Original Article
Clinical investigation of thrombolytic therapy with rt-PA in the emergency department

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Abstract: Objectives: To compare the effects of emergency thrombolytic therapy and in-hospital thrombolytic therapy and determine whether shortening the in-hospital delay time of thrombolytic therapy contributes to more benefits to patients with acute cerebral infarction at the ultra early stage. Methods: Patients who visited hospital within four and a half hours of symptom onset and received thrombolytic therapy in the emergency department were taken as the research group, patients treated with thrombolytic therapy in the neurology ward over the same period were taken as the control group. Results: The average time for the research group in starting thrombolytic therapy was 45 minutes and 39 patients received thrombolytic therapy within 4.5 hours after the initial symptom onset (14.4%). The average time for the control group was 80 minutes and 29 patients received thrombolytic therapy within 4.5 hours after symptoms manifested (10.5%). There were significant differences between the two groups on the score of NIHSS after thrombolytic therapy and the full or nearly full recovery rate of barthel index. Discussion: Emergency thrombolytic therapy of rt-PA in ultra early cerebral infarction can shorten the in-hospital delay time, enabling more suitable patients to be treated, relieve neurological deficits and improve the prognosis. Besides, such treatment is relatively convenient, safe, with little side effects in practice, which can be widely applied in the emergency department of the primary hospital.

Keywords: Emergenc, thrombolytic therapy, cerebral infarction

Introduction

Cerebral infarction is one of the most common diseases encountered in the emergency department, which is characterized by its high incidence and mortality rate, severe disability and results in a great burden being placed on both society and family members. Up to now, thrombolytic therapy at the ultra early stage has been considered the most available effective intervention. However, the time window for thrombolytic therapy is just limited 4.5 hours from symptoms first appearing [1], which makes it is imperative to shorten the delay time for thrombolytic treatment after symptom onset as much as possible. We began to employ thrombolytic therapy of rt-PA (recombinant tissue plasminogen activator) for the treatment of ultra acute cerebral infarction in the emergency department from Jan. 2005-Dec. 2009 and made comparisons with patients who received in-hospital thrombolytic treatment (on the neurology ward) over the same period.

Materials and methods

Inclusion Criteria: patients who visited our emergency department from Jan. 2005-Dec. 2009 were enrolled. All cases were diagnosed according to the criteria of cerebral infarction recommended on the 4th national cerebrovascular diseases academic meeting in 1995 [2] and also suitable for the following standard: ① age ≤ 75; ② within 4.5 hours of symptom onset; ③ CT scan excludes intracerebral haemorrhage and apparent low density infarction changes; ④ severe limb weakness (muscle power: 0-3); ⑤ no consciousness level change, such as stupor, coma, etc [3].

Exclusion Criteria ① active bleeding or known bleeding tendency; ② history of intracerebral haemorrhage and cerebral infarction within 6

Table 1. Demographic information and basic clinic information of both groups

Group	n	Age (years)	Genders Male	Genders Female	NIHSS (before reatment)
Research group	39	62 ± 6	21	18	15.2 ± 4.3
Control group	29	59 ± 7	15	14	13.7 ± 5.6
"t/X^2" value		4.927	3.6733		1.298
"P" value		0.035	0.0445		0.20

Table 2. Comparison of NIHSS assessment after thrombolytic treatment in control and research group

Group	n	Before treatment	24 h after treatment	21 d after treatment
Research group	39	15.2 ± 4.3	7.5 ± 2.7	6.0 ± 1.9
Control group	29	13.7 ± 5.6	8.8 ± 3.6	6.9 ± 2.1
"t" value		1.25	1.8701	1.8469
"P" value		0.1079	0.0330	0.0346

Table 3. Comparison of barthel index 90 days after thrombolytic treatment in the two groups

Group	n	< 50	50-95	≥ 95
Research group	39	7	12	20
Control group	29	7	14	8
"X^2" value				3.8557
"P" value				0.0496

months; ③ uncontrollable hypertension, 180/110 mmHg or more even after two adjustments; ④ intracranial aneurysm or arteriovenous malformation; ⑤ anticoagulation treatment; ⑥ severe organ failure, such as heart, liver and renal, etc.; ⑦ PLT count < 100 × 10⁹/L [4].

As to the controlled clinical trial, the patients given odd outpatient numbers were placed in the research group, while those getting even numbers were assigned to the control group. Patients received thrombolysis in the emergency department as a research group and patients who received thrombolysis in the neurology ward in hospital over the same period were used as the control.

Drug Treatment Both groups received rt-PA 0.9 mg/Kg body weight, IV within 1 h combined with danshen injection + edaravone injection with the same dosage and treatment duration simultaneously. 24 hours after thrombolysis, aspirin 100 mg/d was prescribed. Mannitol

added for those with signs of brain oedema [5].

Effects Assessment NIHSS was used for evaluation of the research and control group just before, 24 hours and 21 days after thrombolytic treatment, a total of 3 times. Barthel index was applied to assess activities of daily life 90 days after thrombolytic treatment.

Statistical Analysis Data was expressed as mean ± SD. Statistical difference was analysed by the SAS 8.1 software package. Student t test and X^2 test were employed respectively. Probability value < 0.05 was considered as statistically significant.

Results

Comparison of general information in both groups

There were 39 cases in the research group. Average time from visiting hospital to receiving thrombolytic treatment (Door to Treatment) was 45 minutes. All 39 cases received treatment within 4.5 hours of symptom onset, about 14.4% of patients with cerebral infarction, male 21 and female 18, 44-74 years old, average age (62 ± 6). 29 cases were enrolled in the control group. The average time was 80 minutes. Also, all 29 cases received treatment within 4.5 hours of symptom onset, about 10.5% of patients with cerebral infarction, male 15 and female 14, 43-75 years old, average age (59 ± 7). Both groups demonstrated no significant statistical differences in gender, age, time from symptom onset to visiting hospital and the NIHSS evaluation before thrombolytic treatment. See **Table 1**.

Comparison of NIHSS assessment after thrombolytic treatment

The NIHSS assessment of both 24 hours and 21 days after treatment revealed statistically significant differences in the control and research group (P < 0.05). See **Table 2**.

Comparison of barthel index assessment after thrombolytic treatment

The rate of full recovery and nearly full recovery (barthel index ≥ 95) demonstrated significant differences in the research group (51.3%) and

the control group (27.6%) (P < 0.05). However, no statistical significance could be found in severe disability rate (barthel index < 50) between the two groups. See **Table 3**.

Comparison of intracranial haemorrhage after thrombolytic therapy

All of the cases were scanned by CT 24 h later in order to observe intracranial haemorrhage. Intracranial haemorrhage occurred in 1 case (3.45%) in the control group and 1 case (2.56%) in the research group, both were asymptomatic intracranial haemorrhages. There is no statistical significance between the two groups.

Discussion

Pathological injury to ischaemic brain tissues evolves progressively after acute cerebral infarction. It is the "time window" for thrombolytic treatment which limits its extensive utilization in clinical practice [6]. Astrup [7] et al proposed the theory of ischaemia penumbra in 1981 which established the foundation for a time window conception. The time window for thrombolysis is well known to be one of the most critical factors which has a great effect on the outcome. Large amounts of evidence revealed that the time window should be defined as being within 4.5 hours of symptom onset [8-10].

"Time is brain" may fully imply the importance of the therapeutic time window. Conner [11] et al revealed that the recanalization rate of thrombolytic treatment within 4 hours after symptom onset was 94% (15/16), 4-6 h 45% (9/20) and > 6 h 43% (3/7), respectively. They pointed out that the commencement time for thrombolysis could significantly influence recanalization (P = 0.002). It was relatively easy for occluded vessels to be reopened by thrombolytic treatment within 4 h; however, with extended time passing before treatment being given, the recanalization rate decreased sharply and was accompanied by severe ischaemia-reperfusion injury [12, 13].

However, most of the patients cannot arrive at hospital rapidly (out-of-hospital delay) which greatly decreases the opportunity for patients to receive thrombolytic therapy at the ultra early stage in cerebral infarction [14-16]. Besides, some patients cannot receive urgent treatment because of unnecessary in-hospital delay [17]. In our study, the average time from

arriving in hospital to initialization of thrombolytic treatment was 45 minutes in the research group, 39 patients received thrombolytic treatment within 4.5 h after symptom onset, represented 14.4% of visiting patients with cerebral infarction over the same period. For the control group, there were 29 cases, the average time was 80 minutes and all of these patients received thrombolytic treatment within 4.5 h, about 10.5% of visiting patients with cerebral infarction. The evaluation of NIHSS of 24 hours and 21 days after thrombolytic treatment revealed significant differences between the two groups (P < 0.05). 90 days after treatment, the rate of full recovery and nearly full recovery (barthel index ≥ 95) was 51.3% in the research group and 27.6% in the control group (P < 0.05); for severe disability rate (barthel index < 50), 17.9% in the research group and 24.1% in the control group.

Our research indicated that emergency thrombolytic therapy could shorten in-hospital delay time, enhance effects of thrombolytic treatment, make more patients receive treatment at the ultra early stage, relieve neurologic deficits and improve prognosis.

To ensure more patients who have suffered a stroke receive thrombolytic therapy and to be effective, a specialized ambulance equipped with integrated CT, rapid point-of-care laboratory system and telemedicine capabilities will be needed for prehospital stroke treatment at the site of the emergency [18]. In the future, large randomized multi-centre studies are needed to conclusively establish the benefit of this therapeutic strategy.

Disclosure of conflict of interest

None.

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