INPLASY PROTOCOL

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None declared.

The Relationship Between Il-1 RN intron 2 (VNTR) rs2234663 Gene Polymorphism and The Progression of Periodontitis: A systematic Review and Meta-Analysis

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Review question / Objective: **The aim of this systematic review and meta-analysis of case-control studies is to find out the association of IL-1 RN intron 2 (VNTR) rs2234663 Gene Polymorphism and the occurrence and progression of periodontitis(including chronic periodontitis, aggressive periodontitis and early-onset periodontitis).** **Condition being studied:** **Periodontitis is one of the most common ailments affecting the teeth, leading to the destruction of the supporting and surrounding tooth structure. Periodontitis is originally a disease originating from the gingival tissue which if left untreated results in penetration of inflammation to the deeper tissues, altering the bone homeostasis causing tooth loss. Periodontal disease has a multifactorial origin. The main culprit identified in periodontitis is the bacterial biofilm growing on the tooth surfaces. The deleterious effects of periodontopathogens are not limited to the periodontium, but they also exude their ill effects on the systemic health of the patients. While the host response determines the progression of the disease, genetics, environmental factors, systemic health of the patient, lifestyle habits and various social determinants also play a role. Interleukin-1 receptor antagonist encoded by this gene IL-1RN is a member of the interleukin 1 cytokine family. This protein inhibits the activities of interleukin 1, alpha (IL1A) and interleukin 1, beta (IL1B), and modulates a variety of interleukin 1 related immune and inflammatory responses, particularly in the acute phase of infection and inflammation. We aim to study their association by conducting a meta-analysis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2023 and was last updated on 25 March 2023 (registration number INPLASY202330100).

INTRODUCTION

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METHODS

Participant or population: Adults with periodontitis (chronic periodontitis, aggressive periodontitis and early-onset periodontitis).

Intervention: Genotypes that affect the occurrence of periodontitis (chronic periodontitis, aggressive periodontitis and early-onset periodontitis).

Comparator: Genotypes that do not affect the occurrence of periodontitis (chronic periodontitis, aggressive periodontitis and early-onset periodontitis).

Study designs to be included: A case-control, cohort, nested case-control, or cross-sectional design will be included.

Eligibility criteria: Inclusion and exclusion criteria: the following three inclusion criteria should be fulfilled in all retrieved literatures: (1) Evaluation of IL-1RN VNTR polymorphism and periodontitis risk; (2) Usage of a case-control, cohort, nested case-control, or cross-sectional design; (3) With sufficient data to estimate an odds ratio (OR) and corresponding95% confidence interval (CI). Major exclusion criteria as: (1)No control subjects;(2) With systemic diseases;(3) No usable genotype distribution or allele frequency data.

Information sources: We performed a systematic search of studies that addressing the association between IL-1RN VNTR polymorphism and periodontitis. The literature was searched in electronic biomedical databases including the Cochrane Library, PubMed (US National Library of Medicine), Embase, web of science, EBSCO, CNKI, Wanfang and Weipu. A combination of the terms “interleukin-1 receptor antagonist”, “IL-1RN”, “VNTR”, “periodontal disease”, “periodontitis”, “chronic periodontitis”, "aggressive periodontitis", "early onset periodontitiss", “polymorphism" were entered both as Medical Subject Heading (MeSH) components and as free-text words. To avoid selection bias, no language or other restrictions were placed on the search. Moreover, hand search for references cited in the published original and review articles was also performed.

Main outcome(s): Susceptibility to periodontitis (chronic periodontits, aggressive periodontits and early-onset periodontits) may varies by genotypes.

Quality assessment / Risk of bias analysis: We shall use the Newcastle-Ottawa Scale (NOS), it is a commonly used quality assessment tool for case-control and cohort studies. It evaluates cohort and case-control studies by means of eight items in three modules, specifically

selection, comparability, and exposure/outcome. NOS uses a semi-quantitative star system to evaluate the quality of the literature, with the exception of comparability, which is rated up to 2 stars, and all other entries, which are rated up to 1 star out of a possible 9 stars, with higher scores indicating higher quality studies.

Strategy of data synthesis: Hardy-Weinberg equilibrium (HWE) for the controls was calculated, and the chi-squared method was applied to assess whether genotype frequencies in control groups were in HWE. The strength of the association between the IL-1RN VNTR polymorphism and periodontitis was measured by ORs with 95% CIs. The statistical significance of the pooled OR was determined using the Z-test. Genetic contrasts were listed as follows: the mutant allele versus the wild allele, homozygote comparison, heterozygote comparison, dominant model and recessive model. For each genetic contrast, the between-study heterogeneity was evaluated using the chi-squared based Q-test. The Mantel- Haenszel method for fixed effects and the DerSimonian-Laird method for random effects were used to calculate the pooled ORs. Results without heterogeneity were pooled using the fixed-effect model; otherwise the random-effect model was used.
Publication bias was evaluated with the Begg funnel plot and Egger linear regression method, which measures funnel plot asymmetry on a natural logarithm scale of ORs. All statistical analysis were carried out with revman 5.4.1, using two-sided p-values.

Subgroup analysis: Subgroup analysis were also performed for ethnicity, HWE and the severity of periodontitis.

Sensitivity analysis: Not started yet.

Language restriction: None.

Country(ies) involved: China.

Keywords: IL-1RN, Polymorphism, Chronic periodontitis, Aggressive periodontitis, Early onset periodontitis, Meta-analysis.

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