INPLASY PROTOCOL

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Conflicts of interest:
None.

Dietary intake and serum level of folate and lung cancer risk: A Systematic Review and Meta-Analysis

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Review question / Objective: Our patient population is Lung cancer patients. Our intervention is dietary intake and serum level of folate and supplement of folate. And our control measure was to control the intake or content of folic acid at high dose level with folic acid intake or content at low dose level. What we want to achieve is the effect of high or low doses of folate intake and serum level of folate on the incidence rate of lung cancer. Our study design is a systematic review and analysis.

Condition being studied: Lung cancer.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 November 2020 and was last updated on 09 November 2020 (registration number INPLASY2020110033).

INTRODUCTION

Review question / Objective: Our patient population is Lung cancer patients. Our intervention is dietary intake and serum level of folate and supplement of folate. And our control measure was to control the intake or content of folic acid at high dose level with folic acid intake or content at low dose level. What we want to achieve is the effect of high or low doses of folate intake and serum level of folate on the incidence rate of lung cancer. Our study design is a systematic review and analysis.

Rationale: The incidence rate of lung cancer is one of the most widespread cancers. There are many factors that

induce it. Among them, the relationship between folic acid and the pathogenesis of lung cancer has been revealed. The analysis method we adopted was meta analysis, because we found that the meta analysis, which was the last time to explore the risk of lung cancer and folate, was published in 2014. So it is very necessary to update the new meta analysis. Moreover, this meta analysis is more comprehensive in the relationship between dietary intake and supplement intake, and serum level of folic acid and lung cancer incidence rate. So this meta-analysis is innovative and does not repeat the previous meta-analysis.

Condition being studied: Lung cancer.

METHODS

Search strategy: terms: folate lung cancer; folic acid lung cancer. databases: Pubmed; Embase; Web of Science.

Participant or population: Lung cancer patients.

Intervention: Dietary intake and serum level of folate and supplement of folate.

Comparator: Controlling the intake or content of folic acid at high dose level with folic acid intake or content at low dose level. What we want to achieve is the effect of high or low doses of folate intake and serum level of folate on the incidence rate of lung cancer.

Study designs to be included: Systematic review and analysis.

Eligibility criteria: The literature search was independently undertaken by 3 authors (Jia Xu, Canjia Zhang and Yunkai Lin) with a standardized approach and guided by the fourth author (HFL) to make sure this article is rigorous and scientific. The study was eligible for inclusion if the following criteria were met: (1) the study is cohort study for "dietary folate intake" and "folate supplement" or nested case-control study for "serum folate" (2) the study investigated the association between dietary and supplemental intake of folate or serum level of folate and the risk of lung cancer; and (3) effect estimates (risk ratio [RR], hazard ratio [HR], or odds ratio [OR]), and 95% confidence intervals (CIs) were used to compare the highest and lowest dietary and supplemental intake/serum level of folate.

Information sources: The data we obtained are from published articles on electronic databases such as PubMed; EMBASE; Web of Science.

Main outcome(s): Our study revealed that folate intake had little or no influence on the risk of lung cancer and high folate in serum can affect the risk of lung cancer.

Data management: We examined the relationship between folate intake and the risk of lung cancer by pooling the effect estimates (RR, OR, or HR) and 95% CIs of the included studies. CMA (Comprehensive Meta-Analysis) was used to perform meta-analysis comparing the highest with the lowest serum folate and folate intake/supplement. In addition, we ran tree diagram analysis to examine whether this format of data is able to employ and use funnel diagram prove. We also reconducted all data resulted in different research methods. First, this paper use ug/d, ug/mo, ug/1000kcal, nmol/L as units. Second, we regroup some data without unit and only counted in quartering and insert them into proper groups referring to original study. At last, when it comes to different concentration caused by different study, we adjusted and combine data with small differences into appropriate groups, and recount data with large differences and put them into groups whose concentration is near. If the distinction between a specific data and other major data then it will be abandoned.

Quality assessment / Risk of bias analysis: NOS scale (Newcastle-Ottawa scale) was used to evaluate the methodological quality. NOS scale is mainly divided into "study selection", "comparability of cohorts" and "outcome" when evaluating

cohort study and divided into "study selection", "comparability of cases and controls on the basis of the design or analysis" and "Exposure" when it comes to nested case-control study.

Strategy of data synthesis: We examined the relationship between folate intake and the risk of lung cancer by pooling the effect estimates (RR, OR, or HR) and 95% CIs of the included studies. CMA (Comprehensive Meta-Analysis) was used to perform meta-analysis comparing the highest with the lowest serum folate and folate intake/supplement. In addition, we ran tree diagram analysis to examine whether this format of data is able to employ and use funnel diagram prove. We also reconducted all data resulted in different research methods. First, this paper use ug/d, ug/mo, ug/1000kcal, nmol/L as units. Second, we regroup some data without unit and only counted in quartering and insert them into proper groups referring to original study. At last, when it comes to different concentration caused by different study, we adjusted and combine data with small differences into appropriate groups, and recount data with large differences and put them into groups whose concentration is near. If the distinction between a specific data and other major data then it will be abandoned.

Subgroup analysis: Subgroup analysis was conducted to evaluate the effect of folate on the risk of lung cancer in specific continents and different score of articles in NOS scale.

Sensibility analysis: We have carried out sensitivity analysis. Generally, the article is analyzed by folic acid concentration stratification. The stratification value of some articles is quite different from other articles. Therefore, we have carried out sensitivity analysis on these articles. However, the results show that the impact on the results is not significant and can be ignored.

Language: English.

Country(ies) involved: China.

Keywords: folic acid; folate; Vitamin B9; lung cancer; meta analysis.

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