Abstract

Background: Sonolysis is an important factor in therapeutic use of ultrasound in patients with cerebrovascular diseases, it is ultrasound induced lysis of thrombus or embolus. The aim of this study was to assess safety and efficacy of therapeutic ultrasound effect (sonolysis) in acute stroke patients and in patients undergoing carotid artery intervention. First partial aim of this work was to confirm the safety and efficacy of endovascular sonolysis by using the EkoSonic Endovascular System in subjects with acute ischemic stroke. Second partial aim of this work was to test the clinical efficacy of sonolysis for reducing the risk of incidence of new brain ischaemic lesions detected on brain magnetic resonance imaging in patients undergoing elective CEA or CAS for severe internal carotid stenosis. In addition, we assessed the effects of sonolysis on cognitive function, morbidity, and mortality at 30 days post-surgery.

Methods: Patients with acute ischemic stroke and occlusion of the middle cerebral artery or basilar artery were enrolled consecutively to the prospective study tested safety and efficacy of endovascular sonolysis using the EkoSonic Endovascular System (EKOS) in patients with acute stroke. The control group (44 MCA and 12 BA occlusions) was selected from historical controls. EkoSonic Endovascular System was started within 8 hours after stroke onset. The NIHSS score at hospital admission, after 24 hours, and at 7 days; arterial recanalization; early neurologic improvement; symptomatic intracerebral hemorrhage; and favorable 3-month clinical outcome defined as a modified Rankin Scale score of 0–2 were evaluated by statistical means.

All consecutive patients with internal carotid stenosis ≥ 70% indicated for CEA/CAS were screened in the prospective randomized, controlled trial Sonolysis in Prevention of Brain Infarction During Carotid Endarterectomy and Stenting (SONOBUSTER). Patients were allocated randomly to sonolysis and control groups. Neurological examination, cognitive function tests, and brain magnetic resonance imaging were conducted before intervention and at 24 and 30 days post-surgery.

Results: Fourteen patients (10 men; mean age, 65,1 ± 11,2 years; median NIHSS score, 16,5) were enrolled to the study tested safety and efficacy of endovascular sonolysis using the EKOS system and underwent EkoSonic endovascular sonolysis. Arterial recanalization after endovascular treatment was achieved in 6 of 7 (85,7%) patients with MCA occlusion (4 complete recanalizations) and in all 7 (100%) patients with BA occlusion (6 complete recanalizations). No (0%) symptomatic intracerebral hemorrhage or periprocedural
complications occurred. Seven (50%) patients were independent at 3 months (median mRS score, 2). Early neurologic improvement and favorable clinical outcome were significantly more frequent in patients with MCA occlusion undergoing EkoSonic endovascular sonolysis than in controls (100% and 71.4% versus 4.6% and 13.6% of patients; $P = 0.0001$ and $P = 0.003$, respectively). Three-month mortality was significantly lower in patients with BA occlusion undergoing EkoSonic endovascular sonolysis than in controls (0% versus 66.7% patients, $P = 0.013$).

Totaly 242 patients out of the 487 screened patients passed inclusion criteria of the SONOBUSTER Trial; 121 (87 males; mean age, 66.65 ± 7.17 years) were allocated to the sonolysis group and 121 (75; 66.02 ± 8.11 years) to the control group. New brain ischaemic lesions on post-procedure MRI were significantly less frequent in the sonolysis group than in the control group (31.4% of patients vs. 47.1%; $P = 0.018$). Sonolysis and CEA were identified as independent predictors of reduced brain ischaemic risk [sonolysis: odds ratio (OR) = 0.450 (0.215–0.942), $P = 0.034$ and CEA: OR = 0.208 (0.087–0.495), $P < 0.001$]. Stroke or transient ischaemic attack occurred in one sonolysis patient and three control patients ($P = 0.372$). No significant group differences were found in post-intervention cognitive test scores ($P > 0.3$).

**Conclusion:** Sonolysis is safe and effective method in the process of thrombus or embolus lysis, both in acute stroke patients with cerebral artery occlusion and in reducing incidence of new brain ischemic lesions in patients undergoing internal carotid CAS or CEA intervention.

**Key words:** Acute stroke, sonolysis, therapeutic ultrasound, carotid endarterectomy, carotid stenting, cognitive functions.