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The virtual ESO-WSO 2020 Conference, jointly organised by the European Stroke Organisation and the World Stroke Organization, presents latest stroke research results and developments.

EOS: Intravenous alteplase is approved for acute stroke treatment within 4.5 hours of known symptom onset. This individual patient data meta-analysis 'Evaluation of unknown Onset Stroke thrombolysis trials' (EOS) from five large clinical trials (WAKE-UP, EXTEND, THAWS, ECASS-4 and MR WITNESS) investigated a high level of evidence for the use of advanced MRI or CT-perfusion to guide treatment with intravenous alteplase in unknown onset stroke. These results confirm the effectiveness of this new treatment option for acute ischemic stroke, show its efficacy for all ischemic stroke severities, and allow it to be applied more frequently to a larger population of stroke patients who are so far excluded from effective acute revascularization treatments.

BASC: Uncertainty persists over the effects of BP lowering in acute spontaneous intracerebral hemorrhage (ICH), especially over timing and strategy. This systematic review of individual patient data meta-analysis of randomised trials 'Blood pressure in Acute Stroke Collaboration' (BASC) found no overall beneficial effect on functional recovery from acute ICH, despite a clear reduction in hematoma growth.

EOS

Thrombolysis in patients with unknown onset strokes – guided by advanced imaging

Thrombolysis after an ischaemic stroke – i.e. the use of medication to dissolve a blood clot in a cerebral blood vessel – has revolutionised therapy in the past 20 years. Yet this form of treatment has so far mainly been used within 4.5 hours of the stroke onset, a narrow time frame. This excluded patients with unknown onset strokes, including patients with strokes occurring while they were asleep. A new meta-analysis of the "**E**valuation of unknown **O**nset **S**troke thrombolysis trials (EOS) collaborators" from current studies confirms that these patients can also benefit from thrombolysis if it is based on findings on advanced neuroimaging.

Götz Thomalla (Professor for Imaging-based clinical stroke research, Department of Neurology, University Medical Center Hamburg-Eppendorf Germany) and his co-authors tried to confirm whether intravenous thrombolysis is safe and effective for patients for whom the onset of a vascular occlusion is unknown and if so, how safe and effective. For about 20% of people suffering acutely from an ischaemic stroke, the onset of the stroke is unknown.

Individual randomised studies have shown that thrombolysis treatment can be suitable in these cases if advanced imaging procedures such as magnetic resonance imaging (MRI) or computer tomography (CT) are

used to determine the brain tissue that can still be saved through thrombolysis. If this is the case, it would still make sense to restore the blood supply to the affected area of the brain.

In their study, the scientists analysed the individual data of patients with an unknown onset ischaemic stroke from five major randomised clinical studies published up to 21 September 2020, i.e. WAKE-UP, EXTEND, THAWS, ECASS-IV and MR WITNESS. The primary end point (evaluation criterion) was a favourable treatment outcome (no or no significant disability according to the modified Rankin Scale; mRS 0-1) at 90 days after therapy. The safety criteria were the survival rate, severe disability or death (mRS 4-6) and the occurrence of a symptomatic intracerebral haemorrhage.

All in all, the data of 843 patients were analysed from the four selected studies. 429 (51%) had been treated with intravenous thrombolysis (rtPA/alteplase) to dissolve the thrombus in their brain. 414 patients (49%) had received a placebo and were otherwise given standard care.

A favourable treatment outcome (mRS 0-1) occurred in 199 out of 420 patients (47%) who had undergone thrombolysis but only in 160 out of 409 patients (39 %) in the placebo group. The difference between the two patient groups was statistically significant (p=0.011).

Regarding safety, the percentage of patients who exhibited a severe disability or were dead at 90 days (mRS 4-6) amounted to 21% for the thrombolysis group and 25% for the placebo group. This difference was not statistically significant. In the thrombolysis group, more patients died (6%, versus 3% died in the placebo group, statistically significant). Among the participants who had received the drug therapy to dissolve their thrombus, 3% (11 patients) suffered a symptomatic intracerebral haemorrhage; this figure was 1% for the placebo group (2 patients), a difference which was also statistically significant (p=0.024).

Although this new acute treatment of acute stroke may require more extensive imaging (MRI, CT) than the usual thrombolysis with known onset stroke, it is a welcome advance for patients with an unknown onset stroke, especially a stroke detected when waking up. The efficacy of this treatment is now proven despite the already known risks of haemorrhage.

The research is published today in The Lancet.
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32163-2/fulltext

Lowering of blood pressure (BP) in acute intracerebral haemorrhage (ICH): results of an IPD-MA of RCTs

Until now, scientific studies have not yet sufficiently explained what are the benefits from intensive BP lowering in patients with an intracerebral haemorrhage (haemorrhagic stroke), particularly over the timing and type of strategy. In this systematic review with meta-analysis of individual patient data from previous randomized controlled trials, Craig Anderson (Professor of Neurology and Epidemiology, Faculty of Medicine, UNSW Sydney and The George Institute for Global Health, Australia and China) and his co-authors attempted to answer this question.

The authors were able to use individual patient data from 16 randomized controlled trials on BP management within 7 days of the onset of the acute disease process in adult patients with haemorrhagic insult. Overall, these studies included 6,221 patients eligible for analysis (mean age of 64 years, 36% females, median time at enrolment 3.8 hours after onset of symptoms).

An intensive antihypertensive therapy lowered the BP median to 158.6 mmHg systolic within an hour after treatment began (placebo: 166 mmHg) and a median of 144.3 mmHg within 24 hours (placebo: median of 156.4 mmHg). However, the difference between treatment arms was again smaller in the period between 2 to 7 days (median systolic blood pressure 143.7 mmHg in the intensive treatment arm and 151 mmHg with placebo).

The primary outcome (primary evaluation criterion) was functional status, defined by the modified Rankin Scale (mRS score; 0-6) at 90 days after acute ICH. The authors also evaluated the proportional change in haematoma growth with therapy being provided.

Early BP lowering in patients with ICH was not accompanied by a statistically significant improvement in function at day 90 after the acute insult (odds ratio: 0.97; p=0.503). However, patients in the intensive BP treatment arm did show reduced haematoma volume growth in the first 24 hours (odds ratio: 0.75; p=0.007). The subgroup of patients treated with a BP target did show a potential benefit when compared with patients treated based on a drug class.

Further studies are needed to understand this somewhat contradictory finding of the main outcomes and to identify the best timing, BP lowering strategy, and drug classes to show a potential clinical benefit.

Additional information, including video interviews with principle investigators and summary slides are available on the ESO-WSO 2020 Media Portal https://eso-wso-conference.org/media-portal/

You can find the recording of yesterday's press conference on the media portal: https://eso-wso-conference.org/media-portal/

Issued by the ESO-WSO 2020 PR Committee

For more information or to schedule interviews, please send your request to:
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We kindly ask all media representatives to send their press clippings after the congress to urban.schenk@medical-media-consulting.at
Many thanks in advance!