

INPLASY PROTOCOL

To cite: Yang et al. Changes of the corneal nerve in painful diabetic neuropathy compared to painless diabetic neuropathy under corneal confocal microscopy: a systematic review and meta-analysis. Inplasy protocol 202330023. doi: 10.37766/inplasy2023.3.0023

Received: 06 March 2023

Published: 06 March 2023

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Support: Self-financed.

Review Stage at time of this submission: Data analysis.

Conflicts of interest:
None declared.

Changes of the corneal nerve in painful diabetic neuropathy compared to painless diabetic neuropathy under corneal confocal microscopy: a systematic review and meta-analysis

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Review question / Objective: Whether corneal nerve parameters are significantly different under Corneal confocal microscope in Painful diabetic neuropathy compared to Painless diabetic neuropathy.

Condition being studied: Distal symmetric diabetic neuropathy (DSPN) is a common complication of diabetes. According to the American Diabetes Association guidelines, DSPN is defined as a symptom of peripheral nerve disorder in people with diabetes when other causes of the disorder have been excluded. Although the majority of patients with DSPN are asymptomatic (painless diabetic neuropathy), painful diabetic neuropathy occurs in 15–25% of patients. However, the distinction between painless and painful diabetic neuropathy is not clear today. Meanwhile corneal confocal microscopy is a powerful, convenient and rapid technique for detecting DSPN. Thus we consider whether corneal confocal microscopy can distinguish between these two diseases.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 March 2023 and was last updated on 06 March 2023 (registration number INPLASY202330023).

INTRODUCTION

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complication of diabetes. According to the American Diabetes Association guidelines, DSPN is defined as a symptom of peripheral nerve disorder in people with diabetes when other causes of the disorder have been excluded. Although the majority of patients with DSPN are asymptomatic (painless diabetic neuropathy), painful diabetic neuropathy occurs in 15–25% of patients. However, the

distinction between painless and painful diabetic neuropathy is not clear today. Meanwhile corneal confocal microscopy is a powerful, convenient and rapid technique for detecting DSPN. Thus we consider whether corneal confocal microscopy can distinguish between these two diseases.

METHODS

Search strategy: Search papers in pubmed, medline and Embase. Then search reference lists of papers that meet the criteria. And search for grey literature, dissertations at ClinicalTrials.gov, ETHOS.

Participant or population: Adults (>18 years) with diabetes mellitus combined with painful neuropathy.

Intervention: This is an observational systematic review with no interventions. It needs to be detected using corneal confocal microscopy.

Comparator: Diabetic patients with painless neuropathy or without painful neuropathy, healthy people.

Study designs to be included: Observational studies, RCT.

Eligibility criteria: Inclusion: Outcomes: Studies containing any of the following corneal confocal microscopy (CCM) parameters: corneal nerve fiber density (CNFD), corneal nerve branch density (CNBD), corneal nerve fiber length (CNFL); Other: Journal article, grey literature. Exclusion: Population < 18 years old, without painful diabetic neuropathy; Intervention: Not using CCM.

Information sources: Search papers in pubmed, medline and Embase. Then search reference lists of papers that meet the criteria. And search for grey literature, dissertations at ClinicalTrials.gov, ETHOS.

Main outcome(s): Studies - included must find changes in at least one of the following corneal nerve parameters: a. CNFD: number of all major nerve fibres per square

millimetre; b. CNBD: number of branch nerves per square millimetre of source autonomic nerve; c. CNFL: the sum of all nerve fibre lengths per square millimetre.

Additional outcome(s): Corneal nerve fibre tortuosity, Inferior whorl length and the relationship between neurological pain scores and corneal nerve parameters.

Quality assessment / Risk of bias analysis: As the results included are observational, the Newcastle-Ottawa Scale (NOS) will be used for risk of bias assessment.

Strategy of data synthesis: The reviewers will extract the characteristics of the included studies. It will then be judged whether a meta-analysis can be performed. If meta-analysis can be performed, it will be done using Revman software. Heterogeneity between studies will be assessed using the I² statistic. Mean differences (MD) and 95% confidence intervals (CI) will be calculated for corneal parameters. If meta-analysis is not available, a descriptive analysis will be performed.

Subgroup analysis: Subgroup analyses will be performed for factors that may contribute to heterogeneity.

Sensitivity analysis: A sensitivity analysis will also be performed to exclude low-quality articles.

Language restriction: No.

Country(ies) involved: China, UK.

Keywords: Corneal confocal microscopy; CCM; polysymmetric neuropathy; DPN; Distal symmetric diabetic neuropathy; DSPN; painful diabetic neuropathy; PDN; Painless diabetic neuropathy; PLN.

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