INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Association of urinary bisphenol A concentrations with in vitro fertilization outcomes: A meta-analysis protocol

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Review question / Objective: **At present, many studies have focused on the relationship between , but the results are still controversial. At present, there is still a lack of systematic meta-analysis to explain the real relationship between bisphenol A (BPA) concentration in urine and in vitro fertilization(IVF) outcomes two. Therefore, we plan to start from this scientific problem and search Pubmed, Web of science, and Cochrane databases for meta-analysis to provide a theoretical basis for the exact relationship between BPA and IVF outcomes.**
Eligibility criteria: **Inclusion criteria£ş(1) Original epidemiologic studies or observational studies. (2) The exposure way of BPA for IVF women was in daily life. (3) The outcomes included clinical pregnancy. (4) Studies reported odds ratios (OR), hazard ratios (HR), and relative risks (RR) for IVF outcomes as well as their 95% confidence intervals (CIs). (5)Urine samples were taken for BPA exposure assessment before IVF.Exclusion criteria:(1)No concentration data for BPA£ğ(2)Intervention studies.Urine samples were taken for BPA exposure assessment before IVF.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 March 2022 and was last updated on 18 March 2022 (registration number INPLASY202230086).

INTRODUCTION

Review question / Objective: **At present, many studies have focused on the relationship between , but the results are still controversial. At present, there is still a lack of systematic meta-analysis to explain the real relationship between bisphenol A (BPA) concentration in urine and in vitro fertilization(IVF) outcomes two. Therefore, we plan to start from this scientific problem and search Pubmed, Web of science, and**

Cochrane databases for meta-analysis to provide a theoretical basis for the exact relationship between BPA and IVF outcomes.

Rationale: The environment has a profound impact on people's health and can lead to diseases. Bisphenol A (BPA) is a common environmental endocrine disruptor, which exists widely in the environment. People are widely exposed to BPA through many consumer products, including polycarbonate plastics, medical equipment, polymer based dental fillings, glasses and personal care products. At present, many studies have focused on the relationship between BPA concentration in urine and in vitro fertilization(IVF) outcomes, but the results are still controversial.

Condition being studied: Search studies focused on the relationship between BPA concentration in urine and in vitro fertilization (IVF).

METHODS

Search strategy: ((((((((((Bisphenol A) OR (Diphenylolpropane)) OR (Bisphenol B)) OR (Bisphenol F)) OR (tetrachlorobisphenol a)) OR (BFDGE cpd)) OR (Bisphenol S)) OR (BPAF compound)) OR (Bisphenol AF))) AND ((((((((((((((((((((Reproductive Techniques, Assisted) OR (Assisted Reproductive Technique)) OR (Reproductive Technique, Assisted)) OR (Technique, Assisted Reproductive)) OR (Techniques, Assisted Reproductive)) OR (Assisted Reproductive Technics)) OR (Assisted Reproductive Technic)) OR (Reproductive Technic, Assisted)) OR (Reproductive Technics, Assisted)) OR (Technic, Assisted Reproductive)) OR (Technics, Assisted Reproductive)) OR (Assisted Reproductive Techniques)) OR (Reproductive Technology, Assisted)) OR (Assisted Reproductive Technologies)) OR (Assisted Reproductive Technology)) OR (Reproductive Technologies, Assisted)) OR (Technologies, Assisted Reproductive)) OR (Technology, Assisted Reproductive)) OR (ART)) OR ((((((((((((((((((Reproductive Techniques, Assisted) OR (Assisted Reproductive Technique)) OR (Reproductive Technique, Assisted)) OR (Technique, Assisted Reproductive)) OR (Techniques, Assisted Reproductive)) OR (Assisted Reproductive Technics)) OR (Assisted Reproductive Technic)) OR (Reproductive Technic, Assisted)) OR (Reproductive Technics, Assisted)) OR (Technic, Assisted Reproductive)) OR (Technics, Assisted Reproductive)) OR (Assisted Reproductive Techniques)) OR (Reproductive Technology, Assisted)) OR (Assisted Reproductive Technologies)) OR (Assisted Reproductive Technology)) OR (Reproductive Technologies, Assisted)) OR (Technologies, Assisted Reproductive)) OR (Technology, Assisted Reproductive))) OR ((((((((((((((Fertilization in Vitro) OR (In Vitro Fertilization)) OR (In Vitro Fertilizations)) OR (Test-Tube Fertilization)) OR (Fertilization, Test-Tube)) OR (Fertilizations, Test-Tube)) OR (Test Tube Fertilization)) OR (Test-Tube Fertilizations)) OR (Fertilizations in Vitro)) OR (Test-Tube Babies)) OR (Babies, Test-Tube)) OR (Baby, Test-Tube)) OR (Test Tube Babies)) OR (Test-Tube Baby)) OR (IVF))) OR ((((((((Sperm Injections, Intracytoplasmic) OR (Injection, Intracytoplasmic Sperm)) OR (Injections, Intracytoplasmic Sperm)) OR (Intracytoplasmic Sperm Injection)) OR (Sperm Injection, Intracytoplasmic)) OR (Intracytoplasmic Sperm Injections)) OR (ICSI)) OR (Injections, Sperm, Intracytoplasmic))) OR ((((((((((((((Preimplantation Diagnosis) OR (Diagnoses, Preimplantation)) OR (Preimplantation Diagnoses)) OR (Preimplantation Genetic Diagnosis)) OR (Diagnosis, Preimplantation)) OR (Diagnosis, Preimplantation Genetic)) OR (Diagnoses, Preimplantation Genetic)) OR (Genetic Diagnoses, Preimplantation)) OR (Genetic Diagnosis, Preimplantation)) OR (Preimplantation Genetic Diagnoses)) OR (Preimplantation Screening)) OR (Preimplantation Screenings)) OR (Screening, Preimplantation)) OR (Screenings, Preimplantation)) OR (PGT))).

Participant or population: There was no specific population, and the analysis was carried out according to the population in the final literature.

Intervention: Detection of BPA in urine of IVF patients without intervention.

Comparator: To compare the effects of different concentrations of BPA in urine on the clinical outcome of IVF.

Study designs to be included: Observation study or Original epidemiologic studies (including case-control, nested case-control, cross-sectional, and cohort studies).

Eligibility criteria: Inclusion criteria: (1) Original epidemiologic studies or observational studies. (2) The exposure way of BPA for IVF women was in daily life. (3) The outcomes included clinical pregnancy. (4) Studies reported odds ratios (OR), hazard ratios (HR), and relative risks (RR) for IVF outcomes as well as their 95% confidence intervals (CIs). (5)Urine samples were taken for BPA exposure assessment before IVF.Exclusion criteria:(1)No concentration data for BPA; (2)Intervention studies.Urine samples were taken for BPA exposure assessment before IVF.

Information sources: A comprehensive literature search was performed using PubMed, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials (up to March 10,2022). Contact the author for relevant data by email if necessary.

Main outcome(s): The main outcomes are the number of oocytes retrieved, high quality embryo rate, clinical pregnancy rate and live birth rate.

Additional outcome(s): Secondary outcomes are fertilization rate, blastocyst rate, embryo implantation rate.

Data management: The following information was extracted through predesigned data extraction content from each included study: the first author's last name, publication year, main outcomes, study area, study type, study population, sample size, biological sample for BPA exposure measurement, time of sample collection, BPA exposure concentration, urinary dilution adjustment method (urinary concentration adjusted by creatinine/gravidity, unadjusted urinary concentration), covariate adjustment in the model, results expressed as effect estimates (β) and OR and their 95% CIs.In accordance with the PRISMA guidance, the following data were extracted from each eligible study by two reviewers independently: first author's surname, year of publication, country of the study, the ethnicity of subjects, source of the control group, IVF method, numbers of cases and controls, outcomes, and BPA concentrations in cases and controls. Discrepancies were resolved by discussion until reaching a consensus and were arbitrated by a third person when necessary. These data will be recorded in a table for statistical analysis and displayed in the article.

Quality assessment / Risk of bias analysis: The quality of the methods for the included case-control studies was independently assessed by the two reviewers using the Newcastle-Ottawa Scale (NOS).The NOS uses a star rating system to assess quality from three broad perspectives of the case-control study: (a) selection of case and controls; (b) comparability of cases and controls; and (c) ascertainment of exposure.Studies with scores ranging from 0 to 9 stars and ≥7 stars were considered of high quality. Statistical heterogeneity among studies was estimated using the Q test and I2 statistics. Heterogeneity was acceptable as long as I2 ≤ 50%. A random-effects model was used to estimate the pooled log ORs and 95% CIs, as heterogeneity was found with P 50%. We planned to assess funnel plot asymmetry if we identified more than 10 studies. Reasons for asymmetry include publication bias, outcome reporting bias, and heterogeneity.

Strategy of data synthesis: Because all included studies reported risk estimates as ORs for IVF outcomes, the association between the exposure to BPA and IVF outcomes was assessed by calculating pooled OR and 95% confidence interval

(CI). The association between the exposure to BPA and IVF outcomes was assessed by calculating the regression coefficient (β) and 95% confidence interval (CI). All pooled results were conducted by the DerSimonian and Laird random-effects model (DerSimonian and Laird, 1986), which considers both within-study and between-study variations. The summary measures were presented as forest plots where the sizes of the data markers (squares) corresponded to the inverse of the variance of the natural logarithm of the OR or β from each study, and the diamond indicated the pooled OR or β. The squares indicate study-specific odds ratios (size of the square reflects the study-specific statistical weight); the horizontal lines indicate 95% CIs; and the diamond indicates the summary odds ratio with the related 95% CIs. Statistical heterogeneity among studies was quantified using the I2 statistic.

Subgroup analysis: Subgroup analysis was performed according to different races, regions and BPA concentrations, and subgroup analysis will be also performed according to BPA exposure levels of both men and women if possible.

Sensitivity analysis: After the quality evaluation of the included literature, sensitivity analysis is required if there are potentially low-quality studies. When heterogeneity test suggests that there is significant heterogeneity between included studies, sensitivity analysis can also be carried out, and sensitivity analysis is an indirect method to analyze heterogeneity. Use random-effects rather than fixed-effect model. Some studies have larger effects than others because random error means that multiple replications of the same study will produce different effect estimates due to sampling variation, even if replications would yield the right answer on average. The results of smaller studies are subject to greater sampling variation and hence are less precise. Imprecision is reflected in the confidence interval around the intervention effect estimate from each study and in the weight given to the results of each study in a meta-analysis. More precise results are given more weight.

Language: We only include articles written in English.

Country(ies) involved: China.

Other relevant information: Not applicable.

Keywords: Bisphenol A , in vitro fertilization, clinical pregnancy, live birth.

Dissemination plans: Publications are planned in the form of papers and reports are shared at relevant academic meetings.

Contributions of each author:

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