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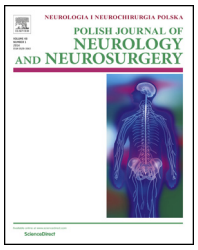

Original research article

Is there a bad time for intravenous thrombolysis? The experience of Polish stroke centers

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ABSTRACT

Background and purpose: The outcome in acute stroke strongly depends on patient-related issues, as well as on the availability of human and diagnostic resources. Our aim was to evaluate safety and effectiveness of intravenous alteplase for stroke according to the time of admission to the hospital.

Materials and methods: We analyzed the data of all acute stroke patients treated with alteplase between October 2003 and December 2010, contributed to the Safe Implementation of Thrombolysis for Stroke registry from 27 Polish stroke centers. According to the time of admission we distinguished between: (1) non-working days (Friday 14:30–Monday 08:00 plus national holidays); (2) out-of-office hours (non-working days plus 14:30–08:00 during working days); and (3) night hours (time from 23:00 to 06:00). Patients admitted during regular working hours (Monday 08:00–Friday 14:30, excluding national holidays) were used as the reference.

Results: Of 1330 patients, 448 (32.5%) were admitted on non-working days, 868 (65.3%) at out-of-office hours, and 105 (7.9%) during night hours. In multivariate logistic regression, none of the evaluated periods showed association with symptomatic intracranial hemorrhage, 7-day mortality, and neurological improvement $\geq$4 points in the National Institutes of Health Stroke Scale score at day 7. Patients admitted during night hours had lower odds (OR 0.53, 95% CI: 0.29–0.95, $p = 0.032$) for achieving favorable outcome (modified Rankin Scale score 0–2).

Conclusions: There is no bad time for thrombolysis. Stroke centers should feel confident about the treatment outside regular working hours, irrespective of equipment and staff availability. However, it may be reasonable to pay additional attention during nighttime.

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1. Introduction

Treatment with recombinant tissue plasminogen activator (rtPA, alteplase) within the first 4.5 h from the onset of symptoms is currently the gold standard of stroke care in developed countries [1–3]. Its effectiveness and safety depend not only on patient-related issues, but also on human and diagnostic resources. As the availability of those resources is not equal 24 h a day and 7 days a week (24/7), the time of admission may affect both the quality of care and the final outcome [4,5].

Several studies have described the so-called 'weekend phenomenon' [5–12]. Some authors also suggest that patients admitted during out-of-office hours [13,14] or night hours [7,15,16] may achieve less favorable outcome. However, the amount of evidence is still not sufficient, especially regarding treatment with rtPA. In Poland, the weekend phenomenon has been previously addressed only in one study that included unselected ischemic stroke patients, and did not account for thrombolysis [12].

The aim of our study was to evaluate safety and effectiveness of intravenous rtPA for ischemic stroke depending on the time of admission to the hospital, including out-of-office hours, non-working days and night hours. Additional emphasis was put on the treatment logistics.

2. Materials and methods

We analyzed the data of all acute stroke patients treated with intravenous rtPA between October 2003 and December 2010 contributed to the Safe Implementation of Treatments in Stroke – Eastern Europe (SITS-EAST) registry by 27 Polish stroke centers.

SITS-EAST is an international study of implementation of evidence-based stroke therapy supported by the SITS International Registry of Thrombolysis in Stroke (SITS-ISTR). The details of the SITS methodology, rationale for SITS-EAST and Polish participation in the registry have been described in detail elsewhere [17–19]. Briefly, SITS was originally a European Union-based, multinational, academic-driven, monitoring study designed to confirm the safety and effectiveness of thrombolysis in clinical practice [20]. Despite achieving its original aim in 2006, the registry as a platform has been constantly expanding. Currently, it is the largest source of data about licensed thrombolysis for stroke.

The registry in Poland has been approved by the local Ethics Committee. Data for the present analysis were acquired in August 2011 with the approval of the National Coordinator (Prof. Anna Czlonkowska). To ensure completeness of the 3-month follow-up, we decided not to include patients treated in the year 2011.

According to the time of admission, we distinguished between: (1) non-working days – defined as Friday 14:30–Monday 08:00 plus national holidays; (2) out-of-office hours – defined as non-working days plus hours 14:30–08:00 during the working days; and (3) night hours – defined as the time from 23:00 to 06:00.

Our major endpoints were the following: (1) symptomatic intracranial hemorrhage (sICH) according to the ECASS II definition (i.e. any intracranial hemorrhage combined with National Institutes of Health Stroke Scale [NIHSS] score worsening of $\geq$4 points or leading to death within 7 days); (2) 7-day mortality; (3) significant neurological improvement (i.e. improvement of $\geq$4 points on the NIHSS or achieving the NIHSS score of 0); (4) favorable outcome at 3-month follow-up (i.e. modified Rankin Scale [mRS] score of 0–2 points, meaning alive and independent) [21]. The ECASS II definition of sICH was chosen because it allows to effectively predict the worst outcome after thrombolysis [22]. As the measures of treatment logistics, we used onset-to-treatment time (OTT), and door-to-needle time (DNT) with special emphasis on DNT $\leq$60 min.

2.1. Statistical analysis

Categorical variables are presented as a number of valid observations with ratio. Proportions were calculated with exclusion of unknown values from the denominator. Due to non-normal distribution, continuous variables are presented as a median with interquartile range (IQR, representing 50% of average observations surrounding the median).

All analyses were made using regular working hours (Monday 08:00–Friday 14:30, excluding national holidays) as a reference. For basic comparisons, we used χ^2 test (with Yates correction if the expected value in at least one cell of a 2×2 contingency table was $<$5) or Mann–Whitney *U*-test. To calculate odds ratios (OR) with 95% confidence interval (95% CI) for each primary endpoint, we used multivariable logistic regression. All regression models were arbitrarily adjusted for age, lack of prestroke disability (mRS score $\leq$1), baseline NIHSS score, and OTT $\leq$90 min.

Calculations were carried out in STATISTICA 10.0 (Stat Soft Inc., Tulsa, USA, 2011). We considered a p-value $<$0.05 statistically significant. In tables, p-values $>$0.100 are presented as non-significant (NS).

3. Results

In the study period, 1330 cases of intravenous thrombolysis were reported to the registry, including 868 (65.3%) patients admitted at out-of-office hours, 448 (32.5%) admitted on non-working days, and 105 (7.9%) admitted during night hours. The reference group consisted of 462 patients admitted during regular working hours (Fig. 1).

3.1. Out-of-office hours

Patients admitted at out-of-office hours did not differ from the patients admitted during working hours in terms of distribution of vascular risk factors, but more frequently presented with no preexisting disability (92.9% vs. 88.2%, $p = 0.004$). They had a significantly lower proportion of mild strokes (NIHSS score $\leq$7) and more frequently showed hyperdense artery sign on the pretreatment brain computed tomography (CT) (Table 1). We found no differences in the median OTT and DNT, but patients admitted at out-of-office hours less frequently received thrombolysis within the first 90 min from the onset of symptoms (7.3% vs. 12.1%, $p = 0.003$) (Table 1). The occurrence of sICH, neurological worsening and the