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Meibomian Gland Dysfunction as an Indicator of Hypercholesterolemia: A Case Control Study.

Preethi P Hegde[1], Sudhir Hegde[1], Akansha Shetty[1]
[1]Department of Ophthalmology, AJ Institute of Medical Sciences and Hospital, Mangalore, Karnataka.

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ABSTRACT

Background: Chemical analysis of lipids secreted from meibomian glands shows that it consists of a mixture of non-polar and polar lipids. Systemic dyslipidemia may theoretically affect the meibomian lipid composition and secretion. The purpose of this study was to investigate a possible correlation between Meibomian gland dysfunction (MGD) and hypercholesterolemia and that MGD may become a marker of previously unknown hypercholesterolemia. **Methods:** After obtaining approval of the Institutional Ethics Committee, a case control study was undertaken in the Department of Ophthalmology, AJ Institute of Medical Sciences and Hospital from August 2016 till January 2017 enrolling 60 MGD cases and 100 controls. Patients satisfying inclusion and exclusion criteria were enrolled and examined using pre-specified clinical criteria. Using statistical analysis serum lipid profile was compared for cases and controls. **Results:** 60 cases of MGD and 100 controls with average age 48.03±12.05 and 44.61±12.11 years respectively were enrolled. Higher serum triglyceride levels were seen in cases (144.03±55.54 mg/dL) and so were higher low density lipid levels (122.16±39.41 mg/dL). MGD cases had higher levels of high density lipids (42.36±13.16 mg/dL) and controls had 41.38±12.17. Using Fisher's exact test, gender of the subjects was found to be statistically significant for MGD development (p=0.006). Distribution of serum cholesterol and low density lipids was found to be statistically different across the different categories of MGD; p=0.006 and p=0.037 respectively. **Conclusion:** This study suggests that MGD can act as a clinical marker for hypercholesterolemia. Larger, multi-centric studies are required to confirm our findings.

Keywords: Hypercholesterolemia, lipid profile, meibomian glands.

INTRODUCTION

Meibomian gland dysfunction (MGD) is an extremely common chronic condition of the posterior eyelids. The International workshop on MGD has defined MGD as a chronic, diffuse abnormality of the meibomian glands commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease. MGD being the most common cause of evaporative dry eye disease, it is important to recognize its presence in a patient complaining of dry eye-like symptoms, although it is not known how many functioning meibomian glands are necessary to maintain the anti-evaporative effects of a normal lipid layer.

Atherosclerosis is the most common underlying pathology in patients with cardiovascular disease (CVD). By evaluating the incidence of coronary events, the contribution of triglyceride-containing lipoproteins to atherosclerosis progression, and the incidence of cerebrovascular ischemic events, the effect of abnormal triglyceride metabolism on atherosclerosis has been studied extensively in the literature. Recent studies have correlated increased cholesterol levels in meibomian secretions to patient's MGD. Meibomian glands, which are tubuloacinar holocrine glands that discharge their entire contents during the secretion process, produce the tear film lipid layer. Chemical analysis of lipids secreted from normal meibomian glands shows that it consists of a mixture of non-polar lipids (wax esters, cholesterol, and cholesterol esters) and polar lipids (phospholipids and glycolipids). Systemic dyslipidemia may theoretically affect the meibomian lipid composition and secretion.

The purpose of this study was to investigate a possible correlation between MGD and hypercholesterolemia. MGD may become a marker of previously unknown hypercholesterolemia and ophthalmologists may increase their role in the early detection of an important risk factor for cardiovascular disease.

Name & Address of Corresponding Author
Dr. Preethi P Hegde
Department of Ophthalmology
AJ Institute of Medical Sciences and Hospital
Mangalore, Karnataka.

MATERIALS AND METHODS

Study Design and Setting

We designed a case control study to understand the correlation of hypercholesterolemia and MGD. This study was conducted in the Department of Ophthalmology, AJ Institute of Medical Sciences and Hospital, India from 1st August 2016 till 31st January 2017. AJ Institute of Medical Sciences and Hospital is located in Mangalore, Karnataka. This over 1000 bedded tertiary level teaching hospital is a major healthcare provider in the region and has a large catchment area. The patients were diagnosed with MGD as per the standard clinical guidelines as described below and as found suitable by the treating ophthalmologist.

Sample population

After obtaining approval of the institutional ethics committee, patients were approached with an informed consent for participation in the study. For the study we recruited 60 cases of MGD and 100 controls. For the diagnosis of MGD we used the definition given by the International Workshop on MGD, as explained above. Exclusion criteria was age less than 18 years, a history of hypercholesterolemia or use of lipid lowering drugs, supplements like omega-3 fatty acids, topical corticosteroids, chronic conditions like Sjogren syndrome, active keratoconjunctivitis, inflammatory or allergic ocular surface diseases unrelated to MGD, or any ocular surgery in the past 9 months, any rheumatologic, or dermatologic disorder affecting the health of the ocular surface. Age and gender matched controls were chosen from accompanying friends, family. All controls underwent ophthalmic examination and were excluded using the same exclusion criteria as for cases.

Data Collection and Data Analysis

The diagnosis of MGD was made by clinical examination, based on glandular obstruction and quality of the secretions. While observing the ease of excretion and quality of the secretions under slit-lamp microscope the grading was obtained by firm digital pressure over the central third of the upper and lower eyelid. Meibomian gland obstruction was graded as 0 if there is no obstruction or the secretion is easily expressed, 1 if mild obstruction is present and secretions are expressible with mild pressure, 2 if moderate obstruction is seen or the meibum is expressible with moderate pressure, and 3 if complete obstruction is there or no glands are expressible, even with hard pressure. Quality of expressed meibum was graded as follows: 0 (clear fluid), 1 (cloudy fluid), 2 (cloudy particulate fluid), and 3 (toothpaste-like). Patients graded 2 or higher on either of these scales in either eye during their baseline meibomian gland evaluation were diagnosed with moderate to severe MGD and included in this survey. All cases and controls underwent lipid profile tests. For each patient, we noted serum cholesterol, high and low density lipids and triglyceride levels. Data obtained from hospital was codified and entered into Microsoft excel sheets. Data were then imported in to Statistical Package for Social Sciences (SPSS) version 21 and descriptive analysis was performed. Analysis was done using Fisher's exact test and Mann Whitney U test to check for statistical significance. P value less than 0.05 was taken as statistically significant.

RESULTS

Table 1: Baseline characteristics of patients included in the study

Variable	Cases	Controls
Number	60	100
Average age	48.03 ± 12.05	44.61± 12.11
Males	27	62
Average serum cholesterol level (mg/dL)	177.63 ± 55.08	152.43 ± 43.91
Average serum triglyceride level (mg/dL)	144.03 ± 55.54	129.17 ± 55.62
Average serum high density lipid level (mg/dL)	42.36 ± 13.16	41.38 ± 12.17
Average serum low density lipid level (mg/dL)	122.16 ± 39.41	109.53 ± 32.16

Table 2: Variation among cases and controls

Variable	Cases	Controls	p value
Males	27	62	0.48
Females	33	38	
Smoking history	5	8	1.000
Hypertension	11	11	0.237
Diabetes mellitus	6	6	0.368
Distribution of serum cholesterol across all categories of cases			0.006
Distribution of serum low density lipids across all categories of cases			0.037
Distribution of serum high density lipids across all categories of cases			0.669
Distribution of serum triglycerides across all categories of cases			0.054

During the study period, we recruited 60 cases of MGD and 100 controls. Average age of MGD cases was 48.03±12.05 and that of controls was 44.61±12.11 [Table 1]. There were 89 males in total, 27 of which were cases. Average serum cholesterol of MGD cases was 177.63±55.08 mg/dL and that of controls was 152.43±43.91 mg/dL. Higher serum triglyceride levels were seen in cases (144.03±55.54 mg/dL) and so were higher low density lipid levels (122.16±39.41 mg/dL). MGD cases had higher levels of high density lipids (42.36±13.16 mg/dL) and controls had 41.38±12.17. Using Fisher's exact test, gender of the subjects was found to be statistically significant for MGD development (p=0.006) [Table 2]. No other variable like smoking history, diabetes or hypertension were

found to be statistically significant with the diagnosis of MGD. Distribution of serum cholesterol was found to be statistically different across the different categories of MGD (p=0.006). Similarly, distribution of low density lipids was found to be statistically different across different categories of MGD (p=0.037). [Table 2]

DISCUSSION

This study looked at the possibilty of using MGD as a clinical indicator of hypercholesterolemia. We found significant association of serum cholesterol and serum low density lipids with different grades of MGD. Symptoms of MGD are nonspecific and include burning, irritation, itching, red eyes, and decreased or fluctuating vision. The etiopathological mechanism behind MGD are not fully understood, but studies have suggested that it is probably caused by an altered composition of meibum or an obstruction of the meibomian glands secondary to hyper-keratinization of the duct epithelium and plugging with a solidified secretion. These changes result in altered tear film lipid layer which can evaporate more easily, resulting in dry eye signs and symptoms.

Meibomian gland secretion consists largely of neutral sterol and wax esters with relatively lesser proportions of polar lipids, diesters, triesters, triglycerides, free fatty acids, and free sterols. Considerable variation in lipid composition among normal individuals has been shown by previous literature. Also it is known that the lipid composition in normal individuals varies greatly from that in patients with meibomian gland dysfunction. Spectroscopic studies have demonstrated a gradual decline in the phase transition temperature of meibum with age in normal subjects but a marked increase in phase transition temperature in MGD. All these changes result in increased viscosity of the lipid secretion. A higher cholesterol concentration in meibum would increase the meibum melting point, also increasing its viscosity and causing meibomian gland plugging. Overall, previous data suggest that elevated cholesterol may be implicated in the development of MGD.

Total cholesterol level should be less than 200 mg/dl according to the US National Cholesterol Education Program. Increased levels of LDL or decreased levels of HDL, with or without other risk factors, have been reported to increase the risk of cardiovascular disease. Dao et al showed that patients with moderate to severe MGD have a higher incidence of elevated total cholesterol than the general population. These authors also observed that the HDL levels contributed most to this increase in incidence of MGD.

Our study has some limitations. Due to the small sample size, the results of our study might not be generalizable to other geographical regions. Secondly, we sampled our population from a single centre, thereby limiting our ability to apply our findings to racially different populations.

CONCLUSION

Our findings suggest that MGD can act as a clinical marker for hypercholesterolemia. Larger, multi-centric studies are required to confirm our findings. MGD may become an important clinical marker of previously unknown hypercholesterolemia and there is an increased role of ophthalmologists in the early detection of an important risk factor for cardiovascular disease.

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