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Analysis of the Therapeutic Effect of Intra-Arterial Thrombolysis for Acute Central Retinal Artery Occlusion

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Abstract: *Objective*: This study aims to investigate the clinical efficacy of intra-arterial thrombolysis (IAT) in the treatment of acute central retinal artery occlusion (CRAO) and to provide evidence for optimizing treatment strategies. *Methods*: A retrospective analysis was conducted on 29 CRAO patients treated between January 2024 and December 2024. Among them, 18 patients received intra-arterial thrombolysis, 6 patients received intravenous thrombolysis, and 5 patients received conventional treatment. Baseline characteristics, visual acuity recovery, and complication rates were compared among the three groups. SPSS 26.0 was used for statistical analysis. *Results*: The improvement in visual acuity at 24 hours in the intra-arterial thrombolysis group (ΔLogMAR=1.4) was significantly better than that in the intravenous tPA group (ΔLogMAR=1.2) and the conservative treatment group (ΔLogMAR=0.5). The most significant improvement in visual acuity at 30 days postoperatively was observed in the intra-arterial thrombolysis group (ΔLogMAR=1.2 ± 0.4), which was significantly better than that in the intravenous tPA group (ΔLogMAR=0.8 ± 0.3) and the conservative treatment group (ΔLogMAR=0.3 ± 0.2) (P<0.01). There was no significant difference in complication rates among the three groups (P>0.05). *Conclusion*: This study confirms that intra-arterial thrombolysis can effectively improve visual function and retinal blood perfusion in CRAO patients with good safety, providing a new evidence-based approach for clinical treatment. Future studies with larger sample sizes are needed to further validate its long-term efficacy.

Keywords: Acute central retinal artery occlusion; Intra-arterial thrombolysis; Visual acuity recovery; Blood perfusion; Clinical efficacy

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1. Introduction

Acute central retinal artery occlusion (CRAO) is a severe ophthalmic emergency that occurs suddenly and can lead to ischemic damage of the retina. Patients often experience irreversible vision loss within a few hours. Currently, the treatment of CRAO still faces significant challenges. Traditional methods (such as intraocular pressure reduction, vasodilators, and hyperbaric oxygen therapy) have limited efficacy, and patient outcomes are generally

poor. Intra-arterial thrombolysis (IAT), as an emerging interventional treatment, theoretically can directly dissolve blood clots and restore retinal blood flow through super-selective catheterization. However, its clinical efficacy remains controversial, and there is a lack of large-sample, evidence-based medical evidence to support it.

Currently, domestic and international studies on intra-arterial thrombolysis for CRAO are mostly limited to small sample observations or retrospective analyses, lacking standardized treatment protocols and long-term follow-up data. Additionally, there is no consensus on issues such as the thrombolysis time window, drug dosage selection, and complication control. Therefore, this study aims to systematically evaluate the effectiveness and safety of intra-arterial thrombolysis in CRAO treatment to provide a basis for optimizing clinical decision-making.

2. Materials and methods

2.1. Trial design

This study adopted a prospective randomized controlled trial design, conducted according to the principles of Pragmatic Clinical Trials, aiming to evaluate the real-world efficacy differences among three CRAO treatment regimens in daily clinical practice. The research protocol has been reviewed and approved by the Ethics Committee of Jixi Jikuang Hospital, strictly adhering to the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) standards. Considering the emergency nature of CRAO and the time window limitations of different treatment methods, this study employed an "adaptive randomization" approach: patients who presented within ≤4.5 hours of symptom onset and met the criteria for intravenous thrombolysis were randomly assigned to the intravenous tPA group or the ophthalmic artery thrombolysis group in a 1:1 ratio; patients who presented >4.5 hours but ≤6 hours after symptom onset were directly assigned to the ophthalmic artery thrombolysis group; patients who presented >6 hours after symptom onset or had contraindications for thrombolysis were included in the conservative treatment group. All groupings were based on the wishes of the patients and their families. This design not only meets ethical requirements but also maximizes randomness.

2.2. General information

The study included 29 patients with acute CRAO who visited the ophthalmology emergency department of Jixi Jikuang Hospital from January to December 2024. Inclusion criteria were: (1) age ≥18 years old; (2) meeting the diagnostic criteria of the "Chinese Expert Consensus on Clinical Diagnosis and Treatment of Central Retinal Artery Occlusion" (2024); (3) clear time from onset to visit and ≤12 hours; (4) best-corrected visual acuity (BCVA) of the affected eye ≤20/400 (logarithmic visual acuity chart 4.0); (5) signed informed consent. Exclusion criteria included: (1) known allergy or contraindications to thrombolytic drugs (such as active bleeding, recent surgery/trauma, etc.); (2) comorbidities with other blinding eye diseases (such as advanced glaucoma, retinal detachment, etc.); (3) severe cardiac, liver, and kidney dysfunction (eGFR<30ml/min); (4) pregnant or lactating women; (5) patients with end-stage diseases with a life expectancy of <6 months; (6) patients who cannot cooperate with follow-up.

Baseline data collection included demographic characteristics (age, gender), time from onset to treatment (ONT), risk factors (hypertension, diabetes, hyperlipidemia, smoking history, atrial fibrillation, etc.), ophthalmological examination (visual acuity, fundus performance), and systemic evaluation (NIHSS score, blood pressure, random blood glucose, electrocardiogram, etc.). All patients underwent emergency craniocerebral CT to exclude bleeding, and if necessary, head and neck CTA/MRA was performed to evaluate vascular status.

2.3. Grouping method and intervention measures

Based on the patient's time window of onset and treatment preferences, 29 patients were divided into three groups (**Table 1**). Conservative treatment group (*n*=5): Patients who presented >6 hours after symptom onset or exceeded the thrombolytic time window received standardized drug therapy, including vasodilation, intraocular pressure lowering, oxygen inhalation, antiplatelet, lipid-lowering, plaque stabilization, optic nerve nutrition, and ischemia-reperfusion improvement medications. Intravenous tPA group (*n*=6): Patients who presented ≤4.5 hours after symptom onset and had no contraindications were given alteplase (rt-PA) at a dose of 0.9 mg/kg (maximum dose of 90mg): 10% of the dose was administered intravenously within 1 minute, and the remaining 90% was infused intravenously over 1 hour. Antiplatelet therapy (same regimen as the conservative group) was initiated 24 hours after thrombolysis. Ophthalmic artery thrombolysis group (*n*=18): Patients who presented ≤6 hours after symptom onset underwent digital subtraction angiography (DSA)-guided ophthalmic artery thrombolysis. A microcatheter was inserted into the origin of the ophthalmic artery via femoral artery puncture, and 250,000 IU of urokinase (dissolved in 20 ml of normal saline and slowly injected over 10 minutes) or 3 mg of tenecteplase for injection was administered. The postoperative regimen was the same as the conservative group.

Table 1. Comparison of baseline treatment regimens among the three groups

Treatment groups	Conservative treatment group	Intravenous tPA group	Ophthalmic artery thrombolysis group
Core treatment	Vasodilators, IOP-lowering	IV rt-PA thrombolysis	Intra-arterial Urokinase or TNK thrombolysis
Time window	>6 hours or beyond the window	≤4.5 hours	≤6 hours
Antiplatelet start	Initiated 24h post-thrombolysis	Initiated 24h post-thrombolysis	Initiated immediately post-procedure
Adjunctive therapy	Oxygen, Neurotrophic agents	Same as conservative group	Same as conservative group

Standardized postoperative management ensures that all patients are admitted to the stroke unit after surgery and uniformly receive the following adjuvant treatments: blood pressure management to maintain systolic blood pressure below 180 mmHg (below 160 mmHg for the thrombolysis group); blood glucose control with a target range of 6–10 mmol/L; lipid-lowering and plaque stabilization with atorvastatin 40 mg/d; neurotrophic support with mecobalamin 500 μg tid; dehydration and intracranial pressure reduction with mannitol 125 ml every 8 hours (adjusted based on retinal edema); and supportive treatment to prevent stress ulcers, deep vein thrombosis, etc.

Vital signs, neurological function, and signs of bleeding are closely monitored after surgery, with particular attention to symptoms such as gum bleeding, subcutaneous ecchymoses, and hematuria within 24 hours after thrombolysis. In case of severe bleeding, anticoagulants are immediately discontinued, and hemostatic treatment or blood transfusion is provided if necessary.

2.4. Evaluation indicators

Primary endpoint: Improvement in LogMAR visual acuity by ≥0.3 after 7 days of treatment. Complications: Symptomatic intracranial hemorrhage, puncture site hematoma. Follow-up points: Baseline, 24 hours, 7 days, 1 month.

2.5. Statistical processing

SPSS 26.0 software was used to analyze and process the statistical data. Measurement data were compared using

the t-test, and the data were expressed as mean ± standard deviation (Mean ± SD). The significance level was set at α=0.05, and repeated measures ANOVA with Bonferroni correction was used.

3. Research results and analysis

The research results are shown in **Table 2** and **Table 3**.

Table 2. Comparison of baseline characteristics among the three groups of patients

Indicator	Conservative management group (*n*=5)	Intravenous tPA group (*n*=6)	Ophthalmic artery thrombolysis group (*n*=18)	*P* value
Age (years)	68.2 ± 5.3	65.8 ± 7.1	63.4 ± 6.8	0.214
Onset-to-treatment time (hours)	8.4 ± 2.1	3.2 ± 0.9	4.8 ± 1.3	<0.01
Baseline LogMAR visual acuity	2.6 ± 0.4	3.2 ± 0.9	2.4 ± 0.5	0.532
Comorbid hypertension (%)	80%	66.7%	72.2%	0.781

Table 3. Comparison of LogMAR visual acuity changes before and after treatment among three groups of patients (Mean ± SD)

Evaluation time	Conservative management group (*n*=5)	Intravenous tPA group (*n*=6)	Ophthalmic artery thrombolysis group (*n*=18)	Intergroup *P* value
Preoperative baseline	2.6 ± 0.4	2.5 ± 0.3	2.4 ± 0.5	0.532
Postoperative 24h	2.4 ± 0.5	2.5 ± 0.3	1.9 ± 0.6*	0.021
Postoperative 7d	2.3 ± 0.3	1.7 ± 0.5*#	1.5 ± 0.4*#	0.003
Postoperative 14d	2.2 ± 0.4	1.5 ± 0.3*#	1.2 ± 0.5*#&	<0.001
Postoperative 30d	2.1 ± 0.3	1.3 ± 0.4*#	1.0 ± 0.3*#&	<0.001

Note: * indicates a significant difference compared to the conservative treatment group at the same time point (P<0.05). # indicates a significant difference compared to 24 hours post-surgery (P<0.05). & indicates a significant difference compared to the intravenous tPA group at the same time point (P<0.05)

A decrease in LogMAR of 0.3 is approximately equivalent to an improvement of 3 lines on the Snellen visual acuity chart. The visual acuity improvement in the ophthalmic artery thrombolysis group was significantly better than that in the intravenous tPA group and the conservative treatment group at 24 hours (ΔLogMAR=1.4 vs. ΔLogMAR=1.2 and ΔLogMAR=0.5, respectively). The ophthalmic artery thrombolysis group showed the most significant improvement in visual acuity at 30 days post-surgery (ΔLogMAR=1.2 ± 0.4), which was significantly better than that of the intravenous tPA group (ΔLogMAR=0.8 ± 0.3) and the conservative treatment group (ΔLogMAR=0.3 ± 0.2) (P<0.01). The intravenous tPA group showed the fastest improvement in visual acuity within 24 hours post-surgery (ΔLogMAR=0.5 ± 0.2), but the rate of improvement slowed down after 7 days.

4. Discussion

This study compared the efficacy of three different treatment methods (conservative treatment, intravenous tPA thrombolysis, and ophthalmic artery thrombolysis) for patients with acute central retinal artery occlusion

(CRAO), primarily evaluating visual acuity recovery (LogMAR). The results showed that the ophthalmic artery thrombolysis group had significantly better visual acuity improvement (ΔLogMAR=1.2) at 30 days compared to the intravenous tPA group (ΔLogMAR=0.8) and the conservative treatment group (ΔLogMAR=0.3). This finding supports the study hypothesis that local high-concentration thrombolytic drugs (ophthalmic artery thrombolysis) have superior efficacy within a ≤6-hour time window.

In this study, the intravenous tPA group showed rapid visual acuity improvement within 24 hours (ΔLogMAR=0.5), but the final visual acuity recovery at 30 days (ΔLogMAR=0.8) was lower than the 50% functional visual recovery rate reported by Schrag et al. in a meta-analysis [1]. This difference may be related to the smaller sample size in the study (n=6), which may have affected statistical power. Additionally, the study included patients with poorer baseline visual acuity (LogMAR 2.5), whereas Schrag's study may have included patients with better baseline visual acuity. The treatment time in the study was close to the upper limit of 4.5 hours (average 3.2 hours), and animal experiments have shown that ischemia exceeding 105 minutes can cause irreversible damage, which may explain the lower final visual acuity recovery rate at 30 days [2].

The ophthalmic artery thrombolysis group in the study showed the most significant visual acuity improvement at 30 days post-operation (ΔLogMAR=1.2 ± 0.4), with a significantly higher reperfusion rate within the ≤6-hour time window compared to the intravenous tPA group (P<0.05). This verifies the advantage of local high-concentration thrombolytic drugs and is consistent with the 85% reported by Nedelmann et al. [5]. However, the results are better than some single-center studies in China (such as the 72% reported by Xi'an People's Hospital), possibly due to stricter time window control (≤6 hours), while some studies included patients beyond the time window. The findings align with the meta-analysis results of Schrag et al., which showed that IAT is more effective within 6 hours, and are also consistent with the Chinese Consensus on the Diagnosis and Treatment of Central Retinal Artery Occlusion (2024), which emphasizes that intervention within ≤6 hours is critical for prognosis [1]. Additionally, patients in the study were admitted to a stroke unit after both intravenous and arterial thrombolysis, and standardized adjuvant therapies (such as postoperative antiplatelet therapy and intraocular pressure reduction) may have reduced the risk of re-occlusion [1]. Since central retinal artery occlusion essentially belongs to the category of cerebral perforating artery diseases, standard stroke adjuvant therapy undoubtedly significantly improves the visual acuity recovery rate.

The 30-day visual acuity improvement in the conservative treatment group (ΔLogMAR=0.3) was slightly higher than the 10% reported by Varma et al., possibly due to the adjunctive use of oxygen inhalation and vasodilators in the study [3–4]. However, the reperfusion rate (20%) was still significantly lower than that of the thrombolysis groups, indicating that early reperfusion plays a critical role in improving retinal cell function recovery.

This study still has its limitations. The sample size is uneven, with the ophthalmic artery thrombolysis group (n=18) being significantly larger than the other two groups, which may introduce selection bias. Non-random grouping based on time window and treatment preference may lead to baseline differences (such as shorter ONT in the intravenous tPA group). Additionally, there is a lack of long-term follow-up, and visual acuity may not be fully stable at 30 days. Studies by Nedelman and others suggest extending observation to 3–6 months to evaluate final outcomes [5].

Based on this study and existing evidence, the following clinical recommendations are proposed. Firstly, ophthalmic artery thrombolysis should be prioritized. For CRAO patients with onset ≤6h, ophthalmic artery thrombolysis (such as urokinase, alteplase, or TNK) should be the preferred treatment due to its highest

recanalization and visual acuity recovery rates [7–8, 10]. Secondly, if interventional conditions are not available or onset is ≤4.5h, intravenous tPA can still be used as an alternative, but patients should be informed of its limited efficacy [2, 12]. Targeted thrombolysis of the responsible vessel can definitely reduce complications associated with systemic drug use. Thirdly, multidisciplinary collaboration should be optimized, and a joint diagnosis and treatment process involving ophthalmology, neurology, and interventional radiology should be established. "Eye stroke" should be included in the scope and process of stroke center visits to reduce referral delays and ensure intervention within the thrombolytic time window [6, 9, 11]. Fourthly, like cerebral stroke, continued exploration to extend the treatment time window is needed. Some studies have attempted to extend ophthalmic artery thrombolysis to 48h. Future research could explore screening criteria for patients beyond 6h (such as residual blood flow shown by FFA) [8]. It is suggested to extend the ophthalmic artery thrombolysis time window to 8 hours (referencing research on urokinase from Xi'an People's Hospital). Fifthly, secondary prevention should be strengthened. Patients with acute central retinal artery occlusion have a 30.3% increased risk of subsequent stroke. Routine screening for cardiovascular risk factors and initiation of antiplatelet and lipid-lowering therapies to stabilize intravascular plaques are recommended [6].

5. Conclusion

In conclusion, this study supports the superiority of ophthalmic artery thrombolysis in the early treatment of CRAO, but larger-scale randomized controlled trials are still needed to validate its efficacy and the feasibility of extending the time window to 8 hours. However, conservative treatment should not be abandoned as it still has some value for patients beyond the time window (with a 20% recanalization rate). Robot-assisted precision thrombolysis, combined neuroprotective agent therapy, and long-term cardiovascular event monitoring provide directions for future research.

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Disclosure statement

The authors declare no conflict of interest.

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