Efficacy of Intense Pulsed Light Therapy in Meibomian Gland Dysfunction: A Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: Dry eyedisease(DED)is a chronic ocular surface disease(OSD), with severe impact on vision-related quality of life. Depending on geography and populations, prevalence ranges from 5% to 50%, reaching up to 75% in one publication. Most DED cases are caused by excessive evaporation of the tear film, mainly due to obstructive meibomian gland dysfunction (MGD). Meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands characterized by terminal duct obstruction and/or qualitative/quantitative changes in glandular secretion. This results in the alteration of the tear film, eye irritation, clinically apparent inflammation of the eyelid margin, and ocular surface diseases. Common therapies for MGD include lid hygiene, lid warm compressors, heat application, meibomian gland expression (MGX), artificial tears, topical and systemic antibiotics, and anti-inflammatory agents. However, these treatments provide limited relief and are generally unsatisfactory. In recent years, many studies have reported that Intense pulsed light (IPL) treatment relieves dry eye symptoms, improves meibomian gland secretion, and lengthens tear film break-up time (TBUT) in patients with MGD/dry eye. Hence, this study conducted a meta-analysis of published articles to explore the efficacy and safety of Intense Pulsed Light Therapy in Meibomian Gland Dysfunction.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 June 2020 and was last updated on 19 June 2020 (registration number INPLASY202060069).

INTRODUCTION

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**Condition being studied:** Most DED cases are caused by excessive evaporation of the tear film, mainly due to obstructive meibomian gland dysfunction (MGD). Common therapies for MGD include lid hygiene, lid warm compresses, heat application, meibomian gland expression (MGX), artificial tears, topical and systemic antibiotics, and anti-inflammatory agents. However, these treatments provide limited relief and are generally unsatisfactory. In recent years, many studies have reported that Intense pulsed light (IPL) IPL treatment relieves dry eye symptoms, improves meibomian gland secretion, and lengthens tear film break-up time (TBUT) in patients with MGD/dry eye.

**METHODS**

**Participant or population:** We included adults (i.e. aged 18 years or older) with MGD or dry eye disease, as defined by the study investigators.

**Intervention:** We included RCTs that compared IPL therapy applied to the facial area with the intent of treating MGD or dry eye disease.

**Comparator:** Standard therapy (e.g. warm compresses, MGX), placebo therapy (e.g. sham IPL) or no treatment.

**Study designs to be included:** Randomized controlled trials (RCTs) will be included.

**Eligibility criteria:** RCTs evaluating the outcomes of IPL and Standard therapy (e.g. warm compresses, MGX), placebo therapy (e.g. sham IPL) or no treatment in MGD were included in this study. Trials were required to report the inclusion and exclusion criteria for patients and intervention procedures, and those that involved patients undergoing other interventions or not following complete randomization were excluded.

**Information sources:** Relevant trials published before June 2020 were identified from the PubMed, Embase, and Cochrane databases.

**Main outcome(s):** The primary outcome was meibomian gland function determined using the meibomian gland evaluator or other methods.

**Quality assessment / Risk of bias analysis:** Two review authors independently assessed risk of bias in the included studies according to the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Chapter 8; Higgins 2011a). We assessed the risk of bias in the following domains: selection bias (sequence generation and allocation concealment), performance and detection bias (masking (blinding) of participants, study personnel and outcome assessors), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting) and other sources of bias. Risk of bias was graded as 'low risk', 'high risk' or 'unclear risk' for each included study.
Subgroup analysis, metaregression and sensitivity analysis were to define the origin of heterogeneity. Publication bias was assessed by visual inspection of Begg's funnel plot. P<0.05 was considered significant.

**Strategy of data synthesis:** The effect size of the continuous outcomes was reported as mean difference (MD). The precision of an effect size was reported as 95% confidence interval (CI). If not provided, the SD of a mean was estimated from the provided CI limits or standard error. A pooled estimate of the MD was computed using the DerSimonian and Laird random-effect model. The Cochrane Q tests and statistics were used to evaluate the statistical heterogeneity and inconsistency of treatment effects across trials, respectively. Statistical significance was set at P < 0.10 for Cochrane Q tests. Subgroups were analyzed through pooling of available estimates to obtain similar subsets of patients across trials.

**Subgroup analysis:** Subgroups were analyzed through pooling of available estimates to obtain similar subsets of patients across trials.

**Sensibility analysis:** If necessary, a sensitivity analysis will be conducted.

**Country(ies) involved:** China.

**Keywords:** dry eye disease, meibomian gland dysfunction, intense pulsed light therapy, meibomian gland expression.

**Contributions of each author:**
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