Safety and Time Course of Drip-and-Ship in Treatment of Acute Ischemic Stroke

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Background: The drip-and-ship approach allows intravenous tissue plasminogen activator therapy and adjuvant endovascular treatment in acute ischemic stroke, even in rural areas. Here, we examined the safety and time course of the drip-and-ship approach. *Methods:* Fifty consecutive cases treated with the drip-and-ship approach (drip-and-ship group) in June 2009 to March 2016 were retrospectively examined. Changes in mean blood pressure, systemic complications, and neurological complications were compared according to method of transportation. Time courses were compared between drip-and-ship and direct admission groups during the same period. *Results:* In the drip-and-ship group, 33 and 17 patients were transferred to hospital by ambulance and helicopter, respectively. One patient suffered hemorrhagic infarction during transportation by ambulance. Mean blood pressure change was lower in patients transferred by helicopter than ambulance (<5 mmHg versus 12.2 mmHg, respectively). The mean onset-to-door times in the drip-and-ship and direct admission groups were 71 and 64 minutes, respectively, and mean door-to-needle times were 70 and 47 minutes, respectively ($P = .002$). Although mean transportation time from the primary stroke hospital to our hospital was 32 minutes, the entry-to-exit time from the primary stroke hospital was 113 minutes. Thereafter, there was an average delay of 100 minutes until reperfusion compared with the direct admission group. *Conclusions:* Drip-and-ship was relatively safe in this small series. Transportation by helicopter was less stressful for acute ischemic stroke patients. It is important to reduce door-to-needle time and needle-to-departure time in the primary stroke hospital to minimize the time until treatment in cases of acute ischemic stroke. **Key Words:** Acute ischemic stroke—endovascular treatment—reperfusion—t-PA—transportation.

Introduction

Intravenous tissue plasminogen activator (iv t-PA) plays a critical role in treatment of acute ischemic stroke (AIS). However, only a small percentage of AIS patients receive t-PA treatment because of a lack of neurologists or neurosurgeons, especially in community hospitals. The recanalization rate of iv t-PA alone is low in cases of internal carotid artery or proximal middle cerebral artery occlusion.[1] Although several recent clinical trials indicated the efficacy of rapid endovascular treatment in patients with AIS with proximal vessel occlusion,[2-6] such

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treatment can only be provided in a comprehensive stroke center.

Drip-and-ship treatment represents a solution to these issues as it allows greater numbers of patients with AIS to receive iv t-PA even in community hospitals,[7] and more patients can receive adjuvant endovascular treatment when iv t-PA cannot recanalize major vessel occlusion.[8] Moreover, the clinical outcome of patients with severe ischemic stroke can be improved by neurointensive care.[9]

As iv t-PA has a relatively high risk of hemorrhagic complications, it is necessary to confirm the safety of drip-and-ship treatment. As the clinical outcome of patients with severe ischemic stroke is correlated with reperfusion time,[10] it is important to verify the time course of drip-and-ship treatment. To examine these issues, changes in vital signs by transportation were analyzed and compared between ambulance and helicopter transportation, and the time course of drip-and-ship patients was compared with those admitted directly to our hospital and receiving iv t-PA and endovascular treatment.

Methods

In this retrospective observational study, we compared consecutive patients with AIS who were transferred from a primary hospital to our hospital after treatment with iv t-PA between June 2009 and March 2016 (drip-and-ship group) with AIS patients who were directly admitted to our hospital and underwent endovascular treatment after iv t-PA during the same period (direct admission group). Our hospital is a comprehensive stroke center that covers the entire area of a mountainous prefecture in Japan. Patients in the drip-and-ship group were transferred by helicopter or ambulance. A helicopter was used mainly in remote areas, but an ambulance was used after sunset or under rainy conditions even in such areas. The linear distance from stroke-ready hospitals ranged from 10 to 80 km. Both the flight team and the ambulance transport team consisted of a nurse and physician. Neurological severity and outcome were evaluated using the National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS), respectively.

For evaluation of safety, changes over time in mean blood pressure (mBP) and heart rate, and medical condition were collected from clinical records and compared between patients transferred by ambulance and by helicopter. Head computed tomography (CT) was performed on admission to our hospital and 24 hours after treatment in all cases.

The time course was compared between the drip-and-ship group and the direct admission group at the following time points: onset, admission to primary hospital, beginning of iv t-PA, departure from primary hospital, admission to our hospital, groin puncture, and time of reperfusion. In the drip-and-ship group, onset to second door time indicates the time from onset to admission to our hospital.

The data are presented as the means ± standard deviation. The paired *t*-test was used to characterize the changes in vital signs. In all analyses, $P < .05$ was taken to indicate statistical significance. All calculations were performed with Statcel software (version 2; OMS Publishing Inc., Saitama, Japan) running on Macintosh OS X.

Results

The drip-and-ship group was composed of 50 patients (31 men, 19 women, age range 38-86 years, median age 72 years) who were transferred after administration of t-PA, and infusion was continued during transfer in all of these cases. Thirty-three patients were transferred by ambulance and 17 patients were transferred by helicopter. The NIHSS scores before transfer ranged from 5 to 32 points, with a median of 19. The median NIHSS score after transfer was 17 points.

During the same period, 32 patients with AIS who were directly admitted to our hospital underwent endovascular treatment after iv t-PA (direct admission group). The direct admission group was composed of 24 men and 8 women, ranging in age from 42 to 88 years, with a median age of 77 years. The NIHSS scores at admission ranged from 8 to 32 points, with a median of 18. The baseline characteristics and clinical parameters in the 2 groups are shown in Table 1.

With the exception of 1 patient, there were no cases of life-threatening complications or major neurological deterioration in either transport subgroup. One of the patients transferred by ambulance suffered hemorrhagic infarction during transportation. This patient was a 78-year-old woman with severe acute basilar occlusion. As the onset occurred at night, a helicopter could not be used. She was transferred by ambulance with a drive of more than 1 hour. With regard to other events, 1 patient transferred by helicopter and 2 patients transferred by ambulance were administered antiemetic medication during transport. One of the patients transferred by helicopter and 2 of the patients transferred by ambulance were administered antihypertensive drugs during transport. CT was performed just after transfer to our hospital in all cases. No intracranial hemorrhages were detected, except in the patient who developed hemorrhagic infarction. There was no statistically significant difference in mRS at 90 days between the drip-and-ship group and direct admission group.

The change in mBP was lower in patients transferred by helicopter than in those transferred by ambulance, and their mean change in mBP was <5 mmHg. The mean change in mBP just after transport increased to 12.2 mmHg in patients transferred by ambulance (Fig 1). Changes in heart rate showed a similar tendency to mBP (data not shown).