Stroke Scale Items Associated with Neurologic Deterioration within 24 Hours after Recombinant Tissue Plasminogen Activator Therapy

Yusuke Nanri, MD,* Yusuke Yakushiji, MD, PhD,* Megumi Hara, MD, PhD,† Makoto Eriguchi, MD, PhD,* Ryuichirou Okada, MD,* Motohiro Yukitake, MD, PhD,* and Hideo Hara, MD, PhD*

It is unclear when and which neurologic deficits should be examined within 24 hours after intravenous recombinant tissue plasminogen activator (rt-PA) therapy for acute ischemic stroke. Relationships between serial changes in National Institutes of Health Stroke Scale (NIHSS) subscores and neurologic deterioration (ND) within the first 24 hours after therapy were investigated in 43 consecutive patients. The NIHSS score was measured by neurologists 28 times within 24 hours after therapy. Assessments of subscores associated with ND, defined as the first change 4 or more points from baseline, were performed at 15 minutes (most frequent time of the first ND), 120 minutes (median time of the first ND), and 24 hours after therapy. Seventeen of 43 patients (age range, 55-94 years) showed ND. Of the NIHSS subscores, increases in scores for loss of consciousness (15 minutes, $P = .001$; 120 minutes, $P = .026$; 24 hours, $P = .018$) and motor limbs total (15 minutes, $P = .014$; 120 minutes, $P = .031$) were related to deterioration. Items such as questions, gaze, visual fields, ataxia, language, dysarthria, and extinction/inattention were not related to deterioration at any time. In conclusion, ND of ischemic stroke patients treated with intravenous rt-PA therapy was frequently seen within 120 minutes after therapy. Items such as loss of consciousness and motor limbs total may be considered indices for monitoring neurologic deficits after therapy. **Key Words:** Intravenous recombinant tissue plasminogen activator therapy—acute ischemic stroke—National Institutes of Health Stroke Scale—neurologic deterioration.

Introduction

Intravenous administration of recombinant tissue plasminogen activator (rt-PA) is generally accepted as first-line treatment for acute ischemic stroke within 3 hours of onset; however, such therapy causes 10 times the incidence of intracranial hemorrhage (ICH) compared with placebo.[1] Because most symptomatic ICHs (sICHs) occur within the first 24 hours after the start of rt-PA therapy,[2-4] repetitive neurologic and physiological monitoring of patients during this period is critical.[5,6]

The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study[1] and the Japan Alteplase Clinical Trial (J-ACT)[4] demonstrated the efficacy of intravenous rt-PA therapy for acute ischemic stroke within 3 hours of onset. Both studies used the National Institutes of Health Stroke Scale (NIHSS) to evaluate neurologic deterioration (ND). However, only the results of total score changes between baseline and 24 hours after stroke onset were reported in these studies. In the NINDS

From the *Division of Neurology, Department of Internal Medicine; and †Department of Preventive Medicine, Faculty of Medicine, Saga University, Saga, Japan.

Received May 21, 2012; revision received September 28, 2012; accepted October 1, 2012.

Grant support: None.

Address correspondence to Yusuke Nanri, MD, Division of Neurology, Department of Internal Medicine, Faculty of Medicine, Saga University, Nabeshima 5-1-1, Saga 849-8501, Japan. E-mail: nanriyu@cc.saga-u.ac.jp.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2012.10.006

rt-PA study, repetitive neurologic evaluations after rt-PA therapy initiation were performed using the abbreviated NIHSS. During these repetitive assessments, a nurse evaluated the level of consciousness (LOC), extremity strength, and designated cardinal signs for each patient (such as language). A decline of 2 points in the total abbreviated NIHSS score indicates the need for reassessment with the complete NIHSS.[7] In a subgroup analysis of the NINDS rt-PA study that assessed clinical variables associated with ICH, the complete NIHSS score was obtained 5 times, that is, at baseline, 2 hours after therapy, and 24 hours, 7-10 days, and 3 months after therapy.[2] However, when and how neurologic deficits should be assessed within 24 hours after intravenous rt-PA therapy for acute ischemic stroke is not well known.

To develop evidence-based protocols for management of ND after rt-PA therapy for acute ischemic stroke, relationships between serial changes in complete NIHSS subscores and ND within the first 24 hours after the start of rt-PA therapy for acute ischemic stroke were examined.

Patients and Methods

Patients

Forty-five consecutive patients admitted to our division and treated with intravenous rt-PA for acute ischemic stroke within 3 hours of onset between May 1, 2006 and January 31, 2011 were considered potential subjects for this study. Intravenous rt-PA therapy was done with a single dose of alteplase (.6 mg/kg; not exceeding 60 mg), with 10% given as a bolus, followed by continuous infusion of the remaining dose over 1 hour, according to the J-ACT study.[4] The inclusion and exclusion criteria for intravenous rt-PA therapy were the same as in the J-ACT study[4] and matched the guidelines for intravenous use of rt-PA (alteplase) in Japan.[6] In brief, in addition to the inclusion and exclusion criteria of the NINDS study, patients with an NIHSS score 4 or less and who demonstrated early ischemic changes on computed tomography (CT) affecting more than one third of the middle cerebral artery territory were excluded. Two patients were excluded as they could not be assessed because of clinical circumstances (one had adult respiratory distress syndrome, and the other had hematemesis from advanced gastric cancer). In both cases, they developed coma, and because of treatment for acute respiratory distress syndrome or hematemesis, NIHSS evaluations could not be performed. In both cases, the patients' outcomes 3 months after rt-PA therapy were modified Rankin scale[8] (mRS) scores of 5.

Thus, 43 patients were studied prospectively. Informed consent was not obtained from the patients because the data needed for this study were collected while patients were treated according to the guidelines for intravenous use of rt-PA (alteplase) in Japan[6] without additional invasive examinations or treatments. Instead, our intention to use data from patients who were treated was posted on the hospital's Web site between October 4, 2010 and February 28, 2011. All protocols were approved by the institutional review board on October 4, 2010 (approval number: 2010-10-02).

Neurologic Assessments

The NIHSS has established reliability and validity for use in prospective clinical research, predictive validity for long-term stroke outcome,[9-11] and appears to be the most sensitive way to detect changes associated with acute stroke.[12] Thus, in this study, neurologic examination was assessed by the complete NIHSS, which consists of the following 15 items: 1A, LOC; 1B, questions; 1C, commands; 2, gaze; 3, visual fields; 4, facial palsy; 5a, motor left arm; 5b, motor right arm; 6a, motor left leg; 6b, motor right leg; 7, limb ataxia; 8, sensory; 9, language; 10, dysarthria; and 11, extinction/inattention. In each patient, the complete NIHSS was measured a total of 28 times by neurologists as follows: pre–rt-PA (baseline) and post–rt-PA at 15, 30, 45 minutes, and every hour from 1 to 24 hours. The neurologist in charge of NIHSS measurements rotated every 4 or 5 hours within 24 hours after the start of rt-PA therapy. The interrater variability for each NIHSS item score measured using the NIHSS training and demonstration digital video disk,[13] expressed as Cohen κ, was as follows: 1A, .64; 1B, .64-.82; 1C, 1.00; 2, .68; 3, .75; 4, .03-.21; 5a, .40-.62; 5b, .79-1.00; 6a, .36-.63; 6b, .35-.48; 7, −.10; 8, .56-.89; 9, .73-1.82; 10, .71-.90; and 11, 1.41-1.73. Of the 1204 NIHSS measurements (43 subjects × 28 examinations as planned), 54 (4.5%) NIHSS evaluations could not be performed because of the following: head magnetic resonance imaging or CT examination, 13 times; operation for hemorrhagic infarction, 4; treatment for nasal hemorrhage, 1; medical care for other patients, 4; transfer to general medical ward, 1; and unknown, 31. Thus, the data of 1150 NIHSS total scores and subscores were used for the analysis. Based on previous studies,[14-17] ND was defined as an increase of 4 or more points from the baseline NIHSS score. No change or improvement was defined as an increase of less than 4 points. sICH was defined as CT evidence of ICH accompanied by apparent ND, defined as conditions that could be documented objectively or an increase of 4 or more points from the last NIHSS score.[16] Recurrence of infarction was diagnosed when there was both clinical and imaging evidence of ischemic stroke in an independent arterial territory, so as to exclude deficits explainable by arterial reocclusion, proximal extension, or distal embolism of the original thrombus.[18] Early ND of the original cerebral infarction (CI) was defined as an increase of 4 or more points from the baseline NIHSS score without sICH or recurrent infarction. Activities of daily living of each patient were assessed before and 3 months after rt-PA therapy using the mRS.[8]

Statistics

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL)