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Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial

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Summary

Background

Long-term loss of arm function after ischaemic stroke is common and might be improved by vagus nerve stimulation paired with rehabilitation. We aimed to determine whether this strategy is a safe and effective treatment for improving arm function after stroke.

Methods

In this pivotal, randomised, triple-blind, sham-controlled trial, done in 19 stroke rehabilitation services in the UK and the USA, participants with moderate-to-severe arm weakness, at least 9 months after ischaemic stroke, were randomly assigned (1:1) to either rehabilitation paired with active vagus nerve stimulation (VNS group) or rehabilitation paired with sham stimulation (control group). Randomisation was done by ResearchPoint Global (Austin, TX, USA) using SAS PROC PLAN (SAS Institute Software, Cary, NC, USA), with stratification by region (USA *vs* UK), age (≤30 years *vs* >30 years), and baseline Fugl-Meyer Assessment-Upper Extremity (FMA-UE) score (20–35 *vs* 36–50). Participants, outcomes assessors, and treating therapists were masked to group assignment. All participants were implanted with a vagus nerve stimulation device. The VNS group received 0·8 mA, 100 μs, 30 Hz stimulation pulses, lasting 0·5 s. The control group received 0 mA pulses. Participants received

6 weeks of in-clinic therapy (three times per week; total of 18 sessions) followed by a home exercise programme. The primary outcome was the change in impairment measured by the FMA-UE score on the first day after completion of in-clinic therapy. FMA-UE response rates were also assessed at 90 days after in-clinic therapy (secondary endpoint). All analyses were by intention to treat. This trial is registered at ClinicalTrials.gov, NCT03131960.

Findings

Between Oct 2, 2017, and Sept 12, 2019, 108 participants were randomly assigned to treatment (53 to the VNS group and 55 to the control group). 106 completed the study (one patient for each group did not complete the study). On the first day after completion of in-clinic therapy, the mean FMA-UE score increased by 5·0 points (SD 4·4) in the VNS group and by 2·4 points (3·8) in the control group (between group difference 2·6, 95% CI 1·0–4·2, p=0·0014). 90 days after in-clinic therapy, a clinically meaningful response on the FMA-UE score was achieved in 23 (47%) of 53 patients in the VNS group versus 13 (24%) of 55 patients in the control group (between group difference 24%, 6–41; p=0·0098). There was one serious adverse event related to surgery (vocal cord paresis) in the control group.

Interpretation

Vagus nerve stimulation paired with rehabilitation is a novel potential treatment option for people with long-term moderate-to-severe arm impairment after ischaemic stroke.

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