Effectiveness of acupuncture at acupoint BL1 (Jingming) in comparison with artificial tears for moderate to severe dry eye disease: a randomized controlled trial

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Abstract

Background: The global incidence of dry eye disease (DED) is very high. DED seriously affects the quality of life of patients; however, the current curative effect of medicine for moderate to severe DED is poor. This randomized clinical trial was planned to investigate the effect of acupuncture compared with artificial tears (AT) on moderate to severe DED.

Methods: A randomized clinical trial was performed at 2 hospitals in China. 120 DED patients were randomly equally divided into an acupuncture and an artificial tear group. Either acupuncture or artificial tears was performed for an 8-week period, and a 24-week follow-up was performed. The primary outcome measure was the Schirmer-I test (SIT) change from baseline. The secondary outcome measures included the numerical rating scale (NRS) change from baseline for improvement in ocular symptoms, the ocular surface disease index (OSDI), the tear-film break-up time (TBUT), corneal fluorescein staining (CFS), and acupuncture acceptability. Adverse events also were monitored and documented.

Results: For the primary outcome, the mean changes from baseline in the SIT values were significantly different between the acupuncture (5.75 [2.53–9.75]) and AT (0.52 [−1.18–2.46]) groups at week 8 with a between difference of 5.23 (P < 0.05). Between-group differences of 8.49 in OSDI score change from baseline differed significantly at week 8 (P < 0.05). However, between-group differences of the changes in the average symptom NRS score, TBUT, and CFS did not differ significantly at week 8. Five cases experienced acupuncture-related adverse events.

Conclusions: This randomized clinical trial found that acupuncture at BL1 significantly promoted tear secretion. Acupuncture showed greater benefits than AT for moderate to severe DED. However, the study findings warrant verification.

Trial registration: Registration number: ChiCTR1800015831. Name of trial registry: Efficacy and safety of acupuncture in the treatment of moderate to severe dry eye disease: a randomized controlled trial. Registered on 23 April 2018 (https://clinicaltrials.gov/).

Keywords: Dry eye, Acupuncture, RCT, Artificial tears, SIT

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dynamics, of any cause, resulting in tear-film instability and/or eye surface abnormalities. DED symptoms include eye dryness, foreign body sensation, pain, visual fatigue, and blurred vision. The global DED incidence varies (5–34%) [2], and is higher in Asian countries. Moreover, the incidence has increased with the recently increased exposure to display screens, abuse of eye medicines, and continuous improvement in DED diagnosis. DED causes include tear-film instability, tear hyperosmolality, ocular surface inflammation, injury, and neurosensory abnormalities [3]. It increases financial burden and reduces work efficiency, and quality of life [4–6].

Based on expert consensus [7], Artificial tears (ATs) are among the most commonly used drug treatments; ATs lubricate the eye surface, supplement tears, and reduce tear osmotic pressure, but only temporarily relieve DED symptoms. Effective treatment for severe DED is currently lacking. Non-drug treatments include surgery, lacrimal duct embolism, psychological counseling, physiotherapy, health guidance, wet chamber mirror, and silicone eye masks. Surgical treatment may have risks and side effects, making it a less acceptable treatment strategy. The efficacy of other therapies is not established; thus, these are not widely used [8].

Acupuncture therapy has a long history of use in China. Systematic reviews of randomized controlled trials (RCTs) have demonstrated that acupuncture is effective for DED [9–11]. However, previous studies [12, 13] showed that acupuncture treatment only improved subjective symptoms and lack the effectiveness of objective indicators for DED. Moreover, previous clinical studies of acupuncture generally included participants with mild to moderate disease, and the efficacy of acupuncture on moderate to severe DED remains uncertain [14]. Furthermore, the effect of only using periocular acupoints for treating DED was not significant based on a systematic review [15]. Thus, further studies with periocular acupoints accompanied by effective acupuncture manipulation are needed to investigate the effects for patients with moderate to severe DED. Although ATs are currently recommended as a conservative and effective treatment, they cannot replace naturally secreted tears as the lack of oxygen, vitamin A, mucoprotein, and other nutrients present in naturally secreted tears. In our previous clinical study [16], only acupuncture at the BL1 (Jingming) was effective in promoting tear secretion and improving DED symptoms.

In this RCT, we compared the effectiveness of acupuncture at BL1, with repeated needle manipulation until tear flow, with ATs for treating moderate to severe DED. We evaluated the improvements in objective and subjective indicators after an 8-week treatment period and a subsequent 24-week follow-up period.

Methods
This 2-center, RCT was approved by the Ethics Committee of Guang’anmen Hospital of China Academy of Chinese Medical Sciences. The study commenced on September 1, 2018, and was completed on December 31, 2020. The flow chart is shown in Fig. 1. Before inclusion, each participant provided written informed consent. The study protocol has been published previously [17]. The original trial protocol and statistical analysis methods are available (Supplementary 1). The trial was conducted and reported in accordance with CONSORT guidelines.

Study design
Patients were randomized to the acupuncture or AT groups based on a random distribution sequence. Clinical Laboratory of affiliated drugs of Guang’anmen Hospital was responsible for random grouping by computer. Patients were randomly assigned to the acupuncture or AT group using a block size of 4 stratified by centers, the final group assignments were placed in 120 opaque sealed envelopes, which were serially numbered and kept by a researcher not involved in treatment procedures or data analysis. After informed consent was obtained, the researcher opened the envelope according to the order in which the participant entered the trial and was provided for the prescribed treatment. All participants received either acupuncture or ATs 3 times per week over the 8-week period, and both groups were followed up for another 24 weeks.

Study population
DED participants were recruited from advertisements posted by the hospital. Participants were eligible only if they were 18–60 years old and met the diagnostic criteria of moderate-to-severe DED [18, 19]: They were required to have one or more symptoms of DED (e.g. eye dryness,
The primary outcome was the increase from baseline in the value of the SIT, with anesthesia, at week 8. The SIT was performed using a tear secretion test paper (Color Bar™ Schirmer tear test, Eagle Vision, Inc., Memphis, TN, USA). Tear volume was measured by placing the strip down the outer third of the eyelid and measuring the length of the wet part of the test strip 5 min later (the SIT value). Although there is no clinical significance yet, the SIT value is considered an important indicator of DED severity and positively correlates with DED symptoms and quality of life [20].

Secondary outcome measures
Secondary outcomes included the following. The SIT value with anesthesia at baseline, week 4, and week 32 was measured, similarly to week 8.

The average DED symptom intensity of the past week, as assessed by the participant with a self-administered numerical rating scale (NRS) (range: 0–10), was based on well-known DED symptoms (eye dryness, foreign body sensation, itching, burning, stinging, visual fatigue, photophobia, blurred vision) at baseline, weeks 4, 8, and 32. The individual score and the mean of these 8 symptom scores (global symptom score) were calculated and compared.

The Ocular Surface Disease Index (OSDI) was assessed at baseline, weeks 4, 8, and 32. The OSDI is commonly used to evaluate the influence of ocular surface disease on patients’ daily life. The scale includes 3 aspects: eye symptoms, visual-related function, and environmental stimulus factors; the higher the OSDI score (range: 0–100), the more serious the impact of the disease on daily life. The change in the total scores reflected the overall improvement in the patients’ eye symptoms.

The tear break-up time (TBUT) was measured at baseline, weeks 4, 8, and 32. The TBUT test is used to assess tear-film stability and reflects different pathophysiology according to rupture mode [21]. After staining with sodium fluorescein (2.5%), the time taken for the first dry spot on the tear-film was measured thrice with a slit lamp, and the average time was taken as the TBUT.
Corneal fluorescein staining (CFS), which was used to assess ocular surface damage as well as monitor the clinical response to therapy, was measured at baseline, weeks 4, 8, and 32. Corneal staining was examined under standard illumination with a slit lamp, using a cobalt blue filter, and was graded using the modified Oxford scale [22].

Acceptability of acupuncture or AT was evaluated at week 8, using a 4-point scale, with 1 representing “very difficult to accept,” 2 representing “difficult to accept,” 3 representing “easy to accept,” and 4 representing “very easy to accept” [23].

All participants were requested to report Adverse events (AEs) in the study during the treatment and follow-up periods. The severity (divided into mild, moderate, and severe) of AEs was evaluated by the investigator.

### Calculation of sample size and statistical analyses

The sample size was calculated based on the mean SIT value. According to our pilot trial [16], the increase in the mean SIT value in the acupuncture group at week 8 was $3.41 \pm 3.04$. A previous report indicated a mean increase in the SIT value in an artificial tear group of $1.8 \pm 1.6$ [24]. Based on these values, a sample size of 120 was needed to detect a difference of 1.61 between the two groups, which provided 90% power with a two-sided 5% level of significance, considering a 20% dropout rate.

SPSS Version 26.0 software was used for statistical analysis. All statistical analyses used bilateral tests. P values less than 0.05 were considered to be statistically significant. The analysis of efficacy was based on the principle of intentionality analysis. All participants who had at least one efficacy assessment were all included in the efficacy analysis. A sensitivity analysis was performed considering the loss during the study. The missing data was replaced by using the last observation carried forward method [25].

For data with a natural or adjusted normal distribution, we used mean and 95% confidence interval (CIs). For data with a non-normal distribution, we used the median and 95% CI. Group t-tests or non-parametric rank and sum tests were used for between-group comparisons. For within-group comparisons to baseline values, t-tests or non-parametric rank and sum tests were used. Independent sample t-tests were used to compare different time-points. Categorical variables were described using composition ratios and/or 95% confidence intervals. Chi-square test or Fisher’s exact test was used for comparisons between groups.

### Results

#### Enrollment

We screened 167 participants with DED for eligibility, and excluded 47; thus, 120 participants were assigned to either the acupuncture group ($n = 60$) or the AT group ($n = 60$), at a ratio of 1:1. Among them, 113 (94.2%) participants completed at least 4-week treatments and 110

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**Fig. 2** Flow of participants
(91.7%) participants completed all the trials (Fig. 2). Baseline characteristics are shown in Table 1; these were similar between the groups.

### Missing data and dropouts
Adherence to acupuncture treatments (3 times per week for 8 weeks) or AT treatments (4 times per day for 8 weeks) was similar in both groups, 90.0% and 96.7%, respectively. Of the 120 patients, 113 patients completed 4-week treatments and 110 patients completed all treatments and follow-ups. The data of the 120 participants was analyzed in the full analysis set based on the intention-to-treat principle. A sensitivity analysis was performed in the per-protocol set, which included the participants that completed all the treatments and follow-ups. The original results in this study were stable and reliable based on the sensitivity analysis.

### Outcomes

#### Primary outcome measures
For the primary outcome (Table 2), the mean SIT value was 4.37 (95%CI, 3.37–5.25) at baseline and 9.25 (95%CI, 6.00–12.75) at week 8 in the acupuncture group, and 3.82 (95%CI, 2.84–4.86) at baseline and 4.34 (95%CI, 2.94–5.98) at week 8 in the AT group. The increase in the SIT value at week 8 was greater in the acupuncture group (mean, 5.75) than in the AT group (mean, 0.52), with a mean difference of 5.23 (95%CI, 1.34–9.12; \( P = 0.01 \)).

Similar results were observed at week 4 (Table 2). The increase in the SIT value at week 4 was greater in the acupuncture group (mean, 5.16) than in the AT group (mean, −0.3) with a mean difference of 5.46 (95%CI, 2.73–8.18; \( P < 0.001 \)). However, the SIT values were not significantly different between both groups at week 32.

#### Secondary outcome measures
No significant differences in the change in mean DED symptom NRS scores were found between the groups (all \( P > 0.05 \)). Symptoms varied among participants, and not all participants experience every listed symptom. The acupuncture group had significantly decreased NRS scores for eye dryness, eye pain, and blurred vision compared to the AT group at multiple time-points. There was no significant difference between both groups for other symptoms.

### Table 1  Participant baseline characteristics

| Characteristic | Acupuncture group (n=60) | Artificial tear group (n=60) | \( P \) value |
|---------------|--------------------------|-----------------------------|------------|
| Age (years) (mean, 95%CI) | 44.16 (35.54 to 49.43) | 41.28 (31.78 to 45.78) | 0.224 |
| Sex, M/F (No.) | 22/38 | 29/31 | 0.437 |
| Educational level (No. [%]) | | | |
| Primary education or less | 16 (26.7) | 11 (18.3) | 0.246 |
| Secondary education | 38 (63.3) | 42 (70.0) | 0.413 |
| Tertiary education | 6 (10.0) | 7 (11.7) | 0.421 |
| DED duration, median (IQR), months | 26 (6–60) | 22 (5–60) | 0.259 |
| Profession (No. [%]) | | | |
| Office worker | 30 (50.0) | 34 (56.7) | 0.341 |
| Physical work | 12 (20.0) | 11 (18.5) | 0.512 |
| Retired or unemployed | 18 (30.0) | 15 (25.0) | 0.218 |
| Comorbidities (No. [%]) | | | |
| Cardio vascular and cerebro vascular diseases | 6 (10.0) | 4 (6.7) | 0.362 |
| Metabolic disorders | 5 (8.3) | 6 (10.0) | 0.438 |
| Eye conditions | 9 (15.0) | 7 (11.7) | 0.327 |
| Other | 2 (3.3) | 3 (5.0) | 0.357 |
| Sleep disorders (No. [%]) | 3 (5.0) | 3 (5.0) | 0.553 |
| SIT | 4.37 (3.37 to 5.25) | 3.82 (2.84 to 4.86) | 0.255 |
| Average symptom NRS (mean, 95%CI) | 7.14 (4.29 to 8.85) | 6.83 (4.27 to 8.63) | 0.316 |
| OSDI (mean, 95%CI) | 34.50 (29.15 to 41.23) | 32.20 (27.80 to 40.12) | 0.426 |
| TBUT (mean, 95%CI) | 4.31 (3.38 to 5.25) | 4.40 (3.56 to 5.32) | 0.418 |
| CFS (mean, 95%CI) | 3.25 (2.93 to 3.62) | 2.80 (2.56 to 3.08) | 0.227 |

SD: standard deviation, DED: dry eye disease, SIT: Schirmer-I test, NRS: numerical rating scale, OSDI: ocular surface disease index, TBUT: tear break-up time, CFS: corneal fluorescence staining, IQR: inter-quartile range.

a There were no significant between-group differences at baseline.
b Two participants in the acupuncture group and one participant in the artificial tear group had no the records of complications and concomitant medication.
The acupuncture group showed a more significant decrease than the AT group in the OSDI score at weeks 8 (8.49 [95%CI, −5.26–22.14]) and 32 (12.15 [95%CI, −4.68–15.46]) (all P < 0.05), but not at week 4 (P > 0.05).

There were no significant differences in the change in TBUT between both groups. A minor difference of 1.4 (95%CI, −0.46–3.27) was detected at week 4, 1.28 (95%CI, −1.01–3.26) at week 8, and 0.34 (95%CI, −1.01–2.26) at week 32. The differences between both groups were not significant (all P > 0.05).

There were no significant differences in the change in CFS from baseline to all time-points between both groups. The reduction in CFS was similar between both groups.

Acupuncture and AT acceptability were assessed after 8 weeks of intervention. 63.3% of participants in the acupuncture group and 75.0% in the AT group is easily acceptable or very easily acceptable. No significant differences were observed between the groups (P = 0.13). The detailed data are shown in Table 2.

### Safety outcomes

Treatment-related AEs occurred in 8.3% of participants in the acupuncture group; AEs included mild bleeding, which was absorbed quickly, or moderate bleeding, which was resolved by cold compress repeatedly for 24 h, and there were no other AEs. Common termination criteria adverse events (CTCAE) were used to evaluate the level of use in the study. AEs were divided into five grades according to CTCAE, in which 3 participants were grade one and 2 participants were grade two. To avoid the occurrence of AEs related to acupuncture,
acupuncturists were advised to slow down the frequency of acupuncture manipulation and routinely use cold compress for a while after acupuncture, which may reduce the occurrence of bleeding related to AEs. Incidence of AEs in the AT group was 3.4%, which included nausea (1 participant) and dizziness (1 participant). However, it was unclear whether these AEs were related to the treatment. No other has occurred (Table 3).

**Discussion**

In this RCT, we compared acupuncture and ATs for DED. After 4 and 8 weeks of treatment, acupuncture resulted in greater improvement in the SIT value than AT. OSDI score change in the acupuncture group was also significantly better than AT group. However, between-group differences of the changes in the average symptom NRS score, TBUT, and CFS did not differ significantly at week 8. The overall incidence of AEs was low.

The SIT value provides direct objective evidence for the therapeutic value of acupuncture. In this study, the SIT value in the acupuncture group increased by 5.16 and 5.75 after 4 and 8 weeks, respectively. Previous studies showed an increase of 0.41 [12] and 0.96 [13], which was significantly lower than that in our study. The acupuncture method used in this study may have been more conducive to promoting tear secretion than those used in previous studies, due to the acupuncture used, the stronger and longer duration of needling manipulation, and the tear-flow method after needling manipulation.

The OSDI is also an important indicator of DED symptoms. In this trial, the change in the OSDI score in the acupuncture group (Table 2) was consistent with previous findings. In our study, the OSDI score decreased by 16.14 after 8 weeks in the acupuncture group, similar to the decrease of 16.11 found previously [12]. A median reduction of 13.9 in the OSDI score represents the minimal clinically important difference [26].

Although previous studies have shown that acupuncture can improve DED symptoms, there were some differences in findings. In our study, acupuncture significantly improved the symptoms of dry eye, itching, eye pain, and blurred vision; however, it was less effective in improving other DED symptoms (photophobia, blurred vision, visual fatigue, and foreign body sensation) than AT, possibly due to the acupuncture point used, needle manipulation, and inclusion of moderate to severe DED participants. In this study, acupuncture stimulated lacrimal secretion and improved lacrimal gland function, rapidly relieving many DED symptoms in a sustained manner. A previous study showed that acupuncture could release opioid peptides, which may explain the relief of eye pain by acupuncture [27]. Acupuncture also altered the tear composition and regulated the immune system, thereby reducing inflammation or an allergic reaction at the eye surface [28].

In this study, objective indicators other than the SIT value did not improve significantly. A previous study on DED showed that the TBUT increased significantly, by 0.95, after acupuncture, but not after sham acupuncture [29]. Another study showed that TBUT increased by 1.93 after acupuncture treatment [13].

Participants in both groups generally found their treatment acceptable. The use of a single acupoint, rather than multiple acupoints as in previous studies, reduced the pain of acupuncture, possibly contributing to its acceptability.

Most previous studies showed that acupuncture treatment only improved subjective DED assessments, but did not investigate objective assessments or did not find significant improvement in the objective indicators (SIT, TBUT, CFS) [30, 31]. In this study, acupuncture treatment at BL1 with needle manipulation resulted in approximately 10 times more tear secretion than in the AT group, suggesting the mechanism underlying the efficacy of acupuncture. The BL1 point is located on the lacrimal caruncle of the inner canthus, and the tissues in the lacrimal caruncle and Krause glands may come in contact during acupuncture, which could regulate basic tear secretion and help maintain ocular surface homeostasis. When acupuncture was performed in the nasal direction, the sensory neurons in the lacrimal reflex arc may have been stimulated, thus triggering reflexes through the trigeminal nerve, which were transmitted to the lacrimal gland to promote tear production and regulate tear secretion [32].

The anatomical position of BL1 may be related to the better curative effect observed in many previous acupuncture trials for ophthalmic diseases [33]. Modern neuroanatomy indicates that the BL1 point belongs to

**Table 3** Adverse events

| Adverse event       | Participants (No. [%]) | Acupuncture group (n=60) | Artificial tear group (n=60) |
|---------------------|------------------------|--------------------------|----------------------------|
| Overall             | 5 (8.3)                | 2 (3.4)                  |                            |
| Bleeding (mild)     | 3 (5)                  | 0                        |                            |
| Bleeding (moderate) | 1 (1.7)                | 0                        |                            |
| Sharp pain          | 1 (1.7)                | 0                        |                            |
| Feel nauseated      | 0                      | 1 (1.7)                  |                            |
| Dizziness           | 0                      | 1 (1.7)                  |                            |

Adverse events were analyzed in all participants who received treatment. Adverse events were counted by type other than the frequency in the same participant. Adverse events with different types occurring in a single participant were defined as independent adverse events. An adverse event with multiple occurrences in a single participant was defined as 1 adverse event.
the trigeminal nerve distribution. When the BL1 point is
stimulated, the trigeminal nerve could produce excitatory
signals in the brain, which could improve visual function.

This study had some limitations. First, we did not
limit the subtype of DED when including study partici-
pants. Our findings may be more relevant to the lacri-
mal deficiency type. Second, because the AT group was
the control group not performed blinding, which may
have affected the study results. The environment of the
treatment room and the repeated health education of
acupuncturists may give participants some positive psy-
chological hints, which may contribute to improving the
effect. Thirdly, the effect of acupuncture may be related
to the psychological expectation of the subjects before
treatment. This should be investigated in the future.

Based on these limitations, stratification of partici-
pants can be added to trials in the future. Acupuncture
may have a better effect on DED with water deficiency
than other types of DED, as it can promote tear secre-
tion. Once there are many significant differences between
groups on the types of DED in the included participants,
the results will be biased. The placebo control group may
be set up in the trials in the future, and an appropriate
placebo group which can not be recognized by partici-
pants will be needed. Finally, expectations of the partici-
pants should be investigated before the trial in the future.

Conclusions
Acupuncture at the BL1 point alone can significantly
improve lacrimal secretion and symptoms of moderate
and severe DED, with a better curative effect than that
of AT. Acupuncture treatment was acceptable to patients
and there were no serious AEs. Thus, this simple acu-
puncture treatment could be considered safe, effective,
and acceptable for moderate to severe DED.

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Authors’ contributions
ZWZ had full access to all of the data in the study and takes responsibility for
the integrity of the data and the accuracy of the data analysis. Concept and
design: ZWZ, ZX. Acquisition, analysis, or interpretation of data: ZX, PSY, ZB.
Drafting of the manuscript: ZX. Critical revision of the manuscript for impor-
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Availability of data and materials
The full data set will be made available. Requests for the data to be released
should be sent to ZWZ (principal investigator).

Declarations

Ethics approval and consent to participate
Central ethical approval has been confirmed by the China Academy of Chi-
nese Medical Sciences (ethical number: 2018-012-KY-01).

Competing interests
The authors declare no conflicts of interest. The lead author confirms that
this manuscript is an accurate, honest, and transparent account of the study
undertaken and reported, with no aspects being omitted and any discrepan-
cies explained.

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References
1. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye
workshop (2007). Ocul Surf. 2007;5(2):75–92.
2. Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye
disease. Dtsch Arztebl Int. 2015;112(5):71–81 quiz 82.
3. Simsek C, Dogru M, Kojima T, Tsubota K. Current management and treat-
ment of dry eye disease. Turk J Ophthalmol. 2018;48(6):309–13.
4. Zeew MS, Miller DD, Latkany R. Diagnosis of dry eye disease and emerging
technologies. Clin Ophthalmol. 2014;8:581–90.
5. Dana R, Bradley J, Guerin A, et al. Estimated prevalence and incidence of
dry eye disease based on coding analysis of a large, all-age united states
health care system. Am J Ophthalmol. 2019;202:47–54.
6. Barabino S, Labetoulle M, Rolando M, Messmer EM. Understanding
symptoms and quality of life in patients with dry eye syndrome. Ocul
Surf. 2016;14(3):365–76.
7. Management and therapy of dry eye disease: report of the management
and therapy subcommittee of the international dry eye workshop (2007).
Ocul Surf. 2007;5(2):163–78.
8. Shen Lee B, Kabat AG, Bacharach J, Karpecki P, Luchs J. Managing dry eye disease and facilitating realistic patient expectations: a review and appraisal of current therapies. Clin Ophthalmol. 2020;14:119–26.

9. Yang L, Yang Z, Yu H, Song H. Acupuncture therapy is more effective than artificial tears for dry eye syndrome: evidence based on a meta-analysis. Evid Based Complement Alternat Med. 2015;2015:143858.

10. Kim BH, Kim MH, Kang SH, Nam HJ. Optimizing acupuncture treatment for dry eye syndrome: a systematic review. BMC Complement Altern Med. 2018;18(1):145.

11. Lee MS, Shin BC, Choi TY, Ernst E. Acupuncture for treating dry eye: a systematic review. Acta Ophthalmol. 2011;89(2):101–6.

12. Kim TH, Kang JW, Kim KH, et al. Acupuncture for the treatment of dry eye: a multicenter randomized controlled trial with active comparison intervention (artificial teardrops). PLoS One. 2012;7(5):e36638.

13. Liu Q, Liu J, Ren C, et al. Proteomic analysis of tears following acupuncture treatment for menopausal dry eye disease by two-dimensional nano-liquid chromatography coupled with tandem mass spectrometry. Int J Nanomedicine. 2017;12:1663–71.

14. Kuo YK, Lin IC, Chien LN, et al. Dry eye disease: a review of epidemiology in Taiwan, and its clinical treatment and merits. J Clin Med. 2019;8(8):1227.

15. Wei QB, Ding N, Wang JJ, Wang W, Gao WP. Acupoint selection for the treatment of dry eye: a systematic review and meta-analysis of randomized controlled trials. Exp Ther Med. 2020;19(4):2851–60.

16. Zhu WZ, Ni J, et al. A preliminary observational study of 27 cases of acupuncture for dry eye disease by Jingming acupuncture point. Chin Acupuncture Moxibustion. 2017;1:37 (Chinese).

17. Zhang X, Liu Z, Ding W, Zhang J, Shi H, Zhu W. Efficacy and safety of acupuncture at a single BL1 acupoint in the treatment of moderate to severe dry eye disease: protocol for a randomized controlled trial. Medicine (Baltimore). 2018;97(22):e10924.

18. Thulasi P, Djallilari AN. Update in current diagnostics and therapeutics of dry eye disease. Ophthalmology. 2017;124:527–33.

19. Baudouin C, Figueiredo Francisco C, Messmer Elisabeth M, et al. A randomized study of the efficacy and safety of 0.1% cyclosporine A cationic emulsion in treatment of moderate to severe dry eye. Eur J Ophthalmol. 2017;27:520–30.

20. Brott NR, Ronquillo Y. Schirmer Test. 2022 May 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–.

21. Eom HD, Jung JU, Lee KP, et al. Simplified classification of tear film breakup patterns and their clinicopathological correlations in patients with dry eye disease: Eye Contact Lens. 2021;47(1):15–19.

22. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003;22(7):640–50.

23. Zhang X, Wang Y, Wang Z, Wang C, Ding W, Liu Z. A randomized clinical trial comparing the effectiveness of electroacupuncture versus medium-frequency electrotherapy for discogenic sciatica. Evid Based Complement Alternat Med. 2017;2017:9502718.

24. Robert PY, Cochener B, Amrane M, et al. Efficacy and safety of a cationic emulsion in the treatment of moderate to severe dry eye disease: a randomized controlled study. Eur J Ophthalmol. 2016;26(6):546–55.

25. Zhao L, Chen J, Li Y, et al. The long-term effect of acupuncture for migraine prophylaxis: a randomized clinical trial. JAMA Intern Med. 2017;177:508–15. https://doi.org/10.1001/jamainternmed.2016.9378.

26. Miller KL, Walt JG, Mink DR, et al. Minimal clinically important difference for the ocular surface disease index. Arch Ophthalmol. 2010;128(1):94–101.

27. Nepp J, Jandrasits K, Schaersberger J, et al. Is acupuncture an useful tool for pain-treatment in ophthalmology? Acupunct Electrother Res. 2002;27(3-4):171–82.

28. Shi JL, Miao WH. Effects of acupuncture on lactoferrin content in tears and tear secretion in patients suffering from dry eyes: a randomized controlled trial. Zhong Xi Yi Jie He Xue Bao. 2012;10(9):1003–8.

29. Lan W, Tong L. Acupuncture has effect on increasing tear break-up time: acupuncture for treating dry eye, a randomized placebo-controlled trial. Acta Ophthalmol. 2012;90(1):e73.

30. Dhaliali DK, Zhou S, Samudre SS, Lo NJ, Rhee MK. Acupuncture and dry eye: current perspectives. A double-blinded randomized controlled trial and review of the literature. Clin Ophthalmol. 2019;13:731–40.

31. Jeon JH, Shin MS, Lee MS, et al. Acupuncture reduces symptoms of dry eye syndrome: a preliminary observational study. J Altern Complement Med. 2010;16(12):1291–4.

32. Gong L, Sun X. Treatment of intractable dry eyes: tear secretion increase and morphological changes of the lacrimal gland of rabbit after acupuncture. Acupuncture Electrother Res. 2007;32(3-4):223–33.

33. Zhang W, Li HZ, Zhao N, Hai X, Dong H, Wang J. Bridge role of Jingming (BL 1) for VDT asthenopia and brainfatigue based on human instinct. Zhongguo Zhen Jiu. 2017;37(1):85–7 (Chinese).

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