Prevalence of Meibomian Gland Dysfunction through a Novel Automated Non- invasive Ocular Surface Analyser: A hospital-based study

Introduction

Meibomian gland dysfunction (MGD) has grown as one of the most common causes for seeking ophthalmological consultation in today's modern world. It is defined as a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/ quantitative changes in glandular secretion, which can result in alteration of the tear film, inflammation, ocular surface disease, and symptoms of eye irritation.[1] Obstruction of the terminal duct and orifice due to hyperkeratinization is one of the important factors in the causation of MGD as the meibum is stuck inside the gland leading to qualitative and quantitative changes in glandular secretions. MGD is the leading cause of evaporative dry eye[2] and is also frequently found in aqueous-deficient dry eye. The prevalence of MGD is usually underestimated due to nonspecific nature of patient's symptoms and poor correlation between severity of symptoms and signs of the disease. Systemic factors like androgen deficiency and dyslipidaemia have been reported to be associated with MGD.

Prevalence of MGD in different populations has been reported to range from 38% to 68%[3] with a higher prevalence in Asians.[4] In this study we aimed to study the prevalence of both asymptomatic and symptomatic MGD and assess its ocular and systemic associations in a hospital based setting using a non-invasive ocular response analyser.

Materials and Methods

Study design This was an observational, cross-sectional study conducted at Dr. R.P. Centre, AIIMS, Delhi. The study was in accordance with the Declaration of Helsinki and was commenced after obtaining approval from Institutional Ethics Committee, All India Institute of Medical Sciences, New Delhi, India. Consecutive patients, aged 18 years or above, attending the ophthalmology outpatient department of our hospital and consenting to participate in the study were included.

Subject Recruitment and Screening All participants of the study underwent a standardized symptom questionnaire specific to dry eye symptoms and as modified by the Lekhanont et al.[R] Demographic details, systemic illness and ophthalmic/ non-ophthalmic medication use was noted. Similar to Lekhanont et al[R] presence of 1 or more symptoms often or all the time was considered significant. After an initial assessment of visual acuity, measurement of meibomian gland and tear film related parameters was performed using a non-invasive Ocular Surface Analyzer (I.C.P. OSA, SBM Sistemi). Non-invasive break up time (NIBUT), tear meniscus height (TMH), lipid layer thickness (LLT), non- contact meibography of upper lid was performed on OSA in the above mentioned order. For measurement of NNIBUT, median of three readings on interferometry was taken using I.C.P. Tearscope (SBM Sistemi, Turin, Italy). LLT was recorded after asking the participants to quickly blink three times, which ensured an even distribution of the lipid layer over the cornea. The observed patterns of lipid layer on interferometric evaluation of LLT were graded from 0-5. Infrared meibography of the upper lid was performed for estimating the morphological changes in the glandular tissue. Meibomian gland loss was represented as the percentage of area of the missing glands in upper tarsal plate. Subjects with meibomian gland loss of ≥ 20 % were labelled as those affected with MGD and the remaining subjects served as controls.

On slit lamp examination each lid margin was carefully examined for evidence of meibomian gland dysfunction. Presence of one or all of the following clinical signs; meibomian orifice obstruction (MOO), meibomian gland blockage, lid margin telangiectasia and eyelash contamination was labelled as MGD. Following this, corneal staining was performed using 1% Sodium Fluorescein strips and presence, area and pattern of corneal stain was documented. Presence or absence of filamentary keratitis was also looked for.

Participants with acute ocular infection or inflammation, history of ocular surgery (< 3 months) and ocular trauma, recent use of contact lens (<2 weeks) and uncontrolled systemic disease were excluded from the study.

Statistical analysis Pearson chi square/ Fischer's exact for qualitative data, Mann-Whitney U test for non-parametric data, Two- sample t test for normal distribution data. The correlation between OSA parameters was performed using Spearman correlation test. Receiver operating characteristic (ROC) curves with calculations of the area under the curve (AUC)

were used to describe the accuracy of each parameter for differentiating patients with MGD from controls. Results were considered statistically significant for P<0.05.

Results

Demographic characteristics and clinical features A total of 225 eyes of 113 patients were included in the study of which 62 (54.9%) were males and 51(45.13%) females. The mean age of the patients was 41.56±13.23 years (Range, 17- 65 years). The overall prevalence of MGD was 46.02% which was non-significantly distributed across all age groups (P=0.288). The MGD group had significantly older subjects as compared to non- MGD group (39.1± 12.8 vs 44.46± 13.3; P=0.03) and slightly higher percentage of males (53.85%) but this difference was statistically insignificant (P=0.84). Systemic comorbidities (diabetes mellitus, hypertension, rheumatoid arthritis and coronary artery disease) were identified in 46 of the participants but none were significantly associated with prevalence of MGD. The demographic profile of the subjects is summarized in Table 1. History of cataract surgery was present in 10 subjects of which 8 (80%) had MGD (P=0.024). 30 subjects in our study were identified with computer vision syndrome of which 12 (66.7%) were affected with MGD (P=0.524). 14 (26.92%) patients with MGD had visual acuity of 6/6 and 38 (73.08%) patients had a visual acuity of >6/6.

Dryness (42.31%) and foreign body sensation (42.31%) were the commonest ocular symptoms associated with MGD (P=0.749 and P= 0.110 respectively) followed by burning (40.38%; P=0.401) and redness (36.54%; P=0.625). 34 (65.38%) subjects with MGD had 1-2 ocular symptoms and 18 (34.62%) subjects with MGD had 3 or more symptoms (P= 0.845) (Table 2).

OSA parameters Median values of the MGL, LLT, NIBUT and TMH in MGD group are mentioned in Table 3. NIBUT (5.65 ± 3.49 vs. 6.9 ±4.1; P=0.023) and LLT (28.26±17.59 vs. 21.72±14.54; P=0.013) were significantly lower and MGL was significantly higher (32±11.04 vs. 19.75±19.16; P<0.001) in MGD group than in controls. There was no significant difference in TMH (0.18±0.05 vs. 0.17±0.04; P=0.892) between both groups. Distribution of MGL in patients with MGD is depicted in Figure 1. Maximum numbers of patients were seen to have meibomian gland loss between 26%-50% and no patient had MGL between 51%-75%. On correlation analysis a negative correlation was found between NIBUT and MGL (r=-0.32, P= 0.052) and MGL and LLT (r= -0.30, P= 0.016) and positive correlation was found between LLT

and TMH (r= 0.336, P= 0.014). No significant correlation was seen among other parameters. The ROC curves of NIBUT, LLT, MGL are shown in Figure 1. MGL had the highest AUC followed by LLT and NIBUT (Table 3).

Lipid layer type: distribution of various lipid layer patterns in MGD patient.

Discussion

Prevalence In this study an overall MGD prevalence of 46.02% was estimated in a clinic based setting using a non- invasive ocular surface analyser. Prevalence of MGD has been reported by various population based studies to be in the range of 3.5%-68.3% with higher prevalence noted in Asian population and lower in Caucasian population. Prevalence of 20%-90% have been reported by clinical studies targeting specific population like contact lens wearers and dry eye patients. All of these studies have used presence of clinical signs (meibomian orifice obstruction, lid telengectasia) as criteria to diagnose MGD. Till date there is no universally accepted definition and criteria for diagnosing MGD. The use of infrared meibography gives a more objective assessment of disease status. In our study, we have used percentage of meibomian gland loss in the upper lid as the criteria for diagnosing MGD. This helps by removing observer bias and can even detects asymptomatic cases of MGD.

Age An increase in the prevalence of MGD with increasing age has been reported by several studies. Similarly, in our study, the MGD group had significantly older population compared to controls. Most of the studies in literature whether population or clinic based have included older population (> 40 years) which can explain an increased prevalence of MGD in those studies. Our study had relatively younger participants over a wide range (17-65 years) as compared to other studies. An increase in the usage of electronic devices is believed to be responsible for more and more young people getting affected. (Schaumberg et al. 2011) Although the overall prevalence of MGD varied non-significantly across various age groups the older population (>60 years) did have a

Gender MGD group had relatively greater percentage of men than women in our study although this difference was non-significant. Similarly, et al also reported a non-significant higher prevalence in men. Studies with larger sample sizes have reported that MGD affects men more than the pre- menopausal women, and a protective role of estrogen role of sex hormones thus affecting postmenopausal women.

Systemic diseases MGD is a lifestyle disorder often by systemic factors increased diastolic BP a risk factor

H/O Cataract sx A history of cataract surgery is a definitive risk factor for MGD as 80% of those who had undergone cataract surgery at least 3 months before enrolment were affected. Computer vision syndrome is reported by to be a risk factor for MGD but it did not show any significance in our study. Often patients with MGD will complain of irritation and excessive weeping that occur more frequently at night or in the morning, when using the computer or perhaps spending time in excessively overheated and dehumidified environments.

Clinical signs and symptoms The non-specific signs and symptoms of MGD also pose a challenge in accurate diagnosis and management of the disease. The clinical tests correlated weakly to MG morphology and symptoms score was not related to changes in MG morphology. Contrary to our findings, Pult et al. reported significantly stronger correlation coefficients. Most studies have, however, reported inconsistent results with regard to the relationship between MG loss and clinical tests. Consistent with our findings, these studies also show that the strongest relationships were seen between MG morphology and meibum expression.

OSA Parameters Meibography allows in-vivo visualisation of meibomian gland morphology allows automatic determination. Meibography grading has been established as a reliable clinical test. Arita et al. demonstrated the diagnostic ability of their meibography grading scheme to discriminate between patients with MGD and healthy subjects. al that upper lid is the preferred lid for estimating MGL as it provides better interobserver variability

A previous report revealed that MG loss is directly linked to reduction of the lipid layer thickness in the tear-film which leads to shorter TFBUT. Thinner lipid layer thickness is associated with increased friction during blinking. Similarly in our study MGL had a negative correlation with NIBUT and LLT.

Meibomian gland dysfunction leads to reduced thickness of lipid layer in the tear film consecutively leading to unstable tear film and decreased tear break up time. NIBUT and LLT were significantly reduced in MGD group as compared to controls consistent with previous

studies. A negative correlation was seen between MGL and NIBUT and MGL and LTT indicating that

Giannaccare et al reported the highest AUC of non-invasive BUT. In contrast in our study the highest AUC was of MGL followed by LLT and NIBUT.

LLT

Slightly lower prevalence as compared to other Asian studies, but these studies targeted specific populations (dry eye patients, contact lens wearers) which could explain higher prevalence reported by them.

There is no study from Indian population estimating MGD prevalence. The OSA offers an effective, non-invasive, cost effective screening and diagnostic tool for MGD in busy clinics.

References

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