Study confirms benefit and safety of extending treatment window for stroke to 4.5 hours

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Extension of the timeframe for alteplase treatment after acute stroke from 3 hours up to 4.5 hours is a safe option and has not resulted in delayed treatment of patients. The longer time window offers an opportunity to patients who cannot be treated earlier, but the benefits quickly lessen with time, and patients should be treated as early as possible. These are the conclusions of an Article published Online First and in the August edition of the *Lancet Neurology*, written by Professor Nils Wahlgren from Karolinska University Hospital in Sweden and international colleagues.

Previous research from ECASS III and SITS-ISTR has shown the benefit and safety of alteplase treatment in the 3-4.5 hour window after stroke. However, the SITS-ISTR study reported a possible increase in symptomatic intracerebral haemorrhage and death within 3 months in patients treated late (within 3□□.5 hours) compared with early (within 3 hours). Additionally, questions remained about whether the increased time window could result in a longer delay in the treatment of patients and potentially effect outcome, as fast treatment still offers the best chance of recovery.

In this study, the authors did a follow-up safety analysis from SITS-ISTR to assess the implementation of the longer time window after publication of the ECASS III and SITS-ISTR studies in September 2008, the effect on admission-to-treatment time, and to confirm or refute whether

alteplase remains safe when given beyond 3 hours.

23 942 patients were registered in SITS-ISTR between December 2002 and February 2010 and grouped according to whether they were registered before or after October 2008.

Findings showed that the proportion of patients receiving alteplase treatment within 3-4.5 hours in the last quarter of 2009 was three times higher than in the first quarter of 2008 (282 of 1293 [22%] vs 67 of 1023 [7%]).

The median admission-to-treatment time was 65 minutes for patients registered both before and after October 2008, suggesting that the extended time window had not resulted in delayed treatment of patients.

After adjusting for confounding variables, patients treated within 3-4.5 hours had higher rates of symptomatic haemorrhage and death and worse functional outcome at 3 months than patients treated within 3 hours.

The authors say: "Since October 2008, thrombolysis within 3-4.5 hours after stroke has been implemented rapidly, with a simultaneous increase in the number of patients treated within 3 h…This has not been at the expense of increased delay from admission-to-treatment time. Increases in the risk of symptomatic intracerebral haemorrhage and mortality in the time window are minor and are outweighed by the benefit of treatment."

They conclude: "Alteplase remains safe when given with short treatment delays beyond 3 h. Nevertheless, our results emphasise that patients should be treated as early as possible."

In a Comment, Scott E Kasner from the University of Pennsylvania Medical Center, Philadelphia, USA, and Steven R Levine from State

University of New York Health Science Center and School of Medicine, New York, USA, point out that despite the ample evidence of the efficacy and effectiveness of alteplase, neither the European Medicines Agency or the US Food and Drug Administration have approved alteplase for use in the extended time window. They conclude by calling for regulatory approval to ensure that this treatment option is available to all patients.

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