INPLASY

Meta-analysis of the effects of CYP3A5*3 gene polymorphisms on tacrolimus blood concentration and efficacy in Chinese patients with membranous nephropathy

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 March 2024 and was last updated on 20 March 2024.

INTRODUCTION

Review question / Objective To systematically evaluate the relationship between CYP3A5*3 gene polymorphisms and the blood concentration and efficacy of tacrolimus (FK506) in patients with membranous nephropathy.

Condition being studied In recent years, the incidence of membranous nephropathy has increased significantly in China.The 2021 KDIGO guideline recommends tacrolimus for patients with intermediate and high-risk membranous nephropathy.However, tacrolimus is characterized by a narrow therapeutic window and variable oral bioavailability. it has been shown that individual differences in tacrolimus pharmacokinetics are largely influenced by genetic factors.Previous studies have shown that CYP3A5*3 gene polymorphism is associated with tacrolimus blood concentrations in liver, kidney, heart, and bone marrow transplant patients.However, there are no evidence-based studies on the association of CYP3A5*3 gene polymorphisms with tacrolimus blood concentrations in membranous nephropathy patients. The results of studies about CYP3A5*3 gene polymorphism and the efficacy of tacrolimus in Chinese MN patients are conflicting. Therefore, we conducted a systematic review and meta-analysis of the published studies to determine the effects of CYP3A5*3 gene polymorphism on tacrolimus blood concentration and efficacy in Chinese MN patients.

METHODS

Participant or population Chinese membranousnephropathy patients.

Intervention Altered expressions of CYP3A5*3 gene polymorphisms.

Comparator Healthy controls.

Study designs to be included Case-control studies.

Eligibility criteria Inclusion criteria: (1) all published domestic and international correlative studies on the effects of CYP3A5*3 gene polymorphisms and efficacy on tacrolimus blood concentration in Chinese MN patients, in any language. (2) MN patients treated with tacrolimus-based immunosuppressants, not using other drugs affecting tacrolimus blood concentrations, and all tested for CYP3A5*3 gene polymorphisms, with no restrictions on patient age, gender, race, nationality, or test method. (3) Patients were classified into 3 different genotypes AA (*1/*1), AG (*1/*3) and GG (*3/*3) genotypes, or separately in GG(*3/*3) and AA+AG(*1/*3+*1/*1) genotypes. (4) Studies should provide either tacrolimus whole blood trough concentration (C0) or the dose-adjusted trough concentration (C0/D).Studies were excluded if (1) they were repeatedly published literature; (2) not original studies (e.g. reviews, synthesis, case report type articles); (3) have incomplete study outcomes;(4) have inconsistent study content and results.

Information sources A search will be performed to identify relevant studies in PubMed, Cochrane Library, Web of Science (WOS), CBM, Embase, China Knowledge Network (CNKI), Wanfang, Vipers (VIP), ReadShow, and clinicaltrail.gov databases (updated on 28 October 2022). The search terms were: Tacrolimus, FK506, membranous nephropathy, membranous glomerulonephritis, CYP3A5, and cytochrome P4503A5.

Main outcome(s) Relationship between CYP3A5*3 genotypes polymorphisms and tacrolimus blood trough concentrations.

Quality assessment / Risk of bias analysis STREGA was used to assess the quality of each included study in terms of (1) the adequacy of the sample size, (2) the clarity of diagnostic criteria, (3) problems with the matching of subgroups, (4) whether study groups were comparable, (5) whether the genetic testing methods were reasonable, (6) adequacy of data. For each of the above 6 items, meet 1 item obtain 1 point, with a total score of ≥3 being considered reliable in terms of quality.

Strategy of data synthesis Stata.16 software will be used for forest plots. The relationship between genotypes and tacrolimus blood concentrations will be evaluated by standard mean differences (SMD) and their corresponding 95% confidence intervals (95%CI). The Mantel-Haenszel(M-H) method will be used to analyze dichotomous data, and the strength of their association with efficacy will be determined by odds ratio (OR). Heterogeneity assumptions were assessed using Q-tests based on chi-square tests. The mean±standard deviation will be estimated using the formula of McGrath S et al, if the study reported only median and interquartile spacing.

Subgroup analysis N/A.

Sensitivity analysis Sensitivity analysis: Sensitivity analyses were conducted by one-study remove approach to assess the influence of single study on the combined effect.

Country(ies) involved China.

Keywords gene polymorphism; CYP3A5; tacrolimus; membranous nephropathy;meta-analysis.

Contributions of each author

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