Effect of the traditional Chinese medicine fumigation combined with the meibomian gland squeezer for treatment of dry eye associated with meibomian gland dysfunction

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Abstract

Background: To observe the effect of traditional Chinese medicine fumigation combined with the meibomian gland squeezer for the treatment of dry eye associated with meibomian gland dysfunction (MGD). Methods: This is a randomized, controlled, non-masked, single-center study. Seventy-four cases (74 eyes) of dry eye associated with MGD were randomly divided into two groups. Thirty-seven patients were chosen as the treatment group was treated by the traditional Chinese medicine fumigation 3 times a week combined with the meibomian gland squeezer once a week for one month. The other 37 cases were sorted as the control group and only treated with the meibomian gland squeezer once a week for one month. Both groups received the primary treatment for 1 month, including Tobradex eye ointment once a day and 0.1% sodium hyaluronate eye drops 4–6 times daily. Patients were evaluated at baseline and 2-week and 1-month visits for the ocular symptom scores, international ocular surface disease index (OSDI), fluorescein tear break-up time (TBUT), corneal fluorescein staining test (CFS), Schirmer I test, meibum quality and meibum expressibility. Results: Sixty-seven patients were followed in the study, and the mean age was 57 (± 12.6) years. Thirty-three patients (11 males) in the treatment group and 34 patients (8 males) in the control group were followed in the study, and the mean age of the two groups was 45.36 ± 15.02 years and 43.68 ± 13.43 years, respectively. Before treatment, there was no significant difference between the two groups in gender, age, ocular symptom scores, OSDI, TBUT, CFS, Schirmer I test, meibum quality, and meibum expressibility (P > 0.05). Compared with baseline, the 2 groups had different degrees of improvement in the ocular symptom scores, OSDI, TBUT, CFS, meibum quality, and meibum expressibility at the 2-week and 1-month visits (P < 0.05), and the treatment group showed a more significant improvement in the ocular symptom scores, OSDI, TBUT, CFS, meibum quality and meibum expressibility compared with the control group (P < 0.05). In addition, no serious adverse events were observed in each group. Conclusions: The traditional Chinese medicine fumigation combined with the meibomian gland squeezer may be safe, effective, and helpful for the treatment of dry eye associated with MGD.

Keywords: meibomian gland squeezer; traditional Chinese medicine; dry eye disease; meibomian gland dysfunction
Introduction

Meibomian gland dysfunction (MGD) is a common ocular condition that can cause changes in the tear film and eye discomfort [1]. The main pathogenic mechanisms of MGD are the obstruction of the meibomian gland’s terminal ducts and qualitative/quantitative changes in glandular secretion [2]. In Asia, the prevalence of MGD among dry eye patients ranges from 46.2% to 69.3% [3-5]. A multicenter study in the United States and Europe showed that over 80% of dry eye patients exhibited signs of MGD [6]. Additionally, epidemiological investigations of dry eye have revealed that approximately 10% of patients with severe aqueous deficiency dry eye may have Sjögren’s syndrome [7]. Therefore, MGD is considered the most common form of dry eye [8].

Currently, the primary methods for treating MGD-related dry eye include physical therapy (lid hygiene, warm compresses, lid massage), artificial tears, systemic and topical antibiotics, topical anti-inflammatory treatments (such as non-steroidal anti-inflammatory drugs, glucocorticoids, cyclosporine A, tacrolimus, biologics), surgical interventions, dietary adjustments, environmental modifications, and psychological management [9, 10]. Among these, physical therapy serves as the foundation for MGD treatment. It effectively clears the obstruction in the meibomian gland ducts caused by epithelial hyperplasia and solidified sebum, allowing the elimination of accumulated abnormal secretions and promoting normal lipid excretion to enhance tear film stability [11].

Clinical studies have demonstrated that combining traditional Chinese medicine fumigation and lid massage is a safe and effective method for treating MGD [12]. In our clinical practice, we have employed the combination of traditional Chinese medicine fumigation and a novel type of lid massage using forceps to treat MGD-related dry eye and have observed significant relief of eye discomfort in patients. In order to objectively evaluate the clinical efficacy of this treatment approach, we conducted a randomized controlled trial. The following report presents the relevant findings from our clinical study.

Methods

Study design and patients

74 patients with MGD-related dry eye were recruited from the Outpatient Department of Longhua Hospital. Based on our previous research findings, sample size calculation was conducted using G-power (3.1) [13]. The primary outcome measure “tear film break-up time” was estimated. An expected dropout rate of 20% was considered, resulting in the inclusion of a total of 60 patients. Using SPSS 25.0 software, the patients were randomly assigned to two groups, each consisting of 37 patients. The study received approval from the Ethics Committee of Shanghai University of Traditional Chinese Medicine Affiliated Longhua Hospital (Approval No. 2021LGLSY077) and was registered with the Chinese Clinical Trial Registry (ChiCTR2200055299). After explaining the purpose of the study, all patients provided informed consent by signing consent forms.

Study inclusion and exclusion criteria

Inclusion criteria [14]: Patients meeting the diagnostic criteria for dry eye and meibomian gland dysfunction [15], aged between 18 and 75, of any gender, and capable of comprehending and providing informed consent.

Exclusion criteria [16]: Patients with concurrent ocular infections; patients with eyelid disorders, corneal diseases, prophylaxis, glaucoma, or lens dislocation; patients who have not fully recovered from recent eye surgeries such as glaucoma filtration surgery or retinal detachment repositioning surgery; patients with known allergies to the prescribed medications; patients with a history of chalazion within the past 3 months; patients who have worn contact lenses in the past 3 months; patients who have used isotretinoin (vitamin A acid) in the past 6 months; patients with poorly controlled systemic diseases such as hypertension, coronary artery atherosclerosis, etc.; pregnant or lactating women; patients currently participating in other drug clinical trials or using other ocular medications; patients with mental illness or compromised overall health status that may impede the examination.

Treatment

The study duration was one month, with follow-up visits scheduled at 2 weeks and 1 month after the treatment. Both groups of patients received basic treatment consisting of tobramycin and dexamethasone eye ointment (a compounded formulation containing 0.3% tobramycin and 0.1% dexamethasone) (Alcon Laboratories, Inc., Fort Worth, TX, USA) applied once daily. Sodium hyaluronate eye drops 0.1% (5 ml.5 mg) (Zhuhai Federal Pharmaceutical Co., Ltd., Zhuhai, China) were used 4-6 times daily. The same practitioner used the novel meibomian gland massage tweezers to administer weekly treatments, totaling 4 sessions.

In the treatment group, “Chinese medicine fumigation” was incorporated, involving a concentrated decoction of Chinese herbs (Phellodendri Chinensis Cortex, Bidens pilosa, Chrysanthemum Flos, Lycii Cortex, Menhadea Herba, and Mori Folium) at approximately 100 ml per session at a temperature of 42–45 °C to prevent burns. Fumigation was performed thrice a week, each lasting approximately 15 minutes. The control group received only the primary treatment without “Chinese medicine fumigation.”

Clinical assessments

The main evaluation parameters encompass clinical symptom scores, the Ocular Surface Disease Index (OSDI), tear break-up time (TBUT), Schirmer 1 test (SIT), corneal fluorescein staining (CFS), and assessment of meibomian gland secretion function. These metrics were assessed both prior to the commencement of treatment and at the 2-week and 1-month intervals post-treatment.

Utilizing an ocular survey questionnaire for the assessment of Primary Clinical Symptom Scores, the scale encompasses 12 ocular symptoms, including burning sensation, irritation, dryness, foreign body sensation, itching, ocular swelling and pain, blurred vision, eye fatigue, frequent blinking, photophobia with tearing, redness, and increased white discharge from the eyes [13]. Each symptom is graded based on its severity, categorized into non-existent, mild, moderate, moderately severe, and severe, with corresponding scores of 0, 1, 2, 3, and 4, respectively. The maximum cumulative score for symptoms for each patient is 48 points, with higher scores indicating a more pronounced severity of symptoms.

Fluorescein sodium test strips (Tianjin Jinmingxin Technology Development Co., Ltd., Tianjin, China) were used to detect TBUT [17]. Moisten fluorescein sodium test strips with sterile physiological saline and instill a fluorescein drop into the conjunctival sac of each eye. Instruct patients to blink several times to ensure the uniform distribution of fluorescein on the cornea. Direct patients to maintain a straight-ahead gaze and assess the tear film under a microscope using a cobalt blue filter. Observe and meticulously record the interval from the uniform distribution of fluorescein to the initial tear film break. Perform three measurements for each eye and compute the average.

A 12-point grading system was employed to assess CFS [18]; the cornea was divided into four quadrants - upper, lower, nasal, and temporal. After staining each quadrant separately, the scores were aggregated to yield the total score, with a maximum of 12 points. Scoring criteria were as follows: 0 points - absence of punctate staining; 1 point - 1-30 punctate stainings; 2 points - > 30 punctate stainings without fusion; 3 points - presence of fused punctate staining, filamentary material, and ulcers on the cornea.

![Figure 1 New type meibomian gland massage tweezers](https://www.tmrjournals.com/im)
To perform the SIT, place a tear detection filter paper strip (Tianjin Jinming New Technology Development Co., Ltd., Tianjin, China) in the lower conjunctival sac of the affected eye, positioning it approximately one-third from the outer edge (without surface anesthesia). Record the extent of wetting after a 5-minute interval.


Meibomian Gland Secretion Capacity Score: gently compress the central meibomian glands of the lower eyelid and evaluate the ease of secretion discharge from the central five glands (under normal circumstances, secretion should occur from all five glands). Scoring criteria: 0 points - secretion observed from all glands; 1 point - secretion observed from 3–4 glands; 2 points - secretion observed from 1–2 glands; 3 points - no secretion observed from any glands.

Meibomian Gland Secretion Quality Score: assess the secretion characteristics of the eight meibomian glands in the lower 1/3 region. Observe the appearance of the secretion from each gland. Scoring criteria: 0 points - normal meibum, clear and transparent; 1 point - meibum is cloudy; 2 points - meibum is cloudy with debris (particles); 3 points - meibum is thick and toothpaste-like. The maximum score is 24 points, with higher scores indicating poorer quality of meibomian gland secretions.

Safety assessment
The same individual operated the meibomian gland massage tweezers. During the follow-up visits at 2 weeks and 1 month, the safety of the eyes was assessed by examining the patient’s best-corrected visual acuity and intraocular pressure and performing a slit lamp examination of the eyelashes, eyelids, conjunctiva, cornea, anterior chamber, and lens. Furthermore, patients were questioned about any occurrence of severe adverse events, and their responses were recorded.

Statistical analysis
Statistical analysis was conducted using SPSS 25.0 software to analyze all the observed variables mentioned above. Continuous data were reported as mean ± standard deviation (x ± s) and analyzed using t-tests. Categorical data were presented as percentages (%) and analyzed using the chi-square test. A significance level of P < 0.05 was considered statistically significant to detect differences.

Results
74 patients were included in this study, with 33 cases (22 females) in the treatment group and 34 cases (26 females) in the control group who completed the trial. The average age in the treatment group was 45.36 ± 15.02 years, and in the control group, it was 43.68 ± 13.43 years. There were no statistically significant differences between the two groups regarding age, gender distribution, and other characteristics (P > 0.05), indicating that the groups were comparable. Please refer to Table 1 for further details.

Before treatment, there were no statistically significant differences (P > 0.05) in the scores of major clinical symptoms, OSDI, TIBUT, CFS, SIT, meibomian gland secretion capacity, and meibomian gland secretion quality between the two groups. After 2 weeks and 1 month of treatment, except for SIT, significant differences (P < 0.05) were observed in the scores of major clinical symptoms, OSDI, TIBUT, CFS, meibomian gland secretion capacity, and meibomian gland secretion quality compared to before treatment. The treatment group exhibited more significant improvements in clinical symptom scores, OSDI, CFS, TIBUT, meibomian gland secretion capacity, and meibomian gland secretion quality compared to the control group (P < 0.05). For detailed information, please refer to Table 2.

In addition, during treatment, traditional Chinese medicine fumigation and meibomian gland massage may lead to discomforts, such as conjunctival congestion and tearing. However, no serious adverse events were reported, such as acute conjunctivitis, keratitis, or meibomian gland inflammation.

Table 1 Demographic data for all patients

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>33</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>45.36 ± 15.02</td>
<td>43.68 ± 13.43</td>
<td>0.79</td>
</tr>
<tr>
<td>Median</td>
<td>44.0</td>
<td>40.5</td>
<td></td>
</tr>
<tr>
<td>Minimum, maximum</td>
<td>25, 72</td>
<td>26, 67</td>
<td></td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (33.3)</td>
<td>8 (23.5)</td>
<td>0.37</td>
</tr>
<tr>
<td>Female</td>
<td>22 (66.7)</td>
<td>26 (76.5)</td>
<td></td>
</tr>
</tbody>
</table>

SD, standard deviation.

Table 2 Clinical parameters for all subjects at baseline, 2-week and 1-month visit

<table>
<thead>
<tr>
<th>Ocular symptom scores</th>
<th>Group</th>
<th>Severity score (mean ± SD)</th>
<th>Baseline</th>
<th>2-week</th>
<th>1-month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>8.21 ± 3.18</td>
<td>5.52 ± 2.77*</td>
<td>3.79 ± 2.57*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>8.50 ± 3.31</td>
<td>6.15 ± 2.86*</td>
<td>5.12 ± 3.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OSID</td>
<td>42.28 ± 17.61</td>
<td>31.07 ± 12.06*</td>
<td>26.73 ± 14.52*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>42.49 ± 12.56</td>
<td>38.10 ± 14.83*</td>
<td>30.71 ± 11.52*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>2.26 ± 1.19</td>
<td>2.57 ± 1.14</td>
<td>2.59 ± 1.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIBUT (seconds)</td>
<td>2.72 ± 1.55</td>
<td>4.61 ± 3.05*</td>
<td>4.94 ± 3.05*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>1.33 ± 2.15</td>
<td>0.61 ± 1.62*</td>
<td>0.70 ± 1.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.32 ± 2.58</td>
<td>2.00 ± 2.86</td>
<td>1.65 ± 2.93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIT (mm)</td>
<td>14.45 ± 8.60</td>
<td>12.52 ± 9.45</td>
<td>12.39 ± 9.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>11.85 ± 8.09</td>
<td>12.24 ± 8.67</td>
<td>10.88 ± 7.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>1.29 ± 0.63</td>
<td>0.85 ± 0.56</td>
<td>0.76 ± 0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meibum expressibility</td>
<td>1.30 ± 0.85</td>
<td>0.94 ± 0.75</td>
<td>0.42 ± 0.50*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>1.29 ± 0.63</td>
<td>0.85 ± 0.56</td>
<td>0.76 ± 0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>12.42 ± 5.70</td>
<td>8.94 ± 4.22*</td>
<td>6.27 ± 3.81*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meibum quality</td>
<td>12.15 ± 4.06</td>
<td>9.68 ± 4.50*</td>
<td>7.76 ± 3.68*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data used are from the worse eye according to TIBUT, * compared with baseline, the difference within the group was significant (P < 0.05); ** compared with baseline, the difference between the two groups was significant (P < 0.05). OSDI, Ocular Surface Disease Index; TIBUT, tear break-up time; CFS, corneal fluorescein staining; SIT, Schirmer I test; SD, standard deviation.
Discussion

MGD is a common eye condition closely associated with evaporative dry eye [19]. Current studies have indicated an increased prevalence of MGD with advancing age, especially among individuals aged 50 years and above [20, 21]. The extensive use of video display terminals (VDTs) such as computers, tablets, and smartphones in daily work and life has also contributed to a high prevalence of MGD among VDT workers (74.3%), further exacerbating the severity of VDT-related dry eye [22–24]. Moreover, MGD in adolescents has emerged as an area of concern among ophthalmologists [25].

Structural abnormalities of the glands and changes in the viscosity of the lipid secretions characterize obstructive MGD [26]. Eyelid warming, with or without humidification, can help melt the pathologically altered meibum [27]. At the same time, meibomian gland massage effectively clears the blocked meibomian gland ducts caused by excessive epithelial hyperplasia and sebaceous accumulation [28]. The combined use of eyelid warming and meibomian gland massage is a commonly recommended treatment approach for MGD [29]. It helps eliminate accumulated abnormal secretions, facilitate the proper flow of normal lipids, enhance tear film stability, and improve symptoms [30].

In current clinical practice, innovative treatment methods that combine heating with meibomian gland massage have been utilized, such as the Lipiflow thermal pulsation system ( Tears Science, Morrisville, NC, USA) [31]. This system combines eyelid warming at 42.5 °C with glandular expression. A single 12-minute treatment session with Lipiflow has shown significant improvements in meibomian gland function and a reduction in dry eye symptoms, with effects lasting up to 12 months [32].

Recent research has substantiated the beneficial impact of traditional Chinese medicine in addressing MGD. Chinese herbal steaming therapy, a traditional external treatment method in Chinese medicine, employs the "medicinal vapor" produced by boiling Chinese herbs to steam the eyes, creating a synergistic effect of herbal and thermal influences. Traditional Chinese medicine believes that this therapy achieves the effects of releasing the exterior, dispelling pathogens, detoxifying, resolving stasis, and alleviating swelling by inducing sweating, expelling pathogens, regulating nutrient and Wei-defensive Qi (Wei-defensive Qi is a form of Qi with functions of defending against external pathogens, warming and nourishing the entire body, and regulating the pores), and promoting the circulation of Qi and blood [12, 33]. This meets the pathogenesis of MGD in traditional Chinese medicine theory. Numerous clinical studies have affirmed the safety and efficacy of localized Chinese herbal steaming treatment for MGD or MGD-induced dry eyes [14, 16]. In a randomized controlled study conducted by Zhang et al., Chinese herbal steaming was found to enhance eye symptoms, meibum quality scores, and TBUT in MGD patients [34]. Importantly, this treatment was well-tolerated and deemed safe by the patients.

The herbal blend for Chinese herbal steaming includes components such as Phellodendri Chinensis Cortex, Bidens pilosa, Chrysanthemi Flos, Lycii Fructus, Menthae Herba, and Mori Folium. These ingredients collaboratively not only alleviate eye discomfort associated with MGD but also enhance the secretion function of the meibomian glands. A network pharmacology study of a traditional Chinese medicine formula containing Lycii Fructus and Chrysanthemi Flos reveals its therapeutic effects on dry eye syndrome through multiple targets and pathways [35]. Another study found that the decoction of traditional Chinese medicine containing Lycii Fructus can improve epithelial erosion and desquamation in a dry eye model of mice, maintaining the integrity of corneal epithelium and restoring tear osmotic pressure [36].

Expanding on the treatment with 0.1% sodium hyaluronate eye drops and diclofenac eye ointment, this study introduced the use of traditional Chinese medicine fumigation combined with a novel meibomian gland massage tweezer for the management of MGD-related dry eye. Following a treatment period of 2 weeks and 1 month, significant improvements were observed in the treatment group compared to baseline, with notable differences in the scores of major clinical symptoms, OSDI, TBUT, CFS, meibomian gland secretion capacity, and meibomian gland secretion quality (P < 0.05), excluding SIT. Moreover, the treatment group demonstrated superior enhancements in clinical symptom scores, OSDI, CFS, TBUT, meibomian gland secretion capacity, and meibomian gland secretion quality compared to the control group (P < 0.05). Notably, no severe adverse events were reported throughout the entire duration of the trial.

Conclusions

In conclusion, combining traditional Chinese medicine fumigation and the novel meibomian gland massage tweezer demonstrates significant efficacy in alleviating symptoms of MGD-related dry eye. This treatment approach is safe and effective, showcasing the potential and benefits of incorporating traditional Chinese ophthalmology techniques. The localized application of traditional Chinese medicine offers advantages such as simplicity, convenience, efficacy, and affordability, underscoring its prominent role and demonstrating its effectiveness.

However, some things could be improved in this study. Firstly, the lack of a large-scale multicenter controlled study limits the generalizability of the findings. Additionally, the long-term effects of MGD-induced dry eye were not assessed, necessitating further investigation to ascertain this treatment approach’s efficacy fully. Future research should focus on exploring and elucidating these aspects to provide a more comprehensive understanding of its therapeutic potential.

References


