INPLASY PROTOCOL

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Support: **None.**

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Conflicts of interest:
None declared.

Efficacy and Safety of a Vectored Thermal Pulsation System (Lipiflow®) in the Treatment of Meibomian Gland Dysfunction: A Systematic Review and Meta-analysis

Hu, J[1]; Zhu, S[2]; Liu, X[3].

Review question / Objective: **To evaluate the efficacy and safety of a vectored thermal pulsation system (Lipiflow®) for the management dry eye disease resulting from meibomian gland dysfunction (MGD).**
Condition being studied: **Meibomian gland dysfunction (MGD) is one of the most common ophthalmic disorders and the leading cause of dry eye disease (DED) in clinical, which may result in alterations of the tear film, symptoms of eye irritation, inflammation and ocular surface disease. Not only have the MGD patients suffered from the discomfort, but also their life quality would be lowered, the economic burden increased and the normal social networking affected. In terms of the scope of the disease (among different countries, races, ages and genders) or the harm it may cause, MGD is a serious issue that deserves our attention. There is no gold standard treatment for MGD. Lipiflow® is a novel approach combined heat therapy with massage for MGD. However, its efficacy and safety are still unclear.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 March 2021 and was last updated on 06 March 2021 (registration number INPLASY202130015).

INTRODUCTION

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METHODS

Participant or population: Adults with a definite diagnosis of MGD or evaporative dry eye disease, but did not have acute conditions that could potentially affected the assessment or interfered with the treatment effectiveness or increased the risk of operation-related injury. We did not exclude studies in which both groups had chronic conditions such as glaucoma, cataracts, or contact lens wear.

Intervention: We will include studies that compared Lipiflow® versus other forms of MGD treatment, such as Lid Hygiene (application of heat and mechanical massage), placebo therapy or no treatment.

Comparator: Lid Hygiene (application of heat and mechanical massage), placebo therapy or no treatment.

Study designs to be included: We will include only randomized controlled trials (RCTs).

Eligibility criteria: We will include randomized controlled trials (RCTs) studying the effectiveness or safety of a vectored thermal pulsation system (Lipiflow®) for treating MGD. And RCTs with outcomes or data were presented in a format which can be extracted for analysis.

Information sources: We searched MEDLINE and EMBASE via the OVID platform, PubMed, Web of Science databases, ClinicalTrials.gov and Cochrane Central Register of Controlled Trials (CENTRAL) for RCTs that evaluated Lipiflow® therapy for MGD from database inception until 4 January 2021. There was no language or other restrictions set in the literature search.

Main outcome(s): Change from baseline in subjective dry eye symptoms with SPEED or OSDI.

Additional outcome(s): 1. Meibomian gland assessment with number of meibomian glands yielding liquid secretion (MGYLS), meibomian glands yielding secretion score (MGYSS) or lipid layer thickness (LLT); 2. Objective dry eye tests with tear break-up time (TBUT), Ocular surface staining (corneal fluorescein staining, conjunctival lissamine green staining), Schirmer test, Osmotic pressure of tear film; 3. Safety endpoints with incidence of device-related adverse events or intraocular pressure (IOP).

Data management: Two reviewers will independently extract relevant information and outcome data with a pilot-tested data extraction form from each included study: name of first author, year of publication, country, methods (study design, study site, sample size, unit of randomization, unit of analysis); participants(baseline characteristics include age, gender, severity of MGD); interventions(details of the intervention, length of follow-up, co-interventions); outcomes (meibomian gland assessment: MGYLS, MGYSS, LLT; objective dry eye tests: TBUT, ocular surface staining (corneal fluorescein staining, conjunctival lissamine green staining), SIT , osmotic pressure of tear film; subjective dry eye symptoms: SPEED, OSDI ; safety endpoints: incidence of device-related adverse events , IOP.

Quality assessment / Risk of bias analysis: Two review authors will independently evaluate the risk of bias of included studies according to the recommended methods of

the Cochrane Handbook, any discrepancies were resolved by discussion. Risk of bias will be assessed as 'low risk', 'high risk' or 'unclear risk' for each included study.

Strategy of data synthesis: The meta-analyses will be performed with Review Manager 5.4 only when there is absence of heterogeneity. A fixed-effect model will be used when there is fewer than three trials available; otherwise a random-effects model will be adopted. We will focus on units of analysis and randomization units. If any significant heterogeneity is observed ($I^2 \geq 50\%$ or $P < 0.1$), a random-effects model will be used; otherwise, a fixed effects model will be used.

Subgroup analysis: We will conduct subgroup analyses with seriousness of MGD, causes of MGD, age, gender, races of participants when there is significant heterogeneity. We will divide the analysis into two parts according to the difference of the control group.

Sensitivity analysis: We will perform a sensitivity analysis to observe the change of I2 value by removing each included study once a time to explore the source of heterogeneity.

Country(ies) involved: China.

Keywords: dry eye disease, meibomian gland dysfunction, Lipiflow®, lid hygiene.

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