Tranexamic Acid for Treatment of Residual Subdural Hematoma After Bedside Twist-Drill Evacuation

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■ BACKGROUND: **Management of nonemergent, nonacute subdural hematomas (SDHs) ranges from observation to burr-hole evacuation or craniotomy, but recurrence rates are high. We evaluated the safety and efficacy of tranexamic acid (TXA) for the treatment of residual SDHs after bedside twist-drill evacuation.**

■ METHODS: **We performed a retrospective analysis of a prospectively maintained database from November 2013 to November 2014 for all patients who underwent placement of a bedside subdural evacuating port system (SEPS) followed by treatment with oral TXA (650 mg daily). All demographics, evidence of venous thromboembolism, and volumes of pertinent computed tomography were obtained.**

■ RESULTS: **Twenty subdural hematomas in 14 patients met the inclusion criteria for this study. Most SDHs were mixed density. Mean SDH volume on presentation was 145.96 ± 40.22 cm^3 with a mean midline shift of 9.44 ± 4.84 mm. Mean volumes decreased to 80.00 ± 31.96 cm^3 and midline shift improved to 4.44 ± 3.29 mm after SEPS placement ($P < 0.0001$ and $P = 0.0046$). All patients were placed on TXA after their procedure. Mean follow-up with computed tomography was 92.1 ± 27.5 days, and mean SDH volume at last follow-up was 7.41 ± 15.54 cm^3 with a mean midline shift of 0.19 ± 0.69 mm ($P < 0.0001$ and $P = 0.0002$). Percent volume reduction was significantly higher after TXA than after SEPS (91.31% vs. 40.74%; $P < 0.0001$). No increase or delayed recurrence of the SDH was noted during TXA treatment. All but 1 clinical presenting symptom improved at follow-up. No venous thromboembolisms were noted among the patients.**

■ CONCLUSIONS: **In our pilot study, chronic SDH volumes were reduced by 40.74% after SEPS drainage. The residual volume was reduced by an additional 91.31% during oral TXA treatment. No patients developed delayed recurrence or expansion of their SDHs. Further prospective studies are needed to evaluate the role of TXA for adjunctive treatment of chronic SDHs.**

INTRODUCTION

Nonacute subdural hematomas can cause significant morbidity and mortality. Previous studies have cited an incidence of 8–58 per 100,000 individuals.[1,2] With an aging population, the incidence of subdural hematomas (SDHs) is likely to increase significantly.

These are several options for treatment, ranging from observation to burr-hole drainage at the bedside or in the operative room to craniotomy. No clear consensus exists among practitioners concerning the best mode of treatment, although there has been an increasing trend toward bedside procedures, especially for poor surgical candidates.[2] Furthermore, most studies have analyzed outcomes with pure chronic SDHs; less information is available for mixed density hematomas.

All current treatments have associated risks and significant recurrence rates. In a systematic review of chronic SDHs treated by various modalities, 11.7%–28% of patients developed a recurrence.[2]

Key words
- Bedside evacuation
- Fibrinolysis
- Subdural hematoma
- Tranexamic acid
- Traumatic brain injury
- Venous thromboembolism

Abbreviations and Acronyms
CT: Computed tomography
SDH: Subdural hematoma
SEPS: Subdural evacuating port system
TDC: Twist-drill craniostomy
TXA: Tranexamic acid
VTE: Venous thromboembolism

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Multiple factors contribute to recurrence after evacuation. Hyperfibrinolytic activity may play a major role in the liquefaction and enlargement of chronic SDHs, and increased fibrinogen levels in the subdural fluid are associated with the presence of layering and mixed density SDHs with membranes.[3]

Theoretically, medications targeting hyperfibrinolytic activity may reduce the incidence of recurrence. Recently, the use of tranexamic acid (TXA), an antifibrinolytic agent, was shown to resolve small chronic SDHs managed nonoperatively.[4] The purpose of this pilot study was to examine the role of TXA as an adjunct to bedside evacuation of large mixed density SDHs.

METHODS

After obtaining institutional review board approval, we performed a retrospective search of a prospectively collected database for all patients at Bellevue Hospital Center undergoing bedside twist-drill evacuation of SDHs with a subdural evacuating port system (SEPS) from November 2013 to November 2014. In general, patients who had symptomatic subacute or chronic SDHs were candidates for SEPS. Those with mixed density acute and chronic components were candidates if the acute component was <50% of the overall hematoma volume. Multiple loculations were not a contraindication for SEPS. Patients who were noncompliant with their medications or did not have a follow-up computed tomography (CT) scan at a minimum of 3 months after treatment were excluded from analysis. Demographics, diagnosis, clinical presentation, use of oral anticoagulants, platelets, and international normalized ratio were recorded for each patient. All CT images were analyzed by a physician blinded to patient identifiers and time to imaging. SDH dimensions were measured from the CT scans, and hematoma volumes were calculated using the modified a × b × c/2 method.[5]

The SEPS placement procedure was performed in an intensive care unit setting and coagulopathies were corrected before the procedure. In all cases, conscious sedation with local anesthetic was used. The procedure details have been outlined previously.[6,7] After the procedure, the patients were monitored in an intensive care unit setting. Immediate postprocedure head CT was obtained if there was a concern for a complication. Otherwise, CT was obtained immediately before removal of the SEPS.

Patients were started on oral TXA at 650 mg daily after the SEPS was removed and were continued on the medication as outpatients for 6 months or until SDH resolution was shown on follow-up CT. All patients were seen in the clinic at 2 weeks, 1 month, and 3 months, with additional visits up to 6 months if there was a persistent residual on the 3-month scan. Lower extremity ultrasonography or contrast CT scans were obtained at the discretion of the treating physicians during the patients' hospital course and outpatient follow-up if there was a clinical suspicion for a deep vein thrombosis or pulmonary embolus.

The data were entered into a spreadsheet and analyzed using XLSTAT version 2015.1.01 (Addinsoft SARL, Paris, France). Statistical differences between groups were assessed using the Mann-Whitney U test. A P value of ≤ 0.05 was deemed to be significant.

RESULTS

Fourteen patients met the inclusion criteria for this study. Six patients harbored bilateral chronic SDHs, which were treated as separate units, so the analysis encompasses 20 SDHs. Three patients were excluded: 2 patients lacked follow-up imaging, and 1 patient was noncompliant with his medication. The average age was 56.4 ± 16 years and most were male (86%).

All patients were symptomatic on presentation. The most common symptoms were altered mental status, headache, and gait disturbance (Table 1). Most SDHs were mixed density (Table 2). The average volume of the SDH was 145.96 ± 40.22 cm^3 with a mean midline shift of 9.44 ± 4.84 mm. SEPS was performed on all patients. One patient required a craniotomy as a result of expansion of SDH after SEPS. After the initial bedside evacuation, SDH volume was reduced by 40.74% to a mean volume of 80.00 ± 31.96 cm^3 ($P < 0.0001$, Mann-Whitney), and mean midline shift decreased to 4.44 ± 3.29 mm ($P = 0.0046$, Mann-Whitney, Figure 1). TXA was started immediately in all patients after SEPS removal, except in 1 patient in whom TXA was initially deferred because of a history of atrial fibrillation. TXA was started after a recurrence of the SDH was seen on follow-up CT at 2 weeks after SEPS. Mean and median duration of TXA treatment were 90.3 ± 27 days and 87 days, respectively. Mean time to last radiographic follow-up was 92.1 ± 27 days after initiation of TXA. Mean SDH volume at last follow-up was 7.41 ± 15.54 cm^3, representing an additional 91.3% reduction from post-SEPS volumes ($P < 0.0001$, Mann-Whitney, Figures 2 and 3). Midline shift also continued to improve (0.19 ± 0.69 mm; $P = 0.0002$, Mann-Whitney).

TXA was discontinued once the follow-up CT scan showed significant resolution of the SDH. Most patients experienced rapid clinical improvement after the SEPS treatment, and this was maintained during the TXA treatment period. Ten of 14 patients (71%) had complete resolution of their presenting symptoms at last follow-up. Three patients reported persistent but improved symptoms, and 1 patient had baseline dementia, which persisted.

One patient had clinical suspicion for a venous thromboembolism (VTE), but lower extremity ultrasonography showed no evidence of deep vein thrombosis. The remainder of the patients were asymptomatic and further investigation was not pursued.

DISCUSSION

In our cohort of patients who underwent bedside evacuation of moderate to large mixed density SDHs followed by an oral TXA regimen, we achieved a 95% reduction of the initial SDH. SDH volumes were reduced by 40.74% after the initial SEPS drainage, and TXA treatment reduced the residual volumes by an additional 91.3%. More importantly, we noted no increase in the size of the

Table 1. Symptoms on Presentation and at 3-Month Follow-Up

Symptom	Presentation	Improvement?	%
Altered mental status	6	5	83
Headache	4	4	100
Gait disturbance	2	2	100
Focal neurologic deficit (speech, motor)	2	2	100
Total	14	13	93