# INPLASY PROTOCOL

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# Meta-analysis of the efficacy of hemoperfusion combined with hemodialysis in treating acute severe organophosphorus pesticide poisoning

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Review question / Objective: Organophosphorus pesticides are one of the most widely used pesticides in the world. Our meta-analysis aims to conduct a more comprehensive and indepth analysis of the efficacy of hemoperfusion combined with hemodialysis on ASOPP patients through several different outcome indicators, providing clinical evidence for ASOPP blood purification therapy. P: Patients with acute severe organophosphorus pesticide poisoning; I: Hemoperfusion combined with hemodialysis; C: Conventional emergency treatment; O: Cure rate, efficacy, incidence of complications, time for cholinesterase level to return to normal, coma time, time of hospitalization and atropine dosage; S: RCT.

Information sources: The PubMed, EMbase, Cochrane, Web of sciense, Ovid, Scopus, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical literature (CBM), WanFang, Weipu (VIP), Chinese clinical trial Registry and Clinical Trials.gov databases.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 November 2021 and was last updated on 16 November 2021 (registration number INPLASY2021110056).

# INTRODUCTION

**Review question / Objective:** Organophosphorus pesticides are one of the most widely used pesticides in the world. Our meta-analysis aims to conduct a more comprehensive and in-depth analysis of the efficacy of hemoperfusion combined with hemodialysis on ASOPP patients through several different outcome indicators, providing clinical evidence for ASOPP blood purification therapy. P: Patients with acute severe organophosphorus pesticide poisoning; I: Hemoperfusion combined with hemodialysis; C: Conventional emergency treatment; O: Cure rate, efficacy, incidence of complications, time for cholinesterase level to return to normal, coma time, time of hospitalization and atropine dosage; S: RCT.

**Rationale:** Acute organophosphorus pesticide poisoning (AOPP) is a common clinical disease, according to WHO's estimates, millions of people worldwide suffer from AOPP every year, of which about 200,000 die, most of which occur in developing countries. Early emetic, gastric lavage, catharsis, and early use of conventional emergency treatments such as pralidoxime, atropinization and a series of advanced life support measures have greatly improved the cure rate. However. the mortality rate is still high, especially for patients who are acute severe organophosphorus pesticide poisoning (ASOPP). For ASOPP patients, blood purification is also a common rescue method in emergency departments. However, up to now, blood purification therapy is still controversial in the treatment of ASOPP.

#### Condition being studied:

Organophosphorus pesticides are one of the most widely used pesticides in the world. Acute organophosphorus pesticide poisoning (AOPP) is a common clinical disease, according to WHO's estimates, millions of people worldwide suffer from AOPP every year, of which about 200,000 die, most of which occur in developing countries. Early emetic, gastric lavage, catharsis, and early use of conventional emergency treatments such as pralidoxime, atropinization and a series of advanced life support measures have greatly improved the cure rate. However, the mortality rate is still high, especially for patients who are acute severe organophosphorus pesticide poisoning (ASOPP). For ASOPP patients, blood purification is also a common rescue method in emergency departments. However,up to now, blood purification therapy is still controversial in the treatment of ASOPP, and the clinical evidence for the efficacy of blood purification on ASOPP is insufficient which is not totally recognized by the medical community. Because hemoperfusion,

hemodialysis or CRRT, while removing toxins, they also absorb and remove antidotes and therapeutic drugs from the blood to varying degrees, which reduce the efficacy of these drugs, and there is a potential risk of inducing poisoning aggravation. Despite this, there are a large number of literature reports that blood purification therapy, especially the current mainstream hemoperfusion combined with hemodialvsis to treat ASOPP, is effective. but there is a lack of clinical evidence, especially in English-language studies. After searching the medical database, we found that there is only one Chinese metaanalysis about the efficacy of hemoperfusion combined with hemodialysis in treating ASOPP. Whereas, the outcome index of this meta-analysis is only the cure rate, which is not comprehensive, and the publication year of the included articles is relatively old because in 2016, the Chinese Society of Toxicology Poisoning and Treatment of Specialized Committee issued the Clinical guideline for the diagnosis and treatment of acute organophosphorus pesticide poisoning (2016). After that, the diagnosis and treatment of AOPP by emergency doctors in China became more standardized and reasonable. So,the treatment methods in the articles included in this meta-analysis may not be standardized. Our meta-analysis aims to conduct a more comprehensive and indepth analysis of the efficacy of hemoperfusion combined with hemodialysis on ASOPP patients through several different outcome indicators, providing clinical evidence for ASOPP blood purification therapy.

#### **METHODS**

Search strategy: The PubMed, EMbase, Cochrane, Web of sciense, Ovid, Scopus, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical literature (CBM), WanFang, Weipu (VIP), Chinese clinical trial Registry and Clinical <u>Trials.gov</u> databases were searched from January 1, 2017 until November 11, 2021. English search terms included organophosphate poisoning (MeSH term), organophosphate

poisonings, organothiophosphonate poisoning, organophosphorus poisoning, organothiophosphate poisoning, organothiophosphate poisonings, hemoperfusion (MeSH term), hemoperfusions, hemosorption, hemosorptions, renal dialysis (MeSH term), renal dialyses, extracorporeal dialyses, hemodialysis, hemodialyses, within the restriction limit of randomized controlled trial. Due to the complexity and particularity of Chinese, we have formulated a more perfect search strategy. Chinese search term included words meaning acute severe organophosphorus pesticide poisoning, hemoperfusion, hemodialysis, and randomized controlled trial. In response to the Chinese term "acute severe organophosphorus pesticide poisoning", we have formulated 10 different search strategies. Similarly, 7 different retrieval strategies have been developed for hemoperfusion combined with hemodialysis in interventions. For study design, our search strategy includes RCT, randomized control, random number table, lottery and so on.

Participant or population: Acute severe organophosphorus pesticide poisoning.

Intervention: Hemoperfusion combined with hemodialysis.

**Comparator:** Conventional emergency treatment.

Study designs to be included: RCT.

Eligibility criteria: Articles were included if they met all of the following criteria:1) Randomized controlled study (RCT) 2) Study population consisted of accidental or suicidal OP poisoning patients, and diagnosed as acute severe organophosphorus pesticide poisoning (ASOPP) and there are clinical manifestations of pulmonary edema, respiratory failure, coma, cerebral edema or other important organ failures. 3) Study population consisted of patients who potentially received hemoperfusion combined with hemodialysis on the basis of conventional emergency treatment once they presented to the emergency department. 4) One or more of the following were reported:cure rate, efficacy, incidence of complications, time for cholinesterase level to return to normal, coma time, time of hospitalization and atropine dosage. 5) Articles were from January 1, 2017 to November 11, 2021.Articles were excluded if any of the following were present: 1)The article did not clearly state that the research was RCT.2) Studies were not published in Chinese or English. 3) Study data was unavailable or the content of article was not rigorous.4) Studies involving primarily special populations (e.g. AIDS or tuberculosis patients)5)Repeated literature6)Sample size was too small.

Information sources: The PubMed, EMbase, Cochrane, Web of sciense, Ovid, Scopus, Chinese National Knowledge Infrastructure (CNKI), Chinese Biomedical literature (CBM), WanFang, Weipu (VIP), Chinese clinical trial Registry and Clinical Trials.gov databases.

Main outcome(s): Cure rate, efficacy and incidence of complications.

Additional outcome(s): Time for cholinesterase level to return to normal, coma time, time of hospitalization and atropine dosage.

Data management: NoteExpress.

Quality assessment / Risk of bias analysis: Cochrane collaboration tool.

Strategy of data synthesis: Dichotomous variable was presented as Risk ratios (RR) and ordinal categorical variable was presented as Odds ratios (OR). Continuous outcomes such as time for cholinesterase level to return to normal, coma time, time of hospitalization, and atropine dosage were presented as the mean difference and with a 95% confidential interval (CI) rate. Statistical heterogeneity was assessed according to the Cochrane Handbook of Systematic Review of Interventions (version 5.1). Chi-square and I2 tests were used to test the heterogeneity. If necessary,

we would also use L'Abbe graph and Galbraith plot to assess heterogeneity. If there was heterogeneity between the studies (I2>50%, P<0.05), the cause of heterogeneity such as the year of publication, the proportion of men, average age, sample size and unit, and subgroup analysis was searched for. We will use meta regression to find these factors that may cause heterogeneity. If the cause was not found, the random effects model for metaanalysis was used. If there was no heterogeneity between the studies, the fixed effect model was applied. At the same time, we would conduct a sensitivity analysis to explore whether the results of each meta-analysis are robust. Publication bias was assessed by using a funnel plot. We would also use Begg's test and Egger's test to assess publication bias. If there was obvious publication bias, we would use the trim and fill method to correct or eliminate the publication bias and detect how much the publication bias has affected the results of the meta-analysis.

Subgroup analysis: According to the publication year of the article, the proportion of men, the sample size, the average age and the unit of measurement for subgroup analysis.

Sensitivity analysis: After deleting any one of the documents, merge them again. If the effect size is not much different, then pass the sensitivity analysis.

Language: English and Chinese.

Country(ies) involved: China.

Keywords: hemoperfusion combined with h e m o d i a l y s i s, a c u t e s e v e r e organophosphorus pesticide poisoning.

#### **Contributions of each author:**

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