

DOI: 10.15225/PNN.2019.8.4.6

Thrombolysis and Mechanical Thrombectomy as Leading Treatments for Acute Ischemic Stroke

Tromboliza i trombektomia mechaniczna jako wiodące sposoby leczenia ostrego udaru niedokrwiennego mózgu

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Abstract

Brain vascular diseases, especially strokes, are still a very serious public health and medicine problem. The world is still facing an epidemic of stroke. With the impact load increasing all over the world, there is a continuing need to understand the characteristics of this disease and its impact in different countries. Despite significant improvements in primary prevention and treatment efficacy over the past decades, stroke is still a debilitating disease. Early treatment is the key to successful recovery of patients with ischemic stroke.

The aim of the study is to show the most effective methods of treating patients in the acute phase of ischemic stroke. (JNNN 2019;8(4):177–181)

Key Words: ischemic stroke, treatment, thrombolysis, thrombectomy

Streszczenie

Choroby naczyniowe mózgu, a zwłaszcza udary, to nadal bardzo poważny problem zdrowia publicznego i medycyny. Świat nadal stoi w obliczu epidemii udaru mózgu. Przy rosnącym na całym świecie obciążeniu udarowym istnieje ciągła potrzeba zrozumienia cech tej choroby i jej wpływu w różnych krajach. Pomimo znacznej poprawy w zakresie pierwotnej profilaktyki i skuteczności leczenia w ciągu ostatnich dziesięcioleci udar jest nadal wyniszczającą chorobą. Wczesne leczenie jest kluczem do pomyślnego powrotu do zdrowia pacjentów z udarem niedokrwiennym.

Celem pracy jest ukazanie najskuteczniejszych metod leczenia pacjentów w ostrej fazie udaru mózgu niedokrwiennego. (PNN 2019;8(4):177–181)

Słowa kluczowe: udar niedokrwienny, leczenie, tromboliza, trombektomia

Introduction

Despite significant improvements in primary prevention and treatment efficiency over the past decades, stroke is still a debilitating disease. The world is still facing an epidemic of stroke. With the growing impact of stroke load worldwide, there is a continuing need to understand the characteristics of this disease and its impact in various countries [1].

At present, strokes are the second most common cause of death and the third most common cause of disability

in the adult population [2]. Early treatment is the key to successful recovery of patients with ischemic stroke. From time of onset, the chances of a patient's permanent disability increase only until they can receive reperfusion intervention. Such intravenous tissue plasminogen activator (IVr-tPA) interventions and mechanical thrombectomy (MT), when used quickly, can minimize the extent of brain damage in the event of ischemic stroke [3].

The aim of the study is to show the most effective methods of treating patients in the acute phase of ischemic stroke.

Recombinant Tissue-Type Plasminogen Activator

Thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA) is a standard treatment for acute ischemic stroke (AIS). It is used within 4.5 hours of the onset of symptoms. It is invariably the gold standard of AIS treatment. It is used at a dose of 0.9 mg/kg of body weight. The frequency of r-tPA treatment has been increasing over the past 15 years [4–6].

Requirements of using rt-Pa:

- diagnosis of ischemic stroke with a significant neurological deficit by a doctor experienced in the treatment of stroke;
- determining the exact time of onset of symptoms based on reliable and credible medical history from the patient or witness of the event;
- exclusion of intracranial bleeding by computed tomography or magnetic resonance imaging;
- determination of basic life parameters [4–6].

Intravenous thrombolysis is the basis for the AIS treatment in any patient with a disability causing deficits within 4.6 hours of the onset of symptoms. Randomized studies have shown that more patients return to good function (defined as independence and minor disability or less) when they are treated within 4.5 hours after the onset of symptoms using rt-Pa [7]. Intravenous thrombolysis is the only approved pharmacological treatment in patients with AIS, but the immediate response to thrombolysis varies from patient to patient. In a study by Mehrpour et al. [8], among 118 patients with ischemic stroke, who were treated with a standard dose of rt-Pa, the effect of rt-Pa on patient performance was examined, as well as the factors predicting the outcome of intravenous thrombolysis in stroke patients before rt-PA administration. After 3 months of admission, 51% of patients achieved a good outcome [Rankin Scale (mRS)=2], while the poor outcome was seen in 49%. Important predictors of the result after 3 months according to the multivariate regression analysis was the result of the higher National Institute Health Stroke Scale — NIHSS (odds ratio [OR], 0.61; 95% confidence interval [CI], 0.498–0.750; $p < 0.001$), systolic and diastolic blood pressure on admission (OR, 0.95; 95% CI, 0.925–0.991; $P = 0.01$), atrial fibrillation (OR, 0.09; 95% CI, 0.013–0.708; $P = 0.02$), coronary artery disease (OR, 17.08; 95% CI, 0.013–0.708; $p = 0.003$). On the other hand, in a study conducted by Huang et al. [9], among 101 subjects who received rt-Pa, 55 patients obtained a good result (mRS 0–1). It has also been shown that patients with no history of diabetes, low

blood glucose level, low systolic blood pressure level and low baseline NIHSS score before thrombolysis have a better outcome.

Thrombolysis has proved effective in patients with acute ischemic stroke for over two decades. The medical and health care systems fully agree that stroke is fast and time is crucial. The demonstration of the effectiveness of rt-Pa as a highly time dependent treatment has brought the rapid progression of ischemic stroke to the fore. On average, 1.9 million neurons die every minute, which suggests that the implementation of stroke treatment as soon as possible can be significantly reflected in the results and effectiveness [10]. In the event of delayed thrombolytic treatment, the likelihood of improving the patient's functional condition decreases and the risk of bleeding increases [11]. A large multi-site observational study, in which 90-day results using a modified Rankin Scale were observed, showed that even a minute saved on treating a patient with thrombolysis was associated with an additional 1.8 day of healthy life and a reduction of 15 min generated up to 1 month of disability-free life for all ischaemic strokes [12]. The treatment time is onset of symptoms to the start of treatment with alteplase and it can be divided into two key elements, pre-hospital and hospital. Although most delays occur in pre-hospital settings, hospitals play a key role in providing rapid treatment of patients with ischemic stroke by providing rapid treatment from the time they arrive at the hospital, which is called the door-to-needle time (DNT) [10]. A quick diagnosis, adequate logistics and rapid response of the stroke team are key determinants of this variable. Due to the demonstrated improvement in clinical results, current guidelines recommend performing at least 80% of rt-Pa treatments within 60 minutes of DTN [13]. DNT provides valuable insight into the course of work in treating stroke and is an indicator of the efficiency of the stroke department. The patient care systems workflow has to be harmonized for a rapid delivery of rt-Pa. This proved difficult due to the interdisciplinarity involvement of emergency, radiological and neurological services. Therefore, goals were set for the rapid identification and treatment of acute stroke that every hospital should strive for. The target time were chosen arbitrarily to expedite the stroke treatment in an already busy emergency department; with door to physician time as 10 min, door to computed tomography (CT) time as 25 min, door to CT reading time as 45 min and door-to-needle (DTN) time as 60 min [14].

Endovascular Thrombectomy

Despite several effective stroke prevention strategies, the stroke epidemic continues to be a major cause of permanent disability. A recent series of well-diagnosed,

convincingly positive, randomized controlled trials of intravascular thrombectomy (EVT) in stroke patients with large vessel obstruction initiated a paradigm shift and a new era in the treatment of acute stroke. More than twelve years ago, the first reports appeared about mechanical thrombectomy, i.e. the removal of thrombi from cerebral arteries using special devices under the control of an X-ray lamp in ischemic stroke [15]. In 2018, the American Heart Association (AHA) and the American Stroke Association (ASA) published updated guidelines on endovascular interventions in acute ischemic stroke. The most important recommendations regarding the selection of candidates for intravascular therapy include:

- “Severity of neurological deficit: a patient should have been functionally independent pre-stroke, and have a National Institute of Health Stroke Scale (NIHSS) score at least 6. Patients with lower NIHSS would unlikely benefit from endovascular intervention.
- Identifiable large vessel occlusions (LVO) of the internal carotid artery (ICA) or proximal middle cerebral artery (MCA — M1 branch) must exist. Benefits of endovascular therapy when applied to occlusions of the M2 or M3 portions of the MCA, anterior cerebral arteries, vertebral arteries, basilar artery or posterior cerebral arteries are uncertain but can be tried (Class IIb; Level of Evidence C).
- An ischemic core that is not large. The volume of the ischemic core can be estimated with the Alberta Stroke Program Early CT Score (ASPECTS) and it should be at least 6.
- Age at least 18 years” [16].

It has been proven that EVT is effective in large artery occlusion (LAO) in the anterior cerebral circulation within the first 6 hours of stroke onset [17]. Recent randomized clinical trials (RCTs) have demonstrated a strong efficacy of intravascular thrombectomy in acute ischemic stroke due to obstruction of large vessels. The Sedation versus Intubation for Endovascular Stroke Treatment (SIESTA), The Anaesthesia During Stroke (AnSTROKE), The General or Local Anaesthesia in Intra Arterial Therapy (GOLIATH) did not show a harmful effect of general anaesthesia on EVT treatment results compared to conscious sedation. In turn, two randomized clinical trials DAWN (Clinical Mismatch in the Triage of Wake up and Late Presenting Strokes Undergoing Neurointervention with Trevo Thrombectomy Procedure) and DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischaemic Stroke 3) showed that the time window for the treatment of stroke has been extended from 6 hours to 24 hours provided that a small infarct core and significant tissue at risk is documented [18,19]. DAWN and DEFUSE 3 studies showed that

thrombectomy in acute/ischemic stroke, given to patients with standard care within 6–24 hours or 6–16 hours after onset, had better disability/activity results after 90 days than in patients who received only standard care [20,21].

Another randomized controlled study based on magnetic resonance imaging (MRI), WAKE-UP (Efficacy and Safety of MRI-based Thrombolysis in Wake-up Stroke) showed the benefits of intravenous thrombolysis in wake-up stroke patients. If the patient wakes up with a stroke, the time of onset cannot be determined. In the WAKE-UP study, this onset was estimated via DWI and fluid-attenuated inversion recovery (FLAIR) MRI. The infarction, which is clearly visible on FLAIR, is likely to be older than 4.5 hours and these patients are not considered suitable for thrombolysis. However, it is difficult to determine what can be considered a clearly visible infarction in the FLAIR system. This was demonstrated in a post hoc analysis, in which 5% of intravenous thrombolytic patients were considered to have a myocardial infarction in the FLAIR study [22–24].

Despite the existence of the stroke subunit infrastructure in Poland, providing adequate care to virtually all patients with acute stroke, and despite fully funded thrombolytic treatment, the introduction of mechanical thrombectomy is a huge logistical and organizational undertaking. It is extremely important to create intervention centres for stroke that will provide primary care for stroke units within an organized network. The creation of many small centres will lead to the situation that the operators and the entire staff will not have adequate experience, which will directly translate into a deterioration in the quality of procedures performed and the whole care. Since thrombectomy is a recent procedure and there are practically few teams and specialists with relevant experience, it is necessary to put a lot of emphasis on training. We currently have hard evidence of the effectiveness of mechanical thrombectomy in stroke. Therefore, it is necessary to implement it in a way that will allow effective and safe treatment. To this end, a needs analysis, preparation of appropriate impact centres and their connection in a network with basic subunits with planned logistics is carried out. Personnel preparation and quality monitoring is also a key element. After meeting all of the above-mentioned conditions, there is a chance to improve the stroke care system aimed at providing all eligible patients with access to mechanical thrombectomy [24,25].

Implications for Nursing Practice

Currently used modern principles of organization of treatment in the acute phase of ischemic stroke have contributed to reducing the risk of death and severe

long-term neurological deficits in patients. Stroke wards are units that have been created to provide specialist care in stroke. The comprehensiveness of activities in accordance with the latest recommendations is the priority. The nurse plays an important role at every stage of therapeutic activities. During AIS treatment, the role of a nurse is primarily to closely monitor the vital signs and clinical condition of the patient, continuous observation and constant presence with the patient as well as providing him with psychological support.

Conclusions

Stroke is a hard and destabilizing experience for the patient and his family. As a result of illness, the health and life situation of a person affected by stroke changes significantly. Over the past decade, remarkable progress has been made in the treatment and prevention of stroke. Effective treatment of the acute phase of stroke is only possible if pre- and in-hospital delays are reduced. That is why it is so important to recognize the symptoms quickly and to provide medical assistance quickly. These factors are one of the most important links in the patient's survival and prognosis chain after a stroke, as well as his later functional fitness. Therefore, knowledge on the above topics must be promoted not only among patients and their families, but also among health care professionals taking care of the patient at all stages of the survival chain.

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Conflict of Interest: None

Funding: None

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(A — Concept and design of research, B — Collection and/or compilation of data, C — Analysis and interpretation of data, D — Statistical analysis, E — Writing an article, F — Search of the literature, G — Critical article analysis, H — Approval of the final version of the article)

Received: 6.08.2019

Accepted: 15.10.2019