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Intravenous thrombolysis for ischaemic stroke is also safe and efficient without a specialised neuro-intensive care unit

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Summary

Background: Treatment with intravenous (i.v.) recombinant tissue plasminogen activator (rt-PA) is recommended for selected patients with acute ischaemic stroke. We evaluated the feasibility and safety of this treatment in clinical practice in a hospital without a specialised neuro-intensive care unit.

Methods: We prospectively studied all patients who were treated with i.v. rt-PA for ischaemic stroke at our hospital between January 2001 and June 2002. The selection criteria corresponded to those published by the NINDS [1] and ECASS [2] groups. Time intervals between stroke symptom onset, hospital arrival and treatment with rt-PA were measured. A modified NIH stroke scale was used to assess clinical outcome 24 hours after stroke onset and before discharge. Cerebral computed tomography was performed prior to thrombolysis and again if the neurological status failed to improve or deteriorated.

Results: Thrombolytic therapy was administered to 15 acute ischaemic stroke patients, 13 men and two women with a median age of 69 years. The median time from stroke onset to rt-PA therapy was 135 minutes and from arrival in the emergency room to the start of thrombolysis 74 minutes. Ten patients exhibited early clinical improvement, defined as a decrease in NIHSS score by 4 points at 24 hours. Further improvement until discharge was observed in nine of these ten patients. One patient developed a non-fatal intracerebral haemorrhage. Another patient with severe stroke and clinical failure of thrombolysis died after 25 days.

Conclusions: This study in a small patient population suggests that thrombolysis with rt-PA for acute ischaemic stroke is feasible without excess risk in a hospital experienced in the management of stroke patients, with a neurological consultant service but without a specialised neuro-intensive care unit (NICU). The outcome in this small series of patients corresponds to the results described in the randomised trials.

Key words: acute ischaemic stroke; thrombolysis; rt-PA; feasibility

Introduction

Randomised placebo-controlled studies [1–5] and meta-analysis [6, 7] have demonstrated the beneficial effect of i.v. rt-PA in patients with acute ischaemic stroke if treatment is given within 3 hours of the onset of symptoms and the inclusion and exclusion criteria are strictly respected. However, the clinical setting in which thrombolysis should be performed remains controversial. Some authors advocate restricting it to neurological centres at university level with specialised intensive care stroke units [8], while others favour its extension to hospitals with expertise in the treatment of neurovascular patients and adequate neuroimaging facilities, but without designated NICUs. Today only a small proportion of stroke patients in Switzerland have the benefit of thrombolytic therapy. The reasons are referral patterns, local unavailability of thrombolytic therapy, logistic problems and limited capacity of existing stroke units. The aim of this study was to evaluate the feasibility, outcome and safety of intravenous thrombolysis with rt-PA in acute ischaemic stroke patients treated in a centre hospital with a unit specialised in early stroke treatment and a consultant neurological service, but without a designated NICU. The population studied were patients admitted and treated with intravenous rt-PA during the first 15 months from implementation of this therapy at our hospital to registration of i.v. rt-PA for this indication in Switzerland in July 2002.

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Methods

We prospectively recorded all patients treated with i.v. rt-PA for ischaemic stroke at our hospital between January 2001 and June 2002 in an ongoing register. The protocol was approved by the local ethics committee. All patients with acute ischaemic stroke admitted within three hours of stroke onset were considered for intravenous thrombolytic therapy. Inclusion and exclusion criteria for systemic rt-PA treatment were those of the National Institute of Neurological Disorders and Stroke (NINDS) study [1], with the following additional exclusion criteria taken over from the European-Australasian Acute Stroke Study (ECASS) [2]: severely impaired consciousness (coma or stupor) and/or hypodensity of more than ⅓ of the middle cerebral artery territory on initial computed tomography (CT) [8, 9]. Patients admitted to our hospital with acute stroke were first examined clinically in the emergency room. CT brain scan was performed as soon as possible and interpreted by an experienced radiologist. Informed consent was obtained from the patient (or the next of kin if the patient was unable to understand the information). Patients received 0.9 mg/kg of i.v. rt-PA (alteplase; Actilyse®), 10% as bolus and 90% as continuous infusion over 60 min, up to a maximum of 90 mg. I.v. rt-PA was administered immediately after screening and admission to the emergency room or intensive care unit (ICU). All patients were monitored for the first 24 hours in our ICU. Aspirin and heparin were withheld for the first 24 hours after thrombolytic therapy. Time intervals between stroke symptom onset, hospital arrival and treatment with rt-PA were recorded. Neurological deficits were assessed on admission, 24 hours after onset of stroke symptoms and before discharge, using a modified National Institute of Health Stroke Scale (NIHSS) (0–36 points) [10]. If not documented, an absent NIHSS score was deduced from the neurological examination records. Early clinical improvement was defined as a decrease in the NIHSS score of 4 points at 24 hours after onset of symptoms. An examination by our consultant neurologist was performed during the hospital stay. A cerebral CT scan was performed before discharge if the neurological status did not improve or immediately if it deteriorated.

Results

From January 2001 to June 2002, i.v. thrombolytic therapy was administered to 15 patients (13 men and 2 women) with acute ischaemic stroke in our hospital (Table 1). The median age was 69 years (range 56–81). Thrombolysis was started after a median time interval of 135 minutes (range 10–180) after stroke onset. The median time interval from arrival in the emergency room to the beginning of lysis was 74 minutes (range 10–103; see Table 1). One patient with a favourable outcome was treated 10 minutes after onset of stroke symptoms while undergoing coronary angiography in our hospital without prior CT scan. Thrombolytic therapy was usually administered in the ICU, but was also started (4 patients) or even completed (one patient) in the emergency room if ICU beds were not immediately available. The place of administration had no detectable impact. On hospital admission 3 patients had an NIHSS score ranging from 5–10 points, 8 patients a score from 10–20 points, and 4 a score over 20 points. Median pretreatment NIHSS score was 14 points (range 6–24; n = 15). 24 hours after symptom onset the median NIHSS score decreased to 7 points (range 1–24; n = 15). Before discharge after a median period of 20 days (range 3–79) the

Table 1

Demography, time intervals and NIH stroke scales on admission, 24 h after stroke onset and before discharge in the 15 patients with acute ischaemic stroke treated by i.v. thrombolysis.

Patient	Age [y]	Time sympt. – lysis [h:m]	Time hosp. – lysis [h:m]	Complications of thrombolysis	NIHSS on admission	NIHSS day 1	NIHSS on discharge
1	68	02:10	01:10	0	14	5	1
2	77	02:00	01:14	0	18	20	20
3	56	02:10	00:55	0	7	3	1
4	81	00:10	00:10	0	17	1	0
5	76	02:25	01:27	0	13	8	10
6	66	01:55	01:15	0	21	6	3
7	66	03:00	01:20	0	12	8	7
8	78	02:40	01:14	0	19	17	19
9	62	01:57	00:49	0	12	4	0
10	77	02:50	01:20	0	14	7	3
11	69	02:45	00:35	0	21	21	19
12	66	02:00	01:25	haemorrhage	22	22	18
13	73	03:00	01:43	0	6	2	0
14	67	02:35	00:20	0	9	5	3
15	77	02:15	00:55	0	24	24	18
Mean	**71**	**02:15**	**01:03**		**15**	**10**	**8**
Median	69	02:15	01:14		14	7	3

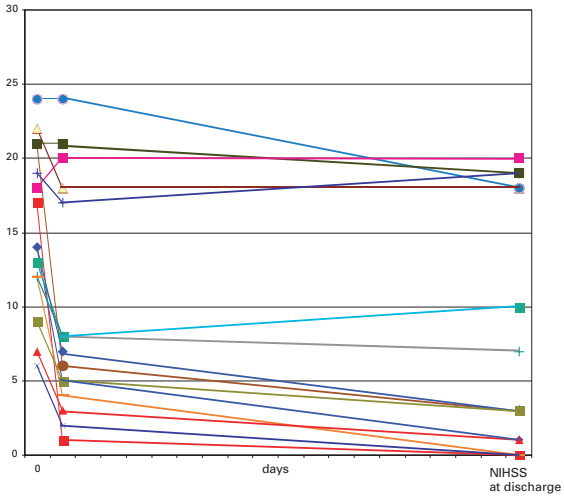

Figure 1

Neurological development of the 15 patients with acute ischaemic stroke treated by i.v. thrombolysis.

median NIHSS score was 3 points (range 0–20; n = 15) (Figure 1). Early clinical improvement, defined as a decrease in NIHSS score of 4 points 24 hours after stroke onset, was observed in 10 patients. Further improvement was seen in 9 of these 10 patients, with a median NIHSS score of 1 (range 0–7) before discharge after a median stay of 15 days (range 3–26). Thrombolysis was considered to have failed in five patients. In one of these a non-fatal intracerebral haemorrhage occurred, fortunately without deleterious effects. One patient in whom thrombolysis failed died after 25 days of pneumonia and left heart failure with pulmonary oedema.

Discussion

The results of this clinical study suggest that i.v. thrombolytic therapy for ischaemic stroke is feasible and safe in the setting of a hospital experienced in the treatment of acute stroke but without a designated NICU. This is important because many patients with acute stroke arrive at non-university hospitals first and any transfer delays treatment. Overall outcome will only be improved when the majority of these patients can be given the benefit of thrombolytic therapy. However, the treatment's safety must be guaranteed by a defined quality of structure, process and outcome. Recommendations are discussed elsewhere [20, 23]. The physician guiding thrombolytic therapy must be able to recognise the aetiology of the neurological deficiency, assess the risk of thrombolysis and recognise possible complications. The quality of the thrombolytic treatment outcome should be continuously monitored.

Before our department introduced i.v. thrombolysis as a treatment option for acute ischaemic stroke, most of the patients considered for this therapy could not receive thrombolytic therapy, chiefly because the time limit had been missed. Patients in the NINDS trial [1] who were treated within 90 minutes of the onset of symptoms had a more favourable response to rt-PA than those treated within 91–180 minutes [11]. This again argues in favour of starting i.v. thrombolytic therapy as soon as the criteria are met and possibly before transfer to the ICU. No excess risk was detected in our patient subgroup in whom treatment was begun or even completed in the emergency room with the necessary surveillance.

The median time interval from arrival in hospital to the start of thrombolysis (door-to-needle time) was 1 h 14 min (range 20 min to 1 h 43 min, excluding the one patient with thrombolysis during angiography). This seems to be long compared to door-to-needle times recorded in the thrombolytic treatment of myocardial infarction (median 30 min in Switzerland [12]). However, it corresponds to the time frame reported in other studies [13, 14, 16, 18, 19] and is explained by the extent of investigations necessary to evaluate inclusion and exclusion criteria including CT scan. No patient was excluded from treatment in our study because of delays after arrival in hospital. Equally important is the time interval between onset of symptoms and admission (in our study a median of 1 h 06 min, range 0 h 35 min to 2 h 15 min). Broad education of the public and referring physicians regarding the importance of early treatment may help to shorten these time intervals. Improvement of pre-hospital and in-hospital fast-track mechanisms may further improve the outcome.

Intracranial haemorrhage is the major complication of thrombolytic treatment. The only adverse event observed in our study was one non-fatal intracranial haemorrhage not requiring surgical intervention. In line with the recommendations by the American Brain Attack Coalition, neurosurgical care for stroke patients should be available within two hours [20]. It therefore appears to be safe to use thrombolytic therapy in patients with acute ischaemic stroke in hospitals without in-house neurosurgery but with the possibility of immediate referral.

Another treatment option for patients with acute ischaemic stroke is local intra-arterial therapy with prourokinase [21]. The advantages of this therapy are the wider time window of six hours, the lower number of exclusion criteria, the known pathological anatomy and the possibility of local intervention with thrombus extraction resulting in a higher rate of recanalisation [22]. Local therapy also reduces the systemic risks of thrombolytic therapy. However, logistic problems prevent the broad application of this therapy in Switzerland today.

Although the outcome in patients treated by thrombolysis was not a primary endpoint in our study and the numbers are small, we analysed the results observed in our study population. Ten of

our 15 patients showed substantial clinical improvement. The median NIHSS score was reduced from 14 points before treatment to seven points 24 hours after treatment and three points at the time of discharge. These results compare well with those reported in the literature. They support the conclusion of recent studies [13–19] that the outcome observed in randomised trials [1–4] can be reproduced in clinical practice and also in hospitals without designated neurological ICUs. To further improve this treatment option and coordinate its development, national registers should be kept of the results obtained in individual institutions.

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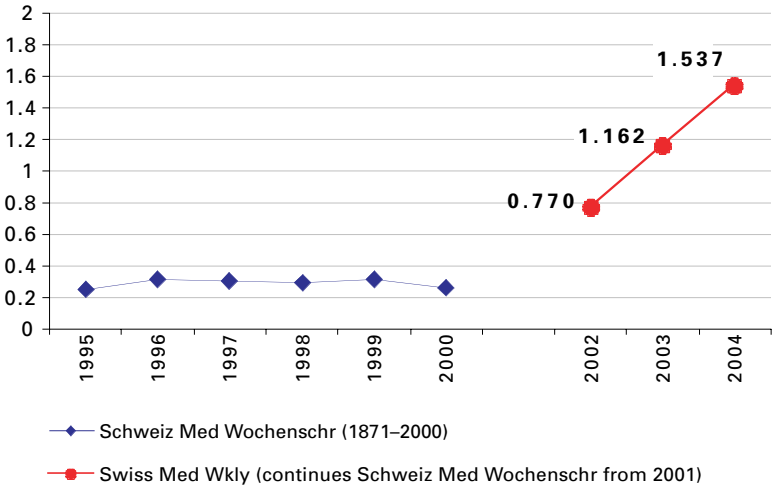

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