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REVIEW

A Network Meta-Analysis Comparing the Efficacy Differences of Different Acupuncture and Sodium Hyaluronate Eye Drops in the Treatment of Dry Eye Disease

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Objective: To systematically evaluate the efficacy of different acupuncture methods and sodium hyaluronate eye drops in the treatment of dry eye disease, and to rank the interventions through a network meta-analysis.

Methods: Chinese and English databases were searched to collect randomized controlled trials (RCTs) published from the establishment of the databases to October 14, 2025. The Cochrane Risk of Bias tool was used to assess the quality of the literature. Bayesian network Meta-analysis was performed using R software to calculate relative risk (RR), mean difference (MD), and SUCRA value to evaluate the efficacy of the interventions.

Results: A total of 30 RCTs were included, involving 2,514 patients and 10 acupuncture methods. Network meta-analysis showed that electroacupuncture was the best in terms of total effective rate (SUCRA = 0.98). With respect to Schirmer I test (SIT) and tear film break-up time (BUT), fascia release acupuncture combined with acupuncture had the best effect (SUCRA = 0.87 and 0.95, respectively). In general, fascia release acupuncture combined with acupuncture was the optimal intervention among the evaluated modalities.

Conclusion: Acupuncture is superior to sodium hyaluronate eye drops in the treatment of dry eye disease. Fascia release acupuncture combined with acupuncture performs best in improving tear secretion and tear film stability, while electroacupuncture is most likely to be optimal in improving the overall effective rate.

Keywords: dry eye disease, acupuncture, sodium hyaluronate eye drops, network meta-analysis

Introduction

Dry Eye Disease (DED) is a chronic ocular surface disease that is widely prevalent worldwide. Global prevalence studies show that the overall prevalence of dry eye disease ranges from 5% to 50%.[1] Notably, the prevalence increases with age.[2] The impact of DED on the quality of life of patients cannot be ignored. DED not only leads to visual dysfunction but also significantly impairs work efficiency, increases psychological burden, and triggers chronic pain.[1] The medical expenses and productivity losses associated with DED constitute a substantial socio-economic burden, especially among people of working age.[3] In addition, the comorbidity of DED with a variety of systemic diseases, such as rheumatoid arthritis and systemic lupus erythematosus, further exacerbates the health burden of patients.[4]

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Although diverse therapeutic options exist for DED, current treatment methods still face significant limitations. Regarding pharmacological interventions, artificial tears such as sodium hyaluronate remain the primary treatment. However, they offer only temporary symptomatic relief and fail to fundamentally restore tear secretion or tear film stability.[5] For inflammation-mediated DED, immunomodulators such as cyclosporine A and lifitegrast can improve the ocular surface microenvironment by inhibiting the activation of T cells and the release of inflammatory cytokines.[6] While corticosteroids can rapidly control acute inflammation, their long-term application is limited by risks such as elevated intraocular pressure. In recent years, new pathogenesis-targeted drugs, such as androgen replacement therapy and topical insulin preparations, have shown promise in clinical trials, yet further robust clinical evidence is required to confirm their efficacy.[7] Among non-pharmaceutical treatments, while biological agents like autologous serum and platelet-rich plasma have demonstrated certain potential, their clinical widespread adoption is constrained by complex preparation protocols, high costs, and the uncertainty regarding the long-term efficacy.[8] Moreover, the individualized treatment strategy of DED is still insufficient, and a dearth of precise treatment regimens for distinct etiologies and pathological mechanisms persists. In real-world clinical settings, treatment persistence remains a concern, as patients may discontinue therapy when faced with cumbersome dosing schedules or inadequate symptomatic relief.[9] These limitations highlight the urgent need to explore novel treatment approaches and optimize existing therapeutic strategies.

In this context, acupuncture has emerged as a promising alternative, with mounting evidence supporting its efficacy in the management of DED.[10,11] Despite its potential advantages as an alternative therapy, significant evidence gaps remain to be addressed. Randomized controlled trials (RCTs) are the gold standard for efficacy evaluation, but the quality of studies in the field of acupuncture is uneven. Initially, a lack of standardized intervention regimens persists, where diverse forms such as traditional acupuncture, electroacupuncture, and guiding acupuncture coexist. In parallel, significant variations in acupoint selection and stimulation parameters result in marked inter-study heterogeneity.[12] Another critical limitation involves efficacy evaluation; while numerous studies indicate that acupuncture is superior to artificial tears in improving ocular surface disease index (OSDI) and prolonging tear film break-up time (BUT), results for certain indicators, such as the Schirmer I test (SIT), remain controversial.[13] Accordingly, comparative studies between artificial tears (eg, sodium hyaluronate) and acupuncture modalities hold significant clinical importance. This comparison is primarily grounded in the following aspects. Mechanism-wise, while artificial tears mainly relieve symptoms by physically supplementing tear components and lubricating the ocular surface, acupuncture exerts multi-target therapeutic effects by modulating the neuro-endocrine-immune network, improving local microcirculation, and inhibiting the release of pro-inflammatory cytokines such as IL-6 and TNF-α.[14] Clinically, acupuncture has been shown to alleviate patients' subjective symptoms more effectively.[15] Additionally, explorations of combined treatment strategies suggest that acupuncture integrated with artificial tears can produce synergistic effects, showing superiority in enhancing tear secretion (increased TMH) and reducing corneal fluorescein staining (CFS) scores.[16] Such comparisons not only provide an evidence-based basis for clinical decision making, but also lay a theoretical foundation for understanding the complementarity of different treatment modalities. More importantly, there is a notable paucity of direct comparative studies between different acupuncture interventions, which makes it difficult to determine an optimal treatment plan. These evidence gaps seriously restrict the clinical application and promotion of acupuncture in the treatment of DED. Therefore, we conducted a network meta-analysis to compare the efficacy of various acupuncture methods with sodium hyaluronate, aiming to provide evidence for clinical practice.

Methods

Register

This study follow PRISMA manual (PRISMA - NMA) report, and registered in PROSPERO (ID: 420251172501) https://www.crd.york.ac.uk/PROSPERO/view/CRD420251172501

Inclusion Criteria

Study subjects: Patients diagnosed with DED according to authoritative diagnostic criteria.[17,18] No restrictions on gender, age, race or nationality.

Intervention measures: acupuncture (acupuncture, electroacupuncture, Fu's Subcutaneous Needling, acupoint application, moxibustion, etc.) or combined with other treatments (medicine, etc).

Control group: Sodium hyaluronate eye drops.

Outcomes: Efficacy: clinical efficacy was assessed based on the *Criteria for Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine* issued by the National Administration of Traditional Chinese Medicine.[19] The Total Effective Rate (TER) was calculated as follows: TER = (number of recovered + markedly effective + effective cases) / total number of patients × 100%. The specific criteria were: (1) Recovery: Complete resolution of clinical symptoms and signs, with multiple SIT values > 10 mm / 5 min; (2) Markedly effective: Significant improvement in clinical symptoms and signs, with multiple SIT values > 7 mm / 5 min; (3) Effective: Moderate improvement in clinical symptoms and signs, with multiple SIT values > 4 mm / 5 min; (4) Ineffective: No improvement or aggravation of clinical symptoms, with multiple SIT values < 4 mm / 5 min. Schirmer I test (SIT) and Break up time (BUT): Although minor operational variations existed among the studies (eg, filter paper placement or fluorescein sodium volume), all the included RCTs adhered to standardized international protocols for SIT and BUT.[19] For SIT, a standardized filter paper was placed in the outer third of the lower eyelid conjunctival sac, and the length of tear infiltration was measured after 5 minutes. For BUT, the interval between a complete blink and the first appearance of a dry spot on the corneal surface was recorded following fluorescein sodium staining. Therefore, the consistency in these measurement techniques ensured that data from different studies were highly comparable without the need for additional data conversion or standardized score transformation.

Type of study: Randomized Controlled Trial.

Exclusion Criteria

Studies were excluded if they met any of the following criteria: (1) duplicate publications; (2) non-randomized controlled trials, including reviews and meeting abstracts; (3) trials employing a blank control; (4) trials comparing the identical acupuncture modality with variations only in acupoints, manipulation, or frequency; (5) studies with incomplete data or evident errors; and (6) interventions appearing only in a single study or those limited to a specific practitioner's unique protocol.

Data Sources and Search Strategies

Randomized controlled trials (RCTs) regarding acupuncture for DED were systematically searched across Chinese and English databases, including PubMed, Embase, the Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), WanFang Database for Academic Journals (WanFang), VIP database (VIP), and SinoMed. The search was conducted from the inception of each database to October 14, 2025. The detailed search strategies for all databases are provided in Supplementary Tables 1–4.

Literature Screening

Literature screening was conducted independently by two researchers (Xin Yan and Jinlu Hu). First, duplicate records were removed using EndNote X9 software.[20] Subsequently, the titles and abstracts were screened to exclude studies that did not meet the eligibility criteria. The full texts of the remaining articles were then obtained and thoroughly reviewed to determine final inclusion. Any disagreements between the two researchers were resolved through consensus or by consultation with a third researcher (Mu Qin).

Data Extraction

Two researchers (Xin Yan and Jinlu Hu) independently extracted data using a predesigned data extraction form. The extracted information included: (1) basic study characteristics, such as author, year, sample size, interventions for both

groups, course of treatment, and follow-up period; (2) outcome measures, including primary and secondary metric values; and (3) methodological characteristics and information related to the risk of bias. The extracted data were cross-checked, and any discrepancies were resolved through discussion.

Risk of Bias Assessment

The included literature was evaluated for quality and risk of bias using the Cochrane Risk of Bias tool (RoB 2).[21] The assessment covered five evaluation domains: (1) bias arising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in outcome measurement; and (5) bias in selection of the reported result. Each domain was categorized into three levels: "low risk", "some concerns" and "high risk". The overall risk of bias was determined as follows: "low risk" if all domains were at low risk; "some concerns" if at least one domain was judged to some concerns but no domain was at high risk; and "high risk" if at least one domain was judged to be at high risk. Two researchers (Xin Yan and Shiqi Lei) performed the assessments independently, and any discrepancies were resolved through discussion or by consulting a third researcher (Mu Qin).

Statistical Analysis

Relative risk (RR) and mean difference (MD) were employed as the effect measures for binary and continuous variables, respectively. Meta-analysis was performed using R software (version 4.2.2). The point estimate and 95% confidence interval (CI) for direct comparisons were given, and the network evidence map was drawn. A comparison-adjusted funnel plot was utilized to identify the small-study effects and publication bias within the intervention network. Markov chain Monte Carlo (MCMC) methods were used for Bayesian inference. Specifically, four chains were established with 10,000 iterations each; the initial 5,000 iterations were discarded as burn-in to ensure stable convergence, with a thinning interval of 20. Posterior probabilities were inferred from prior distributions once the Markov chains reached a steady state. Both fixed-effects and random-effects models were fitted, and the goodness of fit was judged according to the Deviance information criterion (DIC), with the lower DIC value indicating a superior fit. League tables were constructed based on the effect values of pairwise comparisons between interventions. Meanwhile, the probability of being the optimal treatment and the Surface Under the Cumulative Ranking (SUCRA) area were calculated to rank the interventions. A SUCRA value closer to 1 indicates a higher probability of superior clinical efficacy. Finally, sensitivity analysis was performed to assess the robustness of the results, and meta-regression was employed to explore the potential influence of heterogeneous factors.

Results

Results of Literature Screening

A total of 2,032 articles were retrieved, and 1,616 duplicate articles were removed. After a preliminary screening of titles and abstracts, 383 records were excluded. Subsequently, the remaining articles underwent a full-text review, resulting in the exclusion of 3 additional studies. Ultimately, 30 studies[16,22–50] were identified as eligible and included in the final analysis. The detailed literature screening process is illustrated in Figure 1.

Basic Characteristics

A total of 30 studies[16,22–50] were included, involving 2,514 participants (1,278 in the intervention group and 1,236 in the control group). The analysis encompassed 10 acupuncture-related interventions: Fu's Subcutaneous Needling, acupuncture, traditional Chinese medicine combined with acupuncture, walnut-shell moxibustion, thunder-fire moxibustion, thumbtack needling, heat-sensitive moxibustion, electroacupuncture, acupoint application, and fascia release needling technique. The main characteristics of the included studies are summarized in Table 1.

Risk of Bias Assessment results

Regarding random sequence generation, 20 studies had a low risk, 3 had a high risk, and 7 had some concerns. Only one study implemented allocation concealment (using the envelope method). Due to the nature of acupuncture interventions,

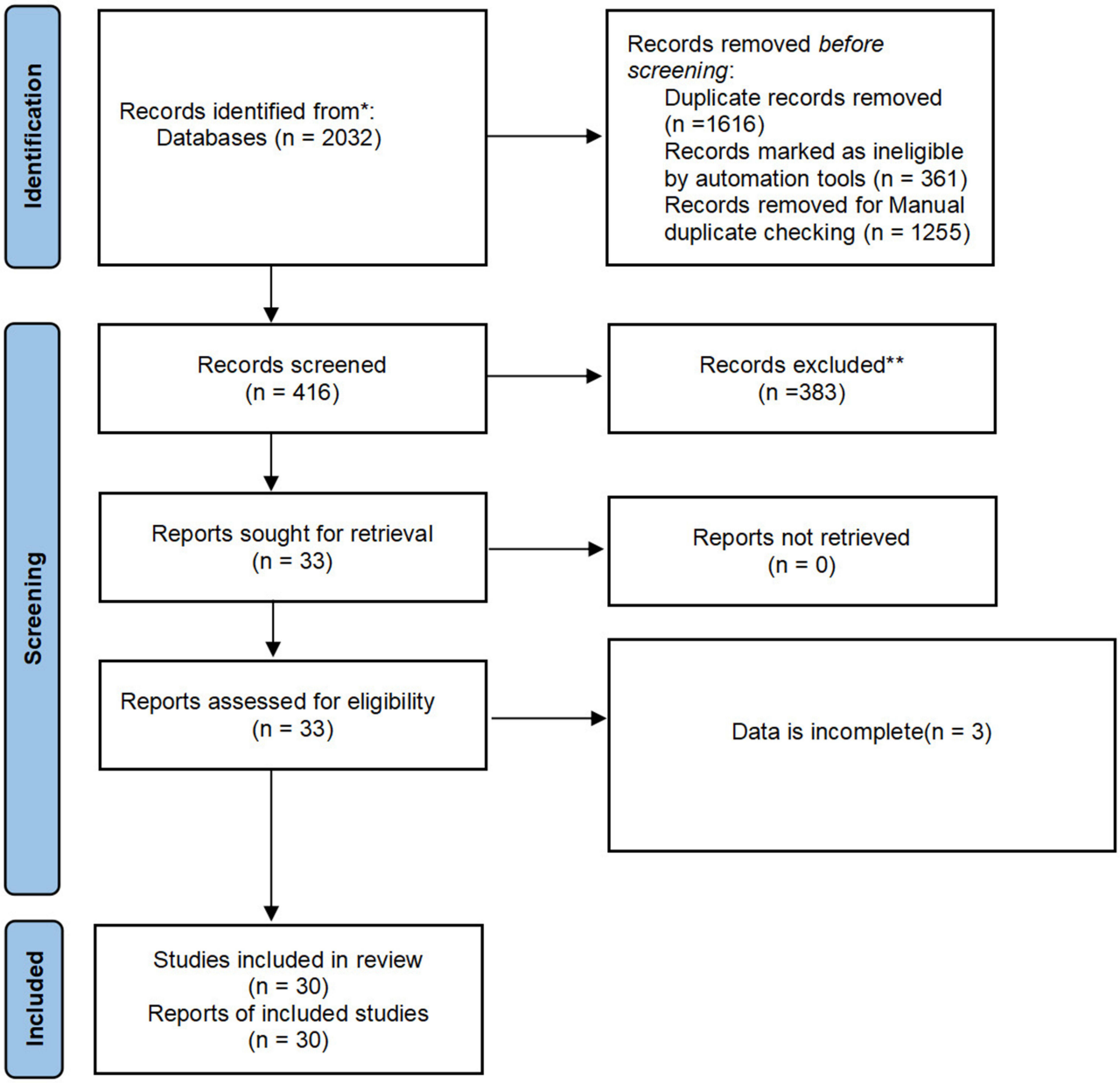

Figure 1 Literature screening process (*Consider,if feasible to do so,reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers.**If automation tools were used,indicate how many records were excluded by a human and how many were excluded by automation tools.).

implementing blinding of participants and personnel was inherently challenging; consequently, only one study reported using a blinding method. However, the potential impact of this lack of blinding on objective outcomes was considered limited. All included studies provided complete outcome data, and no evidence of selective reporting or other significant sources of bias was found. Overall, 3% (1/30) of the studies had a low risk of bias, 10% (3/30) had a high risk, and 87% (26/30) had some concerns (Figure 2).

Meta-Analysis

Efficacy

Twenty-four studies reported efficacy, including 10 acupuncture-related interventions, with the most studies on acupuncture (Figure 3). The results of the inconsistency test showed a P-value > 0.05, indicating no significant inconsistency;

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Table 1 Basic Characteristics of the Included Studies

Author	Year	Sample Size (I/C)	DED type	Duration of DED (I/C)	Gender (M/F)		Age (I/C)	Interventions	Control measures	Frequency	Outcomes	Course
					I	C						
CGF[22]	2022	30/30	Senile DED	±29.1±13.5/28.7 ±12.0(m)	11/19	10/20	65.67±5.24/ 64.80±4.23	2	1	Twice a week	Efficacy, BUT, SIT	4w
CCY[23]	2021	40/40		12.56±5.32/13.61 ±4.52(m)	18/22	17/23	38.12±7.36/ 38.85±8.36	3+4	1	Once a day	Efficacy, BUT, SIT	4w
ZQ[24]	2024	60/60	Perimenopausal DED	1.5±0.8/1.4 ±0.7(m)	0/30	0/30	49.8±4.3/49.7 ±4.3	3+5	1	Three times a week	Efficacy, BUT, SIT	4w
ZJ[25]	2023	150/150			79/71	78/72	48.77±3.11/ 49.25±2.96	3+4	1	Four times a week	Efficacy, BUT, SIT,AE	4w
CTT[26]	2019	20/20			5/15	6/14	48.2±11.2/47.6 ±10.5	3	1	Three times a week	Efficacy	12w
CMM[27]	2021	75/75	Middle-aged and elderly DED	27.60±7.56/25.80 ±7.08(m)	33/42	34/41	53.44±6.12/ 53.78±6.40	3+4	1	Once a day	Efficacy, BUT, SIT	4w
DSQ[28]	2024	47/47	DED after phacoemulsification of cataract	10.39±3.18/10.17 ±3.69(d)	23/24	25/22	63.27±6.88/ 62.89±7.34	6+4	1	Once a day	Efficacy, BUT, SIT	4w
GH[29]	2023	30/30		16.8±10.8/18.0 ±12.0(m)	18/12	14/16	45.8±12.5/47.2 ±10.6	7+4	1	Twice a week	Efficacy, BUT, SIT	12w
JY[30]	2022	40/40	Meibomian gland dysfunction associated with DED	21.38±4.14/21.23 ±4.07(m)	23/17	21/19	45.73±6.81/ 45.62±6.77	3	1	Once every two days	Efficacy, BUT, SIT	12w
LYM[31]	2025	32/32			9/23	10/22	30.57±1.80/ 26.38±0.92	8	1	Once every three days	Efficacy, BUT, SIT	4w
LGX[32]	2012	36/36	Schirmer hyposecretion DED	2d-12m	30/42		40~70	3	1		Efficacy	4w
LX[16]	2023	30/30	Aqueous deficiency type DED	11.3±3.3/10.2 ±2.4(m)	14/15	12/17	47±14/41±11	3	1	Once a day	BUT, SIT	2w

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LYL[33]	2012	20/20		8±1.5/7±1.2(m)	11/9	10/9	31.4±1.3/32.5 ±1.4	9	1	Once a day	Efficacy, BUT, SIT	3w
LYY[34]	2025	45/45	DED after cataract surgery		25/20	24/21	66.02±3.77/ 65.98±3.80	10+4	1	Once a day	Efficacy, BUT, SIT	4w
WQN[35]	2024	30/30	DED of lung Yin deficiency type	10.75±3.46/11.26 ±2.92(m)	19/11	17/13	51.06±8.26/ 52.81±7.39	3+4	1	Once a day	Efficacy, BUT, SIT	4w
WLX[36]	2010	40/40		30.18±31.69/ 30.20±43.76(m)	10/30	13/27	44.75±17.06/ 42.98±12.54	3	1	Once every two days	BUT, SIT	3w
WQM[37]	2023	45/45	Meibomian gland dysfunction type DED		13/32	15/30	53.87±13.17/ 53.16±13.28	6	1	Once a day	BUT	4w
WZX[38]	2023	42/41/41		16.3±9.8/16.2 ±10.2/16.1 ±9.6(m)	20/2220/2118/23		43.0±14.4/44.2 ±15.1/45.1±13.0	11+33	1	Once a day	Efficacy, BUT, SIT	4w
XH[39]	2014	30/30		22.4±13.4/14.5 ±11.0(m)	5/25	4/26	39±15/41±13	3	1	Three times a week	BUT, SIT	4w
ZHY[40]	2021	30/30					18~70	3+4	1	Once every two days	Efficacy, BUT, SIT	4w
ZJ[41]	2022	30/30		0.58±0.29/0.62 ±0.34(m)	13/17	12/18	46.8±3.6/45.5 ±2.3	3+4	1	Once a day	Efficacy, BUT, SIT	4w
ZX[42]	2022	30/30	Moderate to severe DED		7/23	8/22	44.16+7.8/41.28 +8.8	3	1	Three times a week	BUT, SIT,AE	8w
ZY[43]	2009	28/26	Perimenopausal DED		0/28	0/26	52.00±5.23/ 51.50±5.96	3	1	Once a day	BUT, SIT	4w
ZJ[44]	2022	65/65			35/30	33/32	38.60±7.66/ 37.89±7.05	3+4	1	Once a day	Efficacy, BUT, SIT	2w
ZD[45]	2013	36/36	Perimenopausal DED		0/36	0/36	50.0±3.5/49.0 ±3.9	3	1	Once a day	Efficacy	2w
ZD[46]	2019	30/30		30.3±31.7/30.2 ±42.7(m)	10/20	11/19	41±14/41±12	3	1	Once every two days	Efficacy, BUT	4w

(*Continued*)

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Table 1 (Continued).

Author	Year	Sample Size (I/C)	DED type	Duration of DED (I/C)	Gender (M/F)		Age (I/C)	Interventions	Control measures	Frequency	Outcomes	Course
					I	C						
GY[47]	2021	67/67			22/45	21/46	44.27±7.16/ 45.01±6.84	3	1	Once a day	Efficacy, BUT, SIT	4w
LJY[48]	2022	30/30	DED after myopic laser surgery	4.43±1.23/4.36 ±1.13(m)	17/13	14/16	25.83±4.62/ 25.16±3.67	3+4	1	Once every two days	Efficacy, BUT, SIT	3w
LJ[49]	2025	20/20		14.16±4.68/15.00 ±2.52(m)	9/11	8/12	43.02±5.30/ 42.35±4.18	3	1	Three times a week	Efficacy, BUT, SIT	4w
JHR[50]	2021	30/30			13/17	14/16	40.83±10.08/ 42.73±13.06	9	1	Three times a week	Efficacy, BUT, SIT	4w

Notes: I, Intervention group; C, Control group; M, Male; F, Female. Interventions: 1, Sodium hyaluronate eye drops; 2, Fu's Subcutaneous Needling; 3, Acupuncture; 4, Traditional Chinese medicine; 5, Walnut-shell moxibustion; 6, Thunder-fire moxibustion; 7, Thumbtack needling; 8, Heat-sensitive moxibustion; 9, Electroacupuncture; 10, Acupoint application; 11, Fascia release needling technique.

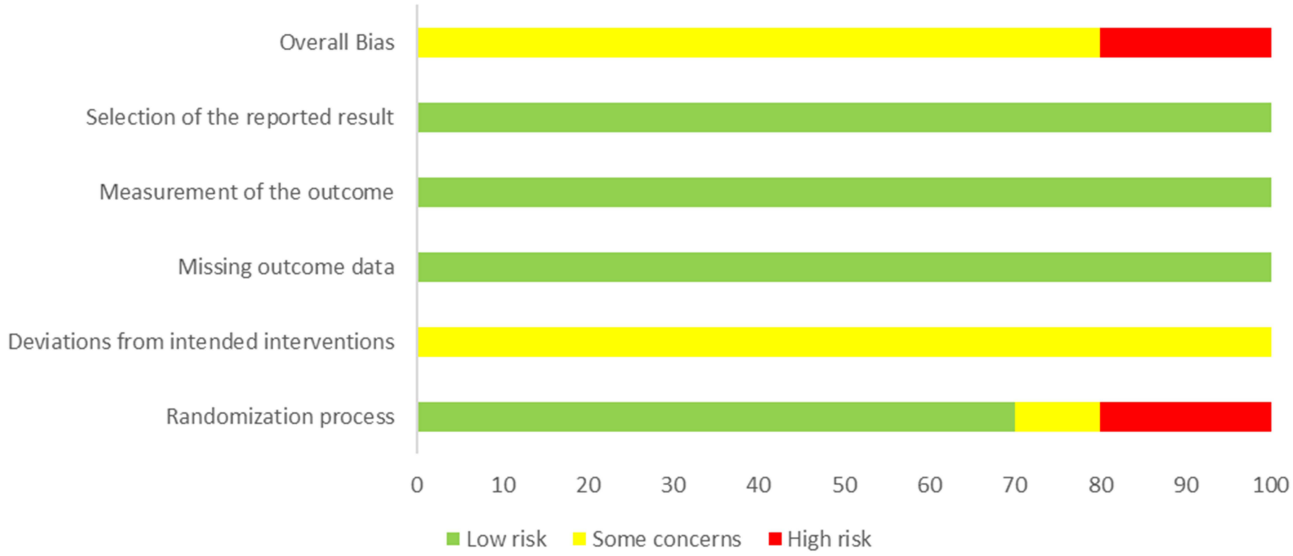

Figure 2 Risk of bias graph.

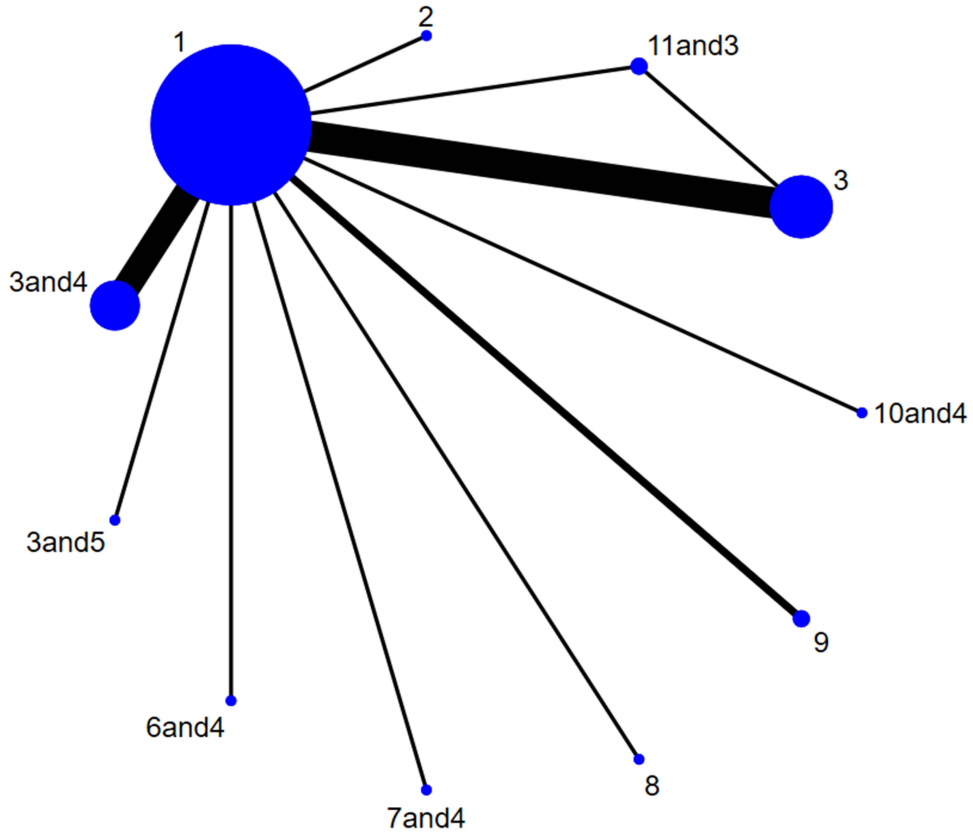

Figure 3 Network Diagram of acupuncture combined with DED for AS (Efficacy).

therefore, a consistency model was employed for the analysis. Heterogeneity test results showed I^2=23%, suggesting low heterogeneity. Network meta-analysis results revealed that, compared with the control group, the following interventions were significantly superior ($P < 0.05$): fascia release needling technique combined with acupuncture [RR = 1.5, 95% CI (1.1, 2.0)], acupuncture [RR = 1.3, 95% CI (1.2, 1.6)], traditional Chinese medicine combined with acupuncture [RR = 1.3, 95% CI (1.1, 1.4)], and electroacupuncture [RR = 2.4, 95% CI (1.6, 3.9)] (Figure 4). Notably, electroacupuncture

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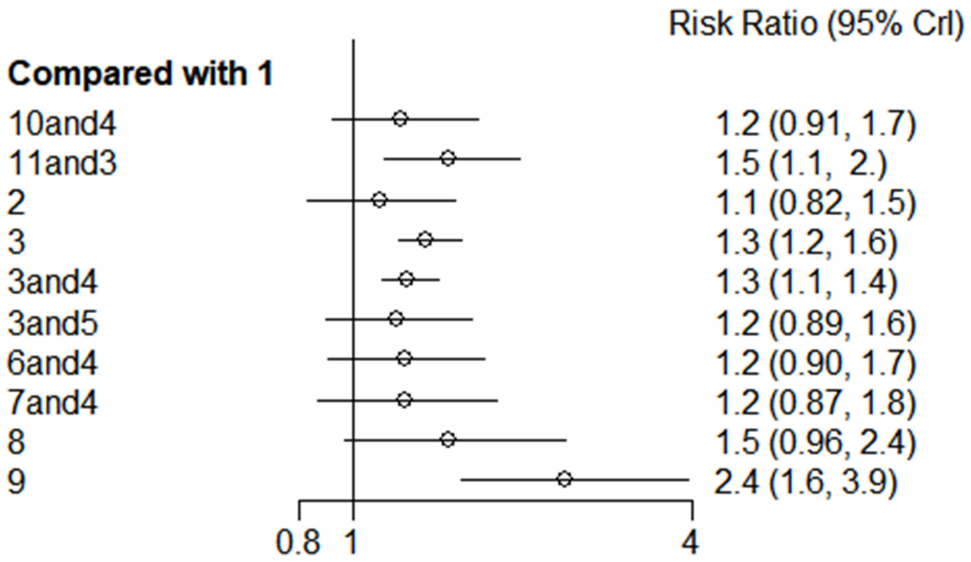

Figure 4 Forest map of acupuncture combined with DED for AS (Efficacy).

demonstrated superior efficacy compared to other acupuncture methods (Supplementary Table 5). According to the SUCRA values, the top three interventions were electroacupuncture (SUCRA = 0.98), fascia release needling technique combined with acupuncture (SUCRA = 0.72), and heat-sensitive moxibustion (SUCRA = 0.69) (Table 2).

SIT

Twenty-five studies reported SIT, including 10 acupuncture-related interventions, with the largest number of studies on acupuncture (Figure 5). The results of the inconsistency test showed a P-value > 0.05, indicating no significant inconsistency;

Table 2 SUCRA Ranking

Intervention	Efficacy		SIT		BUT	
	SUCRA	No	SUCRA	No	SUCRA	No
1	0.05	11	0.14	10	0.07	11
10and4	0.42	8	0.66	3	0.60	4
11and3	0.72	2	0.87	1	0.95	1
2	0.25	10	0.63	4	0.62	3
3	0.63	4	0.42	8	0.37	9
3and4	0.46	5	0.57	5	0.50	7
3and5	0.38	9	0.46	7	0.45	8
6and4	0.43	7	0.14	11	0.31	10
7and4	0.43	6	0.28	9	0.54	5
8	0.69	3	0.49	6	0.50	6
9	0.98	1	0.80	2	0.69	2
6and4					0.34	10

Notes: 1, Sodium hyaluronate eye drops; 2, Fu's Subcutaneous Needling; 3, Acupuncture; 4, Traditional Chinese medicine; 5, Walnut-shell moxibustion; 6, Thunder-fire moxibustion; 7, Thumbtack needling; 8, Heat-sensitive moxibustion; 9, Electroacupuncture; 10, Acupoint application; 11, Fascia release needling technique.

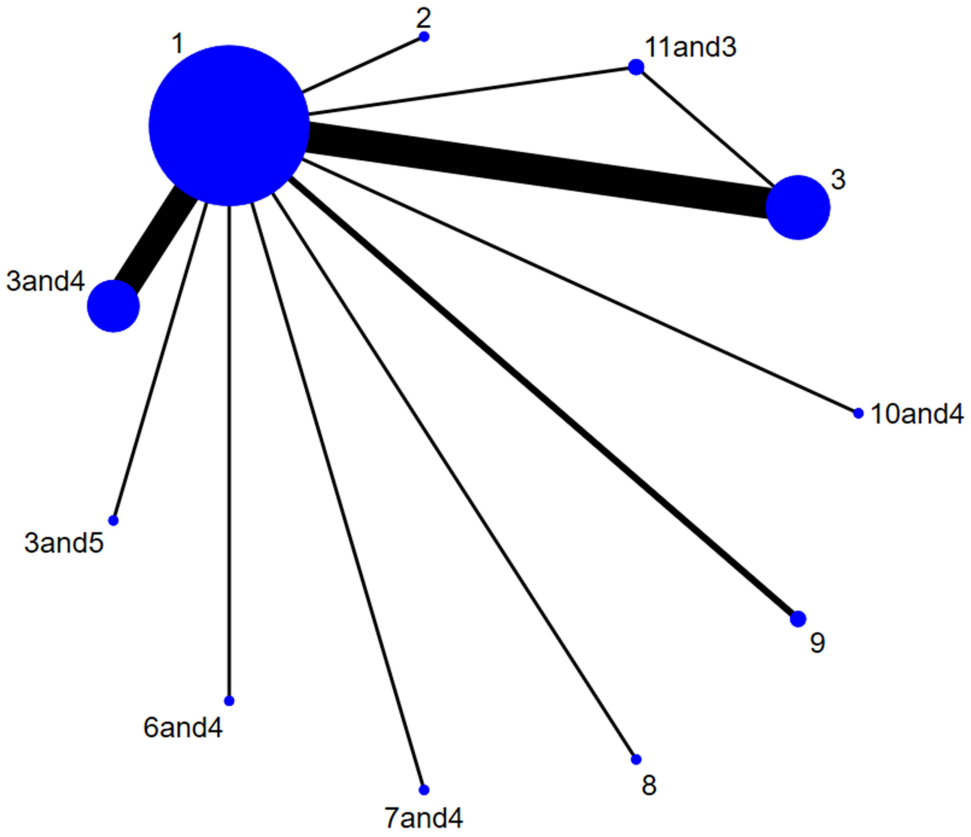

Figure 5 Network diagram of acupuncture combined with DED for AS (SIT).

therefore, a consistency model was employed for the analysis. Heterogeneity test results showed I^2=23%, suggesting low heterogeneity. Network meta-analysis results revealed that, compared with the control group, the following interventions were significantly superior (P < 0.05): fascia release needling technique combined with acupuncture [MD = 4.9, 95% CI (1.2, 8.7)], acupuncture [MD = 1.7, 95% CI (0.3, 3.3)], traditional Chinese medicine combined with acupuncture [MD = 2.6, 95% CI (1.1, 4.1)], and electroacupuncture [MD = 4.4, 95% CI (1.4, 7.4)] (Figure 6). Significant differences were observed among the interventions (Supplementary Table 6). According to the SUCRA values, the top three interventions were fascia release

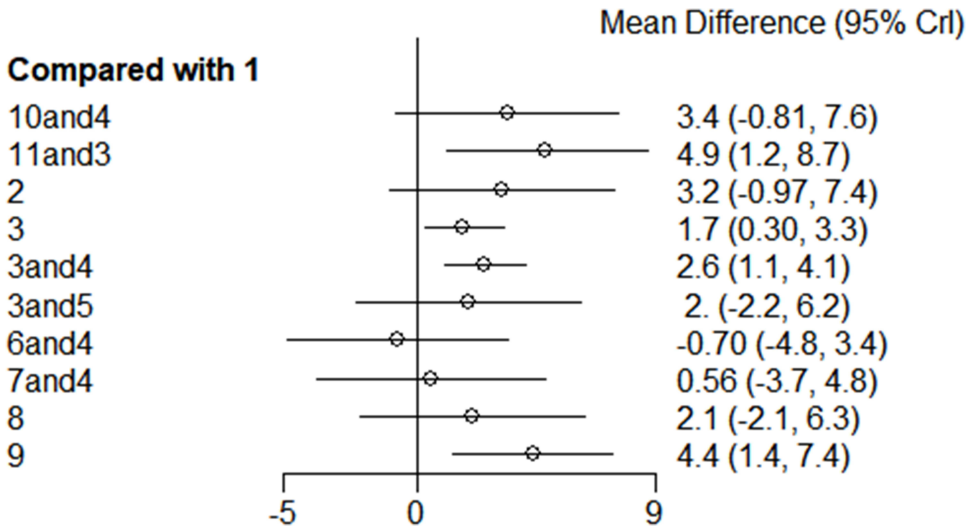

Figure 6 Forest map of acupuncture combined with DED for AS(SIT).

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needling technique combined with acupuncture (SUCRA = 0.87), electroacupuncture (SUCRA = 0.80), and acupoint application combined with traditional Chinese medicine (SUCRA = 0.66) (Table 2).

BUT

Twenty-seven studies reported on BUT, including 10 acupuncture-related interventions, with the largest number of studies on acupuncture (Figure 7). The results of the inconsistency test showed a P-value > 0.05, indicating no significant inconsistency; therefore, a consistency model was employed for the analysis. Heterogeneity test results showed I^2=0.7%, suggesting low heterogeneity. Network meta-analysis results revealed that, compared with the control group, the following interventions were significantly superior (P < 0.05): fascia release needling technique combined with acupuncture [MD = 6.0, 95% CI (2.6, 9.4)], acupuncture [MD = 1.8, 95% CI (0.59, 3.0)], traditional Chinese medicine combined with acupuncture [MD = 2.4, 95% CI (1.1, 3.8)], and electroacupuncture [MD = 3.6, 95% CI (0.9, 6.3)] (Figure 8). Significant differences were observed among the interventions (Supplementary Table 7). According to the SUCRA values, the top three interventions were: fascia release needling technique combined with acupuncture (SUCRA = 0.95), electroacupuncture (SUCRA = 0.69), and Fu's Subcutaneous Needling (SUCRA = 0.62) (Table 2).

Publication Bias

The results were tested for publication bias (Figure 9a–9c), and the results showed that efficacy (Figure 9a) and BUT (Figure 9c) had a high possibility of publication bias (P < 0.05).

Sensitivity Analysis and Meta-Regression

We performed a sensitivity analysis of the results using one-by-one exclusion and found that the results did not change significantly and were stable (Supplementary Figures 1–3). Meta-regression was conducted to explore the influence of

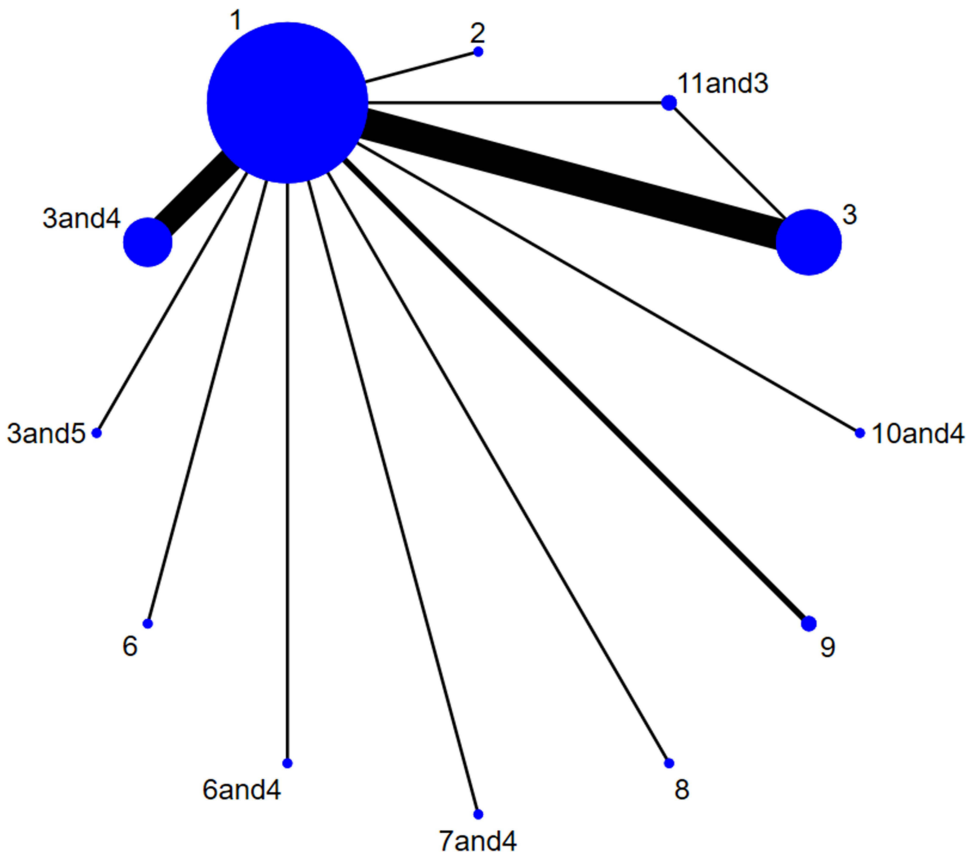

Figure 7 Network diagram of acupuncture combined with DED for AS (BUT).

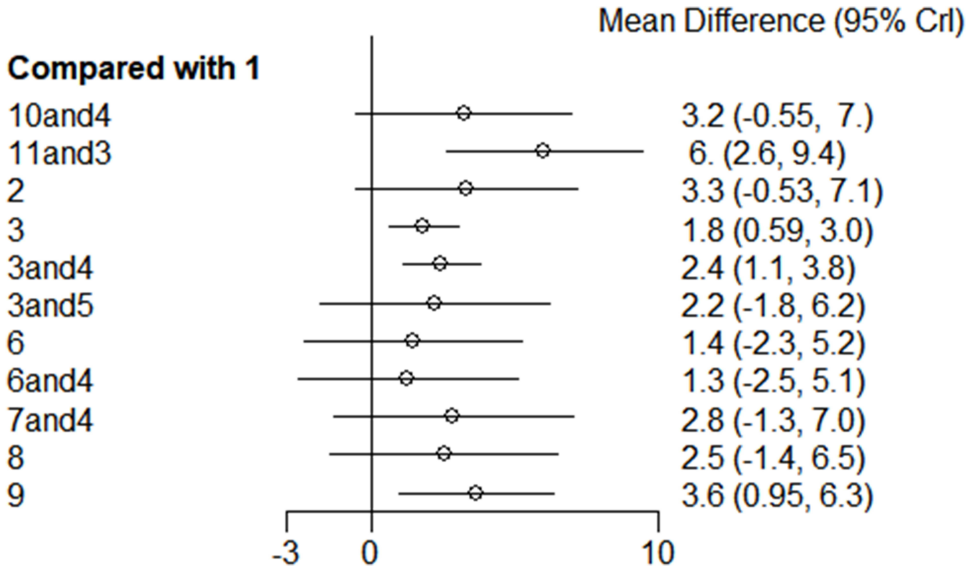

Figure 8 Forest map of acupuncture combined with DED for AS (BUT).

frequency and duration of treatment on the results relative to sodium hyaluronate eye drops (Supplementary Table 8). Regarding efficacy, the effects of electroacupuncture and acupuncture were proportional to both the frequency and duration of treatment. For SIT, the effects of acupuncture, acupuncture and traditional Chinese medicine were proportional to both the frequency and duration of treatment. Meanwhile, the effect of electroacupuncture was specifically proportional to the frequency. In terms of BUT, the effects of acupuncture, traditional Chinese medicine combined with acupuncture, fascia release needling technique combined with acupuncture, and electroacupuncture were proportional to the frequency of treatment. Additionally, the effects of acupuncture, traditional Chinese medicine combined with acupuncture, and electroacupuncture were directly proportional to the duration of treatment.

Discussion

Currently, the prevalence of DED has been increasing year by year. At present, while artificial tears serve as a primary supplement to temporarily stabilize the tear film, they offer only transient relief. For formulations containing preservatives, long-term administration carries the risk of inducing or exacerbating corneal epithelial damage. Consequently, it is urgent to seek a safer, more effective and more sustainable therapeutic interventions. As an important part of complementary and alternative medicine, acupuncture therapy has gained widespread clinical acceptance due to its safety, stability and high operability.[51] Despite a wealth of clinical studies, a deficit remains in direct comparisons among diverse acupuncture modalities. This study employed a network meta-analysis to systematically evaluate the relative efficacy of 10 acupuncture-related interventions versus sodium hyaluronate eye drops in the treatment of DED. Based on the quantitative and comprehensive analysis of 30 included RCTs involving 2,514 patients, the following core evidence was obtained. All the evaluated acupuncture interventions demonstrated superior efficacy to sodium hyaluronate eye drops in terms of overall effective rate. Specifically, electroacupuncture yielded the highest SUCRA value (SUCRA = 0.98), suggesting that it was the most likely to be the best intervention for improving the overall effective rate, followed by fascia release needling technique combined with acupuncture (SUCRA = 0.72) and heat-sensitive moxibustion (SUCRA = 0.69). Regarding the improvement of objective physical signs, fascia release needling technique combined with acupuncture was the most prominent. It ranked first for both SIT (SUCRA = 0.87), which assesses basal tear secretion, and BUT (SUCRA = 0.95), which evaluates tear film stability. Electroacupuncture also exhibited significant advantages in these two objective indicators, ranking second for both (SIT SUCRA = 0.80; BUT SUCRA = 0.69). The results of sensitivity analysis and meta-regression showed that the main conclusions were robust. Furthermore, the analysis suggested that increasing the frequency of treatment and prolonging the course of treatment were positively correlated

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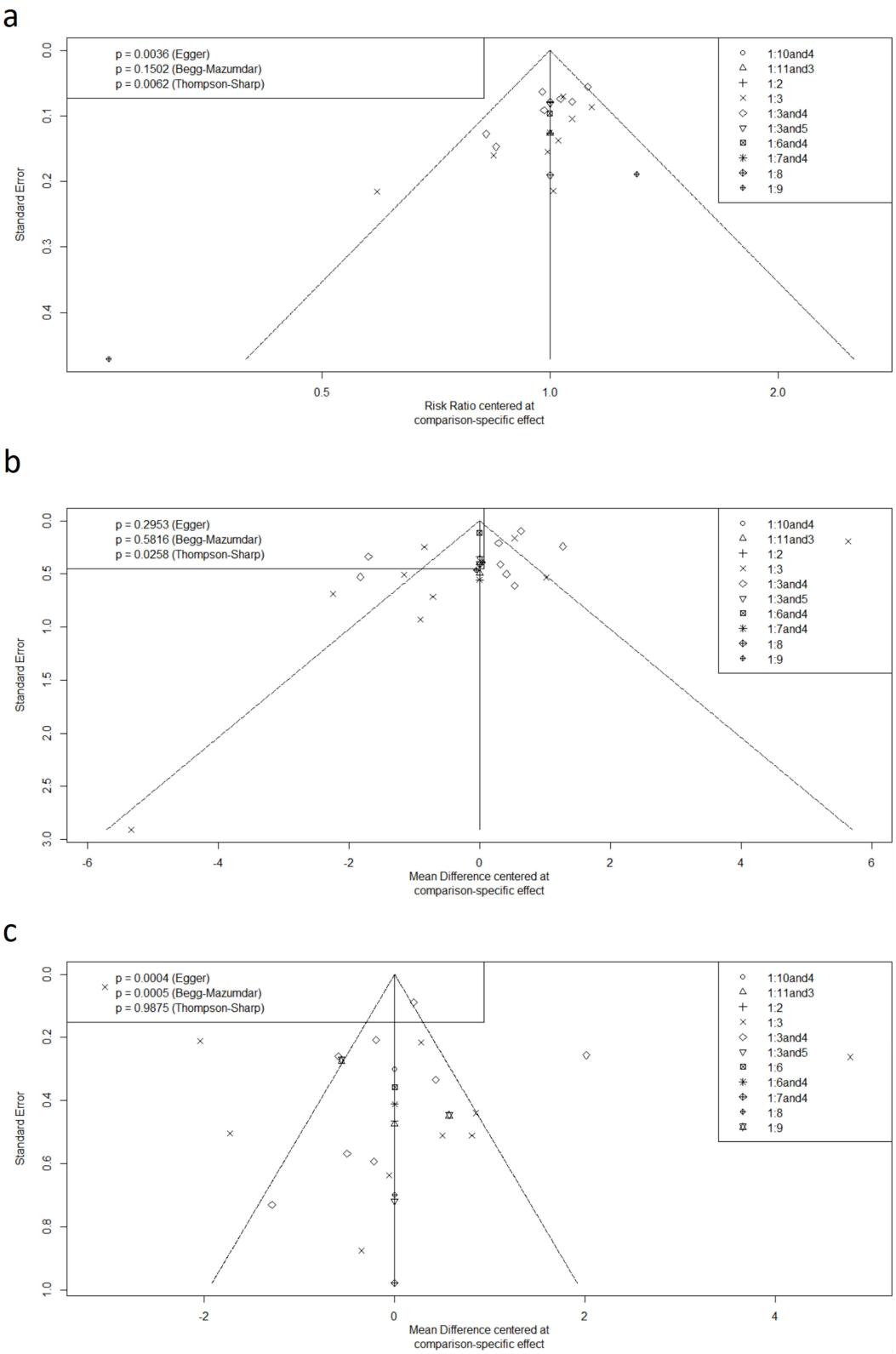

Figure 9 Comparative correction funnel plots for Efficacy (**a**), SIT (**b**), and BUT (**c**).

with enhanced efficacy for some acupuncture therapies, including electroacupuncture, acupuncture, and acupuncture combined with traditional Chinese medicine. This provides a preliminary quantitative reference for the optimization of clinical treatment regimens. Based on the ranking results of each outcome measure, fascia release needling technique combined with acupuncture showed the greatest potential in improving the core pathophysiological link of DED, lacrimal insufficiency and tear film instability. These findings offer differentiated, high-level evidence to support clinical decision making tailored to different treatment goals (eg, improvement of objective signs vs overall efficacy).

The pathological basis of DED is characterized by a self-perpetuating vicious cycle. Tear film instability triggers tear film hyperosmolarity, which subsequently drives corneal cell apoptosis and neuroinflammation. This inflammatory cascade leads to nerve sensitization and overstimulation of the lacrimal gland, further exacerbating tear film instability.[52] Emerging evidence suggests that neuropathic pain-like symptoms related to DED may be the sensitization of central nerves.[53] Central sensitization of the trigeminal nucleus causes a series of hypersensitivity and hyperalgesia reactions in DED.[54] Clinically, this manifests as mechanical pain, heat pain, tenderness and other hyperalgesia, accompanied by myofascial shortening and the formation of Myofascial Trigger Points (MTrPs). MTrPs are typically induced by muscle overload, long-term muscle tension, trauma, or strain. Mechanistically, MTrPs lead to the release of calcium in the sarcoplasmic reticulum, continuous shortening of sarcomere and muscle fiber contraction. Eventually, nodules form in areas where muscle tone is highly sensitive.[55] MTrPs may lead to persistent local contraction of muscles, which further aggravates ischemia and hypoxia, cell damage and metabolic changes, leading to the release of sensitized inflammatory responses and pain mediators (such as bradykinin, calcitonin gene-related peptide, substance P, capsaicin, tumor necrosis factor, 5-hydroxytryptamine, etc.)[56] and further aggravates muscle fiber tension.[57] Therefore, the release of MTrPs may be a key part of relieving the symptoms of DED.

Fascia release needling technique involved palpation of the orbicularis oculi, occipitofrontalis, depressor supercilii, trapezius, sternocleidomastoid muscles on both sides of the neck to identify active MTrPs. Following localized disinfection of the acupuncture site, a disposable sterile needle was inserted transversely. When the needle entered the subcutaneous fascia layer, it continued to penetrate along the fascia layer until there was only 5mm left of the needle, and the needle was stopped. After insertion, lifting and thrusting maneuvers were performed using the thumb and index finger, and the needle was withdrawn after a retention period of 1 hour. The Fascia release needling technique alleviates the symptoms of DED by deactivating MTrPs.[38] Some studies suggest that the peripheral mechanism of neurogenic inflammation is closely related to the axonal reflex dominated by C-nociceptors and dorsal root reflexes (DRR).[58] Acupuncture may release MTrPs and modulate the sensitization of the central nervous system through these pathways, thus treating DED. This lays a key foundation for strengthening the signal transduction generated by acupuncture MTrPs, thereby providing a mechanistic rationale for the treatment of DED via MTrPs-targeted acupuncture.[38] Regarding safety, two included studies reported adverse reactions. These were limited to minor localized bleeding, which resolved with cold compression, confirming the relative safety of the intervention.

Mechanistically, acupuncture has a multi-target regulatory effect in the treatment of DED. The main mechanisms include: (1) enhancing lacrimal gland secretion to improve the amount of tear and the stability of tear film;[59] (2) inhibiting the inflammatory response of ocular surface by downregulating pro-inflammatory cytokines such as TNF-α and IL-6, while upregulating the expression of MUC5AC and MUC19;[60] (3) regulating ocular surface mucin and increasing the number of goblet cells;[61] and (4) modulating the autonomic nervous system and sex hormone levels, particularly in perimenopausal-related DED.[62] Our study also found that the frequency and duration of acupuncture treatment could affect the results of acupuncture. Na et al[11] reported that a 21–30 day treatment cycle with a treatment frequency of 2–3 sessions per week achieved optimal results, whereas Kim et al[63] observed that a treatment cycle of more than 1 month produced more significant effects. However, due to the lack of follow-up data in the included studies, the long-term efficacy of acupuncture warrants further validation through large-scale longitudinal studies.

A search of the Chinese clinical trial registry (https://www.chictr.org.cn/) reveals that numerous clinical trials for acupuncture treatment of DED have been registered (eg, ChiCTR2400087341, evaluating efficacy and patient acceptance of ultrasound-guided floating needle sweeping technique in the treatment of DED; ChiCTR2400084597, observing efficacy of acupuncture for DED and its effects on depression and anxiety; and ChiCTR2300078187, investigating array microneedles in the treatment of DED). This trend indicates that acupuncture for DED is highly valued in current

clinical practice. Previously published meta-analyses have confirmed the effectiveness of acupuncture in the treatment of DED. For instance, the study by Na et al,[11] which included 21 RCTs, showed that acupuncture was superior to artificial tears alone in improving BUT [MD = 1.58, 95% CI (0.91, 2.25)] and SIT [MD = 2.18, 95% CI (1.32, 3.05)]. Similarly, the study by Yang et al,[10] which enrolled 7 RCTs, demonstrated that after treatment, the overall BUT in the acupuncture group was significantly better than that in artificial tears group [MD = 0.48, 95% CI (0.29, 0.67)], which was consistent with the results of our study [MD = 1.80, 95% CI (0.59, 3.00)]. Their study included a variety of artificial tears, which may have more clinical heterogeneity. In this study, only one type of artificial tears was selected for comparison, and the results were more reasonable.

Looking ahead, we believe that the development direction of acupuncture for DED is as follows: (1) Establishment of unified operating standards, such as acupoint compatibility, stimulation parameters, and treatment course settings. (2) Strengthening basic research: using fMRI and microdialysis technology to clarify the neuroendocrine mechanism of acupuncture in regulating lacrimal gland secretion. (3) Multi-center large-sample trials: special attention should be paid to special populations, such as patients after refractive surgery, who have poor response to traditional drug treatment, and preliminary data show that acupuncture can reduce their OSDI scores by more than 50%.[64] (4) Incorporate acupuncture into a step-wise treatment protocol as a second-line option for moderate to severe dry eye, and develop a portable periocular acupoint stimulation device to improve treatment accessibility.

The limitations of this study are as follows: (1) Some included studies have deficiencies in the randomization method, the principle of allocation concealment and the reporting of blinding, which may lead to a potential risk of bias in research results and affect the reliability of relevant conclusions. Due to the particularity of acupuncture (eg, the deqi sensation, acupuncture manipulation, etc)., it is objectively difficult to achieve complete blinding of both practitioners and participants, which is also a common challenge for acupuncture clinical research at home and abroad. Therefore, the possible risks caused by "inadequate implementation of blinding" have been marked in the analysis, and the results were interpreted with caution. In addition, testing for heterogeneity (all I^2 values were very low) and consistency model analysis partially supported the robustness of the pooled results. To minimize blinding-related bias in future research, several strategies are recommended: First, employing non-penetrating sham acupuncture—utilizing devices such as the blunt-tipped, retractable Streitberger needle at non-acupoints or non-therapeutic acupoints — can effectively simulate the tactile sensation and visual appearance of authentic acupuncture. This approach prevents participants from distinguishing between active and sham interventions and is internationally recognized as a highly reliable placebo control method. Second, utilizing an opaque cannula or an adhesive bandage to cover the needling sites ensures that subjects remain blinded to the entry points and procedural details. Third, implementing standardized, neutral procedural description and communication language for both the operator and the subject can avoid suggestive cues. Importantly, assigning independent, blinded assessors to conduct all outcome evaluations and ensuring that data analysts are completely unaware of group allocations are critical steps. This approach is not only highly feasible but also serves as the most effective safeguard against potential measurement bias. Finally, blinded effectiveness tests using structured questionnaires should be administered at study completion to quantify the actual success of the blinding. (2) In the process of literature screening, we systematically searched the English databases including PubMed, EMbase, Cochrane Library, and Web of Science. However, among the studies that met the inclusion criteria, the number of Chinese studies was still dominant, which was determined by the special properties of acupuncture. (3) Variations in acupoint matching, frequency and treatment course across independent studies introduced a certain degree of clinical heterogeneity. (4) The results of direct comparison and indirect comparison of interventions involved in some closed loops in the evidence network were inconsistent, which weakened the strength of recommendation of relevant evidence. (5) No cost-benefit analysis was performed in the included literature. Consequently, in cases where the differences in therapeutic efficacy between certain interventions were not statistically significant, further quantitative analysis regarding safety and economic benefits could not be conducted.

Conclusions

This network meta-analysis demonstrates that acupuncture is superior to sodium hyaluronate eye drops in the treatment of DED, particularly in improving tear secretion, tear film stability and the overall efficacy. In general, fascial release

acupuncture combined with acupuncture exhibits the best effect among the evaluated interventions. However, due to limitations such as uneven methodological quality and clinical heterogeneity, these results should be interpreted with caution. In the future, clinical trials of acupuncture should prioritize third-party assessor, especially for the evaluation of subjective outcome indicators. Furthermore, more high-quality, multi-center and large-sample studies published in English are encouraged to enhance the internationalization and comparability of clinical evidence. It is recommended that future acupuncture trials incorporate sham acupuncture or non-acupoint superficial needling as reliable controls to improve the feasibility of blinding and the rigor of the study.

Data Sharing Statement

The datasets used and analysed during the current study are available from the corresponding author (Jing Chen) on reasonable request.

Ethics Approval and Consent to Participate

This study does not involve human ethical considerations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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