INPLASY PROTOCOL

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None declared.

Intense pulsed light for treating meibomian gland dysfunction: A Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: **P:subjects who were diagnosed meibomian gland dysfunction(MGD). I:intense pulsed light(IPL) therapy was conducted as intervention arms.C:placebo therapy or sham therapy as control arms. O:We extracted identical outcome measures of the endpoint follow-up which were evaluated in different studies,The outcome measures included Ocular Surface Disease Index (OSDI), noninvasive tear break-up time (NIBUT), meibomian gland expressibility (MG expressibility), meibum quality and Adverse Events(AEs). S:Randomised controlled trials (RCTs) with comparation between the IPL arms and Placebo/Sham (control) arms were enrolled for Meta-analysis.**
Eligibility criteria: **We included randomised controlled trials (RCTs) with comparation between the IPL arms and Placebo/Sham (control) arms.and the two arms conbined with or without one or more of same adjuvant therapy such as artificial tears, warm compression, eyelid hygiene.**

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INTRODUCTION

Review question / Objective: **P:subjects who were diagnosed meibomian gland dysfunction(MGD). I:intense pulsed light(IPL) therapy was conducted as intervention arms.C:placebo therapy or sham therapy as control arms. O:We extracted identical outcome measures of the endpoint follow-up which were evaluated in different studies,The outcome measures included Ocular Surface Disease Index (OSDI), noninvasive tear break-up time (NIBUT), meibomian gland expressibility (MG expressibility), meibum quality and Adverse Events(AEs). S:Randomised controlled trials (RCTs) with comparation between the IPL arms and**

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Placebo/Sham (control) arms were enrolled for Meta-analysis.

Rationale: Methodological design was important for a study, RCT and Placebo/ sham control were considered critical in the study designed to reduce risk of bias. we enrolled randomised placebo/sham-controlled trials in the current study, which could maximumly limited confounding variables and isolat the efficacy and safety just for alone IPL treatment on MGD.

Condition being studied: Meibomian Gland Dysfunction (MGD) was first defined as a chronic condition affecting the meibomian gland resulting in decreased secretion or poor quality of meibum by Korb and Henriques in 1980.MGD is one of the most common causes of dry eye.dry eye is widely prevalent worldwide ranging from 3.5% to 70%6-10,and it seriously played negative on individual's work and life. Conventional treatments for MGD included artificial tear supplement, warm compression,eyelid hygiene, meibomian gland expression, topical anti-inflammatory,topical and oral antibiotics. these methods played temporary effects on patient's symptoms and need on going treatment1,but patients often have poor compliance during the treatment process,then MGD relapsed. recent years, intraductal meibomian gland probing, LipiFlow, topical immunomodulatory agents and oral omega-3 essential fatty acids were applicated for MGD, however painfull treatment experience, high cost limited their long-term use. IPL was a broad spectrum, noncoherent light. After filtering, the wavelength of IPL was mostly between 500–1200 nm. IPL was first applied in dermatologic diseases such as facial rosacea, telangiectasia, and pigmented lesions.and it had been proven to be well effective for these diseases.In 2002, Toyos et al found serendipitously that dry eye symptoms significantly improved for rosacea patients who treated with IPL. Since then, IPL was used gradually for treating MGD worldwidely,many studies had investigated the efficacy and safety of IPL for treating MGD.Some researchers tried to conducted meta-analysis on this issue but the results were not satisfactory dued to the lack of appropriate quantity and quality studies,yet there were any inconsistent outcomes.recent years, several new studies on this issue had been published,Therefore, we could conduct the meta-analysis on this issue and wished to provide the best-available evidence relating to the efficacy and safety of IPL as a treatment for MGD.

METHODS

Search strategy: Literatures were searched from Pubmed, Eebase, the Cochrane Library.A thorough search was conducted and was completed on 28 February 2022. search words included intense pulsed light, Blepharitis, Meibomian gland dysfunction, dry eye and dry eye disease. the result was supplemented by hand searching of relevant references from review articles. There were no restrictions on publication date, follow-up period, region,language, ethnicity.Preliminary studies searched from databases were imported into EndNote X3 and duplicate studies were excluded,then the filtered studies underwent 3 stages of screening: screening of the title, screening of absrtact, screening of full-text. ineligible studies were excluded according to inclusion criteria and exclusion criteria by these stages. All stages conducted by two investigators,In case of the two investigators were unable to reach consensus,the third investigator was assisted to resolve these disagreements.

Participant or population: Enrolled subjects: Inclusion criteria:subjects who were diagnosed MGD,age≥18 years; Fitzpatrick skin types 1 to 5; able and willing to comply with the treatment/follow-up schedule and requirements.Exclusion criteria:ontact lens wearers within the past 1 month and throughout the study, any antiglaucomaeye drops use within the past 3 months and throughout the study period, recent ocular or eyelid surgery, neuroparalysis in the planned treatment area, and subjects who have undergone refractive surgery within the past 6 months,IPL treatment and single-dose

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vectored thermal pulsation treatment or any equivalent treatments within the past 12 months,for safety reasons [a. current use of punctual plugs, b. precancerous lesions, skin cancer, or pigmented lesions in the planned treatment area, c. uncontrolled infections or uncontrolled immunosuppressive diseases, d. diseases in the planned treatment area that could be stimulated by light (eg, herpessimplex and lupus disease), e. use of photosensitive medications and/or herbs, such as isotretinoin or tetracycline, f.pregnancy and lactation, g.radiation therapy to the head or neck within the past year or planned radiation therapy throughout study period, h. treatment with a chemotherapeutic agent within the past 8 weeks or planned chemotherapy throughout study period, and i. declared legally blind in 1eye.

Intervention: IPL therapy was conducted as intervention arms.

Comparator: Placebo therapy or sham therapy as control arms.

Study designs to be included: Randomised controlled trials (RCTs).

Eligibility criteria: We included randomised controlled trials (RCTs) with comparation between the IPL arms and Placebo/Sham (control) arms.and the two arms conbined with or without one or more of same adjuvant therapy such as artificial tears, warm compression, eyelid hygiene.

Information sources: Literatures were searched from Pubmed, Eebase, the Cochrane Library.

Main outcome(s): Meibomian gland expressibility(MG expressibility):I nternational Symposium on Meibomian gland Dysfunction pointed out that MGD was a chronic and widespread meibomian gland change, which was manifested as terminal duct occlusion and qualitative or quantitative changes of gland secretions which led to increased tear evaporation, tear hyperosmosis and ocular surface inflammation, epithelial damage.These pathophysiological changes, in turn,led the meibomian glands more damage. so MG expressibility was a important outcome(s) for MGD.

Additional outcome(s): Ocular Surface Disease Index (OSDI), noninvasive tear break-up time (NIBUT), meibum quality and Adverse Events(AEs).

Data management: Two investigators independently extracted data of methodology,intervention, subjects,and outcome parameters from each included studies.any discrepancies in data extraction were resolved by the third investigator by discussion.

Quality assessment / Risk of bias analysis: Review Manager 5.3 was used for evaluding the risk of bias of included studies. assessment indicators of the risk of bias included random sequence generation, allocation concealment, blinding of researchers and subjects, study outcome blind evaluation, completeness of outcome data, selective reporting of results, and bias from other sources. according to the criteria of the rsk of bias,every assessment indicator was categorized as 'low risk', 'high risk' or 'unclear risk' for each included study.

Strategy of data synthesis: Review Manager 5.3 was used to conduct Meta-analysis for these included studies.I2 value was used to assess heterogeneity. I2 value greater than 60% was interpreted to be substantial heterogeneity.forest plots were generated either with fixed or random effects model according to the heterogeneity, fixed-effect model was used to analysis outcome parameter when I2 value was greater than 60%,otherwise, the random-effect model was used to analysis when I2 value was less than 60%.mean difference (MD) was used for estimating continuous outcomes and Risk Difference(RD) was used for incidence rate with 95% confidence intervals (CIs), and $P<0.05$ indicated statistically significant. subgroup analysis was performed if the heterogeneity was substantial among these studies.

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Subgroup analysis: subgroup analysis would be performed if the heterogeneity was substantial among these studies.

Sensitivity analysis: Stata13 was used for performing sensitivity analysis on eligible literatures. it was judged that the study had an significant impact on the total effect size when: (1) the mean value of the combined effect size beyond outside the range of 95% confidence interval of the total effect size after eliminating one of the studies.(2)The upper 95% confidence interval of the combined effect was lower than the mean value of the total effect or the lower 95% confidence interval was higher than the mean value of the total effect after eliminating one of the studies. narrative analysis of results was performed when sensitivity analysis could not be undertook dued to the deficiency of data.

Language restriction: There were no restrictions on language.

Country(ies) involved: China.

Other relevant information: Preliminary studies searched from databases were imported into EndNote X3 and duplicate studies were excluded,then the filtered studies underwent 3 stages of screening: screening of the title, screening of absrtact, screening of full-text. ineligible studies were excluded according to inclusion criteria and exclusion criteria by these stages. All stages conducted by two investigators,In case of the two investigators were unable to reach consensus,the third investigator was assisted to resolve these disagreements.

Keywords: meibomian gland dysfunction; intense pulsed light; sham therapy.

Contributions of each author:

Author 1 - Gao changhua - Undertake the project funding, design, writing and checking of the article, and take full responsibility for the authenticity of the content of the paper, the reliability of the data, the credibility of the conclusion, whether it meets the legal norms, academic norms and ethical norms.

Author 2 - Wu Jingjing - 1.searched records from databases and imported them into EndNote X3 and excluded the duplicate studies,then screened the filtered records underwent 3 stages and excluded ineligible records according to inclusion criteria and exclusion criteria independently. 2. extracted the data of outcome measures from each included studies independently.

Author 3 - Zhang Xiaohan - 1.searched records from databases and imported them into EndNote X3 and excluded the duplicate studies,then screened the filtered records underwent 3 stages and excluded ineligible records according to inclusion criteria and exclusion criteria independently. 2. extracted the data of outcome measures from each included studies independently.

Author 4 - Zhang Jinfeng - was assisted to resolve these disagreements In case of the two investigators were unable to reach consensus on outcomes of the Literatures selection.

Author 5 - Gao Xiaojuan - was assisted to resolve to disagreenment by discussion as the third investigator if any discrepancies in data extraction.

Author 6 - Lin xuesong - Responsible for the funding of the project, design, writing and checking of the article, and most importantly, he is responsible for the reliability of the article.

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