Anticoagulation after thrombolytic treatment for frostbite: A case series

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Introduction

Historically, management of frostbite followed the adage "freeze in January and amputate in July." While rapid rewarming primarily addresses the ice crystal formation phase of damage, vascular injury and subsequent thrombosis result in the overall tissue damage. Through the use of tissue plasminogen activator (tPA), limb salvage for frostbite has been widely employed. tPA treatment of frostbite has reduced the number of digit amputations and benefits of systemic thrombolytic therapy has been demonstrated. Post-thrombolysis anticoagulation has changed as well. Our institution has changed its protocol from using warfarin after tPA therapy to aspirin (ASA) for ease of adherence. This study evaluates the use of warfarin or aspirin for management after tPA therapy.

Specific Aims

- To investigate for differences in the use of aspirin as compared to warfarin after tPA administration
- To describe the use of tPA in the initial management of patients with frostbite injury at an urban academic medical center

Methods

- Retrospective review of patients who received tPA for frostbite between January 2008 and April 2019.
- Data collected included age, height, weight, sex, past medical history, contributing factors to development of frostbite, toxicology screen on admission, cold exposure time, rewarming time, number of digits/limbs affected, and highest grade of injury.
- Outcomes data included medications received, number of digits/limbs amputated, length of stay, and number of follow up visits.

Photo 1: Frostbite of left lower extremity

Photo 2: Frostbite of right hand

Photo 3: Frostbite of left lower extremity

Photo 4: Frostbite of right hand

Results

Table 1: Patient Demographics

	ASA group N = 7	Warfarin group N = 3	P value
Age	31.86 ± 13.43	64.67 ± 4.04	<0.001
Male sex	7 (100%)	3 (100%)	--
Height	178.45 ± 3.79 N = 4	178.63 ± 2.89	0.941
weight	70.29 ± 8.51	86.80 ± 7.80	0.021
BMI	21.54 ± 2.77 N=4	27.18 ± 1.94	0.030
Alcohol abuse	5 (71.4%)	1 (33.3%)	0.500
Drug abuse	3 (42.9%)	1 (33.3%)	1.00
Homelessness	1 (14.3%)	1 (33.3%)	1.00
Mental illness	1 (14.3%)	0 (0%)	1.00
Diabetes	1 (14.3%)	1 (33.3%)	1.00
Exhaustion	0	0	--
Dehydration	0	0	--
Smoker/pack years	13.29 ± 14.37	8.58 ± 14.22	0.647
Delayed presentation	2 (28.6%)	2 (66.7%)	0.500
Cold exposure time	57.50 ± 45.00 N = 4	1192.5 ± 1622.81 N=2	0.503
Rewarming time	203.0 ± 52.33 N= 2	n/a	--
Tox screen positive	4 (57.1%)	2 (100%) N = 2	0.500
Alcohol positive	4 (80%) N = 5	1 (50%) N = 2	1.00
Alcohol level	138.8 ± 169.01 N=5	84.5 ± 119.50 N = 2	0.702
Number of limbs affected	2 ± 1	2 ± 0	1.00
Number of digits affected	12.71 ± 12.31	10.00 ± 0.00	0.722
Highest grade of injury	3.43 ± 0.79	3.00 ± 1.00	0.483

Table 2: Outcomes

	ASA 325 mg group	Warfarin group	P value
LOS	8.0 ≥ 4.0	9.37 ≥ 7.23	0.643
# limbs amputated	0 ± 0.0	0.67 ± 1.15	0.423
# digits amputated	0.14 ≥ 0.38	3.67 ± 5.51	0.383
Days from injury to digit amputation	6.00 N = 1	291.00 N = 1	--
# follow up visits	3.86 ± 4.74	8.0 ± 9.64	0.371
Days from discharge to last follow-up	114.5 ± 53.46 N = 4	158.67 ± 144.14 N=3	0.589

Conclusion

These findings indicate that there may not be a significant difference in clinical outcomes when comparing patients who took ASA to warfarin after tPA therapy. It is common for patients to have a delayed presentation and prolonged rewarming time, resulting in ineligibility to receive tPA. Single center frostbite studies are limited due to sample size and multi-centered studies are necessary for future studies.

Applicability of Research to Practice

ASA 325 mg daily is be a suitable alternative to warfarin therapy after tPA administration following a frostbite injury.

References

1. Activase (alteplase) [prescribing information] San Francisco, CA: Genentech; February 2015.
2. Bruen, Kevin J., et al. "Reduction of the incidence of amputation in frostbite injury with thrombolytic therapy." *Archives of Surgery* 142.6 (2007): 546-55.
3. Gonzaga, Teresa, et al. "Use of Intraarterial Thrombolytic Therapy for Acute Treatment of Frostbite in 62 Patients with Review of Thrombolytic Therapy in Frostbite." *J Burn Care Res* (2015): 211-2.
4. McIntosh, Scott E., et al. "Wilderness medical society practice guidelines for the prevention and treatment of frostbite: 2014 update." *Wilderness & environmental medicine* 25.4 (2014): S43-S54.
5. Twomey, John A., George L. Peltier, and Richard T. Zera. "An open-label study to evaluate the safety and efficacy of tissue plasminogen activator in treatment of severe frostbite." *Journal of Trauma and Acute Care Surgery*59.6 (2005): 1350-1355.
6. Wexler A, Zavala S. The use of thrombolytic therapy in the treatment of frostbite injury. *J Burn Care Res*. 2017 Sep/Oct;38(5):e877-e881.