Clot-busting drugs effective in patients with unwitnessed strokes

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Clot-busting treatment should be considered for patients last seen healthy within a few hours before having a stroke, according to research presented at the American Stroke Association's International Stroke Conference 2010.

A Canadian study analyzed outcomes of clot-busting drugs given to patients based on when they were last seen in their usual state of health ("time last seen normal") compared to patients who had someone witness the start of their stroke symptoms.

The "time last seen normal" patients did just as well as those with witnessed strokes, having no more disabilities when they were discharged from the hospital and being no more likely to require discharge to a nursing facility. In addition, patients treated based on "time last seen normal" were only 65 percent as likely to have bleeding in the brain — a potentially serious complication of treatment (7.9 percent vs. 12.1 percent).

"Every 20-minute delay increases the risk of hemorrhage," said Demetrios Sahlas, M.D., M.Sc., FRCPC, the Michael G. DeGroote Professor in Stroke Management at McMaster University in Hamilton, Ontario. "The patients treated based on 'time last seen normal' may have had their strokes minutes or hours after they were last seen, so overall they may have been at lower risk."

Treatment based on "time last seen normal" within the treatment window

likely overestimates the time of symptom onset, which suggests that these patients are more likely to experience beneficial outcome, Sahlas said.

When a stroke results from a blood clot in a vessel in or leading to the brain (an ischemic stroke), intravenous medication to dissolve the clot, called recombinant tissue-plasminogen activator (tPA), can limit the debilitating effects. However, after several hours, the likelihood that the drug will improve outcome decreases and the risk it will cause bleeding in the brain and result in greater damage increases.

Traditionally, the time window has been three hours from the time of the stroke. But recent studies — including randomized trial data from the European Cooperative Acute Stroke Study (ECASS-3) published in 2009 — suggest that the window could be increased to 4.5 hours for selected patients. The American Stroke Association also changed its recommendation to use tPA up to 4.5 hours in some patients.

In the current study, investigators used the large Registry of the Canadian Stroke Network (RCSN) to compare the outcomes of 1,562 ischemic stroke patients treated at the 11 stroke centers in Ontario between 2003 and 2008. Fifty-one percent were male (average age 72) and 49 percent female (average age 75). Risk factors and the severity of initial symptoms were similar in the 1,082 patients (69 percent) witnessed having a stroke and the 480 (31 percent) treated based on "time last seen normal." Patients with unwitnessed strokes were more likely to be treated greater than 3 hours after "time last seen normal" (27 vs. 12.1 percent).

"If anything, patients identified at the time last seen normal are better candidates for tPA than those in the ECASS trial, which enrolled only those witnessed having a stroke," said Sahlas, who practices at the Central South Ontario Regional Stroke Centre at Hamilton Health

Sciences.

Patients in the registry included many who would have been excluded from the ECASS-3 trial because they were over 80 years of age or had previous strokes or diabetes.

"This study provides added justification for extending the window and taking all comers — not just those witnessed having their strokes," Sahlas said.

"If you come across someone who has had a stroke, act quickly. Be aware that 'time is brain' and seek immediate medical attention. If you last saw someone normal an hour or two ago, that doesn't necessarily disqualify them from receiving tPA."

Researchers who conducted the retrospective study said further prospective research is needed, particularly within the extended time window, to determine whether a difference in clinical outcome is observed.

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