is consistent with Kiyoshi Suzuma et al (2011)[20]. LingYeung et al (2009)[21] found in his study that linear regression chronic HbA1c level also showed reduction in mean CMT. Our study is not consistent with Demir M et al (2013)[22]. His study showed the no statistically significant relationship was found between CMT, HbA1c, and fasting plasma glucose level in either group (p=0.05).

CONCLUSION:

In our study the diagnosis of SMD in patients with diabetic CME by OCT might suggest that these patients have poorer metabolic control than those who have only CME.

Elevated HbA1c is a well-known risk factor for diabetic macular edema. Prolonged hyperglycemia is known to significantly increase the rate of macular edema, while reduction of HbA1c levels with strict glycemic control decreases the rates of clinically significant macular edema, cystoid macular edema, serous macular detachment and other microvascular complications and also noticed the reduction of central macular thickness.

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Cite this article as: Kumar J, Verma A, Dwivedi S, Pathak AK: Serum HbAlc level and Central Macular Thickness in Diabetic Cystoid Macular Edema. PJSR ;2017:10(1):7-11.
Source of Support : Nil, **Conflict of Interest**: None declared.