Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial

In this phase 2 clinical trial, the authors sought to explore whether cerebrolysin, a neuroprotective neuropeptide preparation of porcine origin, also had neurotrophic and neuroprotective effects on recovery after stroke. They enrolled 208 supratentorial ischemic stroke patients with no premorbid stroke disability, aged 18 to 80 years, and with an action research arm test score of <50. Patients were randomized to 30 mL cerebrolysin daily versus placebo, beginning at 24 to 72 hours post stroke, and for a total of 21 days. Patient received accompanying standardized rehabilitation program for 21 days, beginning at 48 to 72 hours after stroke onset. The primary study end point was action research arm test at day 90. The mean age of the patients was 64 years, 63.9% were men, and mean National Institutes of Health Stroke Scale score was 9.2. The mean absolute changes in the action research arm test scores at 90 days compared with those at baseline were 30.7±19.9 (32.0–36.5) for cerebrolysin and 15.9±16.8 (11.0–22.0) for placebo. An increase in the action research arm test score was observed in 92.3% of the cerebrolysin-treated patients versus 84.2% of the placebo-treated patients. Patients in the cerebrolysin group (2.9%) and in the placebo group (6.7%) had serious adverse events, none of which seemed related to the study medications. No patients died in the cerebrolysin group. Therefore, cerebrolysin had a beneficial effect on function and global outcome in early rehabilitation patients after stroke, with a good safety profile. These encouraging results prompt consideration of larger future clinical trials of cerebrolysin for improved early ischemic stroke recovery. See p 151.

Trajectories of Vasomotor Symptoms and Carotid Intima Media Thickness in the Study of Women’s Health Across the Nation

Menopausal vasomotor symptoms (VMSs) have been linked to the development of subclinical cardiovascular disease (CVD) among postmenopausal women. However, it is not entirely well understood whether the time course of presentation of VMS (ie, early versus late onset, duration of symptoms, etc) has any relationship to the development of CVD. In this study, Thurston et al aimed to elucidate this relationship by analyzing carotid intima media thickness in postmenopausal women according to the temporal trends of VMS. They analyzed data from 811 multiethnic women from a longitudinal cohort study, the Study of Women’s Health Across the Nation. At baseline enrolment, women were aged 42 to 52 years; had a uterus and ≥1 ovary; were not pregnant, lactating or on oral contraceptives/hormone therapy; and had ≥1 menstrual cycle in the previous 3 months. Participants were followed up annually for 13 years and had a carotid ultrasound for carotid intima media thickness assessment at year 12. At visit 12, the mean age was 59 years and women were mostly overweight, nonsmoking, and normotensive. Women with consistently high VMS and early onset VMS (starting up to a decade before the last menstrual period) also had a significantly more adverse CVD risk factor profile and significantly higher carotid intima media thickness than women with consistently low VMS. Furthermore, in models adjusted for demographic and CVD risk factors, early onset VMS remained significantly associated with higher mean and maximal carotid intima media thickness. There were no significant interactions between VMS trajectories and race/ethnicity in relation to carotid intima media thickness. These interesting study findings highlight that early VMS may signal poorer future cardiovascular health in women. These results are in line with other studies that have shown that VMS may be related to endothelial disruption, increased inflammatory profile, and adverse adipokine profile. The authors suggest that attention be paid to premenopausal or postmenopausal women with early VMS and that they receive early screening and management for CVD. See p 12.

Large Volumes of Critically Hypoperfused Penumbral Tissue Do Not Preclude Good Outcomes After Complete Endovascular Reperfusion: Redefining Malignant Profile

In this study, Nogueira et al aimed to assess the validity of the malignant profile computed tomographic perfusion component of $T_{max}>10$ s $>100$ mL lesion on the outcomes of patients with acute ischemic stroke undergoing complete arterial reperfusion with contemporary technology. Their hypothesis was that with more rapid reperfusion, such as obtained with stent retrievers, previously established parameters might not adequately identify patients at risk for malignant reperfusion and intracranial hemorrhage after endovascular reperfusion therapy. The authors retrospectively reviewed prospectively collected interventional cases from 2010 to 2015 at a tertiary academic center. They included patient with acute ischemic stroke involving anterior circulation intracranial large-vessel occlusions that achieved full reperfusion (modified Treatment in Cerebral Ischemia grade 3) and that had adequate pretreatment computed tomographic perfusion. The primary outcome variable was the effect of the $T_{max}>10$ s lesion spectrum on infarct growth, as seen by magnetic resonance imaging stroke volumes (86%) or noncontrast computed tomographic volumes within 5 days of therapy. One hundred thirteen patients were included in the study, and mean infarct growth volume was 19.1±41.3 mL. On multivariate analysis, baseline National Institutes of Health Stroke Scale score and baseline infarct core volume were independently associated with malignant profile perfusion lesion ($T_{max}>10$ s $>100$ mL). However, $T_{max}>10$ s $>100$ mL lesions were not associated with parenchymal hematomas, 90-day good outcome, or infarct growth. The authors conclude that in the absence of large infarct cores, large $T_{max}>10$ s lesions should not be considered as an exclusion criterion for contemporary endovascular reperfusion therapies. See p 94.
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