Universität Basel

Research Project

Enhancement of Stroke Rehabilitation with Levodopa (ESTREL): a randomized placebo-controlled trial

Third-party funded project

Project title Enhancement of Stroke Rehabilitation with Levodopa (ESTREL): a randomized placebo-controlled trial
Principal Investigator(s) Engelter, Stefan ;
Co-Investigator(s) Lyrer, Philippe A. ;
Project Members Tränka, Christopher ;
Organisation / Research unit
Bereich Medizinische Fächer (Klinik) / Neurologie
Department
Project start 01.06.2018
Probable end 30.04.2023
Status Completed

In stroke medicine, the large body of high-quality evidence proving benefits of acute revascularization therapies and secondary prevention is offset by a large gap of evidence on means to enhance stroke recovery. Levodopa is a promising candidate for pharmacological enhancement of stroke recovery. Dopamine is a key player in processes of motor learning, reward, and brain plasticity. Preclinical research and studies with healthy individuals suggest, that there is scope for benefit from applying levodopa in addition to standardized rehabilitation. Indeed, there are some, however limited and inconsistent data from small randomized controlled trials (RCTs) testing levodopa in stroke patients. The largest, recently completed but not yet published “Dopamine in Rehabilitation of Stroke” (DARS)-trial did not indicate a benefit of levodopa. A preliminary meta-analysis across 6 RCTs (including DARS) indicated the possibility of a more favorable outcome in levodopa-treated stroke patients than in control patients. Heterogeneity between trials was considerable. The RCTs differed with regard to patient populations (chronic/acute stroke), types of stroke (ischemic/hemorrhagic), dosage and duration of the study treatment, length of follow-up, and outcome measures. None mentioned adaptation of concomitant rehabilitative therapies to the principles of motor learning. Of note, safety concerns were absent. Motor deficits are common and affect quality of life in stroke patients prompting for motor improvement as a top priority. Given the high prevalence and tremendous burden of stroke, a straightforward applicable measure to improve motor outcome is highly relevant. Given the promising but inconclusive clinical trial evidence on benefits, a well-designed, randomized controlled trial studying the usefulness of levodopa in enhancing motor recovery after stroke is warranted.Aim: to study whether levodopa compared to placebo given in addition to standardized rehabilitation based on the principles of motor learning is associated with a patient-relevant enhancement of functional recovery in acute ischemic stroke patients.Design: Multicenter, randomized (ratio 1:1), parallel-group, placebo-controlled superiority trial with blinded patients, care-providers, investigators, and outcome assessors.Patients: Patients with acute ischemic stroke (= 7days) causing clinically meaningful hemiparesis. Eligibility criteria: (i)in-hospital-rehabilitation required and patient capable to participate in standardized rehabilitation therapy; (ii)previous independence in daily living; (iii)absence of indications for dopaminergic agents; (iv)absence of contraindications for levodopa; (v)informed consent.Intervention: Levodopa 100mg/Carbidopa 25mg three times daily, administered for 5 weeks in addition to standardized rehabilitative therapy.Comparison: Matching placebo.Outcome Measures: The primary outcome is the between-group difference of final scores in the Fugl-Meyer-Motor Assessment-(FMA) measured 3 months after randomization. The FMA

will also be assessed at the end of study treatment, at 6 and 12 months. Secondary outcomes include patient-reported outcomes, Rivermead Mobility Index, NIH-Stroke Scale score, modified Rankin Scale, Box-and-Block-Test, Jamar dynamometer test, and as measures of harm: mortality, recurrent stroke, and serious adverse events.Main statistical hypothesis: Levodopa administered in addition to standardized rehabilitative therapy is superior to placebo and standardized rehabilitative therapy, resulting in an at least 6 points higher FMA score at 3 months.Sample Size: 610 patients will be recruited. The sample size is estimated to detect a statistically significant and clinically meaningful difference between treatment groups of =6 points in the FMA at 3 months (primary outcome) assuming it is normally distributed with a standard deviation of 25 points (power 80%, two-sided significance level 5%, drop-out-rate 10%).

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners