Efficacy of neurointervention combined with intravenous thrombolysis in the treatment of ischemic cerebrovascular disease and its influence on neurological function and prognosis of patients

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Abstract. The present study aimed to investigate the efficacy of neurointervention combined with intravenous thrombolysis in the treatment of ischemic cerebrovascular disease (ICD) and its influence on the neurological function and prognosis of patients. A total of 119 patients with ICD admitted to Xinxiang Central Hospital (Xinxiang, China) from May 2013 to September 2015 were selected. Among them, 65 patients were enrolled in the control group and treated with intravenous thrombolysis, whereas the other 54 patients were enrolled in the observation group and were treated with intravenous thrombolysis combined with neurointervention. The National Institute of Health Stroke Scale (NIHSS) system was used to evaluate the neurological function of patients after treatment. Kaplan-Meier survival curve analysis was carried out to assess the survival of patients. The total effective rate, complications, vascular recanalization and the hospitalization time after treatment were compared between the two groups. The NIHSS scores at 1, 3 and 6 months after treatment were statistically lower in the observation group than those in the control group ($P<0.05$). The total effective rate and total vascular recanalization in the observation group were higher than those of the control group ($P<0.05$). The incidence of complications in the observation group was statistically lower than that in the control group ($P<0.05$). In conclusion, neurointervention combined with intravenous thrombolysis can not only effectively improve the diseased blood vessels of patients and restore the damaged nerve function, but also reduce the incidence of complications. Moreover, neurointervention combined with intravenous thrombolysis is safe and can ensure a better quality of life of patients.

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Introduction

Despite the improved living standards nowadays, ischemic cerebrovascular disease (ICD), a disease prevalent in the elderly, is quite common in this increasingly aging society. Featuring high mortality, recurrence and high disability rate, ICD poses a serious threat to people's lives (1-3). ICD can cause temporary blood supply disorder, which leads to neurological deficits and has a serious impact on patients (4). ICD onset is often accompanied by neurological dysfunction (5). Timely treatment is unavailable due to the sudden onset of ICD, making the life of patients severely impacted (6).

The prominent clinical treatment for ICD is intravenous thrombolysis, which can promote the recanalization of the blocked blood vessels and save the life of patients, because of the plasminogen activator in the thrombolytic drug which dissolves the fibrin in the thrombus (7-9). However, the deficiency is that intravenous thrombolysis only works within the first 4 h after the onset of the disease and has certain contraindications for patients (10). Therefore, only a limited number of patients are suitable for intravenous thrombolysis. Due to the increasing incidence of ICD, new research and discoveries have been made. In recent years, neurointervention has been applied in the treatment of ICD (11). Neurointervention is a minimally invasive therapy that is based on a computer to determine the location of arterial stenosis and treat cerebrovascular disease through intubation. The use of intravenous thrombolysis in the course of interventional therapy can directly unblock blood vessels and eliminate infarction (12,13). Neurointervention compensates for the limitations of intravenous thrombolysis regarding treatment time and eligibility of patients. Therefore, the aim of the present study was to combine the two therapies in order to investigate whether intravenous thrombolysis combined with neurointervention could improve the ICD treatment.

The present study explored the efficacy of neurointervention combined with intravenous thrombolysis in the treatment of ICD and its influence on neurological function and prognosis of patients, aiming to provide future reference for the treatment of ICD.

Patients and methods

General information. A total of 119 patients with ICD admitted to Xinxiang Central Hospital (Xinxiang, China)

from May 2013 to September 2015 were selected. Among them, 65 patients were enrolled in the control group and treated with intravenous thrombolysis, whereas the other 54 patients were enrolled in the observation group and were treated with intravenous thrombolysis combined with neurointervention. The control group included 37 males and 28 females, with an average age of 41.3±5.2 years. In the control group, 18 patients had total anterior circulation infarction, 16 partial anterior circulation infarction, 19 posterior circulation infarction and 12 lacunar infarction. The observation group included 28 males and 26 females, with an average age of 42.3±4.7 years. In the observation group, 15 patients had total anterior circulation infarction, 11 partial anterior circulation infarction, 17 posterior circulation infarction and 11 lacunar infarction. The study was approved by the Ethics Committee of Xinxiang Central Hospital. Patients who participated in the study had complete clinical data and signed written informed consents were obtained from the patients and/or guardians.

Inclusion and exclusion criteria. The inclusion criteria were the following: patients with ICD for the first time; patients with treatment indications for neurointervention; patients admitted to the hospital within 6 h after the ICD onset; patients diagnosed with ICD by head CT angiography; and patients with complete clinical data.

The exclusion criteria were the following: patients with severe inflammation; patients with severe mental disorder; patients with intracranial hemorrhage; patients with hereditary diseases; patients with malignant tumors; and patients with other serious cardiovascular or cerebrovascular diseases.

Treatment methods. Patients in the control group were treated with intravenous thrombolysis. After admission, patients were treated with tissue-type plasminogen activator for injection (China FDA approval no. S20150001; Guangzhou Recomgen Biotech Co., Ltd.). An intravenous drop of 300,000-500,000 U of urokinase and 20 ml of saline was firstly administered, followed by an intravenous injection of 1,000,000 U of urokinase and 100 ml of saline.

In the observation group, patients received neurointervention treatment right after the intravenous thrombolysis. Electrocardiography, blood routine tests, liver and kidney function tests, as well as coagulation function tests were performed before treatment. Aspirin (China FDA approval no. H41021076; Henan Fusen Pharmaceutical Co., Ltd.) was orally administrated at a dose of 50-150 mg/day and clopidogrel [China FDA approval no. 20180029; Sinofi (Hangzhou) Pharmaceutical Co., Ltd.] was orally administrated at a dose of 75 mg/day to prevent platelet aggregation. With the support of the digital subtraction angiography system, an injection of a small amount of anesthetic into the inguinal region was administered before puncturing the femoral artery to place the vascular sheath. A 5F arterial sheath was inserted. A contrast tube was inserted to the aortic arch under the guidance of the ultra-sliding guidewire. The blood vessel direction and position was confirmed by angiography. A total of 200,000 U of urokinase (national medicine standard H22023486) was added into 20 ml of 0.9% sodium chloride solution for injection. Next, the solution was pumped in at a rate of 1 ml/min through a micropump autolysis catheter under the guidance of the micro guidewire. A stent was placed at the site of arterial stenosis to determine the unclogging of blocked blood vessels. Antiplatelet therapy was performed 24 h after surgery.

Table I. Efficacy evaluation criteria.

Items	Criteria
Marked response	≥45% decrease in NIHSS score
Moderate response	<45% and ≥18% decrease in NIHSS score
No response	<18% decrease in NIHSS score

Table II. Criteria for vascular recanalization.

Items	Criteria
Complete recanalization	The main branches of the skull are completely recanalized and can be clearly developed
Partial recanalization	The main branches of the skull are not clearly developed and the blood vessels in the posterior part of the embolization are partially recanalized
Blocked	The blood vessels at the back end of the embolization site are blocked and cannot be developed

Outcome measures. Main outcome measures: The National Institutes of Health Stroke Scale (NIHSS) (14) scores of the two groups of patients at 1, 3 and 6 months after treatment were recorded. Kaplan-Meier survival curves were drawn to assess the patients' survival 1 year after treatment.

Secondary outcome measures: The efficacy of treatment (Table I) was evaluated in the two groups. Total effective rate=(cases of marked response + cases of moderate response)/total no. of cases x100%. In addition, the vascular recanalization rates (Table II) of the two groups were calculated. Vascular recanalization rate=(cases of complete recanalization + cases of partial recanalization)/total no. of cases x100%.

Statistical analysis. Statistical analysis was performed using SPSS 19.0 software (IBM Corp.) and the data were plotted using GraphPad Prism 7 software (GraphPad Software, Inc.). Count data were expressed as rate (%) and were compared by Chi-square test. Measurement data were expressed as the mean ± standard deviation (mean ± SD) and were compared between two groups by the independent samples t-test. The measurement data were normally distributed. Repeated measures ANOVA, followed by Bonferroni post hoc test, was used for the comparison of the data at multiple time points. The 1-year survival of patients was assessed by Kaplan-Meier survival analysis and log-rank test was used for the comparison of the survival curves. $P<0.05$ was considered to indicate a statistically significant difference.

Table III. General clinical data of patients in the control and observation groups [n (%), mean ± SD].

Factors	Observation group (n=54)	Control group (n=65)	t/χ^2	P-value
Sex			0.306	0.580
Male	28 (51.85)	37 (56.92)		
Female	26 (48.15)	28 (43.08)		
Age (years)	42.3±4.7	41.3±5.2	1.026	0.307
Disease type			0.681	0.496
Total anterior circulation infarction	15 (27.78)	18 (27.69)		
Partial anterior circulation infarction	11 (20.37)	16 (24.62)		
Posterior circulation infarction	17 (31.48)	19 (29.23)		
Lacunar infarction	11 (20.37)	12 (18.46)		
Low-density lipoprotein (μmol/l)	2.89±0.87	2.81±0.79	1.149	0.251
Hematological disease			0.563	0.453
Yes	18 (33.33)	26 (40.00)		
No	36 (66.67)	39 (60.00)		
Fibrinogen (g/l)	6.43±1.25	6.26±1.43	0.683	0.496
Triglyceride (mmol/l)	1.35±0.23	1.34±0.34	0.184	0.854
Total cholesterol (μmol/l)	4.49±1.04	4.48±1.09	0.051	0.960
Alcohol abuse			0.351	0.553
Yes	22 (40.74)	30 (46.15)		
No	32 (59.26)	35 (53.85)		

Table IV. Comparison of neurological deficits (NIHSS scores) between the two groups before and after treatment (mean ± SD).

Group	Before treatment	1 month after treatment	3 months after treatment	6 months after treatment	F	P-value
Control group (n=65)	12.76±2.85	10.02±2.91[a]	9.24±2.32[a]	8.32±2.16[a,b]	36.259	<0.001
Observation group (n=54)	12.83±2.57	5.23±1.34[a]	3.16±1.54[a,b]	2.53±0.96[a-c]	22.367	<0.001
t	0.135	11.150	16.470	18.250		
P-value	0.892	<0.001	<0.001	<0.001		

[a]P<0.05, compared with the data before treatment; [b]P<0.05, compared with the data 1 month after treatment; [c]P<0.05, compared with the data 3 months after treatment. Marked response, the decrease of NIHSS score was ≥45% compared with that before treatment. Moderate response, the decrease of NIHSS score <45% and ≥18% compared with that before treatment. No response, the decrease of NIHSS score <18%.

Results

General clinical data of patients in the control and observation groups. As shown in Table III, no significant difference was observed between the control and the observation group in terms of age, sex, disease type, low-density lipoprotein levels, hematological disease, fibrinogen, triglyceride and total cholesterol levels and alcohol abuse (P>0.05).

Comparison of neurological deficits and vascular recanalization between the two groups. NHISS scores before treatment were not statistically different between the two groups (P>0.05; Table IV). At 1, 3 and 6 months after treatment, the NHISS scores were lower in the observation group than those in the control group (P<0.001). In the control group, the NIHSS scores at 1, 3 and 6 months after treatment were significantly lower than those before treatment (P<0.05); the NIHSS score at 1 month after treatment was not significantly different from that at 3 months after treatment; however, it was statistically different from that at 6 months after treatment (P<0.05); the NIHSS score 3 months after treatment was not different from that at 6 months after treatment. In the observation group, NIHSS scores at 1, 3 and 6 months after the treatment were significantly lower those before treatment and those in the control group after treatment (P<0.05); the NIHSS score at 1 month after treatment was statistically different from that at 3 and 6 months after treatment (both P<0.05). As presented in Table V, in the control group, there were 21 cases with complete recanalization, 22 cases with partial recanalization and 22 cases with no recanalization. In the observation group, there were 27 cases with complete recanalization, 23 cases with partial recanalization and 4 cases with no recanalization.

Table V. Vascular recanalization after treatment in the control and observation groups [n (%)].

Items	Control group (n=65)	Observation group (n=54)	χ^2	P-value
Complete recanalization	21 (32.31)	27 (50.00)	3.836	0.050
Partial recanalization	22 (33.85)	23 (42.59)	0.960	0.327
Blocked	22 (33.85)	4 (7.41)	12.07	<0.001
Total vascular recanalization	43 (66.15)	50 (92.59)	12.07	<0.001

Table VI. Total effective rate after treatment in the control and observation groups [n (%)].

Items	Control group (n=65)	Observation group (n=54)	χ^2	P-value
Marked response	23 (35.38)	25 (46.30)	1.459	0.227
Moderate response	21 (32.31)	23 (42.59)	1.339	0.247
No response	21 (32.31)	6 (11.11)	9.429	0.002
Total effective rate	44 (67.69)	48 (88.89)	9.429	0.002

Marked response, ≥45% decrease of NIHSS score compared with that before treatment; moderate response, <45% and ≥18% decrease of NIHSS score compared with that before treatment; no response, <18% decrease of NIHSS score compared with that before treatment.

Table VII. Comparison of complications after treatment between the control and the observation group [n (%)].

Complications	Control group (n=65)	Observation group (n=54)	χ^2	P-value
Intracranial hemorrhage	10 (15.38)	2 (3.70)	4.439	0.035
Airway obstruction	19 (29.23)	7 (12.96)	4.571	0.033
Revascularization	18 (27.69)	6 (11.11)	5.037	0.025
Arrhythmia	16 (24.62)	4 (7.41)	6.247	0.012

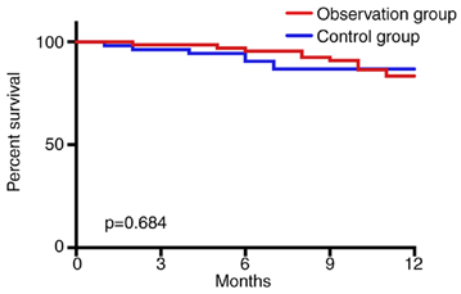

Figure 1. One-year survival curves of patients in the observation and control groups.

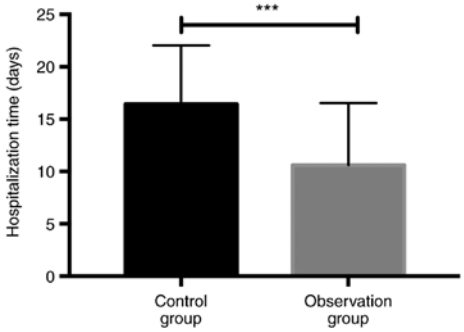

Figure 2. Comparison of total hospitalization time between the two groups. The total hospitalization time in the control group was statistically longer than that in the observation group (t=5.480, ***P<0.001).

Total vascular recanalization was significantly better in the observation group than that in the control group (P<0.001).

One-year survival rate of the patients in the two groups after treatment. As shown in Fig. 1, all 119 patients were successfully followed up after treatment to assess 1-year survival. In the control group, 55 patients survived and 10 patients died within 1 year after treatment, with a survival rate of 84.62%. In the observation group, 46 patients survived and 8 patients died within 1 year after treatment, with a survival rate of 85.19%. According to the Kaplan-Meier survival curve analysis, the 1-year survival rate after treatment was not statistically different between the two groups (P=0.684).

Total effective rate after treatment in the control and observation groups. The rate of marked response was 46.30% in the observation group and 35.38% in the control group (Table VI). The rate of moderate response was 42.59% in the observation group and 32.31% in the control group. The rate of no response was 11.11% in the observation group and 32.31% in

the control group. The observation group had a total effective rate of 88.89%, significantly higher than the total effective rate 67.69% in the control group (χ^2=9.429, P=0.002).

Comparison of complications after treatment between the control and observation groups. As presented in Table VII, in the observation group, 2 patients had intracranial hemorrhage after treatment, 7 airway obstruction, 6 revascularization and 4 arrhythmia. In the control group, 10 patients had intracranial hemorrhage after treatment, 19 airway obstruction, 18 revascularization and 16 arrhythmia. The complication rate in the observation group was statistically lower than that of the control group (P<0.05).

Comparison of total hospitalization time between the two groups. As shown in Fig. 2, the total hospitalization time in the control group was 16.42±5.62 days, statistically longer than that in the observation group which was 10.62±5.90 days (t=5.480, P<0.001).

Discussion

ICD is a disease in which cerebrovascular wall lesions affect the supply of cerebral blood vessels, damaging the brain tissue of patients to varying degrees, and seriously affecting the patients' survival and quality of life (6). The impact of ICD on the nerve function and physical function of patients aggravate the economic burden of the patients and their families. Therefore, the search for an effective and safe treatment for ICD is of great significance (15). Currently, intravenous thrombolysis is the dominant therapy for treating ICD (16-18). However, only a limited number of patients are clinically suitable for intravenous thrombolysis therapy. As studies on cerebrovascular diseases go deeper, the minimally invasive neurointervention therapy begins to play a role in the treatment of cerebrovascular diseases (19-21). Neurointervention, a safe and highly efficient treatment, with fewer complications and less damage to the body functions, has started to be implemented in clinical practice (22).

The present study used the NIHSS score to assess the neurological function of patients. The NIHSS scores of the two groups after treatment were lower than those before treatment, and the NIHSS scores of patients treated with intravenous thrombolysis combined with neurointervention were significantly lower than those treated with intravenous thrombolysis only. The clinical treatment efficacy between the two groups was also compared. The total effective rate, complications, survival, and vascular recanalization for patients treated with intravenous thrombolysis combined with neurointervention were better than those treated with intravenous thrombolysis alone. A previous study (11) reported that neurointervention therapy brought a low incidence of complications and a high recanalization rate. The present study made further progress by combining intravenous thrombolysis with neurointervention, showing that intravenous thrombolysis combined with neurointervention can significantly reduce complications and improve the revascularization of patients with ICD, with better efficacy. The speculation is that the high selectivity of neurointervention compensates for the unspecified targets of intravenous thrombolysis. Moreover, intravenous thrombolysis can improve the problem of thrombus shedding resulted from microcirculation disturbance aroused by neurointervention. Therefore, the combination of neurointervention and intravenous thrombolysis has better efficacy, with less bleeding and side effects. Hao *et al* (23) explored the clinical effects of interventional therapy in ICD and showed that the combination therapy brought better treatment outcomes than the single use of drugs. Such a result is similar to our findings of the combination of neurointervention and intravenous thrombolysis in treating ICD. In the present study, the total hospitalization time after treatment in the observation group was significantly shorter than that in the control group. As reported by Coutinho *et al* (24), intravenous thrombolysis combined with thrombectomy was more effective than intravenous thrombolysis alone, which was similar to the result of the present study, i.e., that the efficacy of the combination therapy was better than that of the intravenous thrombolysis alone. In the present study, the results revealed that the combination therapy was more efficient leading to reduced hospitalization time. The combination of intravenous thrombolysis and mechanical thrombectomy used in Coutinho's *et al* study is defective because of the difficulty of the mechanical thrombectomy to be performed in the tortuous blood vessels. The neurointervention therapy can directly clear the blood vessels through arterial and venous intubation, resulting in high recanalization rates, better safety and treatment efficacy. According to the assessment of the patients' 1-year survival, the survival rate of the observation group was 85.19%, whereas that of the control group was 84.62%. No statistical difference was observed in the survival rate between the two groups. Although the effect of intravenous thrombolysis combined with neurointervention is better than that of intravenous thrombolysis alone, this combination can only recanalize the established thrombus. Numerous patients with ICD have high levels of blood lipids, which makes platelets easy to agglutinate into new thromboses leading to the recurrence of the disease. Unavailability of timely treatment in case of disease recurrence may lead to patient death. Therefore, these two treatment methods have no effect on the patient's survival.

The present study has some limitations. First, the time for the observation of the efficacy and adverse reactions was too short to get a clear understanding of the prognosis of patients, which should be improved in future studies. Second, other treatment methods were not explored for ICD, which are also needed to be discussed in subsequent studies. Finally, healthy individuals were not included in the study, making it unclear whether patients after treatment present differences from healthy subjects in some aspects. In future studies, healthy subjects will be enrolled, the follow-up time will be prolonged, and other treatment options will be investigated to supplement the deficiencies of the present study.

In conclusion, neurointervention combined with intravenous thrombolysis for treating ICD can reduce NHISS score. In addition, this combination can improve the recanalization rate, reduce complications and shorten the hospitalization time, achieving a higher effective rate.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

SL wrote the manuscript. SL and XL interpreted and analyzed the patient data. ZC and CS designed the study and performed the experiment. HL and JH were responsible for the analysis and discussion of the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Xinxiang Central Hospital (Xinxiang, China). Patients who participated in the study had complete clinical data. Signed written informed consents were obtained from the patients and/or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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