Additional Brain Ischemia Protection Time with Prehospital Versus In-Hospital Neuroprotective Agent Start

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Learning Objective

- To determine the additional time gained when implementing a neuroprotective agent in the prehospital setting for acute ischemic stroke treatment

Background

- As time lost is brain lost in acute ischemic stroke, neuroprotective therapies are projected to exert greatest benefit the sooner after onset they are started
- The goal of neuroprotective treatments in development for acute ischemic stroke is to slow infarct growth (penumbra loss), so that more salvageable brain is present when reperfusion is achieved
- Strategies for early neuroprotective therapy start include:
  1) Initiation by paramedics in standard ambulances in the field
  2) Initiation in by MDs/nurse in hospital after initial brain imaging
- This study was undertaken to quantify the additional treatment time gained with field neuroprotective agent start

Method

- Comparative analysis of two randomized trials of neuroprotective agents:

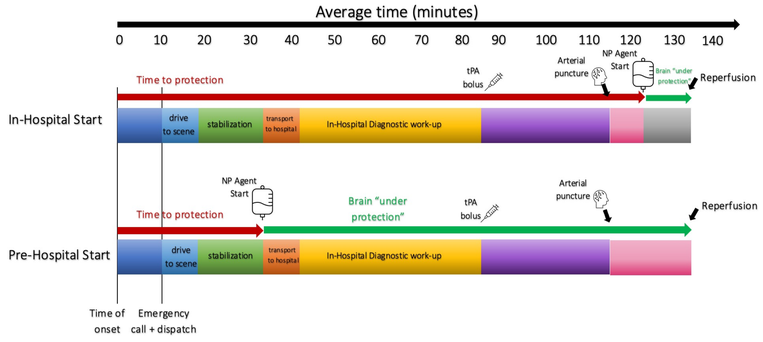
1. Prehospital strategy: Field Administration of Stroke Therapy-Magnesium (FAST-MAG) Trial conducted from 2005 to 2013 within 315 ambulances and 60 receiving hospitals in Southern California
2. In-hospital post-imaging strategy: Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1) trial conducted from 2017 to 2019 at 48 hospitals in North America, Europe, Australia and Asia

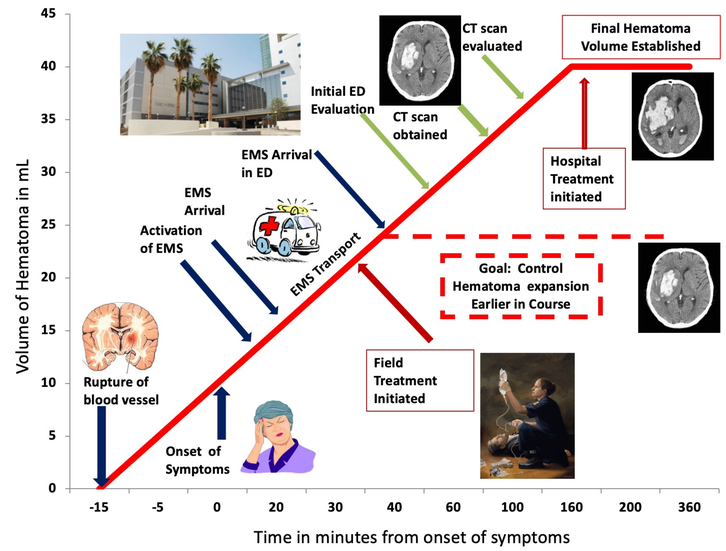
Results

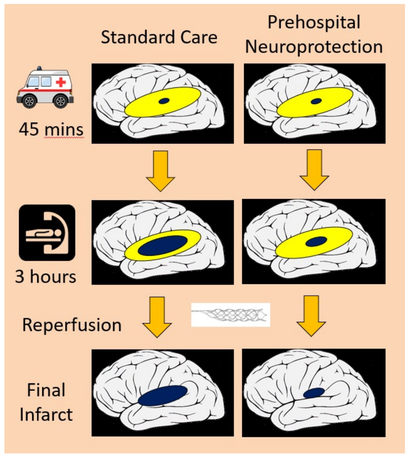
- FAST-MAG (pre-hospital) clinical trial: Stroke onset to neuroprotective agent start time was median 48 minutes; ED arrival to neuroprotective agent start time was median -9 minutes, and time for brain protective effect (NP drug start to expected reperfusion) was median 98 minutes.
- ESCAPE-NA1 (in-hospital) clinical trial: Stroke onset to neuroprotective agent start time was median 201 minutes; ED arrival to neuroprotective agent start time was median 64 minutes, and time for brain protective effect (NP drug start to reperfusion) was median 16 minutes.

Figures/Tables

Neuroprotective Study Agent Treatment Strategies







Figures/Tables

Table 1. Demographic and Baseline Characteristics of Patients Treated with EVT and Patients Treated with IVT

Feature	EVT Patients (n=44)	IVT patients (n=418)
Age, mean (SD), y	69.3 (12.01)	70.3 (13.5)
Female, No. (%)	27 (61.4)	190 (45.5)
Race, No. (%)		
White	38 (86.4)	319 (76.9)
Black/African American	4 (9.1)	56 (13.3)
Asian	2 (4.5)	43 (9.8)
Other	0 (0.0)	0 (0.0)
Hispanic ethnicity, No. (%)	10 (22.7)	84 (22.0)
Medical history, No. (%)		
Hypertension	33 (75.0)	323 (77.3)
Diabetes	10 (22.7)	96 (23.0)
Hyperlipidemia	20 (45.5)	215 (51.4)
Atrial fibrillation	20 (45.5)	98 (23.4)
Heart disease	9 (20.5)	128 (30.6)
Prior Stroke/TIA	5 (11.4)	62 (14.8)
Tobacco use	3 (6.8)	78 (18.7)
Any alcohol use	16 (36.4)	151 (36.1)
SBP, mean (SD), mm Hg		
Prehospital	155.6 (26.4)	155.9 (25.4)
Hospital arrival	158.8 (32.4)	155.0 (25.7)
DBP, mean (SD), mm Hg		
Prehospital	89.8 (17.8)	86.8 (17.4)
Hospital arrival	81.7 (20.1)	82.9 (17.6)
Severity scores		
Prehospital GCS		
Median (IQR)	15.0 (11.0 – 15.0)	15.0 (12.0 – 15.0)
Mean (SD)	13.3 (2.2)	13.6 (2.2)
Prehospital LAMS		
Median (IQR)	5.0 (5.0 – 5.0)	4.5 (3.0 – 5.0)
Mean (SD)	4.7 (0.8)	4.1 (1.1)
Hospital arrival NIHSS		
Median (IQR)	18.5 (11.8 – 23.3)	12.0 (7.0 – 18.0)
Mean (SD)	17.9 (8.7)	12.9 (7.7)

Table 2: Time Interval Results

Strategy	Prehospital	In-Hospital
Trial	FAST-MAG	ESCAPE NA-1
Stroke Onset to NP Start	48 mins	201 mins
"ED Door to NP Start"	- 9 mins	64 mins
Time "Brain Under Protection"	98 mins*	16 mins

*98 minutes with modern workflow as in ESCAPE NA-1; 215 minutes with historical workflow in FAST-MAG

Discussion

- A substantially greater amount of treatable ischemia time can be gained by implementing a neuroprotective agent in the pre-hospital setting
- The additional amount of time during which the brain had potential neuroprotection was 1 hour 22 minutes with prehospital vs in-hospital NP agent start
- Neuroprotective therapy start in the field enabled the majority of patients to receive initial treatment in the "golden hour" – the first 60 minutes after onset

Limitations

- These studies were performed among patients enrolled in randomized clinical trials. Though the trial entry criteria were broad, the results may not be generalizable to patients who did not meet study entry criteria, such as patients with later first activation of the EMS system.
- Available time interval data from the ESCAPE NA-1 trial were in the form of median rather than mean time intervals. Time period values constructed by adding/ subtracting this data may differ mildly from true values that would have been yielded by means. FAST-MAG analyses did use mean values.

Conclusion

- Starting a neuroprotective agent in the pre-hospital (versus in-hospital) enables faster treatment start and an enhanced brain protection interval in acute ischemic stroke
- These findings provide support for the increased performance of ambulance-based, prehospital treatment trials in the development of neuroprotective stroke therapies

References and Acknowledgements

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