INPLASY PROTOCOL

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Corresponding author:
Qihang Yuan

qihangdy@163.com

Author Affiliation:
Dalian Medical University

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Circulating Leptin Level, Soluble Leptin Receptor Level and Their Gene Polymorphism in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-analysis

Yuan, Q[1]; Zhang, L[2]; Tian, Y[3]; Li, W[4]; Li, X[5]; Lu, Z[6].

Review question / Objective: **To compare circulating leptin level, leptin receptor level and related gene polymorphisms between SLE patients and healthy controls, and evaluate the relationship between leptin levels, LepR levels and SLE disease activity.**
Condition being studied: **SLE patients with increased adiposity have a heightened risk for disease-related complications, including neurocognitive decline, renal impairment, dampened physical activity, and poorer prognosis. This suggests that the significance of leptin in the development of SLE is becoming increasingly prominent. However, conflicting associations are reported between circulating leptin level, leptin receptor level, related gene polymorphism and SLE.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 April 2020 and was last updated on 22 April 2020 (registration number INPLASY202040137).

INTRODUCTION

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receptor level, related gene polymorphism and SLE.

METHODS

Search strategy: The complete search used for PubMed will be: #1("leptin [Mesh Terms]" OR "leptin" OR "Obese Protein" OR "Obese Gene Product" OR "Gene Product, Obese" OR "Ob Gene Product" OR "Gene Product, Ob" OR "Ob Protein") #2("Lupus Erythematosus, Systemic [Mesh Terms]" OR "Lupus Erythematosus, Systemic" OR "Systemic Lupus Erythematosus" OR "Lupus Erythematosus Disseminatus" OR "Libman-Sacks Disease" OR "Disease, Libman-Sacks" OR "Libman Sacks Disease") #3=#1 AND #2

Participant or population: Patients with SLE.

Intervention: Abnormal leptin level, leptin receptor level and related single nucleotide gene polymorphisms in SLE patients compared to healthy controls.

Comparator: Healthy controls.

Study designs to be included: All observational studies, including cohort studies, case-control studies and cross-sectional studies.

Eligibility criteria: Inclusion criteria: providing data on the serum/plasma leptin levels, leptin receptor levels and relevant gene polymorphism in SLE cases and healthy controls, having clearly diagnostic criteria for SLE. Exclusion criteria: 1)duplicates; 2)case reports and academic dissertation; 3)editorials, letters and comments; 4)review articles and meta-analyses; 5)conference abstracts; 6)non-human subjects; 7)not complying with the main idea of this meta-analysis.

Information sources: We will search the following databases: PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), China WanFang and China Weipu (VIP) databases. There will be no restriction applied based on language or the publication year. Relevant references cited in included trials will also be hand-searched. Correspondence: Zhimin Lu, MD Email: doctorlzm@ntu.edu.cn; Xia Li, MD, PhD Email: lixia0416@dlmedu.edu.cn.

Main outcome(s): The main outcomes will be: 1)abnormal leptin levels and leptin receptor levels in SLE patients compared to the healthy controls; 2)association of related gene polymorphism with SLE risk. The outcomes will be measured as in each individual study. We will use 1)standardized mean differences (SMD) for calculating the pooled results of abnormal leptin level and leptin receptor level; 2)odds ratios for related gene polymorphism.

Additional outcome(s): The additional outcomes will be the association of circulating leptin level and leptin receptor level with SLE disease activity. We will use standardized mean differences (SMD) for investigating the association of circulating leptin level and leptin receptor level with SLE disease activity.

Quality assessment / Risk of bias analysis: The authors will evaluate each of the included studies for quality assessment, based on the Newcastle-Ottawa Scale (NOS) for case-control studies. The following factors will be taken into account: selection of cases and controls; comparability of cases and controls on the basis of the design or analysis; and exposure of cases and controls. Studies scored above or equal to the median NOS value will be considered as high quality (lower risk of bias) and those scored below the median value will be considered as low quality (higher risk of bias).

Strategy of data synthesis: Odds ratio (OR) and standardized mean difference (SMD) along with 95% confidence intervals (CI) will be applied and the analyses will be carried out by using a random/fixed-effects model. We will use the χ^2 test to evaluate the statistical heterogeneity between different studies. P>0.1 and I^2< 50% will indicate low heterogeneity where a fixed effect model will be used; P50% will indicate statistical heterogeneity where a

random effect model will be applied. All analyses will be conducted using STATA.

Subgroup analysis: We will perform subgroup analyses using the following variables: ethnicity, sample size, gender, source of leptin, assay method.

Sensibility analysis: The leave-one-out method (removing one study each time and repeating the analysis) will be employed, which will allowe us to determine the implication of each study on the pooled effect size.

Country(ies) involved: 中国.

Keywords: Leptin; Leptin receptor; Genetic polymorphisms; Systemic Lupus Erythematosus; Meta-analysis.

Contributions of each author:
Author 1 - Qihang Yuan contributed to the design of the study, collection and interpretation of data, and drafting and revising the manuscript.
Author 2 - Lilong Zhang was responsible for the interpretation of data and drafting the manuscript.
Author 3 - Yao Tian was responsible for the interpretation of data and drafting the manuscript.
Author 4 - Weiping Li was responsible for the interpretation of data and drafting the manuscript.
Author 5 - Xia Li conceived the study and reviewed/edited the manuscript.
Author 6 - Zhimin Lu conceived the study and reviewed/edited the manuscript.