INPLASY

MTHFR C677T, MTRR A66G gene polymorphisms and susceptibility to birth defects: a meta-analysis

INPLASY202460106
doi: 10.37766/inplasy2024.6.0106
Received: 26 June 2024
Published: 26 June 2024

Zhang, YY; Shao, l.

Corresponding author:
Yiyang Zhang

107044016@qq.com

Author Affiliation:
Tibet University for Nationalities.

ADMINISTRATIVE INFORMATION

Support - Tibet University for Nationalities.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460106

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 June 2024 and was last updated on 26 June 2024.

INTRODUCTION

Review question / Objective To evaluate the polymorphism of folate related genes MTHFR C677T and MTRR A66G and their correlation with birth defects through meta-analysis.

Rationale As a complex and high-incidence neonatal disease, birth defects can be caused by many factors such as genetic abnormalities, chromosomal abnormalities, and maternal adverse factors, among which methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (methionine synthase reductase) MTRR) is an indispensable enzyme in the metabolism of folic acid, and its mutation is an important risk factor for birth defects.Based on databases such as PubMed, Cochrane Library, CNKI and Wanfang Data Knowledge Service Platform, this study screened the literature on the association of MTHFR C677T gene and MTRR A66G gene with the pathogenesis of birth defects (including congenital heart disease, cleft lip and palate, neural tube defects, and Down syndrome).

Condition being studied Birth defects refer to various genetic diseases and congenital malformations, defects, metabolic diseases or mental and intellectual disabilities that are found at birth or can only be diagnosed after birth, such as congenital heart disease, cleft lip and palate, neural tube defects, Down syndrome, etc., which are the main causes of miscarriage, embryonic termination, stillbirth, infant death and perinatal death.The incidence of birth defects in newborns is increasing year by year, and it has become a global public health problem, which has brought a great burden to individuals and society, and is the focus of attention in the field of child health.

METHODS

Search strategy Chinese search terms included folic acid, birth defects, cleft lip and palate, congenital heart disease, patent ductus arteriosus,

atrial septal defect, ventricular septal defect, neural tube defect, Down syndrome, polymorphism, 5,10-methylenetetrahydrofolate reductase, methionine synthase reductase, homocysteine; English search terms include birth defects, arbd, congenital anomalies, mtrr, mthfr, hcy, homocysteine, cleft lip and palate, cheilopalatoschisisis, oral clefts, cleftlip, congenital heart disease, chd, pda, patent ductus arteriosus 、atrial septal defect、asd、ventricular septal defects、vsd、neural tube defect、ntds、ntd、down's syndrome。 The search was accompanied by reading the references for retrospective purposes to ensure that the relevant literature was fully included. The limited languages are Chinese and English.

Participant or population Healthy people were used as the control group, and mothers with birth defects were used as the study population.

Intervention No intervention, The genotypes of mothers whose offspring were born defects were selected.

Comparator Healthy people were used as controls.

Study designs to be included (1) The study was a case-control study of the MTHFR C677T gene or the MTRR A66G gene. (2) The control group was controlled by healthy people.(3) The data are complete, and the experimental data contain odds ratios and 95% confidence intervals, or provide relevant data to calculate the distribution frequency of each genotype.(4) The relevant genotype data shall be the genotype data of the mother of the child with birth defects.

Eligibility criteria
Exclusion Criteria:
(1) Literature that is completely unrelated to the research topic.
(2) Repetitive literature, conferences, outcome reports, letter summaries, case reports, etc.
(3) Literature with duplicated, incomplete or inaccessible data.
(4) The Newcastle-Ottawa-scale (NOS) score is less than 5 points.
(5) Non-Chinese and English literature.
(6) The genotype distribution of the control group did not conform to the Hardy-Weinberg equilibrium (HWE): literature..

Information sources Databases such as Pubmed, Cochran Library, CNKI and Wanfang Data Knowledge Service Platform, and reference retrospection.

Main outcome(s) The MTHFR C677T gene and MTRR A66G gene are associated with birthdefects.Different types of maternal gene mutations can affect different birth defect diseases in offspring.

Quality assessment / Risk of bias analysis The two investigators evaluated the quality of the included case-control studies according to the NOS scale, which mainly included the selection of study subjects, component comparability, and exposure factor measurement, and the NOS scale was commonly used to evaluate the ease of use of study design and content, as well as the clarity and completeness of research tasks, aiming to incorporate quality assessment into the interpretation of meta-analysis results. The score ranges from 0 to 9, and we consider the NOS score to be greater than or equal to 5 points for high quality. A score of less than 5 was considered to be of low quality and was not included in this study.

Strategy of data synthesis Firstly, the allele data were calculated from the extracted genotype data of the case group and the control group, and the HWE genetic equilibrium law test was carried out on the data of each control group by using the Excel editing formula in the software WPS office, and the literature that did not conform to the law of genetic equilibrium was excluded. Review Manager 5.4 software was used to meta-analyze different genetic models (including allele model, homozygous model, heterozygous model, dominant model, and implicit model). In order to investigate the more detailed association between MTHFR C677T and MTRR A66G genes and birth defect diseases, we conducted subgroup analyses according to disease types, using OR values and 95% confidence intervals as indicators, and the final analysis results were reflected in forest plots. In this study, the Q test and I2 were used to assess the heterogeneity between groups, when I2 > 50% or P0.05, there was no heterogeneity between studies, and a fixed-effect model was used. Publication bias analysis was performed by funnel plots of the included studies.

Subgroup analysis We performed subgroup analyses by disease type, using OR values and 95% confidence intervals as indicators, and the final results were reflected in forest plots.

Sensitivity analysis In this study, the results of sensitivity analysis showed that the results of the study were relatively stable, and the removal of a single study would not have a significant impact on

the results of the study, and the results were more reliable.

Country(ies) involved China.

Keywords Birth defect Gene polymorphism Meta analysis folic acid.

Contributions of each author

Author 1 - Yiyang Zhang.
Email: 107044016@qq.com
Author 2 - Li Shao.
Email: shaoli@xzmu.edu.cn