INPLASY PROTOCOL

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The Association between Matrix Metalloproteinase-3 -1171 (5A/6A) Promoter Polymorphism and Cancer Susceptibility: An Updated Meta-Analysis and Trial Sequential Analysis

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Review question / Objective: The polymorphism of the 5A/6A promoter region of matrix metalloproteinases-3-1171 has been comprehensively studied to evaluate its risk associated with various cancers. We performed this updated meta-analysis to clarify the inconclusive outcomes of previous studies and to verify the link of this specific variant with the cancer risk.

Eligibility criteria: For the literature covered in this meta-analysis, the authors followed some standards as inclusion criteria: (a) comparative case-control or cohort (different case groups) studies stating the correlation of MMP-3 -1171 (5A/6A) variant with cancer risk; (b) Available genotype and allele data in cases and controls; (c) Sufficient data to determine ORs (odds ratios) with 95% Cis (confidence intervals). The substandard studies were: (a) Review articles, commentaries and duplicate studies; (b) Study graph apart from case-control comparative approaches; (c) Studies having inadequate genotypic information to compute ORs with 95% CIs.

INTRODUCTION

Review question / Objective: The polymorphism of the 5A/6A promoter region of matrix metalloproteinases-3-1171 has been comprehensively studied to evaluate its risk associated with various cancers. We performed this updated meta-analysis to clarify the inconclusive outcomes of previous studies and to verify the link of this specific variant with the cancer risk.

Rationale: MMP-3 -1171 (5A/6A) promoter polymorphism has been found to be connected to the development of cancer. But the outcome is inconsistent due to

small sample size and the variation in ethnicity. We conducted a meta analysis by including 63 studies with 14,252 patients and 15,176 controls. Due to the large sample size, we hope our included studies will meet the required information size (RIS) after performing the TSA analysis that will confirm our outcomes.

Condition being studied: The individual case-control studies evaluated different types of cancer patients and healthy controls to detect the cancer risk. Then, we performed a meta-analysis of these case-control studies to get a pulled outcome risk.

METHODS

Search strategy: The literature search was conducted without restriction on language, time and sample size. We retrieved the literature using the following terms alone or in combination: "MMP-3", "matrix metalloproteinase-3", "stromelysin-1", "cancer" "tumor", "ovarian cancer", "breast cancer", "cervical cancer", "endometrial cancer", "oral cancer", "bladder cancer", "lung cancer", "esophageal cancer", "gastric cancer", "head and neck cancer", "hepatocellular cancer", "colorectal cancer", "prostate cancer","osteosarcoma", and "renal cell carcinoma", "polymorphism", "SNP", "variant", and/or "genotype".

Participant or population: Global population.

Intervention: Cases and controls were evaluated with respect to the presence of different genotypes. The Association of polymorphism was detected as an Odds ratio with 95% confidence interval. Association of polymorphism was detected as Odds ratio with 95% confidence interval.

Comparator: Different genotypes and allele frequency of cases were compared with controls.

Study designs to be included: Case control studies with the respective genotyping data of the mentioned SNP.

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Information sources: The current meta-analysis was designed, redacted, and reported following the updated guidelines for PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). Internet websites and databases like PubMed, Cochrane, EMBASE, MEDLINE,CNKI, and Google Scholar were explored to identify and collect all published case-control studies up to July 27,2021.

Main outcome(s): Our meta-analysis suggests a significant connection between MMP-3-1171 (5A/6A) promoter variant and the risk of overall cancer susceptibility.

Additional outcome(s): An elevated risk of cancer was identified in Asians and Africans. This variant might be associated with esophageal, colorectal, gastrointestinal, breast, gynecological, and hepatocellular cancer risk.

Quality assessment / Risk of bias analysis: Risk bias analysis was performed, and a statistically significant bias was reported in some genetic models from Egger's symmetric funnel plots and p-values. However, no substantial publication bias was found from Begg-Mazumdar's test. The GRADE system was also used to detect the quality of the includedstudies.

Strategy of data synthesis: Dichotomous data will be synthesized to find the pulled odds ratio with a 95% confidence interval.

Fixed effect and Random effect models will be utilized depending on heterogeneity.

Subgroup analysis: Different cancer types, ethnicities, genotyping methods and sources of controls.

Sensitivity analysis: A sensitivity analysis will be performed to evaluate the effect of individual studies on the polled outcomes.

Language restriction: No language restriction was provided during literature searching.

Country(ies) involved: Bangladesh.

Keywords: Cancer; Polymorphism; Matrix Metalloproteinase-3; MMP-3; Meta-analysis.

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