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Original Article

Early neurological improvement after intravenous tissue plasminogen activator infusion in patients with ischemic stroke aged 80 years or older

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Abstract

Background: Early neurological improvement has been observed in patients with stroke receiving treatment with standard intravenous recombinant tissue plasminogen activator. However, the effectiveness of thrombolytic treatment and the risk of hemorrhagic transformation are not well understood in patients aged ≥80 years. In this study, we investigated the influence of age on early neurological improvement and hemorrhagic transformation rates in patients with stroke aged ≥80 years and receiving recombinant tissue plasminogen activator.
Methods: The study included 157 patients who received recombinant tissue plasminogen activator infusion at a teaching hospital. The National Institutes of Health Stroke Scale was used to evaluate stroke severity. Early neurological improvement was defined as an improvement of 8 or more points on this scale (compared with baseline) 24 hours after thrombolytic treatment. Neurological improvement was defined as an improvement of 8 or more points (compared with baseline) at discharge. Neurological deterioration was defined as an increase of 4 or more points (compared with baseline). Multivariate analysis was used to evaluate the associations among age, neurological improvement, and hemorrhagic transformation.
Results: The rate of early neurological improvement was 36.9% (58/157 patients) and the rate of hemorrhagic transformation was 22.3% (35/157 patients). At discharge, the rate of neurological improvement was 50.9% (80/157 patients) and the rate of neurological deterioration was 13.4% (21/157 patients). There was no statistically significant difference between patients aged ≥80 years and those <80 years of age with respect to rates of early neurological improvement, neurological deterioration, or hemorrhagic transformation. Among patients ≥80 years, the rate of neurological improvement in those receiving thrombolytic treatment was higher than the rate in those patients not receiving thrombolytic treatment (58.8% vs. 14.1%, $p < 0.01$). We concluded that thrombolysis increases the rate of neurological improvement in patients aged ≥80 years.
Conclusion: In older patients, thrombolytic treatment increased the rate of neurological improvement compared with patients not receiving the treatment. The study showed that thrombolytic treatment may be beneficial for patients ≥80 years, but should be performed with extreme care.

Keywords: cardioembolism; hemorrhagic transformation; ischemic stroke; outcomes; thrombolytic treatment

1. Introduction

In patients with acute ischemic stroke, intravenous thrombolysis using recombinant tissue plasminogen activator (rt-Pa) is associated with early recanalization and a better outcome.[1] In these patients, the goal of thrombolysis is to restore blood flow in the occluded artery to prevent brain tissue damage during reperfusion. Early neurological improvement (ENI) is defined as an improvement in the National Institutes of Health Stroke Scale (NIHSS) score of 8 or more points, or NIHSS scores equal to 0 or 1 at 24 hours following rt-Pa infusion. One study found that a higher ENI rate was observed in an rt-Pa group than in a control group.[2] The ENI rate is thought to be related to the restoration of blood flow in the occluded

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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artery.[3,4] As the thrombolytic effect of rt-Pa lasts for only 3.5 hours,[5] the response to thrombolysis is best evaluated after the first 24 hours. Among female patients, blood glucose levels of <8 mmol/L and the absence of cortical involvement are associated with major neurological improvement and good outcome at 3 months.[6] Previous studies have reported that intravenous infusion of rt-Pa in patients with stroke aged ≥80 years is associated with a lower probability of favorable outcome, a higher mortality, and an increased rate of hemorrhage.[7–9] However, other studies have shown that thrombolysis induced by rt-Pa in patients with stroke aged ≥80 years is both safe and beneficial.[10,11] A report on the intravenous infusion of rt-Pa in patients with stroke and cardiac myxoma showed that higher hemorrhagic transformation (HT) and lower response rates are observed in older patients.[12] Therefore whether or not the neurological response and HT rates are related to age remain a matter of contention. This study was conducted to investigate the influence of age on the rates of ENI and hemorrhage.

2. Methods

Our data were drawn from the stroke registry database of a teaching hospital in central Taiwan. We have regularly used rt-Pa in patients with acute stroke since January 2007. The data from all patients with stroke who received intravenous rt-Pa treatment between January 2007 and December 2012 were included in the study. All inclusion and exclusion criteria for thrombolytic treatment were based on the guidelines for stroke treatment in Taiwan, which state that patients ≥80 years of age should not be given thrombolytic treatment.[13] However, such patients aged ≥80 years without other contraindications, who arrived within 3 hours of the onset of stroke and requested thrombolytic treatment, were given rt-Pa infusion. The group not receiving rt-Pa included patients ≥80 years old who arrived at our hospital within 3 hours of stroke onset without contraindications for thrombolytic treatment other than old age, but who did not receive the treatment. Patients were followed-up using computed tomography (CT) or magnetic resonance imaging (MRI) of the brain 24 hours after rt-Pa infusion.

The NIHSS scale was used to assess stroke severity. An NIHSS-certified stroke team member at our facility performed the scoring and evaluation after every 6 hours for the first 24 hours, and at discharge. ENI was defined as an improvement of ≥8 points (compared with baseline) 24 hours after thrombolytic treatment, or an improvement in the NIHSS score of 0 or 1 towards the end of rt-Pa infusion. Neurological improvement (NI) was defined as ≥8 point improvement (compared with baseline) or an improvement in NIHSS score of 0 or 1 at discharge.[2] Neurological deterioration (ND) was defined as a ≥4 point increase in the NIHSS score (compared with baseline) at discharge.[10] Early ND was defined as a ≥4 point increase in the NIHSS score (compared with baseline) within 24 hours of rt-Pa infusion. HT was defined as any sign of hemorrhage on the follow-up CT or MRI scans. Symptomatic HT (SHT) was defined as blood clots in the brain observed during follow-up CT or MRI scans, with an increase in the NIHSS score of 4 or more points.[14] The data used in the study were collected from the Chia -Yi Christian Hospital acute stroke registry. This registry has been approved by the ethics committee of the hospital.

Statistical significance between the age groups was analyzed using the Chi-square test or Fisher's exact test for categorical variables and *t* test for continuous parameters, including NIHSS, blood pressure, and time from stroke onset to rt-Pa infusion (rt-Pa time). Logistic regression analysis was used to investigate the risk factors of HT and ENI. MedCalc for Windows, version 12.3 (MedCalc Software, Ostend, Belgium) was used for data analyses.

3. Results

From January 2007 to December 2012 in our hospital, 157 patients received intravenous rt-Pa for acute ischemic stroke within 3 hours of stroke onset. Follow-up by MRI was performed in 45.6% of these patients. During the 6-year study inclusion period, 78 patients presented to our hospital within 3 hours of stroke onset and were considered eligible for thrombolytic treatment (without contraindications for thrombolysis other than old age), but did not receive the treatment because of their age (≥80 years). Follow-up by MRI was performed in 60.2% of these patients. Of the patients who received thrombolytic treatment, 140 were <80 years old (younger group) and 17 were aged ≥80 years (older group). Table 1 gives the baseline characteristics of the patients. The baseline stroke severity was higher in patients aged ≥80 years than in patients aged <80 years. The older age group patients showed a higher prevalence of hypertension, atrial fibrillation,

Table 1
Baseline characteristics of patients (n = 157).

Age (y)	*n*	Male sex	HTN	DM	Prior stroke	AF	Heart disease	SBP-pre (mmHg)	Median NIHSS score	Rt-Pa time (min)	Smoker
<80	140	87	103 (73.4)	51 (36.3)	19 (12.5)	50 (36.3)	67 (48.9)	155.7	14	113.8	57 (42.6)
≥80	17	8	15 (92.8)	3 (7.10)	3 (21.4)	12 (71.4)	14 (92.8)	156.3	22	112.8	6 (21.47)
p			0.24[a]	0.17[a]	0.71[a]	<0.01[a]	0.12[a]	0.20[b]	0.001[b]	0.15[b]	0.79[a]

Data are presented as *n* (%).
AF = atrial fibrillation; DM = diabetes mellitus; HTN = hypertension; NIHSS = National Institutes of Health Stroke Scale; Rt-Pa time = time from stroke onset to recombinant tissue plasminogen activator infusion; SBP-pre = systolic blood pressure prior to thrombolysis.
[a] Chi-square test or Fisher's exact test.
[b] *t* test.