Online Supplement

Systemic Hematologic Status Following Intraventricular rt-PA for Intraventricular Hemorrhage

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Supplemental Methods

Inclusion criteria into CLEAR IVH included age 18-75 years, admission spontaneous ICH volume $\leq$ 30cc (by ABC/2 method), admission systolic blood pressure < 200 mmHg, Historical Rankin score 0 or 1, and obstructive hydrocephalus requiring urgent external ventricular drainage. Patients were excluded if they had a suspected or untreated aneurysm or AVM, clotting disorders, a platelet count < 100,000, INR > 1.7, active internal bleeding, current use of heparin, coagulopathy with prothrombin time (PT) or partial thromboplastin time (PTT) outside of normal range, or infratentorial hemorrhage. All patients with an intraventricular catheter (IVC) inserted in the initial 24 hours of illness to treat IVH were considered. Patients were enrolled within 48 hours after diagnostic head CT. Subjects were randomized to receive either intraventricular rt-PA (0.3mg q12h, 1.0mg q12h, 1.0mg q8h, or 3.0mg q12) or placebo (saline). Subjects could not receive intravenous anticoagulants or low molecular weight heparin for deep venous thrombosis prophylaxis or antiplatelet agents until 72 hours post last dose. Use of subcutaneous unfractionated heparin was not specifically restricted. This study was approved by the Institutional Review Boards of all participating centers.

Seventy-eight patients had clinical data that allowed for pre/post dosing comparison of coagulation parameters. All patients had occlusion of the 3rd and 4th ventricles prior to first dose administration. For a lab draw to be eligible for analysis, it required at least one of three coagulation parameters: PT, PTT, or platelet count. Plasma plasminogen and fibrinogen concentrations were included when available. Subjects were included if they had data for the same coagulation parameter at all time points necessary for analysis. The use of anticoagulants during treatment, such as heparin and warfarin, was recorded.

The percent change for each outcome was calculated as (post treatment – baseline)/baseline. To compare coagulation states of patients who experienced brain bleeding to those who did not, we compared the maximum and minimum coagulation values during treatment.

Supplemental Tables

Table S1. Comparison of Pre- and Post-Ventricle Clearance Coagulation Parameters

Coagulation Parameter	Baseline		Pre-Ventricle Clearance		Post-Ventricle Clearance		% Δ in Coagulation Parameter Between Pre- and Post-III/IV Ventricle Clearance					
	rt-PA	Placebo	rt-PA	Placebo	rt-PA	Placebo	rt-PA (%Δ)			Placebo (%Δ)		
	Mean ± SD (n)	Mean ± SD (n)	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Median	Range	Mean ± SD	Median	Range
Platelet Count (plt/mm^3)	231±50 (19)	226±51 (7)	213±57	191±35	216±48	226±68	3.3±13.1	2.74	-21.8 – 24.5	17.1±15.9	22.0	-4.0 – 40.9
PTT (Sec.)	29.0±3.3 (19)	30.4±4.5 (6)	29.2±3.6	30.6±5.1	29.3±4.9	29.4±4.6	-0.05±9.3	1.57	-26.9 – 12.5	-2.6±16.0	2.9	-28.1 – 14.3
PT (Sec.)	12.4±2.0 (19)	12.2±2.0 (7)	13.2±4.3	11.7±1.7	12.2±2.1	11.6±2.0	-4.8±11.6	-2.31	-48.3 – 7.2	-1.7±4.1	-2.9	-6.2 – 5.0
Fibrinogen (mg/dL)	464±145 (12)	430±110 (6)	574±174	532±166	685±180	508±138	24.1±24.8	20.7	-24.4 – 66.8	0.05±23.9	4.5	-41.1 – 21.5
Plasminogen (%)	103±17 (7)	114±23 (3)	107±27	123±32	109±14	139±50	4.9±16.9	4.27	-23.9 – 29.2	11.5±11.5	7.8	2.3 – 24.3