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Drip-and-Ship Thrombolytic Therapy Supported by the Telestroke System for Acute Ischemic Stroke Patients Living in Medically Under-served Areas

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Abstract

There are a few stroke specialists in medically under-served areas in Japan. Consequently, in remote area patients may not receive thrombolysis with intravenous recombinant tissue plasminogen activator (iv rt-PA), the standard treatment for acute ischemic stroke. Using a mobile telestroke support system (TSS) that accesses the internet via a smart phone, we implemented iv rt-PA infusion therapy under a drip-and-ship protocol to treat the stroke patients in medically under-served areas. The physicians at the Tokushima Prefectural Kaifu Hospital (TPKH), located in rural Japan, can relay CT or MRI scans and other patient data via their smart phone to off-site stroke specialists. In the course of 34 months, we used the TSS in 321 emergencies. A total of 9 of 188 (4.8%) with acute ischemic stroke, received iv rt-PA infusion therapy using a mobile TSS; in 5 among these (55.6%), we obtained partial or complete recanalization of occluded arteries. None suffered post-treatment hemorrhage and their average NIH stroke score fell from 14.6 at the time of admission to 6.8 at 24 h post-infusion. The drip-and-ship protocol contributed to the safe and effective treatment of the stroke patients living in medically under-served rural areas.

Key words: drip-and-ship protocol, recombinant tissue plasminogen activator, telemedicine, telestroke, stroke

Introduction

Recombinant tissue plasminogen activator (rt-PA) infusion therapy is effective in patients with hyperacute cerebral infarction.[1)] The early thrombolytic treatment of patients with acute ischemic stroke is associated with the lower mortality rates, higher rates of independent ambulation at discharge, and discharge to home.[2)]

In Japan, the rt-PA treatment of patients seen within 3 h of stroke onset has been possible since 2005.[3–5)] The use of alteplase in the extended therapeutic time window (within 4.5 h of symptom onset) became covered by insurance in August 2012.[6)] However, the stroke specialists are needed for the appropriate treatment of such patients, and in rural areas without such experts, the delivery of intravenous (iv) rt-PA is difficult. A national survey conducted in 2010 showed that lesser than 5% of eligible Japanese patients had received rt-PA therapy and that by 2009, 44 of 348 emergency medical service areas (12.6%) did not deliver the iv rt-PA treatment.[7)]

In some areas of Japan, the care of acute stroke patients is suboptimal and there are significant disparities in rural communities. Kaifu is a depopulated remote region in the southern Tokushima Prefecture; 23,021 persons live in a 525 km^2 area and their medical care is delivered by the 38 physicians (1.7% of the population). It is under-served with respect to medical and especially acute stroke care, and the rate of iv rt-PA therapy is low.[8–10)]

Tokushima Prefectural Kaifu Hospital (TPKH) is located in the center of Kaifu. The distance to the closest comprehensive stroke center at Tokushima

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University Hospital (TUH) is 80 km. TPKH has 105 beds; the patients are attended by the general physicians and orthopedic surgeons. It has no stroke specialists, and till 2013, it had no experience with iv rt-PA infusion therapy for acute ischemic stroke. Between October 1, 2009 and September 30, 2010, the transport of stroke patients from Kaifu to TUH required an average of 136 min, i.e. 96 min more than that of patients living around TUH in Tokushima city.[11]

The use of telemedicine for stroke care has spread in Western countries.[8,12–14] In 2009, the American Heart Association recommended telestroke systems for the neurological assessment and primary prevention of stroke.[15] We established the telestroke support system (TSS) in our medically under-served area. It involves the standard portable communication devices and the relay of clinical information and high-quality neuroimages to off-site stroke specialists for a real-time clinical diagnosis and treatment advice.

Methods

In collaboration with Tokushima University Hospital (TUH) and Tokushima Red Cross Hospital (TRCH), we developed a drip-and-ship protocol for the initial treatment of off-site patients with acute ischemic stroke. It involves the TSS (called the "k-support system") and the delivery of iv rt-PA infusion therapy at TPKH under the direction of a stroke specialist at TUH and TRCH. After the iv injection of a single alteplase dose of 0.6 mg/kg (not exceeding 60 mg), a 10% dose-bolus is delivered at TPKH. This is followed by the continuous infusion of the remainder of alteplase during transport by ambulance or helicopter from TPKH to a stroke center of TUH or TRCH for post-thrombolytic care.

Our k-support system features an exclusive application developed for smart devices and a dedicated server connected to a picture archiving and communication system (PACS) at TPKH (Fig. 1). The real-time extramural access is via a virtual private network (VPN) connection by wireless LAN, it can deliver patient information, CT-, MR-, and 3D-CTA images, and animated- and 3D-images to the smartphone of a registered physician located off-site. The time-course is established automatically based on individual patients. The communication via a Twitter-style closed communication system is also possible.

The k-support team of our TSS (Fig. 2) consists of emergency medical technicians (EMTs) in the Kaifu area, the physicians at TPKH, and the stroke specialists at the TUH and TRCH stroke center (Table 1). The on-site EMTs send patients' information (time of stroke onset, neurological findings, and vital signs) to TPKH. Upon patient arrival at TPKH, the MRI studies are performed immediately and the findings are conveyed via a smart device to the stroke specialists at TUH and TRCH. If they deem thrombolysis by immediate iv rt-PA therapy appropriate, the patient is transported to the comprehensive stroke center at TUH under the drip-and-ship protocol.

The patient status is evaluated using the National Institutes of Health stroke scale (NIHSS) at the time of admission and 24 h after the start of iv rt-PA infusion.[16] The recanalization of occluded vessels is recorded using the thrombolysis in cerebral infarction (TICI) classification.[17]

Results

Between February 2013 and December 2015, we used the TSS in 321 emergencies (acute stroke in 161 (50%), head injury in 51 (16%), gastrointestinal

Fig. 1 (A) Components of the system (SYNAPSE Erm) for connecting off- and on-site medical care providers. (B) Display of the diagnostic and treatment data on mobile devices.

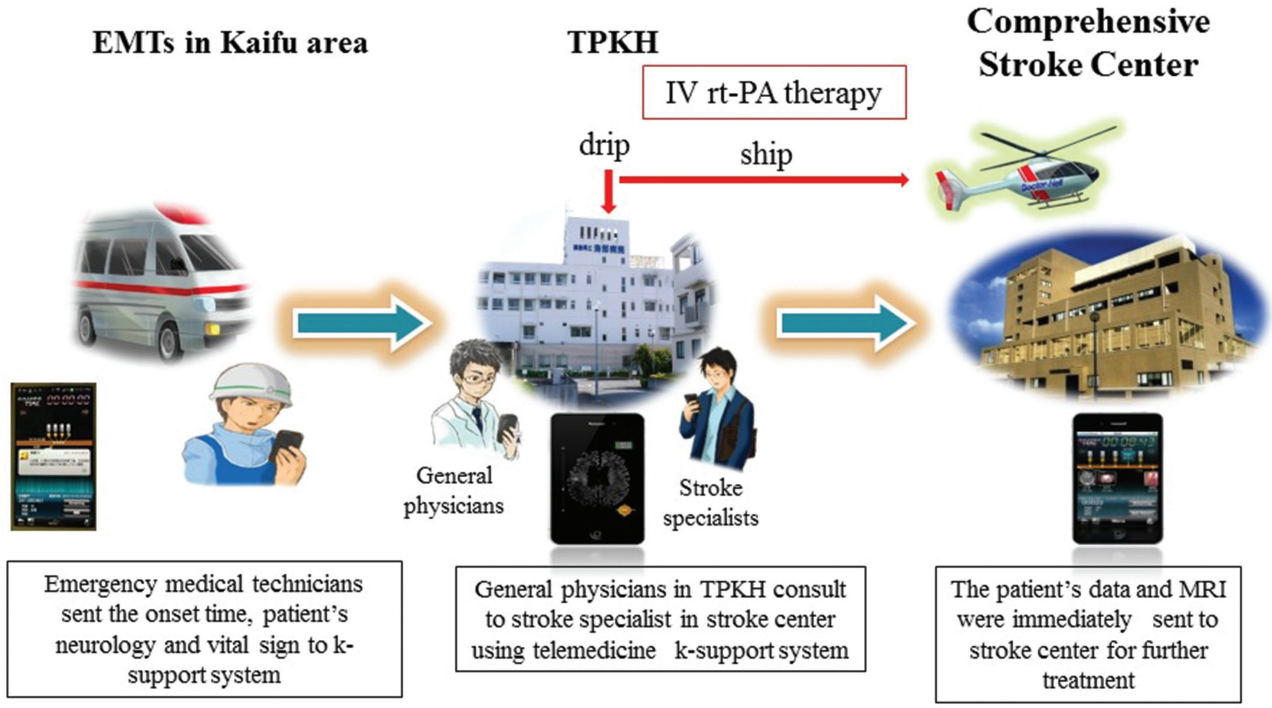

Fig. 2 Concept of the telemedicine "k-support" system. The emergency technicians relay patient information to a physician at TPKH who is in contact with a stroke specialist at TUH. The drip-and-ship protocol for iv rt-PA infusion therapy is implemented at TPKH before patient transport to the stroke center. EMTs: Emergency Medical Technicians, TPKH: Tokushima Prefectural Kaifu Hospital.

Table 1 Member and number of smart devices in our k-support team

Member of k-support team		Number of smart devices
Physicians		
TPKH	General physician	5
	Cardiologist	2
	Orthopedic surgeon	2
	Respiratory physician	1
	Neurosurgeon	1
TUH	Neurosurgeon	2
EMTs in Kaifu area		3
Stroke center		2 (TUH, TRCH)

EMTs: emergency medical technicians, TPKH: Tokushima Prefectural Kaifu Hospital, TRCH: Tokushima Red Cross Hospital, TUH: Tokushima University Hospital.

disease in 38 (12%), and cardiovascular disease in 22 (7%)). We delivered iv rt-PA infusion therapy under the drip-and-ship protocol supported with a mobile TSS (k-support system) to 9 of 188 (4.8%) patients with acute ischemic stroke. All the nine patients are presented with cardiogenic embolism due to atrial fibrillation. For the immediate care of all patients, the general physicians at TPKH consulted with the stroke specialists at TUH via TSS; 5 patients were treated by the general physicians alone at TPKH. The complete (TICI 3) and partial (TICI 2B) recanalization was observed in 4 and 1 patient(s), respectively; in three stroke patients with internal carotid artery occlusion, there was no recanalization (TICI 0). The average NIHSS score was 14.4 (range 3–40); 24 h post-iv rt-PA infusion, it was 6.8 (range 2–15). None of the 9 patients suffered post-treatment intracerebral hemorrhage.

The interval between the stroke onset to arrival at TPKH ranged from 30 to 97 min, the door-to-needle time from 59 to 125 min, the stoke onset-to-needle from 108 to 173 min, and the average transport time from TPKH to TUH from 27 to 86 min (Table 2).

Discussion

Many patients with acute ischemic stroke are initially seen by the general or emergency physicians.[18–20] Consequently, the treatment is heavily dependent on their diagnostic acumen and the stroke patients may not receive emergent iv rt-PA therapy.[21,22] A similar problem exists in medically under-served remote areas of Japan, where there are few stroke specialists.[8–10] Before 2013, TPKH, located in southern

Table 2 Patients profile of drip and ship protocol of intravenous rt-PA infusion therapy in TPKH

Case	Age	Sex	Onset-to-arrival (min)	Door-to-needle (min)	Onset-to-needle (min)	Transport time (min)	Occlusion vessel	NIHSS on admission	TICI classification	NIHSS 24 h after infusion
1.	89	M	30	123	153	44	MCA	10	3	2
2.	96	M	73	89	162	55	ICA	18	0	8
3.	91	M	85	59	144	62	MCA	10	2B	6
4.	84	F	58	50	108	34	ICA	17	0	15
5.	93	M	97	53	150	67	ICA	18	0	15
6.	78	F	53	77	130	27	MCA	9	3	6
7.	70	M	48	125	173	31	PCA	3	3	2
8.	97	F	54	97	151	77	–	5	NE	3
9.	69	F	87	73	160	86	BA	40	3	4

BA: basilar artery, ICA: internal cerebral artery, MCA: middle cerebral artery, NIHSS: National Institute of Health stroke scale, PCA: posterior cerebral artery, TICI: thrombolysis in cerebral infarction, TPKH: Tokushima Prefectural Kaifu Hospital.

Tokushima Prefecture, had never delivered iv rt-PA infusion therapy.

The early thrombolytic treatment of patients with acute ischemic stroke is associated with the reduced rates of mortality and symptomatic intracranial hemorrhage. However, the transfer of patients from a general hospital to a regional stroke center delays the start of rt-PA treatment. Therefore, we implemented a protocol at TPKH, whereby the delivery of iv rt-PA infusion is started locally before the transport of the stroke patients to a comprehensive stroke center at TUH or TRCH for post-thrombolytic care. This strategy is now known as "drip-and-ship," which has been used in 17% of the stroke patients treated by rt-PA infusion therapy living in remote areas of the USA, and the patient discharge rate and the rate of patients able to return to independent living was high.[23] A large study by Sheth et al.[24] found that after the risk adjustment, the rate of in-hospital mortality and symptomatic intracranial hemorrhage was only slightly higher in "drip-and-ship"-treated patients than in patients directly admitted at a stroke center.

The standard real-time cellular video phone can be used to obtain the NIHSS score in patients with acute stroke who present at remote hospitals. The interpretation of the head CT scans sent via smartphone teleradiology to off-site vascular neurologists was in excellent agreement with the reading of on-site radiologists.[14] Takao et al. developed a system that uses smart devices for the real-time relay of patient data, the diagnostic images, and the clinical management information among members of Japanese stroke teams located in remote areas and at stroke centers.[13]

In 2009, The American Heart Association/American Stroke Association promulgated a statement advocating the use of the telestroke system and the drip-and-ship protocol in patients with acute ischemic stroke.[15] The others[8,10] subsequently reported that in stroke patients, the immediate delivery of rt-PA infusion therapy under this protocol, supported by telemedicine technology, is safe and effective. The smart devices with applications adapted to TSS appear to be useful for mobile communications.[12–14] Our mobile TSS (k-support system) involves a drip-and-ship protocol, the stroke specialists at the comprehensive stroke center and EMTs in Kaifu area. Using this method, we delivered the iv rt-PA therapy to 4.8% of patients who had suffered acute ischemic stroke in medically under-served areas of Japan. In all patients, the admitting physician at the remote hospital was directly involved in the implementation of therapy.

The findings of our case–control study in a medically under-served area of Japan require further attention with respect to the responsibility of a local physician initiating iv rt-PA treatment and the cost–benefit ratio. The number of patients treated under the drip-and-ship protocol and the TSS were small and we are continuing to collect data for a better evaluation of this new technology.

Conclusion

The drip-and-ship protocol for iv rt-PA infusion therapy supported by a mobile TSS such as our "k-support system" may benefit patients with acute ischemic stroke living in the remote areas without the stroke centers or the stroke specialists.

Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices cited in this study.

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