INPLASY PROTOCOL

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None declared.

Effect of perfluoroalkyl and polyfluoroalkyl substances on stroke incidence: systematic review and meta-analysis

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Review question / Objective: **We aimed to investigate the association between exposure to perfluoroalkyl and polyfluoroalkyl substances (PFAS) and the occurrence of stroke.**
Eligibility criteria: **We applied the following inclusion criteria for selection of the studies: (1) an observational studies including cohort, cross-sectional, or case-control studies; (2) exposure to at least one PFAS observed; (3) assessment of odds ratio (OR), relative risk (RR), or incidence rate of stroke per 1-log unit increase of PFAS. The exclusion criteria were as follows: (1) case reports and reviews; (2) duplicate publications of the same cohort; and (3) no data on the OR, RR, or incidence of stroke.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2022 and was last updated on 21 November 2022 (registration number INPLASY2022110102).

INTRODUCTION

Review question / Objective: **We aimed to investigate the association between exposure to perfluoroalkyl and polyfluoroalkyl substances (PFAS) and the occurrence of stroke.**

Condition being studied: **The health effect of endocrine disrupting chemical (EDC) is an emerging interest. Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are one of EDC which is highly used in manufacturing nonstick cookware, takeout meal container, firefighting forms, and water-repellent clothing. Compared to general population, those who were exposed to PFAS by drinking contaminated water at residential area were at 1-4 times increased risk of self-reported health problems. Indeed, for recent 5 years, large observational studies reported positive**

association between PFAS and metabolic disorders; dyslipidemia, liver dysfunction, diabetes, and hypertension; which consequently increase the risk of cardiovascular disease.
The major risk factor for stroke is age, sex, ethnicity, metabolic syndrome, smoking, alcohol, diet, and physical inactivity. In addition, environmental pollution is also considered a trigger factor. However, PFAS studies regarding atherosclerosis and cardiovascular diseases shows conflicting results. In this study, we systemically reviewed the literature and performed a meta-analysis to evaluate the effect of four main PFASs; perfluorooctanoic acid, perfluorooctanesulfonic acid, perfluorononanoic acid, and perfluorohexane sulphonic acid; on the occurrence of stroke.

METHODS

Participant or population: Studies that reported the associations between PFAS exposure and stroke incidence.

Intervention: Exposure to PFAS.

Comparator: To determine whether exposure to PFAS has an effect on the occurrence of stroke.

Study designs to be included: Clinical trials in humans were included in this review. Studies published as reviews, letters, or other undistinctive forms were excluded.

Eligibility criteria: We applied the following inclusion criteria for selection of the studies: (1) an observational studies including cohort, cross-sectional, or case-control studies; (2) exposure to at least one PFAS observed; (3) assessment of odds ratio (OR), relative risk (RR), or incidence rate of stroke per 1-log unit increase of PFAS. The exclusion criteria were as follows: (1) case reports and reviews; (2) duplicate publications of the same cohort; and (3) no data on the OR, RR, or incidence of stroke.

Information sources: We systematically searched for relevant articles in the PubMed, Embase, Cochrane Library, and SCOPUS databases for studies published up to November 01, 2022.

Main outcome(s): OR and 95% CI of the development of stroke.

Quality assessment / Risk of bias analysis: The Newcastle–Ottawa scale was used to assess the methodological quality of the included studies based on three aspects: selection of subjects, comparability of the groups, and assessment of outcomes or exposures. The quality of each study was graded as low (0–3), moderate (4–6), or high (7–9). All divergences were resolved by consensus.

Strategy of data synthesis: After discarding the duplicate studies, two reviewers (SMC and MCC) independently evaluated the potentially eligible studies. The studies were screened for eligibility based on a review of the title and abstract, and disagreements were resolved through consensus. After screening, two independent reviewers read the full texts of the studies and re-assessed the eligibility of each. Subsequently, the data, including name of the first author, publication date, study type, number of patients, demographic information (age and sex), follow-up duration, adjusted factors, and outcome data (OR and 95% CI of the development of stroke), were extracted. As PFAS concentrations usually shows skewed distribution, they were natural logarithmically transformed before analysis. Thus, the OR indicates the risk of development of stroke per 1-log unit increment of PFAS.

Subgroup analysis: N/A.

Sensitivity analysis: The studies were excluded one by one, and then the meta-analysis was performed in the remaining studies.

Language restriction: English.

Country(ies) involved: Republic of Korea.

Keywords: Perfluoroalkyl and polyfluoroalkyl substances; incidence; stroke.

Contributions of each author:

Author 1 - Seung Min Chung - The author 1 wrote, read, provided feedback and approved the final manuscript.
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