Treatment Outcomes in Patients with Meibomian Gland Dysfunction: Preliminary Findings of a Retrospective Clinical Study within an Orthoptist-Led Dry Eye Clinic

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ABSTRACT

Purpose: This study aimed to observe the treatment outcomes of participants presenting with meibomian gland dysfunction (MGD) with and without aqueous deficiency to an orthoptist-led dry eye clinic.

Methods: This was a single-site retrospective clinical study. Participants diagnosed and managed for meibomian gland dysfunction in a private Melbourne practice were included. Participants underwent either conservative treatment without meibomian gland expression (CT), conservative treatment with meibomian gland expression (CT-MGE) or combination therapy which included CT-MGE in conjunction with intense pulsed light therapy (CT-MGE-IPL). Outcome data included ocular surface disease index (OSDI), tear meniscus height (TMH), rate of tear film flow (RTFF), non-invasive tear film break-up time (NIBUT) and percentage of meibomian gland loss in the upper (MGUL) and lower lids (MGLL).

Results: Data was extracted from the electronic medical records of 284 participants (568 eyes) affected with dry eye disease (DED) which includes MGD with or without aqueous disease; 68% female with mean age of 63.3 years (±16.4). At baseline, 87.3% of participants had dry, irritated, painful eyes, 89.4% used topical lubricants while omega-3 intake and hydration levels were below recommended daily intake. Participants all underwent conservative treatment and were offered a choice for additional treatment including meibomian gland expression and intense pulsed light therapy which were both considered to be effective for the relief of MGD. All three treatment methods improved patient symptoms on OSDI and decreased the amount of meibomian gland loss. However, there was no improvement in TMH or NIBUT. The post treatment outcomes related to RTFF were mixed and findings suggest that the use of meibomian gland expression may yield better outcomes overall.

Conclusion: The findings of this study suggest that all treatments are effective in managing MGD, although outcomes may be better if management includes meibomian gland expression.

Keywords: dry eye disease, meibomian gland dysfunction, intense pulsed light

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INTRODUCTION

Dry eye disease (DED) is one of the most common ocular morbidities with prevalence estimates ranging from 5%, up to 52.4% with variations in part accounted for by demographic, lifestyle and environmental factors.[1-4] It is suggested that DED arises from a disruption to tear film homeostasis, leading to tear film imbalance and inflammatory events that further contribute to drying of the ocular surface.[5] Associations have been made between DED and a number of factors including infectious and traumatic aetiologies,[6] cardiovascular conditions and diabetes,[7,8] neural and auto-immune conditions,[9,10] and other comorbidities such as skin conditions,[11,12] gut-related illnesses[13,14] and compromised respiratory function.[15,16] In addition, physiological dehydration and a lack of dietary omega-3 are associated with DED, as are the use of some medications which also dry the ocular surface.[17]

DED is subdivided into two types, aqueous deficient and evaporative, with meibomian gland dysfunction (MGD) being the

most common cause of evaporative dry eye disease.[18] MGD is characterised by meibomian gland obstruction and both qualitative and quantitative changes to the gland's secretion of meibum. Symptoms of MGD vary widely and can have a significant effect on individuals world-wide. The effects of the disease cause reduced work productivity, difficulty with activities of daily living and a higher utilisation of specialist and other health care services.[19-22] In addition, the psychosocial impact of dry eye disease includes a higher rate of depression.[22]

First-line treatment for MGD generally involves lid hygiene and pharmaceutical topical lubricants or other topical preparations to treat infection, manage inflammation, thicken the tear film, improve corneal hydration, encourage corneal repair and protect neural tissue.[23,24] Thermal procedures are also often part of first-line treatment and have advanced from the traditional hot flannel warm compresses to specially designed eye masks that distribute heat more consistently across the eyelids, facilitating circulation and meibomian gland secretions.[25] However, such conservative treatment methods do not always lead to long term alleviation of symptoms.[26] As such, other treatments including intense pulsed light therapy (IPL) with or without meibomian gland expression (MGE), have been introduced as part of managing MGD.

MGE involves the forceful expression of meibomian glands to remove dense obstructions. IPL is designed to improve the outflow of meibum using light/thermal energy, but in contrast to heat masks the main effect occurs within the deeper layers of the skin, targeting cellular metabolism and promoting the quality of secretions to reach physiological homeostasis more quickly. However, the effectiveness of this procedure is yet to be understood[27] and few studies have compared the combination of conservative treatment with IPL and MGE to conservative approaches of treatment and the potential predictors of outcomes in the real word setting.

The aim of this study was to observe the treatment outcomes of participants presenting with MGD to an orthoptist-led ophthalmic clinic and to compare the effectiveness of conservative treatment without meibomian gland expression (CT), conservative treatment with meibomian gland expression (CT-MGE) or combination therapy which included CT-MGE in conjunction with intense pulsed light therapy (CT-MGE-IPL).

METHODS

Study design

This was a retrospective observational study of participants attending a single-site private ophthalmology clinic in Melbourne, over a two-year period between 2019 and 2021. Study procedures were approved by the La Trobe University Human Research Ethics Committee (HREC approval number 21284).

Participants

This study included participants above 18 years of age who were diagnosed with MGD, attended the clinic at least once and undertook either home-based CT, CT-MGE where meibomian gland expression was conducted in the clinic by the orthoptist, or combination therapy (CT-MGE-IPL). All participants diagnosed with MGD were included irrespective of severity, given that severity grading varies between studies depending on the outcome measures used and there are variations with ocular surface disease index (OSDI) score and meibography interpretations. Inclusion of all eyes irrespective of severity may assist to better understand which pattern of DED is associated with positive treatment outcomes.

All participants received a consultation with an ophthalmologist for baseline dilated ocular examination and diagnosis of MGD according to standard clinical procedure. Further investigation and management were provided by a single orthoptist trained in the management of DED. This included a full history and dry eye-related measurements using the Oculus Keratograph 5M®. The service model of care has been previously described[28] and this paper is a retrospective investigation of treatment outcomes, not an audit of the model of care.

Treatment exposure

For management, all participants received education and one course of CT initially. Thereafter, participants who received combination therapy that was unsuccessful in managing their dry eye, were counselled on their options and could choose their own treatment modality based on factors considered important to them such as cost, time and accessibility. This was a strategy thought to improve compliance. A complete description of the procedures used as standard care has been described previously.[28]

Data collection

Data was extracted from the medical files of each patient. This included demographics, treatment type, prior treatments used for DED and dietary intake including weekly omega-3, daily water (mL) consumption and caffeine (cups) intake.

Outcome measures

Outcome data for each eye per participant at baseline (first presentation), and at follow-up (the final dry eye clinic appointment), was extracted directly from medical files. The main outcomes for this study involved the Keratograph to gather the tear-meniscus-height (TMH), non-invasive tear-film break-up time (NIBUT), rate of tear film flow (RTFF) and meibography to grade the percentage of meibomian gland loss (MGUL and MGLL). DED is usually bilateral therefore, data for both eyes were utilised for analysis based on the methodology of other publications incorporating similar analyses.

Measurement of TMH is a repeatable and reproducible method for indirectly estimating aqueous production from the lacrimal and accessory lacrimal glands. The measurements are expressed in millimetres where TMH ≤0.20mm suggests possible aqueous

deficiency, whilst a recording of 0.20mm - 0.34mm is normal and ≥0.35mm indirectly suggests epiphora.[29] Whilst TMH can be more reflective of aqueous deficiency, in the real-world setting MGD does not occur in isolation. Mixed type DED includes an aqueous deficiency component and an evaporative component therefore, this study includes both evaporative DED and mixed DED. In many cases of evaporative DED, the TMH is borderline at initial presentation however, following treatment it appears to improve thus, it is included to determine whether or not it is a statistically significant finding.

The NIBUT is a valid and reliable measurement for assessing tear film balance with generally accepted values of ≤10 seconds considered abnormal.[30]

Tear film viscosity was assessed through a video recording to judge the velocity of particle flow, thereby determining the RTFF. The velocity was categorised as either medium, fast or slow, which suggested a normal state, poor absorbency or excessive absorbency respectively.

Lid margin assessments involved identifying meibomian gland expressibility, presence of telangiectatic vessels and lid hygiene. For this study meibography was the main quantifiable measure used to describe the presence of meibomian gland dysfunction by characterising the percentage of meibomian gland loss in the upper and lower lids using an infrared imaging technique.[31]

In addition to objective investigation of MGD, participants were also administered the OSDI questionnaire which is a validated 12-item questionnaire reporting symptom severity based on visual function, ocular symptoms and environmental triggers.[32] The final score is represented as a percentage where values below 12 are normal, 13 to 22 suggest mild severity, 23 to 32 moderate and ≥33 is severe. The OSDI was used at baseline and all subsequent visits.

Statistical analysis

Data was transferred for statistical analysis from Microsoft Office Excel Standard 2016 to IBM SPSS Statistics for Windows, Version 27.0 (Armonk, NY: IBM Corp). Prior to analysis, data was re-checked for accuracy, screened and cleaned.

Frequency analyses were calculated and the difference in significance of outcome data was checked between pre and post scores within treatment groups as well as between treatment groups. The data was checked for assumptions of normality using the Kolmogorov-Smirnoff test and non-parametric analysis was chosen accordingly.[32] Levels of significance were set at <0.05.

RESULTS

Demographics

This study included 568 eyes from 284 participants with a higher proportion of females (68%) compared to males (32%). The mean age of participants was 63.3 years (range: 21-94, SD 16.4). One hundred and seventy-seven participants (354 eyes) chose to undertake CT, 37 participants (74 eyes) chose CT-MGE and 70 participants (140 eyes) underwent CT-MGE-IPL treatment.

At presentation, most participants complained of dry, irritated or painful eyes (87.3%) and itchy eyes was also common (29.2%). Other complaints included epiphora (25%), blurred vision (24.6%), photophobia (20.1%) and discharge (12.3%). Many reported prior use of ocular lubricants (89.4%), while other prior therapies included anti-inflammatories (19.7%), antibiotics (9.2%), intraocular pressure lowering drops (14.1%), hot compresses (7.4%) and lid hygiene (3.2%).

Participants reported a mean water intake at baseline of 1,289.88mL (SD 772.6mL). 47.2% consumed one or more cups of coffee or black tea daily and a large proportion (71.8%) did not consume omega-3 either by diet or supplementation at baseline.

Effectiveness of treatment

Ocular surface disease index (OSDI)

The OSDI scores pre and post treatment, for all treatment groups are shown in Table 1. Higher scores indicate more severe symptoms. At baseline, the CT-MGE-IPL group had a significantly worse OSDI score (44.13) compared with the CT and CT-MGE groups (35.98 and 35.73, respectively) and this was statistically significant (Kruskall-Wallis H: χ^2 (2, n=568)=12.34, p=0.002). OSDI significantly improved post treatment for all groups (Wilcoxon Signed Rank Test z: p=0.000) with a small to medium effect size. Whilst the OSDI improved for the CT-MGE-IPL group post treatment, this was still significantly poorer than the scores for the CT and CT-MGE groups (Kruskall-Wallis H: χ^2 (2, n=416)=8.9, p=0.011).

Tear meniscus height (TMH)

The TMH before and after treatment, for all treatment groups is shown in Table 1. Mean TMH ranged from 0.30 to 0.34mm at baseline and was 0.32 to 0.41mm post treatment. At baseline, the mean TMH was similar for all groups and no difference was found between groups using the Kruskall-Wallis test (H: χ^2 (2, n=568)=5.11, p=0.78). TMH did not significantly change after treatment for any of the three groups (Wilcoxon Signed Rank Test z: p>0.05) and there was no difference between groups after treatment (H: χ^2 (2, n=411)=3.45, p=0.18). TMH of ≤0.2mm suggests that there is deficiency in the aqueous layer of the tear film which is causing symptoms, while any score between 0.20 and 0.34mm indirectly suggests normal aqueous production.

The proportion of participants with a score of ≤0.2mm at baseline was CT group 33.1%, CT-MGE group 35.5% and CT-MGE-IPL group 43.6%.

Non-invasive tear film break-up time (NIBUT)

A NIBUT measurement of ≥10 seconds is generally considered normal. The NIBUT before and after treatment, for both treatment groups is shown in Table 1 and the findings for all three groups at baseline and post treatment indicate below normal values. The Kruskall-Wallis test showed that the CT group had significantly better baseline NIBUT compared to the other treatment groups (H: χ^2 (2, n=567)=11.87, p=0.003). There was no statistically significant change in NIBUT post treatment for all groups (Wilcoxon Signed Rank Test z: p>0.05) and there was no difference between groups after treatment (H: χ^2 (2, n=396)=5.32, p=0.07).

Rate of tear film flow (RTFF)

The RTFF for all participants was categorised as fast, medium or slow and medium flow is indicative of tear film stability. The proportion of participants in the CT group with medium baseline RTFF was 46.9% and this decreased post treatment to 31.6%. A related samples McNemar Change test indicated that this

Table 1. Pre and post scores and statistical outcome, by treatment group

Outcome variable	Treatment Groups	Pre-treatment Mean	Pre-treatment SD	Pre-treatment Median	Post-treatment Mean	Post-treatment SD	Post-treatment Median	Pre-post outcome
OSDI score	CT	35.98 (n=354)	22.6	33	23.12 (n=216)	21.6	17	*z*=-5.5 p=0.000* r=0.23
	CT-MGE	35.73 (n=74)	23.3	33	19.65 (n=70)	22.5	9	*z*=-3.7 p=0.000* r=0.15
	CT-MGE-IPL	44.13 (n=140)	23.8	42	27.71 (n=130)	23.8	22	*z*=-4.9 p=0.000* r=0.21
TMH (mm)	CT	0.33 (n=354)	0.18	0.29 (Range 0.1-1.9)	0.41 (n=213)	0.85	0.28 (Range 0.2-12.4)	*z*=-0.41 p=0.51
	CT-MGE	0.34 (n=74)	0.16	0.29 (Range 0.1-1.2)	0.33 (n=70)	0.19	0.29 (Range 0.1-1.7)	*z*=-0.87 p=0.38
	CT-MGE-IPL	0.30 (n=140)	0.15	0.27 (Range 0.1-0.9)	0.32 (n=128)	0.18	0.26 (Range 0.1-1.2)	*z*=-0.66 p=0.51
NIBUT (sec)	CT	8.53 (n=353)	8.53	5.74	8.71 (n=201)	6.77	6.88	*z*=-1.71 p=0.86
	CT-MGE	9.55 (n=74)	6.15	7.27	9.42 (n=35)	6.15	7.84	*z*=-0.72 p=0.94
	CT-MGE-IPL	6.71 (n=140)	5.15	5.35	6.87 (n=62)	5.31	5.74	*z*=-1.20 p=0.23
MGUL (% loss)	CT	44.18 (n=354)	27.99	44.18	42.40 (n=173)	26.37	40.0	*z*=-1.27 p=0.22
	CT-MGE	49.33 (n=74)	26.75	48.35	43.06 (n=70)	28.26	40.0	*z*=-2.96 p=0.003*
	CT-MGE-IPL	52.99 (n=140)	26.85	53.30	47.56 (n=122)	27.54	40	*z*=-4.16 p=0.000*
MGLL (% loss)	CT	42.50 (n=354)	29.53	33.30	38.68 (n=172)	26.22	33.30	*z*=-2.58 p=0.010*
	CT-MGE	43.55 (n=74)	31.86	38.30	33.14 (n=70)	30.22	24.85	*z*=-4.59 p=0.010*
	CT-MGE-IPL	48.69 (n=140)	28.05	46.7	43.25 (n=126)	31.02	33.30	*z*=-3.61 p=0.000*

TMH: tear meniscus height; NIBUT: non-invasive tear film break-up time; MGUL: meibomian gland loss of upper lid; MGLL: meibomian gland loss of lower lid. (statistically significant result*).

proportion change was statistically significant (χ^2 (1, n=310)=6.72, p<0.01).

Both treatment groups that received meibomian gland expression had more participants achieving a medium post-RTFF (Table 2), however only the change in proportion for the CT-MGE-IPL group reached statistical significance (χ^2 (1, n=134)=28.93, p<0.01).

Meibomian gland loss

Meibomian gland loss was assessed for the upper and lower eyelids before and after treatment (see Table 1). A higher percentage of meibomian gland loss implies greater severity of disease.

The percentage of meibomian gland loss for the upper and lower lids of the CT-MGE and CT-MGE-IPL groups significantly decreased after treatment (Wilcoxon Signed Rank Test *z*: p<0.05). The CT group also showed a significant reduction in the amount of meibomian gland loss for the lower lid (Wilcoxon Signed Rank Test *z*: p<0.05), but not the upper lid (p>0.05).

The percentage of meibomian gland loss in the upper lids of the CT-MGE-IPL group was significantly higher compared with the other two groups, Kruskall-Wallis test (H: χ^2 (2, n=568)=11.03, p=0.004) and whilst the percentage of loss was also higher for the lower lids, statistically this was only approaching significance (H: χ^2 (2, n=568)=5.14, p=0.07). There was no statistically significant difference between the post treatment meibomian gland loss in the upper eyelids across the three groups (H: χ^2 (2, n=568)=1.75, p=0.45), however the CT-MGE-IPL group did have a higher meibomian gland loss of the lower lids post treatment compared with the other groups (H: χ^2 (2, n=368)=6.79, p=0.03).

DISCUSSION

More than half of the participants in this retrospective study pursued with only CT management (62%), 13% had CT-MGE treatment and 25% had CT-MGE-IPL therapy. There was a slightly larger proportion of females, which is similar to previous research findings.[2,33] Most participants (89.4%) reported using non-specific topical lubricants prior to their first presentation to the dry eye clinic, with limited success. There are a wide range of pharmaceutical lubricants which can be overwhelming to navigate particularly when dry eye disease comprises many different causal factors. This could indicate a need to educate primary care providers including pharmacists and general practitioners to provide targeted advice to participants. Participants in this study tended not to drink adequate water and consumed caffeinated beverages, which potentially leads to dehydration. They also had poor dietary omega-3 consumption. Nutrition from omega-3 foods has been reported to influence development and progression of DED however, there is lack of consensus regarding the impact of omega-3.[34] Given that DED is a multi-factorial condition, both dehydration and limited dietary omega-3 could contribute to increasing recovery time.

Participants who underwent CT-MGE-IPL treatment presented with a higher degree of symptom severity, lower aqueous volume, greater tear film imbalance and higher percentage of meibomian gland drop out compared to those who chose to remain with conservative treatment, with or without meibomian gland expression. In terms of severity of symptoms, analysis showed that all treatment options significantly improved patient symptoms of dry eye by OSDI measurements although, the effect size was small to medium. The overall post treatment score of the CT-MGE-IPL group was statistically worse than the other two groups, reaffirming that this group of participants suffered worse symptoms at presentation and therefore may not be able to achieve equal outcomes to the other treatment groups. The choice of treatment may also have been influenced by financial concerns (CT-MGE-IPL is more expensive), time constraints and level of independence, since CT requires commitment to at-home treatment between visits, requiring adequate dexterity, mobility and time to achieve results. It is plausible that participants with more severe dry eye disease were more likely to seek what they perceived as a more effective and targeted therapy with more specialist involvement/care, ie CT-MGE-IPL. The participants who chose CT-MGE-IPL were very symptomatic with higher OSDI scores. Although all treatments were effective for improving symptoms, due to presenting high severity of symptoms in the CT-MGE-IPL group, there was a higher post-treatment OSDI compared to those participants who were less symptomatic. The limitation of this real-

Table 2: Treatment outcomes – RTTF per treatment group before and after

Outcome variable	Treatment groups	Pre-treatment (% of participants with medium RTFF)	Post-treatment (% of participants with medium RTFF)	Outcome
RTFF	CT (n=310)	46.9	31.6	p<0.01*
	CT-MGE (n=74)	45.9	62.2	p>0.01
	CT-MGE-IPL (n=134)	40	70	p<0.01*

RTFF: rate of tear film flow. (statistically significant result*).

world study design is that we cannot reliably compare those who were severely symptomatic and having CT-MGE or only CT with those who were severely symptomatic and having CT-MGE-IPL. Such a design might show that CT-MGE-IPL is the treatment of choice for improving severe OSDI compared to the other treatment modalities. However, since OSDI is not the sole indicator of severe DED, this would be misleading. A further limitation of this study is that follow-up time and time to resolution was not extracted, and this may have had an impact upon outcomes.

The TMH did not improve post treatment in any of the groups in this cohort of participants. This could be explained by the fact that the treatment modalities used in this study specifically target MGD. However, the finding that approximately 30% of participants showed TMH suggestive of DED linked to partial aqueous deficiency, may also explain this result. Evaporative disease secondary to MGD is best treated using the methods described in this study, and it is possible that there is overestimation of the proportion of participants with evaporative disease. The classification of the underlying cause of DED needs further study.

The outcomes regarding RTFF in this study were variable. As indicated in the results section, medium tear film flow is the preferred result classification for RTFF, and the proportion of participants with medium flow significantly decreased post treatment in the CT group, whilst the proportion increased for the other two groups, although not statistically significant for the CT-MGE group possibly due to the relative smaller size of the sample in the CT-MGE group. A possible explanation is that CT may help temporarily with improving tear film viscosity, however CT-MGE may provide a greater volume of lipid in the tear film which is unstably held. The addition of IPL to CT-MGE may be a way to hold the tear film viscosity for a longer duration since it is thought to target deeper structures surrounding the meibomian glands and ocular tissues than the other two methods are capable of doing. There is a significant limitation with this outcome measure in that it is subjective and examiner dependent. The Oculus Keratograph does not provide a quantifiable measure of RTFF. Future research should incorporate the development of a quantifiable descriptor or grading of RTFF.

There was no significant change to NIBUT post treatment in this cohort of participants, irrespective of treatment. In a comparison study of TBUT methods, the NIBUT showed high sensitivity and specificity compared to traditional fluorescein tear break up time.[35] Researchers suggested that NIBUT was useful to detect dry eye disease, however they applied a cut-off value of 6.2 seconds, where measurements below 6.2 seconds were considered as dry eye. Moderate dry eye was classified with a NIBUT of 4.7 seconds and severe if 2.3 seconds. In this study, the mean baseline and post treatment NIBUT was higher than 6.2 seconds for all groups with those in the CT-MGE-IPL group having the fastest NIBUT and those in the CT-MGE group having the longer NIBUT. This suggests that this measure can be used in conjunction with other tests to determine severity of dry eye disease, but not alone.

The percentage of meibomian gland loss in the upper and lower lids of the CT-MGE and CT-MGE-IPL group decreased after treatment. The common treatment modality that could explain this outcome is that participants in both groups had meibomian gland expression as part of the treatment protocol, whilst the CT group did not. Given that it is likely that over 60% of participants in this study had evaporative disease, targeted therapy for MGD had improved meibomian gland structure in this cohort of participants although, it was expected that CT would also improve meibomian gland structure by increasing oil production by allowing meibum secretion through heating and lid cleansing procedures. Whilst meibography grading can explain the amount of meibum in the glands and ducts in addition to how close the glands and ducts are to the palpebral conjunctiva, it can be useful to provide information about the potential for a lipid layer in the tear film, if the glands express well and the lid margins are otherwise clear. Meibography can also indicate the amount of gland dropout, but it is not a good indicator of improvement or regeneration post treatment specifically because the percentage of loss is an estimate and not specifically quantifiable. Therefore, this also needs to be considered in light of other outcome measures for dry eye disease. Further investigation into quantification of meibomian gland loss or regeneration is therefore warranted.

CONCLUSION

The findings of this study suggest that all treatments are effective in managing meibomian gland dysfunction, although outcomes may be slightly better if management includes meibomian gland expression. Given that this study was retrospective and as a result non-randomised, it is likely that the outcomes for the CT-MGE-IPL group are potentially biased given that these participants presented with more severe disease at baseline. Other factors that may influence outcome are that participants were able to choose their treatment modality and the time between treatment consultations varied due to the real-world nature of the study. However, given these study findings, improved testing modalities with quantifiable results and a dedicated dry eye clinic model, together with an experienced orthoptist allows better outcomes for participants. Given that there are links between dry eye disease and general health conditions including cardiovascular disease, diabetes, auto-immune disease, skin conditions, gut-related illnesses and compromised respiratory function, the aim of further research should be to explore the impact of these comorbidities on dry eye disease and treatment outcomes.

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