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INPLASY

Protective Effects of the TREM1 Inhibitor LP17 on Experimental Acute Brain Injury: A protocol for Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 June 2025 and was last updated on 28 June 2025.

INTRODUCTION

Review question / Objective Does LP17 improve neurological outcomes in animal models of experimental acute braininjury?

Condition being studied Acute brain injury (ABI) is a severe neurological disorder that includes subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), intracerebral hemorrhage, and ischemia-reperfusion injury. These conditions often result in irreversible brain damage and long-term functional disabilities. Inflammatory and immune responses are critical in the pathogenesis of ABI. TREM1, a pattern recognition receptor, plays a key role in recruiting immune cells and transmitting inflammatory signals. Inhibiting TREM1 can reduce inflammation, mitigate neuronal damage, and promote brain tissue repair. Despite advancements in treatment, effective neuroprotective interventions remain limited. The potential of TREM1 inhibition in treating nervous system injuries has gained attention in recent years. Many experimental studies have explored the effects of TREM1 inhibition in animal models of SAH, TBI, intracerebral hemorrhage, and MCAO/R. However, results are inconsistent due to differences in experimental design, animal models, and intervention methods. This study aims to conduct a systematic review and meta-analysis to integrate existing evidence and clarify the therapeutic effects of TREM1 inhibition in these ABI animal models, providing a theoretical basis for future clinical research.

METHODS

Participant or population Animal models of acute brain injury, with no restrictions on the method of

injury induction, species, or strain of experimental animals.

Intervention Interventions are based on the use of the TREM1 inhibitor LP17, with no restrictions on the method of administration, frequency, timing, or incubation time.

Comparator The control group receives no intervention or placebo and sham treatment.

Study designs to be included Controlled animal experimental studies, with articles in Chinese or English.

Eligibility criteria Systematic reviews, systematic reviews, conference abstracts, letters, case reports, and other non-animal experimental studies will be excluded.

Information sources We will conduct a comprehensive search of PubMed, EMBASE, Web of Science, Cochrane Library, CNKI, Wanfang Data, and VIP data using medical subject headings (MeSH or similar). Additionally, we will review reference lists of relevant studies to identify further potential articles.

Main outcome(s) 1. primary indicators: brain water content, neurological function scores. 2. Secondary indicators: inflammatory cytokines (IL-1β, IL-4, IL-6, IL-10, TNF-α), NF-κB, NLRP3, Caspase-1, and cell apoptosisdetection.

Data management The Microsoft Excel software will be used to manage the literature. Two reviewers will independently complete the literature screening according to the inclusion and exclusion criteria. Data extraction will be cross-checked, and any inconsistent data will be reviewed by a third researcher. Information will be extracted using a pre-developed data extraction form. Data on sample size for the intervention and control groups will be extracted from the text. Aggregate statistics such as sample size, mean, standard deviation, or standard error will be extracted. If the data are contained in a graph, data extraction will be performed using digital image analysis software (Plot Digitizer). If information on sample size, mean, standard deviation, or standard error is not available, the corresponding author of the relevant study will be contacted via email, and all relevant information will be provided. If there is no response, two reminder emails will be sent. Discrepancies: The remaining authors will double-check all extracted data. Disputes will be resolved through mutual discussion.

Quality assessment / Risk of bias analysis This study will use the SYRCLE Risk of Bias tool to assess the risk of bias. The SYRCLE tool is an assessment instrument specifically designed to evaluate the intrinsic validity of animal experiments. It comprises 10 items and 22 sub-items, covering six types of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. This tool is applicable for assessing the risk of bias in interventional animal experiments . The assessment results of the 10 items are ultimately indicated by "Yes," "No," and "Uncertain." "Yes" indicates a low risk of bias, "No" indicates a high risk of bias, and "Uncertain" indicates an unclear risk of bias. If the number of included studies for a particular indicator is greater than or equal to 10, publication bias analysis will be performed.

Strategy of data synthesis We plan to conduct a systematic review and meta-analysis, focusing on the potential reasons for the differing efficacy of interventions across various trials. We have performed a statistical analysis of the results from all available studies; however, the implementation depends on the number of relevant studies from which we collect data. If we collect data from at least 10 relevant datasets, we will proceed with a meta-analysis. After all the included data have been collected, two authors will independently calculate the effect size estimates, weights, and I^2 values for each study.
Statistical analyses will be conducted using RevMan 5.4 software, with measures expressed as mean differences (MD). When the units of measurement for outcome indicators differ, standardized mean differences (SMD) will be used as effect size indicators, and each effect size will be expressed as a 95% confidence interval (95% CI). Heterogeneity among studies will be assessed using the I^2 test; if $P>0.1$ and $I^2<50\%$, this suggests low heterogeneity among the included studies, and a fixed-effect model will be used. If P50%, this indicates high heterogeneity among the included studies, and a random-effects model will be used with further sensitivity analysis. In this case, our primary aim is to explore the potential reasons for heterogeneity among studies. However, the final methodology will be determined after data extraction. The final data analysis will be completed using RevMan 5.4 software.

Subgroup analysis Subgroup analyses Animal species, type of modeling, intervention timing, method of intervention, duration of intervention; Outcome indicators of interest and outcome measurement data (e.g., brain water content, neurological function score, inflammatory

cytokines such as IL-1β, IL-6, TNF-α, TREM-1, MyD88,etc.)

Sensitivity analysis When heterogeneity is significant, sensitivity analysis will be conducted on the studies. Sensitivity analysis assesses the stability of the overall results by sequentially excluding eachtrial.

Language restriction English, Chinese.

Country(ies) involved China.

Keywords Acute brain injury; Triggering Receptor Expressed on Myeloid Cells-1; LP17; Systematic review and meta-analysis; Animalmodels.

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