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fficacy and Safety of Tranexamic Acid in Aneurysmal Subarachnoid Hemorrhage: A Meta-Analysis

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Yang, MQ; Wang, S; Guo, YJ.

Corresponding author:
Mengqi Yang

mengqiqiyang@163.com

Author Affiliation:
Jining NO.1 People's Hospital.

ADMINISTRATIVE INFORMATION

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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 8 May 2025 and was last updated on 8 May 2025.

INTRODUCTION

Review question / Objective One of the primary causes of poor prognosis in patients with aneurysmal subarachnoid hemorrhage (aSAH) is rebleeding of the ruptured aneurysm. Antifibrinolytic therapy may serve as a supplementary approach to further prevent rebleeding. However, the role of tranexamic acid (TXA) in the treatment of aSAH remains controversial. This study aims to synthesize existing evidence and elucidate the efficacy and safety of tranexamic acid as an adjunctive therapy for aSAH.

P: Patients with aneurysmal subarachnoid hemorrhage.

I: Patients in the treatment group received TXA treatment and conventional treatment.

C: The control group received conventional treatment without TXA.

O: Rebleeding incidence, mortality, good outcome events, hydrocephalus rate, delayed cerebral ischemia rate, thromboembolic events

S: Randomized controlled trial.

Condition being studied Aneurysmal subarachnoid hemorrhage (aSAH) is a life-threatening condition associated with extremely high rates of disability and mortality. One of the primary causes of poor prognosis in aSAH patients is aneurysmal rebleeding, with reported mortality rates reaching up to 70% in cases of rehemorrhage. According to the latest clinical guidelines for aSAH management, the most effective strategy to prevent rebleeding is early definitive treatment of the aneurysm, such as surgical clipping or endovascular coiling. However, most rebleeding events occur within the first few hours following the initial hemorrhage, leaving insufficient time to complete aneurysm treatment. Consequently, antifibrinolytic therapy may serve as a supplementary intervention to further reduce rebleeding risk.

Tranexamic acid (TXA), an antifibrinolytic agent, reduces bleeding by binding to plasminogen to inhibit fibrinolysis. Since its introduction, TXA has been widely utilized to minimize blood loss in surgical procedures, severe trauma, and heavy menstrual bleeding. Over recent decades, the

application of TXA for subarachnoid hemorrhage (SAH) management has been extensively reported in both domestic and international studies. Nevertheless, the clinical value of TXA in aSAH treatment remains controversial. This study aims to synthesize existing evidence to clarify the efficacy and safety of TXA as an adjunctive therapy for aSAH. Through a comprehensive analysis of randomized controlled trials (RCTs), we seek to elucidate the potential benefits and risks associated with TXA administration in aSAH patients.

METHODS

Search strategy In order to obtain relevant data, we searched various databases involving PubMed, Embase, the Cochrane Library, Web of Science, ClinicalTrials.gov, and Chinese databases (CNKI, WEIPU, WANFANG, China Biology Medicine disc [CBM], Chinese Clinical Trial Registry [ChiCTR]). We identified relevant literature by using combinations terms, including “Tranexamic Acid”, “AMCA”, “AMCHA” etc. and “Subarachnoid Hemorrhage”, “Hemorrhage, Subarachnoid”, “Subarachnoid Hemorrhages” etc. We searched databases for literature published between database inception and April 20, 2025. In addition, we also checked all identified articles carefully to see if we could capture additional relevant studies.

Participant or population Patients with aneurysmal subarachnoid hemorrhage.

Intervention Patients received tranexamic acid treatment and conventional treatment.

Comparator Patients received conventional treatment without tranexamic acid.

Study designs to be included Randomized controlled trial study.

Eligibility criteria Articles were included if they conformed to the following criteria: (1) study type: RCT studies; (2) patient population: patients with aneurysmal subarachnoid hemorrhage; (3) intervention: tranexamic acid treatment and conventional treatment; (4) comparator: conventional treatment without tranexamic acid treatment; (5) outcome: rebleeding incidence, mortality, good outcome events, hydrocephalus rate, delayed cerebral ischemia rate, thromboembolic events and so on.
Articles were excluded on the following basis: (1) not RCT studies; (2) case reports, guidelines, reviews, abstracts and articles involving animal experiments; (3) the content of the research was inconsistent with the study criteria; and (4) the article was not written in English or Chinese.

Information sources PubMed, Embase, the Cochrane Library, Web of Science, ClinicalTrials.gov, and Chinese databases (CNKI, WEIPU, WANFANG, China Biology Medicine disc [CBM], Chinese Clinical Trial Registry [ChiCTR]).

Main outcome(s) Rebleeding incidence, mortality, good outcome events.

Additional outcome(s) Hydrocephalus rate, delayed cerebral ischemia rate, thromboembolicevents.

Quality assessment / Risk of bias analysis The Cochrane risk of bias assessment tool.

Strategy of data synthesis Review Manager version 5.3 software was used for statistical analysis. The Q test and the Chi squared test were used to evaluate the heterogeneity between the original studies. $P < 0.1$ or $I2 \geq 50\%$ indicated that there was heterogeneity between the selected studies; in these cases, we used a random effect model to merge the effect quantity, otherwise the fixed effect model was used. The combined results of outcome indicators were calculated by the combined statistical effect of relative risk (RR) and 95% confidence interval (CI). $P < 0.05$ was considered to indicate statistical significance.

Subgroup analysis Subgroup analysis based on timing of tranexamic acid administration and course of administration.

Sensitivity analysis If the pooled results remain stable after removing any single study, it indicates successful sensitivity analysis.

Country(ies) involved China.

Keywords Tranexamic Acid, aneurysmal subarachnoid hemorrhage.

Contributions of each author
Author 1 - Mengqi Yang.
Author 2 - Yujin Guo.
Author 3 - Shan Wang.