Prolonged statins administration in patients with previous history of ischemic stroke

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Cardiovascular and cerebrovascular diseases (including heart attacks and ischemic stroke (IS)) remain major causes of death and disability incidence in the adult population in many countries.

Purpose of the study: to conduct clinical and pharmacological study of early and long-term (24 months is a lower limit) statins administration in treatment of acute hemispheric ischemic stroke.

Study methodology. A 24-months study was conducted to assess efficacy of early and long-term statins administration in treatment of acute hemispheric ischemic stroke. During the first stage, there were enrolled 210 subjects with peracute ischemic stroke. Arm I (n = 105) therapy included background treatment according to the recommendations for stroke management of European Stroke Initiative (EUSI, 2003), European Stroke Organization (ESO, 2008), or to Roszdrav guidelines (2008-2010) aimed at homeostasis or central/cerebral hemodynamics normalization. Standard therapy in both groups included antiplatelet agents (e.g., aspirin), neurotrophic drugs and neuromodulators, as well as recovery of hypertension, atrial fibrillation and congestive heart failure (CHF). Arm II (n = 105) therapy additionally included simvastatin, 40 mg. Analyzed parameters: lethality, incidence of recurrent cardiovascular events, grade of endothelial dysfunction, neurological status or lipid profile dynamics, and simvastatin safety. During the second stage, dynamic comparative analysis of study parameters depending on the drug (hydroxymethylglutaryl-coenzyme A reductase group) and treatment duration was performed.

Study results. Acute ischemic stroke patients demonstrated 4 to 6 fold increase of desquamated endotheliocytes circulating in blood. Concomitant early administration of simvastatin 40 mg a day on top of neuroprotective and antihypertensive therapy resulted in fats and neurological status normalization, and endothelial dysfunction regression and clinically significant events' incidence decrease (those including fatal cases, strokes, acute myocardial infarctions, pulmonary embolism, or hospitalizations for any reason). Positive dynamics is also observed after delayed (one year after ischemic stroke) but long-term (at least 12 months) administration of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase group drugs. At the end of the follow-up period (Day 720) neither of the drugs (simvastatin, atorvastatin, rosuvastatin) showed Scandinavian Scale or National Institutes of Health Stroke Scale

(NIHSS) score advantage in affecting the end-points or neurological impairment grading. Endothelial dysfunction regression and improvement of Mini-Mental State Examination (MMSE) score were more marked in simvastatin subgroup of subjects who have been regularly administered the drug for 2 years.

Conclusion. Based on the results of our study, early administration of simvastatin 40 mg a day in patients with acute ischemic stroke against neuroprotective and antihypertensive therapy may have favorable effects, particularly, lipid profile normalization or neurological status improvement. The results obtained support mutually dependent positive effect of simvastatin 40 mg therapy onto cardiovascular and renal pathophysiological continuum in subjects with initial hemispheric ischemic stroke and support rationale of the drug's administration in such population. The results of our study demonstrate that long-term (24 months) simvastatin 40 mg/day treatment after ischemic stroke is safe and decreases the incidence of clinically significant events (such as death cases, strokes, acute MIs, pulmonary artery thromboembolia (PATEs), or hospitalizations for any reason). Notably, that positive dynamics is shown even after a year-delayed but prolonged administration of any of the HMG-CoA reductase group drugs. Neither of the drugs (simvastatin, atorvastatin, rosuvastatin) showed Scandinavian Scale or NIHSS score advantage in affecting the end-points or neurological impairment grading by the Day 720. Endothelial dysfunction regression and improvement of Mini-Mental State Examination (MMSE) score were more marked in simvastatin subgroup of subjects who have been regularly administered the drug for 2 years. The results obtained support rationale of statins administration in subjects with acute hemispheric ischemic stroke along with neuroprotective and anti-hypertensive therapy for rapid post-stroke recovery, as well as to achieve neuroprotective effect or to improve endothelial function to have better prognosis in the given subjects population. HMG-CoA reductase group drugs administration should be prolonged (at least for 2 years).