Original article

The outcome of thrombolytic therapy for acute ischemic stroke after extended treatment from 3 to 4.5 hours in Maharaj Nakorn Chiang Mai Hospital

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Objective To present the outcome of acute ischemic stroke patients given thrombolytic therapy from 3 to 4.5 hours after the onset of symptoms.

Methods All acute ischemic stroke (AIS) patients admitted to the Stroke Unit at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand and treated with tissue plasminogen activator (rtPA) between January 1, 2013, and December 31, 2013, were chart reviewed retrospectively. The recovery rate and complications were compared between patients treated within 3 hours and from 3 to 4.5 hours after the onset of symptoms (group A and B, respectively), as was the outcome between patients in Group B and those in Western trials.

Results Ninety two AIS patients were treated with rtPA during the study period, with 68.48% and 31.52% of them being treated in Group A and B, respectively. Only the rate of neurological improvement was significantly different at 24 hours between each group (55.0% vs 27.6%, p =0.03). There was no difference in favorable outcome at 3 months, including the rate of complete recovery (33.3% vs 51.7%, p =0.23) and functional independence (50.7% vs 58.6%, p =0.24). The complication of symptomatic intracranial hemorrhage (1.5% vs 3.4%, p =0.57) and mortality rate (at admission, 3.1% vs 10.3%, p =0.54 and at 3 months, 7.9% vs 10.3%, p =0.54) was similar. The outcome of patients treated in Group B was comparable to that from Western trials.

Conclusion The outcome of patients treated in group B was comparable to that for patients treated in group A. The results of this study confirmed that the window of opportunity for rtPA treatment can extend to 4.5 hours. However, early rather than later treatment had a better outcome. **Chiang Mai Medical Journal 2015;54(2):71-80.**

keywords: thrombolytic therapy, ischemic stroke, outcome

Introduction

Stroke is one of the major causes of death and disability in Thailand. Ischemic stroke caused by vessel occlusion or thrombosis is one of the most common types of stroke, followed by intracranial hemorrhage and subarachnoid hemorrhage. Area reperfusion of hypo-perfusion by reopening the vessel at the appropriate time can save the life and function of patients. However, the treatment should be performed as soon as possible as time is

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limited before a permanently infarct area causes complications through ischemic injury to the blood vessel walls and blood-brain barrier. In 1996, intravenous recombinant tissue plasminogen activator (rtPA) treatment, within 3 hours after onset of symptoms, was approved for acute ischemic stroke (AIS) by the US Federation and Drug Administration (US-FDA) in America, as it was the only thrombolytic agent approved for this indication after the effective result of a pivotal randomized clinical trial sponsored by the National Institute of Neurological Disorders and Stroke (NINDS)[1]. In 2009, the American Heart Association and American Stroke Association (AHA/ASA) published a science advisory statement for expanding the clinical use of rtPA from 3 to 4.5 hours, based on results of the European Cooperative Acute Stroke Study (ECASS III) and Safe Implementation of Treatments in Stroke (SITS), which were safe and effective.[2-4] However, the extended window for rtPA administration has not been approved by the US-FDA because it was not recommended for several populations; although many countries have accepted it. A recent article published in BMJ 2015 raised uncertainty about the bene-fits of using rtPA more than 3 hours after the onset of stroke symptoms, and called for a re-evaluation of current advice on using thrombolysis for up to 4.5 hours after such symptoms manifest[5]. In Thailand, this guideline was implemented less than two years ago. The author has had many years experience at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, in the clinical use of rtPA within 3 hours from AIS, but still has limited data regarding its effectiveness, and especially possible complications of the new time expansion of up to 4.5 hours. The aims of this study were to compare the efficacy and safety of rtPA between patients treated within 3 hours and from 3 to 4.5 hours after the onset of symptoms (group A and B, respectively). Also, the outcome of patients treated in group B was compared with that from major Western studies.

Materials and methods

A retrospective study was carried out by reviewing the medical records of AIS patients, who were admitted to the Stroke Unit at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand and treated with tissue plasminogen activator (rtPA) (Actilyse, Boehringer Ingelheim) between January 1, 2013, and December 31, 2013. All of the patients completely fulfilled the in-hospital protocol, which followed that of the NINDS and European Cooperative Acute Stroke Study (ECASS) III, for patients treated within 3 hours and from 3 to 4.5 hours after the onset of symptoms (group A and B, respectively)[1,3]. They received rtPA at a dose of 0.9 mg/kg body weight (maximum dose 90mg), with 10% given as a bolus and the remaining 90% as a constant infusion over 60 minutes. Evaluated demographic characteristics of the patients were recorded, including age, sex, underlying disease, prior medication and logistic parameters such as time between onset and door to the emergency room (ER), door to computerized axial tomography (CT), and door to needle time. Severity of stroke was rated by the National Institutes of Health Stroke Scale (NIHSS), and serially assessed with a 42-point scale before treatment and after treatment daily during admittance. All of the patients had a baseline CT scan prior to treatment and another one within 24 and 48 hours after thrombolytic therapy in order to check for intracranial hemorrhage. Baseline CT was evaluated by the Alberta Stroke Program Early CT Score (ASPECTS) to evaluate early signs of ischemic change[6]. Blood pressure measurements were recorded before and after treatment, in accordance with the protocol, and the patients were treated with intravenous nicardipine if their systolic blood pressure was >185 mm Hg and/or diastolic blood pressure >110 mmHg. The etiology of stroke was evaluated by a physician, based on medical and radiological data according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria[7]; which were divided into 7 subgroups for analysis as follows: (1) large-artery atherosclerosis (LAA); (2) cardioembolic (CE); (3) small-vessel disease (SVD); (4) other determined etiology; (5a) multiple etiologies; (5b) undetermined etiology with extensive workup; and (5c) undetermined etiology but incomplete evaluation. The stroke subtype was defined by clinical and radiological features according to criteria of the Oxfordshire Community Stroke project, as total anterior circulation infarct (TACI), partial anterior circulation infarct (PACI), posterior circulation infarct (POCI) and lacunar infarction (LACI)[8]. Patient outcome was collected 24 hours after treatment, before discharge and within 3 months after discharge, which included neurological outcome by using NIHSS, functional outcome by using the modified Rankin Scale (mRS), and the Barthel index. The mortality rate was

assessed during admission and within 3 months after treatment.

Definition of outcome measurement

This study used the modified Rankin Scale (mRS), which measures functional dependence on a scale of 0 (no symptoms) to 6 (death), and the the Barthel index (BI) which rated the activities of daily living ranging from 0 (severely disable) to 100 (physically independent). The clinical outcome was defined as "good outcome", when the mRS score = 0-1 or BI= 95-100, "moderate outcome", when the mRS score = 2-3 or BI = 55–90, and "poor outcome", when the mRS = 4-5 or BI = 0-50. Functional independence and complete recovery was defined as mRS score of 0–2 and 0–1 at 3 months, respectively.

Definition of bleeding complication

"Intracranial hemorrhage" was classified by the ECASS classification for radiologic assessment of intracranial hemorrhagic lesions[9], i.e. HI-1= hemorrhagic infarction type 1 (small petechiae along the margin of the infarct), HI-2= hemorrhagic infarction type 2 (confluent petechiae within the infarcted area, but without space-occupying effect), PH-1= parenchymal hematoma type 1 (hematoma in ≤30% of the infarcted area with slight space-occupying effect), and PH-2= parenchymal hematoma type 2 (dense hematoma > 30% of the infarcted area with substantial space-occupying effect, or any hemorrhagic lesion outside the infarcted area).

The "symptomatic intracranial hemorrhage"[1,9,10] (SICH) in this study was divided into 3 definitions, as in previous study trials: 1) NINDS protocol defined as a hemorrhage unseen on a previous CT scan, and subsequent suspicion of hemorrhage or decline in neurological status, 2) ECASS II study defined as any intracranial bleeding, with four or more points worsening in NIHSS score, and 3) Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) protocol, which is defined as intracerebral hemorrhage type 2 (PH-2) on the 24- to 36-hour follow-up imaging scan, after thrombolysis treatment starts with neurological deterioration of four or more points on the NIHSS score from baseline, or from the lowest NIHSS score between baseline and 24 hours after thrombolysis or until death.

Statistical analysis

Demographic data, vascular risk factors and measured outcome variables were described by using descriptive statistics and compared between patients in group A and B. An independent-samples t-test for continuous variables and $\chi 2$ test for dichotomous variables were used. The prevalence of bleeding complication and good outcome were presented as percentage, and a two-tailed $p < 0.05$ was considered as statistically significant. The statistical software SPSS version 22 was employed for data analysis in this study.

Results

Six hundred and thirty four AIS patients were admitted to Maharaj Nakorn Chiang Mai Hospital between January 1,2013 and December 31, 2013, and the stroke team put 301 of them into the fast track program. Only 94 patients were qualified to receive thrombolytic treatment, which accounted for 14.83% of all the AIS patients. Patients were excluded due to time constraints, symptoms resolved, non-stroke diagnosis and intracerebral hemorrhage. Two patients, who received rtPA treatment, were excluded from this study due to a final diagnosis of non-stroke.

Therefore, 92 patients remained in the analysis, of which 63 (68.5%) came by referral from other hospitals and 88 (95.6%) arrived between 6 am and midnight. No significant difference of door to needle time was observed between patients receiving treatment from 6 am to midnight and those being treated between midnight and 6 am (mean time, 56.13min and 42 min: p =0.70). Sixty-three of 92 (68.5%) patients received rtPA in group A, and the remaining 29 (31.52%) were given rtPA in group B. Ninety percent of the patients in group A received rtPA after 90 minutes, whereas 80% of those in group B received it within the first 30 minutes after 3 hours (181-210 min). All 92 patients were ready for clinical follow up within 24 hours after rtPA treatment, with 85 (92.4%) being available at 3 months for clinical data outcome evaluation. Two out of seven patients in group B were missing.

Baseline characteristics and risk factors

Baseline and demographic data including risk factors, concomitant disease, previous medical treatment and degree of neurological severity are given in table 1. All baseline characteristics were not significantly different between the two groups. The mean age of

patients in group A and B was 65±3 (36-91), and 77.6±9.8 (42-84) years, respectively. Hypertension was the most common risk factor of AIS in both groups (52.3% and 62% in group A and B, respectively), followed by atrial fibrillation (AF) (46% and 37.9% in group A and B, respectively) and hyperlipidemia (20.6% and 24.1% in group A and B, respectively). Twenty four patients of 40 (60%) were documented with AF on admission, while the other 16 had been diagnosed for AIS events before. Eleven from 16 patients had indication for long term anticoagulant for cardioembolic prevention. However, only 4 patients received Coumadin,

Table 1. Demographic data and baseline characteristics of all patients

N	63	29	
Male (%)	30 (67.6)	15 (51.7)	0.71
Age (mean,SD)	65±3	77.6±9.8	0.11
Weight (mean)	57.6	51.8	0.23
Past medical history, n (%)			
Previous stroke/TIA	2 (3.1)	2 (6.9)	0.41
Smoker	4 (6.3)	0 (0.0)	0.16
DM	9 (14.2)	5 (17.2)	0.71
Dyslipidemia	13 (20.6)	7 (24.1)	0.7
CAD	4 (6.3)	1 (3.4)	0.56
Cancer	3 (4.7)	1 (3.4)	0.77
AF	29 (46)	11 (37.9)	0.46
Antiplatelet use	11 (17.4)	8 (27.5)	0.26
Hypertension	33 (52.3)	18 (62)	0.38
Mean blood glucose (mg/dl)	174.5±37.4	116.4±50.6	0.7
SBP (mmHg), mean±SD	159.2±16.9	148.2±16.4	0.32
DBP (mmHg), mean±SD	56.2±19	85.9±14.5	0.6
NIHSS: Median	13 (3-27)	9 (2-31)	0.01
NIHSS: Mean	12	11.7	
NIHSS >15, n (%)	20 (31.7)	6 (20.6)	0.27
ASPECT, mean±SD	9.6±1	8.7±1.4	0.21
ASPECT ≤7, n (%)	6 (9.5)	6 (20.6)	0.4
Stroke etiology, n (%)			
Cardioembolism	33 (52.3)	12 (41.3)	0.48
Large vessel occlusive	15 (23.8)	5 (17.2)	0.47
Small vessel occlusive	5 (7.9)	6 (20.7)	0.08
Undetermined etiology	10 (15.9)	6 (20.7)	0.57
Door to CT (mean±SD)	0.27±0.23	0.16±1.08	0.43
Door to needle (mean±SD)	46.51±15.82	39.95±1.39	0.33
Time to treatment			
Median	122	208	0.01
0-90 min, n (%)	5 (7.9)		
91-180, n (%)	58 (92.1)		
181-210, n (%)		23 (79.3)	
211-240, n (%)		4 (13.7)	
240-270, n (%)		2 (8)	
Length of stay (mean±SD)	10.27±10.45	8.10±7.14	0.74
Cost of hospital treatment (mean±SD)	86223±42080	90945±72341	0.59

but all of them had a subtherapeutic level of Coumadin at the time of clinical event. The number of patients taking antiplatelet before treatment was no different between the two groups.

There was no difference in stroke severity between the two groups, when compared by the number of patients with an ASPECT score >7 on baseline brain CT or by those with severe neurological deficit (NIHSS score >15). However, the median NIHSS score at baseline [13 (3-27) vs 9 (2-31), *p* value = 0.01)] of patients in group A was significantly higher than that for those in group B. The proportion of patients with an ASPECTS score ≤7, indicating a large area of infarct, was no different between the two groups.

According to the Oxfordshire Community Stroke Project, the most common pathophysiology of stroke in both groups was cardiogenic embolism (52.3% and 41.3% in group A and B, respectively), followed by large artery atherosclerosis (23.8% and 17.3% in group A and B, respectively) and small vessel occlusive disease (17.2% and 20.7% in group A and B, respectively).

Treatment outcomes

At 24 hours after treatment, patients in group A had significantly better neurological improvement [defined by 4-point improvement in NIHSS score from baseline score or complete resolution of neurological deficit (NIHSS 0–1)] than those in group B [55.5% vs 27.6% (*p* 0.03, CI 1.06-7.41)]. There was no significant difference in good outcome (complete recovery, functional independence) or complication (any ICH, SICH or mortality) between the two groups, as shown in Table 2 and Figures 1 and 2. The total cost during admission and hospital stay was no different for patients in either group. The data of patients in group B of this study were compared to studies of Western data such as ECASS III and SITS, as shown in Table 3. The mean age and NIHSS score of patients in group B were higher when compared to those from patients from SITS and ECASS III studies.

Patients in group B of this study had a median time from onset to treatment of 208 minutes, which was longer than that from SIST (195 minutes) and almost the same as ECASS III (209 minutes) studies. When comparing patients in group B with those in the

Table 2. Comparison of clinical outcome from thrombolytic treatment between patients treated within 3 hours and 3 to 4.5 hours after the onset of symptoms (Group A and B, respectively)

Outcome	Treatment in 3 h	Treatment in 3-4.5 h	*p*
Early improvement at 24 h	35 (55.5%)	8 (27.6%)	0.03
Outcome at 3 months	N= 58	N=27	
Good outcome (mRS0-1)	21 (33.3%)	15 (51.7%)	0.23
Poor outcome (mRS 4-5)	14 (22.2)	1 (3.4)	0.05
Functional independence	32 (50.7%)	17 (58.6%)	0.24
Barthel index (BI) at 3 months			
Good outcome (BI95-100)	28 (44.4%)	16 (55.1%)	0.58
Poor outcome (BI 0-50)	13 (20.6%)	1 (3.4%)	0.45
Hemorrhagic complication			
SICH (NINDS definition)	3 (4.8%)	1 (3.4%)	0.77
SICH (ECASS III definition)	4 (6.3%)	1 (3.4%)	0.56
SICH (SITS-MOST definition)	1 (1.5%)	1 (3.4%)	0.57
Fatal ICH	1 (1.5%)	1 (3.4%)	0.57
Asymtomatic ICH	9 (14.2%)	4 (13.7%)	0.24
Any ICH	13 (20.6)	5 (17.2%)	0.73
Mortality within 7 days	2 (3.1%)	3 (10.3%)	0.54
Mortality within 90 days	5 (7.9%)	3 (10.3%)	0.54

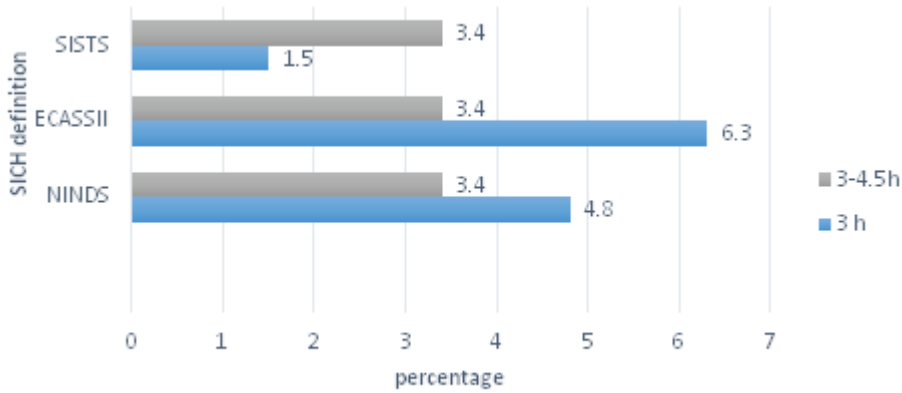

Figure 1. Comparison of symptomatic intracranial hemorrhage in patients treated within 3 hours and 3 to 4.5 hours after the onset of symptoms (group A and B, respectively) using different SICH definitions

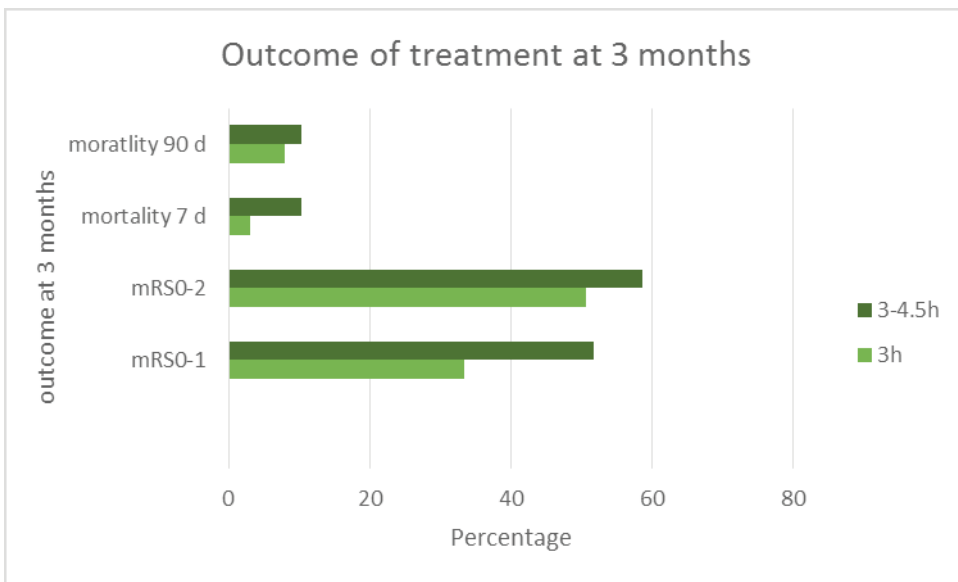

Figure 2. Comparison of mortality and function at 90 days of treatment in patients treated within 3 hours and 3 to 4.5 hours after the onset of symptoms (group A and B, respectively).

SIST study, 79.3% and 72.1% of the patients, respectively, received treatment within 3.5 hours after the onset of symptoms, whereas, 45.7% and 41.6% of patients in the ECASS III study received treatment post symptom onset between 3.5 and 4 hours and 4 and 4.5 hours, respectively.

Treatment complications

The rate of SICH in group B was evaluated by three different definitions from various trials, and it proved to be better in this study when compare to the ECASS III and SIST studies (3.4 vs 5.3 vs 5.3, using SIST definition). Three of 29 (3.4%) patients in Group B died within 7 days after treatment. Two of them died from large middle cerebral infarct with fatal ICH and brainstem infarct, due to basilar artery thrombosis, and the other one from sepsis and cardiovascular failure. No more deaths were identified after discharge. The mortality rate within 7 days of treatment was

Table 3. Comparison of baseline data and outcome between patients treated 3 to 4.5 hours after the onset of symptoms (group B) and those in Western clinical trials

Parameter	rtPA 3-4.5 h	ECASS III	SIST-ISTR
N	29	418	664
Age (mean)	77.6	64.9	65 (55-73)*
NIHSS score (median)	12	9	11
Atrial fibrillation (%)	62.10	12.70	20
Onset to treatment Time (median)	208	209	195
Percent of treatment initiation	79.3	9.6	9.6
≥180 to ≤210 min	13.7	45.7	45.7
>210 to ≤240 min	8	41.6	41.6
>240 to ≤270 min			
Symptomatic intracerebral hemorrhage (%)			
NINDS definition	3.5	7.9	8
ECASS III definition	3.4	1.9	2.2
SITS-MOST definition	3.4	5.3	5.3
Fetal ICH (%)	3.4	0.7	0.6
Mortality 7 days (%)	10.3	no data	7.5
Mortality 90 days (%)	10.3	6.7	12.7
Complete recovery % (mRS0-1)	51.7	52.4	40.5
Functional independence % (mRS0-2)	58.6	66.5	58

higher in this study than in the SIST studies (10.3% vs 7.5%), but the mortality rate within 30 days after treatment was lower in this study (10.3% vs 12.7%). However, the fatal ICH rate was higher in patients in Group B than those in Western studies (3.4% in this study vs. 0.7% in the ECASS III study vs. 0.6% in the SIST study). There was no difference in the rate of complete resolution (mRS 0-1) between this and the ECASS III study [51.7% vs 52.4% and the proportion of functional independence (mRS 0-2)] and between this and the SIST study (58.6% vs 58%).

Discussion

The center of this study was implemented at the Stroke Unit in December 2007. Fast track protocol and thrombolytic treatment within 3 hours after the onset of symptoms were developed and established at that time. Since results from the ECASS III trial in 2008 were reported, recent guidelines have been recommended for extending the treatment window with intravenous (IV) rtPA for up to 4.5 hours after the onset of symptoms. Nevertheless, the authors of this study already knew from many data that early rather than later treatment is better, but no data directly compared between the outcome of patients in Group A and B in Thailand. This study reported its first year's experience of using the guidelines in its center. In this study, 32% of the patients received treatment in group B, but both groups had the same outcome, effectiveness and safety of treatment. Also, neurological improvement at 24 hours was significantly better in patients in group A (55.5% compare to 27.6%, p =0.037, CI =1.06-7.41). There was no difference in any other clinical outcome, including complete recovery and functional independence at 3 months, hemorrhagic complication or any causes of mortality. The cost of hospital stay was comparable between the two groups. When comparing results with major Western trials, the proportion of patients in this study compared substantially to data in the SIST trial. These findings could be due to this study and the SIST trial having the same baseline characteristics of patients, with the researches

carried out in the real community and not in clinical studies, as in the ECASS III trial. However, this study had higher fatal ICH (3.4%), which caused a higher acute mortality rate (10.3%) when compared to the SIST study (0.6% and 7.5%). From a total of 574 patients in the Thrombolysis Implementation and Monitor of Acute Ischemic Stroke in China (TIMS-China), Liao XL and colleague collected data of 165 of them, who had received rtPA in the 3 to 4.5 hour after onset of symptoms group. They also found no significant differences in SICH rate (2.4% vs 1.5%, p =0.70) at 24 to 36 hours, mortalities at 3 months (7.5% vs 7.3%, p =0.84), independence rate (68.9% vs 63.9%, p =0.19), or excellent recovery rate (60.9% vs 52.4%, p =0.11) between patients treated within 3 hours and those treated 3 to 4.5 hours after the onset of symptoms[11].

Atrial fibrillation and cerebral embolism are associated with an increased risk of hemorrhagic transformation (HT)[12,13]. The only fatal ICH case in this study led to acute mortality after receiving thrombolytic treatment for 210 minutes. The incidence of symptomatic intracranial hemorrhage seemed to be independent from the onset time of symptoms to treatment (181-210 min: 1.62, 0.26-10.25; 211-240 min: 1.97, 0.82-4.76; 241-270 min: 3.15, 1.01-9.79; p =0.761) and from results of the ECASS III trial and pooled analysis[14,15]. In contrast, the same pooled analysis showed that mortality increased with increasing onset to treatment time[15]. Other factors that could cause more hemorrhagic lesions in this study might be due to a higher proportion of atrial fibrillation. The same result was found by Tong X and colleague in a predictor study of in-hospital death and symptomatic intracranial hemorrhage in patients with acute ischemic stroke, treated by thrombolytic therapy[16]. There was no difference in effect between treatment given within 3 hours or 3 to 4.5 hours after the onset of symptoms. Older age, male gender, NIHSS, history of myocardial infarction or coronary artery disease, and history of atrial fibrillation were associated with increased in-hospital death from those studies.

The results of this study showed that thrombolytic treatment 3 to 4.5 hours after the onset of symptom remains safe in patients who fulfill the clinical trial guideline. Although the results from the pooled analysis showed good results in patients receiving early treatment within 3 hours after onset of symptoms[14], this study showed that thrombolytic treatment 3 to 4.5 hours after onset of symptoms improves the thrombolysis rate and prognosis of patients with AIS in this center. However, patients should be treated as early as possible after stroke, even though there is a window of opportunity to extend the treatment.

Ethics

This study was exempted from reviewing the research ethics in humans by the Ethics Committee, Faculty of Medicine, Chiang Mai University.

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Conflict of interest

There are no conflicts of interest.

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ผลการรักษาผู้ป่วยอาการสมองขาดเลือดเฉียบพลันในโรงพยาบาลมหาราชนครเชียงใหม่ หลังจากการปรับระยะเวลาการให้ยาเพิ่มขึ้นเป็น 3-4.5 ชั่วโมง

กนกวรรณ วัชระศักดิ์ศิลป์
ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

วัตถุประสงค์ ศึกษาผลการให้ยาละลายลิ่มเลือดในเวลา 3-4.5 ชั่วโมงในผู้ป่วยสมองขาดเลือดเฉียบพลัน

วิธีการ ผู้ป่วยที่ได้รับยาละลายลิ่มเลือดเพื่อรักษาอาการสมองขาดเลือดเฉียบพลันในโรงพยาบาลมหาราชนครเชียงใหม่ในช่วง 1 มกราคม ถึง 31 ธันวาคม พ.ศ. 2556 เทียบผลการให้ยาใน 3 ชั่วโมงกับ 3-4.5 ชั่วโมงและผลการรักษาใน 3-4.5 ชั่วโมงเทียบกับผลการศึกษาในตะวันตก

ผลการศึกษา มีผู้ป่วยได้รับยาจำนวน 92 ราย ร้อยละ 68.48 ได้ยาใน 3 ชั่วโมง ร้อยละ 31.52 ได้ยาใน 3-4.5 ชั่วโมง พบเพียงอาการดีขึ้นทางระบบประสาทที่ 24 ชั่วโมงเท่านั้นที่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 55 กับร้อยละ 27.6, p =0.03) อัตราการหายเป็นปกติและอัตราการช่วยเหลือตัวเองได้ที่สามเดือนไม่พบความแตกต่างกันทางสถิติโดยพบอยู่ที่ ร้อยละ 33.3 กับร้อยละ 51.7 (p =0.23) และร้อยละ 50.7 กับร้อยละ 58.6 (p =0.24) ไม่พบความแตกต่างของการเกิดเลือดออกแบบมีอาการร้อยละ 1.5 กับร้อยละ 3.4 (p =0.57) อัตราการตายในโรงพยาบาลร้อยละ 3.1 กับร้อยละ 10.3 (p =0. 54) และที่ 3 เดือน 7.9% กับร้อยละ 10.3, (p =0.54) รวมถึงผลการรักษาที่ 3-4.5 ชั่วโมงเทียบกับผลการศึกษาในตะวันตก

สรุป การให้ยาละลายลิ่มเลือดใน 3-4.5 ชั่วโมงไม่ต่างกับการให้ยาใน 3 ชั่วโมง ข้อมูลนี้จะเพิ่มโอกาสในการเข้าถึงยาของผู้ป่วย แต่การช่วยให้ได้รับยาเร็วที่สุดโดยการให้ความรู้แก่ประชาชนยังคงเป็นปัจจัยสำคัญเพื่อผลการรักษาที่ดีที่สุด **เชียงใหม่เวชสาร 2558;54(2):71-80.**

คำสำคัญ: ยาละลายลิ่มเลือด สมองขาดเลือด ผลลัพธ์