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Original Article

Tissue Plasminogen Activator in Addition to Twist Drill Drainage as a Treatment for Chronic Subdural Hematomas: A Descriptive Analysis

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BACKGROUND: Current literature lacks robust universal guidelines for first-line treatment of chronic subdural hematomas (cSDH). However, administration of local tissue plasminogen activator (tPA) may enhance the traditional method of twist drill drainage (TDD).

OBJECTIVE: The study aims to explore the efficacy of TDD with and without tPA, at achieving clinically relevant drainage (200mL) and reducing recurrence of cSDH.

PATIENTS AND METHODS: A retrospective review of patients (n=34) with cSDH is presented. Patients who received TDD with tPA (n=17) were identified and matched, based primarily on age and hematoma volume, to a TDD only group (n=17). Variables of interest include hematoma volume, volume drained, length of stay, and recurrence rates. Descriptive analysis was run.

RESULTS: Average age for patients (n=34) was 73.9 years. The majority of the cohort (76%) were males. Mean drainage volume for the tPA cohort was 382.7mL and TDD only cohort was 187.8mL. The addition of tPA resulted in drainage volumes nearly double (1.9x) the clinically relevant amount and had low recurrence rates (6.3%). TDD only failed to result in clinically relevant drainage and had a recurrence rate of 37.5%. Average length of stay in neurosurgical hospital care was 9.71 days for the tPA group, and 7.65 days for TDD only.

CONCLUSION: TDD with tPA was effective at treating cSDH in our population. Patients who received tPA had clinically relevant cSDH drainage, reduced cSDH recurrence, and therefore had decreased risk for complications associated with cSDH recurrence.

KEYWORDS: Chronic subdural hematoma, Tissue plasminogen activator, Twist drill drainage.

INTRODUCTION

Chronic subdural hematoma (cSDH) is defined as a collection of blood between the dura and arachnoid matter in the brain that develops over a period greater than 3 weeks.[1] cSDHs are currently one of the most common neurosurgical diseases,[2] with an estimated yearly incidence in the general population between 1.72 and 20.6 per 100,000 persons.[3] In patients older than 65 years, this number increases to 58.1 per 100,000 persons annually.[4] As our population ages, the incidence of cSDH is predicted to rise significantly in the coming years.[5] It is therefore imperative that risk of recurrence and associated complications be minimized, as elderly patients may not tolerate the invasive care associated with these complications.[6]

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The most common cause of cSDH is mild to moderate head trauma,[1,5] although other risk factors include chronic alcoholism, gender, coagulopathy, and intracranial hypotension.[6] cSDHs are a significant cause of morbidity and mortality, and may be a marker of other underlying health conditions.[2,7]

Despite the high incidence of cSDH, the current literature provides little consensus on universal guidelines for first-line treatment.[2,4,8-10] Common treatment options include clinical monitoring, craniotomy, twist drill drainage (TDD), and burr hole drainage (BHD).[6] Previous meta-analyses have provided support for both the BHD and TDD procedures.[4,11] The lack of consensus is likely sustained due to the failure of one method to outperform in minimization of morbidity and mortality, reduction in recurrence risk, maximization of drainage volume, cost effectiveness, and minimally invasiveness. In comparison to clinical monitoring and craniotomy procedures, many surgeons agree that the BHD and TDD procedures are the most rational therapeutic options.[12]

Although the literature provides support for the BHD and TDD procedures, the risk of recurrence for these procedures varies between 10.5-11.8% and 14.5-31.3%, respectively.[4,8,11,13] One factor that contributes to this risk of recurrence is the volume of drainage achieved by the procedure. Kwon et al. found that those who have less than 200mL of drainage had statistically significant higher rates of recurrence compared to those who had greater then 200mL of drainage.[12] cSDH recurrence increases a patient's chances of experiencing complications that may lead to death, intensive care hospitalization, or require invasive management including surgery or endovascular procedures.[13] It is therefore imperative to maximize drainage of cSDH in order to prevent cSDH recurrence and its associated outcomes.

Preliminary research suggests that using tPA in addition to TDD increases drainage volume of cSDH.[8] The goal of the current study is to build on these previous findings, by assessing the efficacy of TDD with and without tPA, at achieving clinically relevant drainage (200mL) and reducing recurrent of cSDH. Outcomes of interest include the volume of drainage, hematoma recurrence rates, and documented adverse events.

PATIENTS AND METHODS

Ethics approval was obtained from the Horizon Health Network Research Ethics Board on April 8, 2020 under file # 100836, event 14398.

All patients over the age of 19 presenting at a single tertiary care centre with a subdural hematoma, confirmed with computed tomography (CT) imaging, were screened. Patients were identified as having been treated with tPA and TDD or TDD alone. Only patients who had passive drainage systems were included. Patients treated with tPA were then manually matched to patients who were treated with TDD alone. Matching was done by a medical student and confirmed by a neurosurgeon. Primary matching criteria were hematoma volume and patient age. Secondary matching criteria were sex and side of hematoma drained.

Hematoma volume was calculated from CT images by a radiologist using the ABC/2 method as described by Barras et al.[14] This method approximates hematoma volume based on their ellipsoid form. The variables A, B, and C represent hematoma length (tip-to-tip on an axial image), width (maximal width on an axial image), and height (tip-to-tip on a coronal image), respectively.

Recurrence was defined as an increase in the size of the hematoma, at any point following the 24-hour post-drainage imaging, that required re-intervention. The recurrences were stratified based on those that happened within three months of initial presentation and recurrences that occurred after three months.

Technical note

The TDD procedure was done at the bedside using local anesthetic, with or without intravenous sedation. Following preparation of the scalp with iodine solution, a 0.5cm incision was made over the maximum thickness of the hematoma, estimated based on CT imaging. The twist drill was then used to create a burr hole and puncture the dura matter. An antibiotic coated ventricular catheter was then inserted into the subdural space, and secured for continuous passive drainage. Drain removal occurred once there was less than 50mL of drainage within a 24-hour period. This is in addition to clinical improvement and satisfactory decompression on CT. In the tPA group, the decision to use tPA was based on the residual hematoma volume on 24-hour post-drain insertion CT imaging, and volume of drainage in the first 24 hours. Those in the tPA group had 1mg of tPA (Alteplase) injected into their catheter shortly after the 24-hour post-drain insertion CT imaging. The drain was then clamped for one hour following the injection before being reopened to resume continuous passive drainage.

A descriptive analysis of each group was done using SPSS (Statistical Package for the Social Sciences) 26 software. Categorical variables were reported as frequencies and percentages. Continuous variables were reported as means and ranges.

RESULTS

A total of 365 patients were screened resulting in n=34 patients, 17 of which received tPA in addition to the TDD procedure and 17 matched patients who received only the TDD procedure. Demographic information for all patients is presented in **Table 1.**

In the tPA group, the mean age was 74.35 years, with a range of 56 to 87 years. Of the 17 participants, 6 (35.3%) had a left sided cSDH, 5 (29.4%) had a right sided cSDH, and 6 (35.3%) had bilateral cSDH. Five of the six patients with bilateral cSDH had single sided drainage, while one patient had bilateral drain insertions. All of the patients who received tPA had presence of midline shift. The average length of stay on the neurosurgical unit was 9.71 days, with 70.6% being discharged home, 23.5% being transferred to another hospital service, and 5.9% (1 patient) who expired due to respiratory arrest secondary to brain death caused by large bilateral cSDH.

One of the hematomas from the tPA group is presented in **Fig. 1**. These images highlight the size of the hematoma on presentation **(Fig. 1A)**, after TDD **(Fig. 1B)**, and 24-hours following administration of tPA **(Fig. 1C)**.

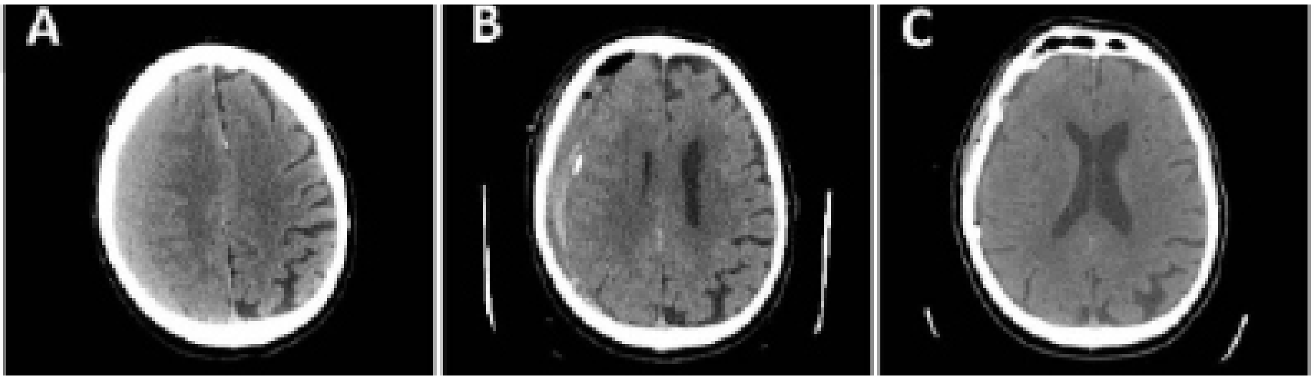

Fig 1: Example patient from treatment group. A: Pre-treatment imaging. B: 24-hour post-drain insertion imaging. C: 24-hours post administration of tissue plasminogen activator (tPA).

Table 1: Demographics of 34 patients with CSDHs included in the study

	Patients with tPA (n=17)	Patients without tPA (n=17)	All Patients (N=34)
	Mean +/- SD	**Mean +/- SD**	**Mean +/- SD**
Age	74.35 years +/- 8.12	73.35 years +/- 11.82	73.85 years +/- 9.97
	n (%)	**n (%)**	**n (%)**
Sex			
Male	13 (76.5%)	13 (76.5%)	26 (76.5%)
Female	4 (23.5%)	4 (23.5%)	8 (23.5%)
Side of hematoma			
Left	6 (35.3%)	8 (47.1%)	14 (41.2%)
Right	5 (29.4%)	5 (29.4%)	10 (29.4%)
Bilateral	6 (35.3%)	4 (23.5%)	10 (29.4%)
Presence of midline shift			
No	0 (0%)	2 (11.8%)	2 (5.9%)
Yes	17 (100%)	15 (88.2%)	32 (94.1%)

*tPA = Tissue plasminogen activator.
n= number.
SD= Standard deviation.

Within the TDD only group, who did not receive tPA, the mean age was 73.35 years, with a range of 50 to 88 years. Among the 17 TDD only patients, 8 (47.1%) had a left sided cSDH, 5 (29.4%) had a right sided cSDH, and 4 (23.5%) had bilateral cSDH. Two of the 4 patients with bilateral cSDH had unilateral drainage, while two patients had drains inserted bilaterally. In contrast to the tPA group, there were 2 (11.8%) patients in the TDD only group who did not have presence of midline shift. The remaining 15 (88.2%) patients did have presence of midline shift. The average length of stay for the TDD only patients was 7.65 days, with 41.2% being discharged home, 52.9% being transferred to another service, and 5.9% (1 patient) who expired. The cause of death was a cardiac event or pulmonary embolism.

Clinical data for the tPA and the TDD only group is presented **(Table 2)**. The tPA group had an average hematoma volume upon presentation of 142.10mL (range of 87.42 to 235.62mL), and the TDD only group had an average volume of 147.76mL (Range of 64.45 to 278.63mL). Additionally, the tPA group had a mean drainage volume of 382.7mL (range of 141.0-774.0mL) while the TDD only group had a mean drainage volume of 187.79mL (range of 48.0-808.0mL). **(Fig. 2).** Within the tPA group, the average volume of drainage before insertion of tPA was 92.0mL, while the volume of drainage following insertion of tPA was 290.7mL. The tPA group had a recurrence rate of 6.3% and the TDD only group had a recurrence rate of 37.5%. All of the recurrences happened within 3 months of their initial presentation. No procedural complications were present, and there were no documented adverse effects related to the use of tPA.

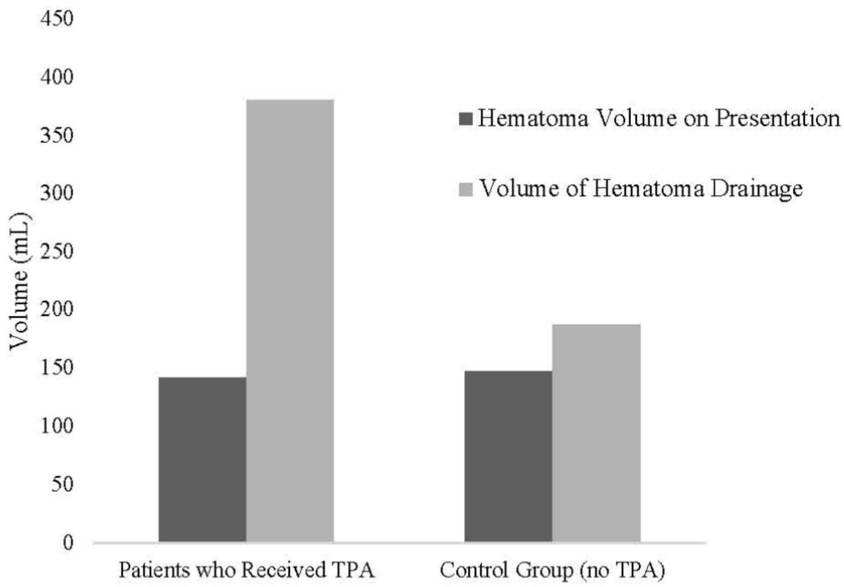

Fig 2: Hematoma volume on presentation and volume of hematoma drained for both the tissue plasminogen activator (tPA) cohort and the TDD only cohort.

Table 2: Clinical data for both the group who received tissue plasminogen activator (tPA) in addition to the twist drill drainage procedure and the control group who did not receive tPA

	Patients with tPA (n=17)		Patients without tPA (n=17)	
	Mean +/- SD	**Range**	**Mean +/- SD**	**Range**
Initial hematoma volume	142.1 +/- 38.8 mL	87.4-235.6 mL	147.76 +/- 55.2 mL	64.5-278.6 mL
Hours spent with drain inserted	63.0 +/- 32.9 h	19.5-142.5 h	34.8 +/- 15.0 h	16.8-69.0 h
Total volume drained	382.7 +/- 186.9 mL	141-774 mL	187.79 +/- 177.85 mL	48.0-808.0 mL
Pre tPA	92.0 +/- 69.9 mL	0-260 mL		
Post tPA	290.7 +/- 193.8 mL	65-734 mL		
Length of stay in neurosurgical services	9.71 d +/- 8.7		7.65 d +/- 6.9	
	n (%)		**n (%)**	
Discharge Details				
Discharge home	12 (70.6%)		7 (41.2%)	
Transferred to another hospital service	4 (23.5%)		9 (52.9%)	
Patient expired	1 (5.9%)		1 (5.9%)	
Hematoma recurrence				
Yes	1 (6.3%)		6 (37.5%)	
No	15 (93.8%)		10 (62.5%)	

*tPA = Tissue plasminogen activator.
n= number.
SD= Standard deviation.

DISCUSSION

As one of the most common neurosurgical presentations, and a disease that primarily targets the elderly, it is important for cSDH drainage to be maximized. cSDH is associated with significant morbidity, and therefore minimizing risk of recurrence is imperative. We found that administration of tPA, in addition to the TDD procedure, is an effective way to achieve clinically relevant drainage values of cSDH. Kwon et al. described a statistically significant difference in hematoma recurrence rates when the volume of drainage achieved is greater than 200mL compared to when it is less than 200mL.[12] Based on the results of the current study, the drainage volume in the tPA group was nearly double (1.9 times) this clinically relevant drainage value, while the volume of drainage in the TDD only group did not meet this value. It is of note that the tPA group had drains inserted for a longer period than the TDD only group (63.0 hours vs 36.4 hours). However, drain removal occurred when drainage had slowed to 0-50mL within a 24-hour period. As such, the discrepancy in length of time for the two groups would not account for the 193.81mL difference between the groups.

Our findings also support those of Neils et. al. who found that tPA (n=12) was effective at achieving average drainage values above 200mL, while their control group (n=73) did not achieve these values.[8] Similarly, Brazdzionis et al. found that administration of tPA in TDD patients who did not achieve significant drainage increased their daily drainage when compared to drainage volumes before tPA administration (n=6).[15] The current study builds on these findings by showing similar results in an increased number of tPA patients.

In the current study, recurrence rates in the tPA group were lower than previously reported epidemiologic studies of cSDH, while those in the TDD group were higher.[3,16] Toi et al. reported a recurrence rate of 13.1% (N=63,358),[16] although Feghali et al. completed a systematic review and found that recurrence rates have been reported to range from 0-76%.[3] They estimated that the reoperation rate for cSDH falls between 10-20%, but noted that there was high variability across different geographic locations and population samples.[3] Our study focused on a single center, and the patients included were otherwise representative of the general cSDH population based on male to female ratio, side of hematoma, and age.[16,17] It is therefore notable that the recurrence rate for the TDD alone group was six times higher than that of the tPA group.

The group who received tPA also had a higher percentage of patients who were discharged home compared to previous studies of patients treated by TDD alone,[18] and similar to the average rate of all cSDH patients.[16] This is clinically relevant as the cSDH patient group as a whole includes patients with smaller hematomas, that are often managed conservatively, thus improving the average prognosis of this group. It is therefore of note that the tPA patients had similar discharge statistics to the entire cSDH population, which includes those managed non-surgically. The TDD only group had a lower proportion of patients discharged home, with the majority of patients being transferred to another service. The discharge home rates were lower than previous studies of TDD patients alone, as well as all cSDH patients.

Adverse effects associated with local tPA have been documented in the context of intraventricular tPA for patients with aneurysmal subarachnoid hemorrhage, and include hemorrhagic complications, sterile meningitis, and ventriculitis.[8] Despite these findings, no adverse effects were noted in both the current and past studies of intrathecal tPA for the treatment of cSDH.[8,15]

Despite a lack of consensus on first line treatment for cSDH, there is a clear benefit to maximizing drainage and preventing recurrence.[12,13] Optimization of current treatment options is imperative, especially as the prevalence of cSDH is increasing with our ageing population. Although the current study was limited by a small sample size, the findings are consistent with current literature and demonstrated the efficacy of using tPA in addition to the TDD procedure in our population.

CONCLUSION

When used in addition to the TDD procedure, tPA was effective at treating cSDH in our population. Patients who received tPA had clinically relevant cSDH drainage, reduced cSDH recurrence, and therefore had decreased risk for complications associated with cSDH recurrence. Patients who received TDD without tPA did not have clinically significant drainage. This case series indicates strong clinical outcomes associated with the use of tPA in addition to TDD for treatment of cSDH.

List of Abbreviations

BHD: Burr hole drainage.
cSDH: Chronic subdural hematoma.
CT: Computed tomography.
SD: Standard deviation.
SPSS: Statistical Package for the Social Sciences.
TDD: Twist drill drainage.
tPA: Tissue plasminogen activator.

Disclosure

The authors report no conflict of interest in the materials or methods used in this study or the findings specified in this paper.

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