Parkinsonism and Related Disorders xxx (2015) 1–5

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Gout is not associated with a lower risk of Parkinson's disease: A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 8 June 2015
Received in revised form
17 August 2015
Accepted 24 August 2015

Keywords:
Gout
Parkinson's disease
Meta-analysis
Epidemiology

ABSTRACT

Background: Uratic acid is a potent anti-oxidant and hyperuricemia is well-linked to a lower risk of Parkinson's disease (PD), one of the most common neurodegenerative disorders. However, data on gout, the major complication of hyperuricemia, remain unclear.
Methods: Two investigators independently searched published studies indexed in MEDLINE, and EMBASE from inception to April 2015 using the terms for gout combined with the terms for PD. The inclusion criteria were as follows: (1) cohort or case-control study evaluating the risk of PD among patients with gout (2) odds ratio, relative risk, hazard ratio or standardized incidence ratio were provided (3) subjects without gout and subjects with PD were used as controls in cohort and case-control study, respectively. RevMan 5.3 software was used to perform the statistical analysis. Point estimates and standard errors were extracted from individual studies and were combined by generic inverse variance method of DerSimonian and Laird. Statistical heterogeneity was assessed using the Cochran's Q test and I^2 statistics.
Results: Three case-control studies and two cohort studies were identified and included in the data analysis. The pooled risk ratio of PD in patients with gout was 0.93 (95% CI, 0.79 to 1.09). The statistical heterogeneity was high with an I^2 of 87%. The results were not significantly different between males and females (RR 0.89; 95% CI, 0.57 to 1.39 and RR 0.95; 95% CI, 0.76 to 1.19, respectively).
Conclusion: This study did not provide support for an inverse relationship between gout and risk of PD.

1. Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative disorders characterized by tremor, bradykinesia, rigidity and postural instability [1]. The worldwide prevalence of PD is approximately 0.3% in individuals over 40 years old [2,3]. Despite the extensive research effort, the exact pathophysiology of selective dopaminergic cell degeneration that underlies PD remains unclear, though oxidative stress and mitochondrial dysfunction are generally believed to play a pivotal role [4–6].

Uric acid is a potent natural antioxidant found throughout extracellular fluid as sodium urate. Uric acid reduces the burden of oxidative stress through several mechanisms including scavenging free radicals and chelating transition metals [7,8]. In particular, a powerful protective antioxidant effect of uric acid on neurons has been demonstrated in several in vivo and in vitro studies [9,10]. Thus, uric acid might be a protective factor against the development of PD. In fact, several epidemiologic studies have consistently demonstrated and inverse relationship between hyperuricemia and risk of PD [11–15].

Gout is the major complication of long-standing hyperuricemia [16]. If hyperuricemia reduces the risk of development of PD, the risk should be lower in the patients with gout as well. However, epidemiologic studies attempting to address this issue have yielded inconsistent results [17–21]. Thus, to clarify this possible association, we conducted a systematic review and meta-analysis of cohort and case-control studies that compared the risk of development of PD in subjects with and without gout.

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http://dx.doi.org/10.1016/j.parkreldis.2015.08.030
1353-8020/

2. Methods

2.1. Search strategy

Two investigators (P.U. and N.S.) independently searched published studies indexed in MEDLINE and EMBASE database from inception to May 2015 using the search strategy that comprised of terms for gout and Parkinson's disease as described supplementary material 1. References of selected retrieved articles were also manually searched. Inclusion criteria The inclusion criteria were as follows: (1) case-control or cohort study (either prospective or retrospective) comparing the risk of PD in subjects with and without gout, (2) odds ratio (OR), relative risk (RR), hazard ratio (HR's) or standardized incidence ratio (SIR) with 95% confidence intervals (CI) were provided, and (3) subjects without PD and subjects without gout were used as control groups in case-control and cohort study, respectively.

Study eligibility was independently determined by each investigator noted above. Newcastle–Ottawa quality assessment scale was used to appraise the quality of the included studies [22]. This scale assessed each study in three areas including (1) the selection of the participants for each group (2) the comparability between the study groups and (3) the ascertainment of the exposure in case-control study and the outcome of interest in cohort study. The senior investigator (C.T.) oversaw this literature review process and resolved any different decisions. Data extraction A standardized data collection form was used to extract the following information: last name of the first author, title of the study, year of publication, year when the study was conducted, country of study, study size, study population, method used to diagnose gout and PD, average duration of follow up, baseline characteristics for each group, confounders that were adjusted and adjusted effect estimates with 95% CI. To ensure the accuracy of data extraction, this process was independently performed by all investigators. Any data discrepancy was resolved by referring back to the original studies.

2.2. Statistical analysis

Data analysis was performed using Review Manager 5.3 software from the Cochrane Collaboration. Point estimates and standard errors were extracted from each study and were combined by the generic inverse variance method of DerSimonian and Laird [23]. In light of the high likelihood of between study variance because of differences in study design and population, we used a random-effect model rather than a fixed-effect model. As the outcome of interest in this study was relatively uncommon, we used OR of case-control study as an estimate for RR to combine this data with RR of cohort study to increase the power and precision of our pooled estimate. Statistical heterogeneity was assessed by Cochran's Q test and I2 statistic. This statistic quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. A value of I2 of 0%–25% represents insignificant

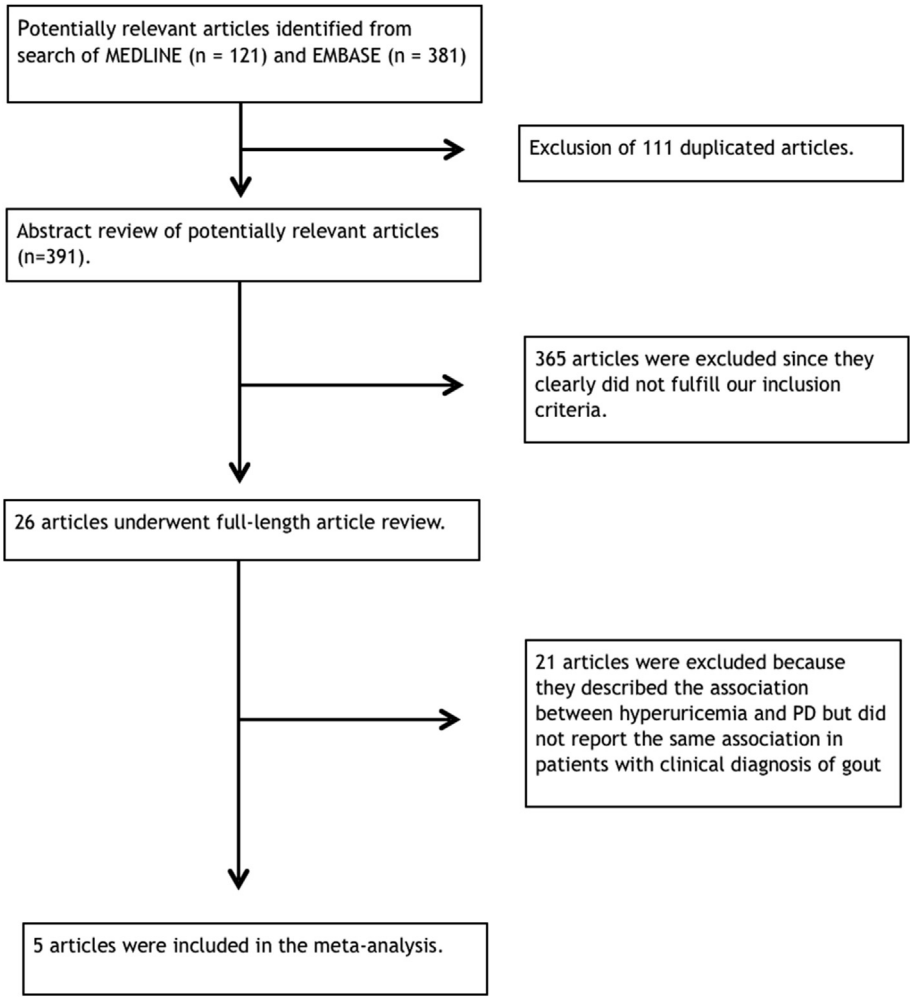

Fig. 1. Outline of our search methodology.

Please cite this article in press as: P. Ungprasert, et al., Gout is not associated with a lower risk of Parkinson's disease: A systematic review and meta-analysis, Parkinsonism and Related Disorders (2015), http://dx.doi.org/10.1016/j.parkreldis.2015.08.030