

**Recovery of hearing loss in patients with sudden sensorineural hearing loss by Batroxobin : a systematic review and meta-analysis**

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**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202620037**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 February 2026 and was last updated on 10 February 2026.**INTRODUCTION**

**Review question / Objective** Review question: Patients with sudden sensorineural hearing loss (SSNHL), does treatment with batroxobin (as an adjunctive or monotherapy) compared to control interventions (The experimental group was treated with batroxobin on the basis of the control group ; or the experimental group was batroxobin, and the control group was other conventional treatment drugs ; or the experimental group was batroxobin + conventional treatment drugs, and the control group was other treatment drugs + the same conventional treatment drugs.) improve hearing recovery and clinical outcomes

**Objective:**To systematically review and meta-analyze the available evidence from randomized controlled trials (RCTs) to evaluate the efficacy and safety of batroxobin in the treatment of SSNHL, with a focus on hearing improvement, recovery rates, and adverse events.

**Population:** adult patients with sudden sensorineural hearing loss

**Intervention:** Batroxobin

**comparison:** The experimental group was treated with Batroxobin on the basis of the control group ; or the experimental group was batroxobin, and the control group was other conventional treatment drugs ; or the experimental group was batroxobin + conventional treatment drugs, and the control group was other treatment drugs + the same conventional treatment drugs.

**Outcome:** After the use of batroxobin, the efficiency of hearing recovery was objectively evaluated.

**Study:** Randomised controlled trial will be included.

**Condition being studied** Sudden deafness is one of the common emergencies in otorhinolaryngology. The etiology is not yet clear. It is generally believed that the dysfunction of the inner ear circulation is the main pathogenic factor. The blood supply of the inner ear comes from the terminal branch of the basilar artery. The lack of collateral circulation is prone to tissue ischemia

and hypoxia, which leads to hearing loss. Batroxobin is a thrombin-like drug that dissolves thrombus and improves microcirculation, which can effectively improve the blood supply of cochlea. Some studies have confirmed that batroxobin has good effect and less adverse reactions in the treatment of sudden deafness. Some studies have confirmed that it is not helpful for the treatment of sudden deafness. At present, there are many studies on batroxobin in the treatment of sudden deafness. However, due to the lack of standardization of clinical research methods and evaluation methods, the clinical treatment effect is still inconclusive, which affects the authenticity of the research results to a certain extent. Therefore, this study used meta-analysis to evaluate the efficacy and safety of randomized controlled trials of batroxobin in the treatment of sudden deafness, and provided evidence-based basis for clinical treatment.

## METHODS

**Participant or population** Patients clearly diagnosed with sudden sensorineural hearing loss (SSNHL)/sudden deafness, age, gender, course of disease and other factors are not limited.

**Intervention** Does treatment with batroxobin (as an adjunctive or monotherapy).

**Comparator** The experimental group was treated with Batroxobin on the basis of the control group ; or the experimental group was batroxobin, and the control group was other conventional treatment drugs ; or the experimental group was batroxobin + conventional treatment drugs, and the control group was other treatment drugs + the same conventional treatment drugs.

**Study designs to be included** Only randomised controlled trial will be included.

**Eligibility criteria** ( 1 ) Patients diagnosed with sudden deafness, age, gender, course of disease and other factors are not limited. ( 2 ) The trial design was a randomized controlled trial. ( 3 ) Intervention measures : the experimental group was treated with batroxobin on the basis of the control group ; or the experimental group was batroxobin, and the control group was other conventional treatment drugs ; or the experimental group was batroxobin + conventional treatment drugs, and the control group was other treatment drugs + the same conventional treatment drugs. ( 4 ) The effective rate was used as the evaluation index in the evaluation of curative effect. ( 5 ) Efficacy evaluation criteria : The main outcome of

this study was the effective rate of treatment. For Chinese studies, the inclusion criteria are based on whether they explicitly adopt domestic established guidelines. Priority was given to studies based on the ' Guidelines for the Diagnosis and Treatment of Sudden Deafness ( 2015 ) '. If the study explicitly refers to an earlier version ( such as the 1997 or 2006 version ), it is also accepted. According to the above guidelines, the efficacy is divided into : recovery, damaged frequency hearing threshold returned to normal or pre-treatment level ; the average hearing improvement was more than 30 dB. Effective, with an average hearing improvement of 15-30 dB ; ineffective, improvement of less than 15 dB. The total effective rate includes three types of patients : cured, markedly effective and effective. For international research, the standard of diagnosis and treatment adopted in the original text shall prevail. Where possible, priority attention is given to research using internationally recognized guidelines, in particular the Clinical Practice Guidelines published by the American Academy of Otorhinolaryngology-Head and Neck Surgery ( AAO-HNSF ) in 2012 and updated in 2019. The guidelines recommend the use of pure tone hearing threshold ( PTA ) and / or speech recognition rate ( SRS ) to assess efficacy, and ' improvement ' is usually defined as clinically significant hearing threshold elevation ( such as  $\geq 15$  dB or  $\geq 20$  dB ). In the process of data extraction, we achieve the comparability of results between Chinese and global studies by mapping different definitions to the unified framework of ' total efficiency '.

**Information sources** A comprehensive literature search will be conducted across 10 electronic databases and trial registries, including both published and gray literature, to identify all relevant randomized controlled trials (RCTs) on batroxobin for the treatment of sudden sensorineural hearing loss (SSNHL). The search will cover the following sources from their inception to February 10, 2026: The information sources are categorized into three groups for clarity and systematic coverage:

- Chinese-language databases (n = 4):
  1. Chinese Biomedical Literature Database (CBM) – A comprehensive Chinese-language database covering biomedical journals in China, including foundational, clinical, and traditional Chinese medicine research.
  2. China National Knowledge Infrastructure (CNKI) – One of the largest integrated academic databases in China, providing access to journal articles, theses, conference papers, and more.

3. Wanfang Data – A leading Chinese digital content platform offering full-text resources in medicine, science, and technology.
4. VIP Information Database – A major Chinese academic resource platform with extensive coverage of scientific and medical journals.
  - International English-language databases (n = 4):
5. PubMed – The U.S. National Library of Medicine's free database, providing access to biomedical literature, including MEDLINE-indexed journals.
6. EMBASE (Excerpta Medica Database) – A comprehensive biomedical and pharmacological database with strong international coverage, particularly in drug-related research.
7. Web of Science Core Collection – A multidisciplinary citation database that includes high-impact scientific and medical journals.
8. Cochrane Central Register of Controlled Trials (CENTRAL) – A highly curated database of RCTs maintained by the Cochrane Collaboration, known for its rigor and relevance to systematic reviews.
- Clinical trial registries (n = 2)
9. Chinese Clinical Trial Registry (ChiCTR) – An internationally recognized registry for clinical trials conducted in China, providing access to protocol and outcome data.
10. ClinicalTrials.gov – A public registry and results database of privately and publicly funded clinical studies conducted around the world, maintained by the U.S. National Institutes of Health. In addition, we will manually screen the reference lists of included studies and relevant systematic reviews to identify potentially eligible trials. Authors of included or ongoing studies may be contacted to obtain additional data, clarify methodological details, or retrieve unpublished results.

- Main outcome(s)**
1. Hearing Recovery Rate: The proportion of patients achieving a clinically significant improvement in pure-tone average (PTA), defined as an increase of  $\geq 15$  dB from baseline to post-treatment.
  2. Total Marked Effective Rate: The proportion of patients achieving either complete recovery or marked improvement (e.g.,  $\geq 30$  dB gain or normalization of hearing).
  3. Incidence of Adverse Events (AEs): The frequency of treatment-related side effects, particularly focusing on hemorrhagic complications and allergic reactions.

#### Additional outcome(s)

Secondary Outcomes:

1. Complete Hearing Recovery Rate: The proportion of patients whose final PTA reached  $\leq 25$  dB after treatment.

2. Mean Change in PTA: The absolute difference in PTA values (in dB) between pre-treatment and post-treatment assessments.
3. Safety Profile: Detailed recording and grading of adverse events according to standard criteria (e.g., CTCAE v5.0) to evaluate the tolerability of batroxobin.

**Quality assessment / Risk of bias analysis** The methodological quality and risk of bias of the included randomized controlled trials (RCTs) will be independently assessed by two reviewers using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2). This tool evaluates bias across five domains:

1. Bias arising from the randomization process – assessing whether the allocation sequence was properly generated and concealed;
2. Bias due to deviations from intended interventions – examining adherence to the assigned intervention and management of crossover or non-adherence;
3. Bias due to missing outcome data – evaluating the extent and handling of incomplete data;
4. Bias in measurement of the outcome – determining whether outcome assessment was blinded and objective;
5. Bias in selection of the reported result – checking for evidence of selective reporting of outcomes or analyses. For each domain, judgments will be made as "Low risk", "Some concerns", or "High risk" of bias, based on predefined signaling questions. Any discrepancies will be resolved through discussion or consultation with a third reviewer. A risk-of-bias summary figure will be generated to visually present the assessment results.

**Strategy of data synthesis** Two authors will independently extract data. Any disagreement will be resolved by discussion until consensus is reached or by consulting a third author. The following data will be extracted: author, year of publication, country where the study was conducted, study period, original inclusion criteria, total number of people included in the study, group, interventions, sample size, age (years), gender, course of the disease, course of treatment and so on.

**Subgroup analysis** Subgroup analyses will be considered to explore potential sources of heterogeneity, if multiple treatment arms are present or significant statistical heterogeneity is observed. Pre-specified factors include:

1. Patient characteristics: Age, sex;
2. Time to treatment: Onset-to-treatment interval ( $< 72$  hours vs.  $\geq 72$  hours);

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3.Treatment regimen: Dose and duration of batroxobin;

4.Concomitant therapies: Use of corticosteroids or hyperbaric oxygen therapy.Additional subgroup analyses may be explored post-hoc if clinically meaningful variables are identified during the screening or data extraction phase (e.g., baseline hearing severity, comorbidities, or geographic region).

All subgroup analyses will only be conducted if sufficient data are available and will be interpreted as exploratory and hypothesis-generating.

**Sensitivity analysis** In order to ensure the stability of the results of the outcome indicators, the sensitivity analysis of each outcome indicator was performed.

**Country(ies) involved** China.

**Keywords** batroxobin; sudden sensorineural hearing loss.

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