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CLINICAL PHARMACY RESEARCH REPORT

Effect on door-to-needle recombinant tissue plasminogen activator administration times for acute ischemic stroke with and without an emergency department pharmacist

Brian W. Gilbert Pharm.D. | **Joel Huffman Pharm.D.**

Emergency Medicine Clinical Pharmacy Specialist, Wesley Medical Center, Wichita, Kansas

Correspondence
Brian W. Gilbert, Emergency Medicine Clinical Pharmacy Specialist, Wesley Medical Center, 550 N Hillside Avenue, Wichita, KS 67214.
Email: brian.gilbert.pharmd@gmail.com

Study Objective: A paucity of data exists on the impact emergency department (ED) pharmacists have on a stroke team's door-to-needle (DTN) administration time of recombinant tissue plasminogen activator (rTPA). The purpose of this study was to assess the odds of achieving a DTN administration time for rTPA of 60 minutes or less with an ED pharmacist present.

Methods: This was a retrospective, cohort study of patients who received rTPA for acute ischemic stroke (AIS) from May 2017 to May 2018. Patients were included if they were at least 18 years old and received tPA for AIS in the ED. The primary outcome for this study was the likelihood of patients receiving a DTN administration time of 60 minutes or less with or without an ED pharmacist present during a stroke alert at a primary stroke center.

Results: The electronic medical record of 184 stroke alert patients was reviewed, and 65 patients were included in the final analysis. Baseline characteristics were similar in all aspects. The odds ratio was 3.3 (95% confidence interval [CI]: 1.1-9.6; $P = 0.04$) to achieve a DTN administration time of 60 minutes or less when an ED pharmacist was present. The ED pharmacist present group had faster median (47 minutes vs 60 minutes; $P = 0.001$) and average (49 minutes vs 63 minutes; $P = 0.003$) DTN administration times compared with the ED pharmacist not present group.

Conclusion: An ED pharmacists present during a stroke alert at our faculty resulted in reduced overall DTN rTPA administration times and increased the odds of a patient receiving rTPA less than 60 minutes from arrival for AIS. Further study is required to determine if this finding can be replicated in other EDs.

KEYWORDS

clinical pharmacist, stroke, thrombolytic

1 | INTRODUCTION

Focus on timely administration of recombinant tissue plasminogen activator (rTPA) remains a central goal for stroke centers. The American Heart Association (AHA) guidelines on the management of acute ischemic stroke (AIS) recommends a door-to-needle (DTN) time for the administration of rTPA be 60 minutes or less in ≥50% of AIS patients as a primary goal.[1] Previous studies have found that early notification by emergency medical services (EMS), quicker triage to computed tomography (CT) times, implementation of a code stroke team, and treatment within CT vs in the emergency department (ED) have all been shown independently to reduce DTN administration times.[2–5] Previous literature have shown some of the beneficial impact that including an ED pharmacist into the stroke team can provide.[6] Most of the literature with regard to pharmacist involvement in AIS have been with a reduction in DTN administration times and more accurate dosing of rTPA, without focusing on the overall goal metric of a DTN administration time of 60 minutes or less.[7–10] Debate will continue as to whether faster administration of rTPA leads to better functional outcomes, but for now, the standard for stroke centers is

rapid rTPA administration based on the AHA guideline of a DTN administration time of 60 minutes or less.[1] The purpose of this study was to assess the odds of achieving a goal DTN administration time of 60 minutes or less with an ED pharmacist present at a primary stroke center.

2 | METHODS

2.1 | Research design

This was a single-center, retrospective, cohort study of a convivence sampling of patients who received rTPA for AIS from May 2017 to May 2018 at a primary stroke center. Patients were included if they were ≥18-years-old and received rTPA for AIS in the ED. Patients were excluded if they received rTPA outside of the ED or if they received rTPA for a diagnosis other than AIS. Factors believed to influence DTN administration times by the authors were evaluated and collected. Other data points collected included: whether the patient developed a symptomatic intracranial hemorrhage (sICH), total hospital length of stay (LOS), and the patients final discharge destination including mortality.

In October 2017, ED pharmacy services were initiated for 11 hours a day (1100-2200), 7 days a week, at Wesley Medical Center in Wichita, Kansas. This institution is a level-1 trauma center, primary stroke center, and community teaching hospital which evaluates over 100 000 patients annually in the ED. Two Post Graduate Year-2 residency trained pharmacists (1 PGY-2 in critical care, 1 PGY-2 in emergency medicine) made up the emergency medicine clinical pharmacy specialist team. The pharmacists were part of a stroke team which included the emergency medicine attending, neurocritical care physician assistants, nursing, radiology, and laboratory services. The stroke team has an algorithm by which it processes each potential stroke patient and different time stamp goals for door to CT, CT to rTPA order, etc. There are two different algorithms based on whether a patient presents via EMS or private vehicle.

An ED pharmacist responded to all stroke alerts during the allotted hours, and the activities of the ED pharmacist during a stroke alert included, but were not limited to, verifying patient weight, gathering supplies for rTPA administration, confirming anti-platelet or anticoagulation use prior to arrival, aiding in blood pressure management via preparation of anti-hypertensive medications, pump administration preparation, dose verification, order verification, and preparation of rTPA. These activities are not currently part of a collaborative practice agreement but are recommendations by the ED pharmacist.

Patients were stratified into two groups with respect to whether an ED pharmacist was present or not during the stroke alert. With respect to the two groups, patients that received rTPA between 1100 and 2200 from October 2017 to May 2018 were included in the ED pharmacist present group and were compared with historical controls from May 2017 to October 2017 during the same working hours without an ED pharmacist present. Because there are historically longer times associated with overnight processes at many institutions, the control group was limited to the hours worked by the ED pharmacist. The decision was made not to include those outside the working hours of the ED pharmacist during the same time period to limit potential confounders. Patients were compared based on factors believed to influence DTN administration times, such as age, sex, initial National Institute of Health Stroke Scale score, whether the patient was on anti-platelet or anticoagulation medication prior to arrival, whether the patient arrived via EMS, and initial blood pressure. Data were queried utilizing ICD-10 codes for acute ischemic strokes and then evaluated for administration of rTPA. Collection of data was performed by both ED pharmacists through the electronic medical record and pharmacy surveillance system. This study was approved by the institutional review board.

2.2 | Outcomes

The primary outcome for this study was the likelihood of patients receiving a DTN administration time of 60 minutes or less with our without an ED pharmacist present. The secondary outcome of the study was to evaluate overall DTN administration times with or without an ED pharmacist present by evaluating the mean and median DTN administration times.

2.3 | Statistical analysis

Categorical variables were summarized using counts and analyzed using non-parametric χ^2 or Fisher exact tests. Continuous variables were summarized using means or medians ± SDs and analyzed with either a Student *t* test or Wilcoxon rank sum test. All analyses were performed using SAS version 9.4 for Windows.

3 | RESULTS

The electronic medical records of 184 stroke alert patients were reviewed, and 65 patients were included in the final analysis (Figure 1). The most common reason for exclusion from the study was that patients did not receive rTPA. There were 33 patients stratified into the ED pharmacist present group and 32 patients stratified into

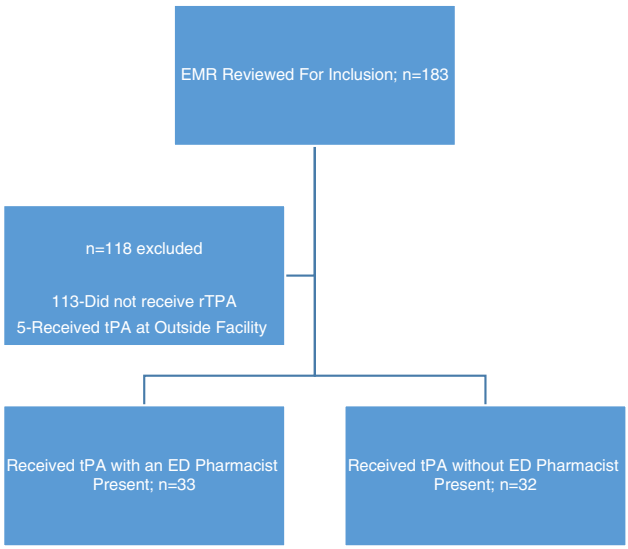

FIGURE 1 Enrollment flow diagram. ED, emergency department; rTPA, recombinant tissue plasminogen activator

the ED pharmacist not present group. The patient demographics and clinical characteristics are identified in Table 1. Baseline characteristics were similar in all aspects. There were more males being treated with an ED pharmacist present, but this did not reach statistical significance. There were more EMS arrivals in the ED pharmacist present group; however, this did not reach statistical significance. Both initial systolic blood pressure (SBP) and initial diastolic blood pressure (DBP) in the ED pharmacist present group had higher initial values than without an ED pharmacist present group, however, this was also not statistically significant. The majority of patients in both groups received rTPA within 3 hours of last known well (LKW) and were similar with respect to having received anti-platelets or anti-coagulation prior to ED arrival.

With an ED pharmacist present, there were 26 (78.8%) patients who had a DTN administration time of 60 minutes or less compared with only 18 (56.3%) patients in the ED pharmacist not present group. The odds ratio was 3.3 (95% confidence interval [CI]: 1.1-9.6; P = 0.04) for patients to have a DTN administration time of 60 minutes or less with an ED pharmacist present (Table 2). The ED pharmacist present group had faster median (47 minutes vs 60 minutes; P = 0.001) and average (49 minutes vs 63 minutes; P = 0.003) DTN administration times compared with the ED pharmacist not present group, which were statistically significant (Table 2).

In the ED pharmacist present group there were three total sICHs, and without an ED pharmacist present there was one sICH. There was one mortality associated with each group and the majority of patients from each group were discharged to home after an average LOS of 4.6 days in the group without an ED pharmacist and 5.8 days in the group with an ED pharmacist group (Table 3).

TABLE 2 Door-to-needle administration time data

Characteristics	ED pharmacist present, n = 33	ED pharmacist not present, n = 32	P value
DTN ≤60 minutes; n (%)	26 (78.8)	17 (53.1)	0.03
DTN; median minutes (range)	47 (22-74)	60 (36-109)	0.001
DTN; mean minutes (range)	49 (22-74)	63 (36-109)	0.003
Odds ratio		P value	
DTN ≤60 minutes, ED pharmacist present		3.3 95% CI (1.1-9.6)	0.04

Abbreviations: DTN, door-to-needle; ED, emergency department.

4 | DISCUSSION

Expedited administration of rTPA for AIS remains an ongoing quality improvement initiative for many stroke centers across the country. The utilization of pharmacists in stroke teams has been shown to improve overall DTN administration times, but this is one of the first studies to examine the impact pharmacist have on the guideline specific recommendation of a DTN administration time of less than 60 minutes.[7–10] Reduction in overall administration times can prove controversial given that the "time is brain" concept is not universally endorsed in the medical community. However, because institutions are measured by guideline recommended DTN rTPA administration times of 60 minutes or less, it becomes important to stroke centers that this metric is met more so than an absolute reduction in administration times.[1,11] Some clinicians within the ED do not endorse the penumbra theory which could potentially confound some DTN administration time results as they may not work in the same expedited fashion that a neurologist may.

This study highlights the impact that a pharmacist can have on meeting the guideline recommended DTN administration time for rTPA of 60 minutes or less for stroke centers across the country.[1] What remains to be seen is whether any clinical outcomes may be affected with the utilization of a pharmacist on the stroke team, which could be answered with larger randomized controlled trials designed to address these functional outcomes. This study adds to the paucity of literature which shows the association of having a pharmacist implemented into the stroke team and a reduction of DTN administration times, and with some data suggesting that faster administration of rTPA leads to better functional outcomes.[6–10] What also remains to be addressed is the potential financial implications of adding a pharmacist into stroke teams. If pharmacist implementation into a stroke team does increase the number of patients with a DTN administration time of 60 minutes or less, there are potential positive financial considerations which could be explored, as well.

This study identified that having a pharmacist present during a stroke alert resulted in greater odds of achieving a DTN administration time of 60 minutes or less, with overall DTN administration times

TABLE 1 Baseline demographics and characteristics

Characteristics	ED pharmacist present, n = 33	ED pharmacist not present, n = 32	P value
Age; years (range)	71 (36-91)	66 (35-99)	0.54
Males; n (%)	17 (51)	10 (30)	0.07
Initial NIHSS; median (range)	6 (1-23)	6 (0-37)	0.45
Arrival via EMS; n (%)	25 (75.7)	17 (51.5)	0.07
rTPA administration ≤3 hours of LKW; n (%)	25 (75.7)	26 (78.8)	0.77
Anti-platelet or anti-coagulation use prior to ED arrival; n (%)	17 (51.5)	18 (54.5)	0.81
Initial SBP; mean	162.3 (119-210)	145.5 (109-216)	0.07
Initial DBP; mean	91.5 (64-110)	83.3 (62-105)	0.09
rTPA dose in mg; mean	75.25 (62-90)	74.3 (65-90)	0.39

Abbreviations: DBP, diastolic blood pressure; ED, emergency department; EMS, emergency medical services; LKW, last known well; NIHSS, National Institute of Health Stroke Scale; rTPA, recombinant tissue plasminogen activator; SBP, systolic blood pressure.

TABLE 3 Post rTPA data

Characteristics	ED pharmacist present, *n* = 33	ED pharmacist not present, *n* = 32	*P* value
LOS; median days	5.8	4.6	0.21
Mortality; *n* (%)	1 (3)	1 (3.1)	0.98
sICH; *n* (%)	3 (9)	1 (3)	0.32
Discharge destination home; *n* (%)	20 (61)	22 (67)	0.23

Abbreviations: ED, emergency department; LOS, length of stay; sICH, symptomatic intracranial hemorrhage; rTPA, recombinant tissue plasminogen activator.

also statistically lower when an ED pharmacist was present. Overall DTN administration times were 60 minutes or less in 78.8% of patients with a pharmacist present, but only 56.3% without a pharmacist present in this study. The overall odds of having a DTN administration time of 60 minutes or less was statistically higher when a pharmacist was present in this study, which is the first study to assess this parameter as a primary end point.

The median DTN administration times with a pharmacist present group was similar, at 47 minutes, compared with previously reported times of 46-69.5 minutes.[7,8] In the ED pharmacist not present group, times were similar to previous studies, with a median administration time of 60 minutes compared with 58-89.5 minutes.[9,10] Variables thought to affect DTN administration times were analyzed and were similar in each group for this study. There were more patients in the ED pharmacist present group that arrived via EMS services, which has been shown to reduce DTN administration times; however, this did not reach statistical significance. Patients in both groups had roughly the same number of patients receive rTPA within 3 hours from LKW, antiplatelet or anti-coagulation use prior to arrival, and rTPA dose. Interestingly, patients in the group that had an ED pharmacist present had a higher initial SBP and DBP, which would affect initial rTPA administration times given the strict initiation criteria by the AHA guidelines; however, this did not reach statistical significance.[1] Factors thought to influence DTN administration times were similar and therefore the effect is limited to finding a correlation that ED pharmacists present during stroke alerts may increase the odds of achieving a DTN administration time of 60 minutes or less.

The outcomes for post administration of rTPA were similar between both groups in this study, as well. There were 3 sICHs in the ED pharmacist present group and 1 in the group without an ED pharmacist present ($P = 0.32$), a median of 5.8 total hospital days in the ED pharmacist present group compared with 4.6 total hospital days without an ED pharmacist present, and roughly the same percentage of patients discharged home in each group (61% vs 67%; $P = 0.23$) which was similar to previously reported data.[1,7–10]

Limitations of our study include its retrospective single-site nature. The retrospective nature of the study relied on accurate documentation to determine administration times; however, to account for this the physician note was also evaluated and if there was a discrepancy in time, the longest administration time was used for analysis. The hours which the ED pharmacists were present in this study may not be generalizable to other institutions, most noticeably in the earlier hours in which wake up strokes can be common, therefore, a temporal relationship may exist that was not addressed. The patient attributes chosen to be evaluated were not all encompassing and instead were those hypothesized by the authors to impact DTN administration times. A number of attributes, such as selective past medical history and prescriber preference cannot be accounted for in terms of their approach to rTPA utilization. While clinical outcomes as they relate to functional status were not obtained, there have been previous data to suggest that faster administration may be associated with better functional outcomes; however, modified Rankin scores to assess functional outcomes were not assessed in this study.[1]

5 | CONCLUSION

An ED pharmacist present during a stroke alert has been shown to reduce overall DTN administration times as well as increase the odds that the patient receives rTPA within 60 minutes of arrival to an ED. This study did not show any other statistically significant factors which could confound the result of higher odds of having a DTN administration time of 60 minutes or less with an ED pharmacist present. Whether an ED pharmacist is present or not does not seem to affect sICH rates, total LOS, or discharge destination.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

ORCID

Brian W. Gilbert https://orcid.org/0000-0002-1385-7500

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