INPLASY PROTOCOL

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The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Association between G1246A polymorphism in HCRTR2 gene and risk of cluster headache: an updated meta-analysis of observational studies

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Review question / Objective: Is there an association between G1246A polymorphism (rs2653349) in HCRTR2 gene and risk of CH?

Condition being studied: The hypocretin receptor 2 (HCRTR2) gene may play a pathological role in cluster headache (CH). However, the conclusions of published reports on the relationship between the G1246A polymorphism (rs2653349) in HCRTR2 gene and risk of CH remain controversial.

Information sources: If multiple studies reported overlapping data, the most comprehensive one will be included in the meta-analysis. If only abstracts are available, the corresponding author of the abstract will be contacted for raw data via email. The record will be discarded if the author can't be contacted after we sent the email for at least three times.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 July 2020 and was last updated on 19 July 2020 (registration number INPLASY202070085).

INTRODUCTION

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pathological role in cluster headache (CH). However, the conclusions of published reports on the relationship between the G1246A polymorphism (rs2653349) in HCRTR2 gene and risk of CH remain controversial.

METHODS

Participant or population: subjects in CH groups should be patients diagnosed with CH according to well-established guidelines, such as the ICHD-II criteria (Society, 2004).

Intervention: The polymorphism of interest is rs2653349 in the HCRTR2 gene.

Comparator: Control subjects should be defined as healthy subjects without history of CH.

Study designs to be included: Observational studies (case control study or cohort study) on human.

Eligibility criteria: Subjects in CH groups should be patients diagnosed with CH according to well-established guidelines, such as the ICHD-II criteria (Society, 2004); (ii) control subjects should be defined as healthy subjects without history of CH; (iii) observational studies (case control study or cohort study) on human; (iv) the polymorphism of interest was rs2653349 in the HCRTR2 gene; (v) the primary outcome was the association between HCRTR2 polymorphism and risk of CH, as indicated by odds ratio (OR) and the associated 95% confidence interval (95%CI) which could be either provided by the original study or calculated based on the allele frequencies of the variant.

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Main outcome(s): The primary outcome is the association between HCRTR2 polymorphism and risk of CH, as indicated by odds ratio (OR) and the associated 95% confidence interval (95%CI) which could be either provided by the original study or calculated based on the allele frequencies of the variant

Quality assessment / Risk of bias analysis: The methodological quality of eligible studies will be evaluated according to the Newcastle-Ottawa Scale (NOS) for observational studies.

Strategy of data synthesis: HWE for the control participants will be evaluated using Chi-square test to assess goodness of fit. In this review, we will conduct the meta-analysis under five different genetic models, including dominant model (AA+AG vs. GG), recessive model (AA vs. AG+GG), allelic model (A vs. G), homozygote model (AA vs. GG) and heterozygote model (AG vs. GG). Q-test and the Higgins I-square test will be used to estimate the intra-study heterogeneity. $p>0.1$ and $I2<50\%$ indicated acceptable variability among included studies.

Subgroup analysis: Subgroup analysis by ethnicity will be performed to determine the role of rs2653349 in different ethnicities.

Sensibility analysis: Meta-regression will be carried out to identify the possible source of variation among studies.

Country(ies) involved: China.

Keywords: cluster headache, HCRTR2, G1246A polymorphism, meta-analysis, rs2653349.

Contributions of each author:
Author 1 - Jiao Yang - Jiao Yang, Jing Kong and Jie Yang participated in the acquisition of data and performed the meta-analyses. Jiao Yang and Zheng-tao Lv helped draft the manuscript.
Author 2 - Si-yi Yu - Si-yi Yu and Zheng-tao Lv designed and supervised the research.

Author 3 - Jie Yang - Jiao Yang, Jing Kong and Jie Yang participated in the acquisition of data and performed the meta-analyses.

Author 4 - Jing Kong - Jiao Yang, Jing Kong and Jie Yang participated in the acquisition of data and performed the meta-analyses.

Author 5 - Fan-rong Liang - Fan-rong Liang and Zheng-tao Lv revised the manuscript.

Author 6 - Zheng-tao Lv - Jiao Yang and Zheng-tao Lv helped draft the manuscript. Fan-rong Liang and Zheng-tao Lv revised the manuscript.