

Relationship between acute lung injury and pulmonary hyaluronic acid deposition after subarachnoid hemorrhage

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Ethics Committee

Tianjin Medical University General hospital

Protocol Abstract

Title	Relationship between acute lung injury and pulmonary hyaluronic acid deposition after subarachnoid hemorrhage
Ethics Committee (Grant Number)	The ethics committee of Tianjin Medical University General Hospital (IRB2024-YX-425-01)
Project Executor	Xintong Ge (M.D. & Ph.D.)
Sponsor	Tianjin Medical University General Hospital
Participant	Tianjin Huanhu Hospital
Principal Investigator	Ye Tian (Ph.D.) - Tianjin Medical University General Hospital Yadan Li (M.D.) - Tianjin Huanhu Hospital
Fundings	High-Level Talent Project of Tianjin Health Research Program (Grant No. TJWJ2024RC002)
Execute Time	10/01/2024-09/30/2025
Recruiting Time	10/01/2024-09/30/2025
Objective	Clarify the correlation between pulmonary inflammatory injury and hyaluoronic acid deposition after subarachnoid hemorrhage
Study Type	Observational
Time Perspective	Prospective
Enrollment	24 participants
Biospecimen	Description: bronchoalveolar lavage fluid and serum Retention: Samples without DNA
Condition	Subarachnoid Hemorrhage
Inclusion Criteria	1) Age between 18 and 80 years old with independent behavior ability or authorized legal representative. 2) A documented diagnosis of SAH within 5 days. 3) A Hunt-Hess scale of IV or V. 4) Absence of clinical and etiological evidence of pulmonary infection.
Exclusion Criteria	1) Pregnant or lactating women. 2) Present history of traumatic brain injury or intracranial hemorrhage.

	<p>3) Past history of neurological disorders, lung infection within the past six months, cancer, chronic cardiopulmonary diseases, hematological diseases or renal failure.</p> <p>4) Have participated in clinical trials in the past 4 weeks.</p> <p>5) The investigator considers that not appropriate for inclusion.</p>
Withdrawal Criteria	<p>1) Clinical or etiological evidence of pulmonary infection after recruitment.</p> <p>2) Failure to complete tracheoscopy treatments within the time frame specified in the study.</p> <p>3) Voluntary withdrawal by the subject.</p> <p>4) Withdrawal requested by the physician or researcher due to issues such as poor compliance.</p>
Outcome Measures	<p>Hyaluronic acid and inflammatory cytokines (IL-1β, TNF-α and IL-10) levels in bronchoalveolar lavage fluid and serum at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) of patients with SAH.</p>
Reference standard	<p>Hyaluronic acid is associated with organ dysfunction in acute respiratory distress syndrome. Critical Care. 2017, 21(1): 304.</p>
Statistical Analysis	<p>All statistical analyses were performed using SPSS Statistics Version 27.0 (IBM, Armonk, NY, USA). A two-tailed p value of less than 0.05 was considered to be statistically significant.</p>

1. Research Background and Objectives

Acute lung injury is a common complication of subarachnoid hematoma (SAH), and a significant risk factor for death in patients with SAH. Unlike neurogenic pulmonary edema and pneumonia following brain injury, the clinical causes of pulmonary injury after SAH are not intracranial hypertension or pulmonary infection. Its occurrence is influenced by the release of catecholamines, the regulatory function of the hypothalamic-pituitary-adrenal (HPA) axis and systemic inflammatory response, but the specific mechanisms are still unclear. Therefore, delving into the pathological mechanisms of SAH-induced lung injury and developing therapeutic strategies based on the findings is of great importance to improve the prognosis of patients.

Abnormal accumulation of hyaluronic acid in the lungs has been reported to be closely related to the pathological progression of various pulmonary injury diseases, such as chest trauma, pulmonary infection and chronic obstructive pulmonary disease. From this, the present research is aimed to explore the levels and dynamic changes of hyaluronic acid in the bronchoalveolar lavage fluid and blood of patients with acute lung injury following SAH, and to analyze its correlation with the prognosis of pulmonary complications, thereby providing assistance for the clinical diagnosis and treatment of SAH.

2. Study design

2.1 Overall design

This research is an observational prospective cohort study.

2.2 Estimated number of subjects

Estimated by statistical analysis, a total of 24 subjects were included from patients admitted to the neurosurgical intensive care unit of Tianjin Medical University General Hospital and the intensive care unit of Tianjin Huanhu Hospital due to aneurysmal SAH.

3. Inclusion, Exclusion and Withdrawal Criteria

3.1 Inclusion Criteria

- 1) Age between 18 and 80 years old with independent behavior ability or authorized legal representative.
- 2) A documented diagnosis of SAH within 5 days.
- 3) A Hunt-Hess scale of IV or V.
- 4) Absence of clinical and etiological evidence of pulmonary infection.

3.2 Exclusion Criteria

- 1) Pregnant or lactating women.
- 2) Present history of traumatic brain injury or intracranial hemorrhage.
- 3) Past history of neurological disorders, lung infection within the past six months, cancer, chronic cardiopulmonary diseases, hematological diseases or renal failure.
- 4) Have participated in clinical trials in the past 4 weeks.
- 5) The investigator considers that not appropriate for inclusion.

3.3 Withdrawal criteria

- 1) Clinical or etiological evidence of pulmonary infection after recruitment.
- 2) Failure to complete tracheoscopy treatments within the time frame specified in the study.
- 3) Voluntary withdrawal by the subject.
- 4) Withdrawal requested by the physician or researcher due to issues such as poor compliance.

4. Study procedure

1) Researchers initiate the study according to the inclusion/exclusion criteria. After confirming the subject has signed the informed consent, doctors will record the basic information, GCS at admission, Hunt-Hess scale and past medical history. Besides, researchers will track the patient's surgical status during hospitalization and GOSE at discharge.

2) The patient undergoes bronchoalveolar lavage treatment under bronchoscopy at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) of SAH. For each session, 5 ml of bronchoalveolar lavage fluid is collected to quantify the levels of hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10). At the same timepoints, 5 ml of venous blood is drawn to assess serum hyaluronic acid and inflammatory factors (IL-1 β , TNF- α and IL-10) levels.

3) The patient undergoes a chest CT scan 14 days after the onset of SAH.

5. Evaluation Parameters

3.1 Primary outcome parameters

Hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels in bronchoalveolar lavage fluid at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) of patients with SAH.

3.2 Secondary outcome parameters

Serum hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) of SAH patients.

6. Withdrawal of the subject

The subject has the right to withdraw from this trial at any time for any reason. The researcher should have a thorough understanding and a record of the reasons for withdrawal. Doctors and researchers also have the right to stop the subject from continuing to participate in the trial at any time during the research. Besides, subjects with early withdrawal should not be replaced by others.

As too many subjects withdrawing from the trial will lead to unreliable results, unnecessary withdrawal should be avoided. The falling rate of the trial should be controlled within 10%.

7. Statistical analysis

1) The difference between hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels in bronchoalveolar lavage fluid at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) was compared using one-way ANOVA followed by LSD post-hoc test.

2) The difference between serum hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels at the acute phase (1-5 days post-onset) and the chronic phase (10-14 days post-onset) was compared using one-way ANOVA followed by LSD post-hoc test.

3) Pearson correlation coefficient was used to evaluate the correlation between hyaluronic acid levels in bronchoalveolar lavage fluid and serum, hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels in bronchoalveolar lavage fluid, as well as serum hyaluronic acid and inflammatory cytokines (IL-1 β , TNF- α and IL-10) levels.

8. Trial Management

8.1 Ethics

To obtain the approval documents of the clinical trial, researchers should submit the trial protocol and a copy of the research documents including the informed consent to the ethics committee.

The approval documents from the ethics committee should be accompanied by the name list of ethics committee members and their respective responsibilities. These documents will be delivered to the researchers in written form before the start of the study.

Any safety-related issues must be promptly reported to the ethics committee, which includes revision on the trial protocol and modification on the subject information page. The end or early termination of the trial should also be reported.

8.2 Informed consent and data protection agreement

It is the responsibility of the researchers to explain the objectives, study procedures, benefits and potential risks of the trial for each subject. The researchers should receive the informed consent signed by the subject before starting the trial, and keep it properly. The subject should also permit researchers and the clinical trial management agency to check his or her original data. Thus, the reliability of the research findings could be ensured.

The personal information of each subject, including name, gender, age, home address and telephone number, should be collected in detail. And the researcher/doctor should give the subject his or her contact information, so that the subject can contact with him or her when needed. This is also helpful for the research and medical care.

8.3 Subjects privacy

The researchers should protect the privacy of the subject. All research documents can only be identified using the subject's number instead of name or physical examination number. In addition, the grouped table that records the correspondence between the subject's name and number can only be kept by the researcher, and could not be submitted to any institution or individual.

8.4 Modification of the trial protocol

The trial protocol is approved by the ethics committee before starting the trial. During the research, any proposed modification on the trial protocol should be reported to the principal investigator, and then be submitted to the ethics committee for review. The clinical research can only be resumed after the re-approval of the ethics committee.

8.5 Original records certification

Researchers should ensure that the subject's privacy is protected when collecting and organizing data. In addition, the data manager is authorized to review the original records in order to confirm the accuracy of the original data.

8.6 Documents on file

According to relevant laws and regulations, researchers should keep the original records properly for at least 5 years from the end of the study.

8.7 Quality control

The clinical trial management agency has the authority to review the study progress, in order to ensure that the trial is carried out as predetermined and that the research data be veritably recorded.