Deep brain stimulation in Parkinson’s disease with early motor complications

A randomised controlled trial suggests that deep brain stimulation may improve quality of life in patients with Parkinson’s disease and recent onset of motor complications.

**Overview:** Parkinson’s disease is a common, chronic, progressive neurological condition, estimated to affect 100–180 people per 100,000 of the UK population. Prevalence rises with age, and 1–2% of people older than 65 years may be affected. The condition is usually treated with dopaminergic drugs. Brain surgery may be considered in people who have responded poorly to drugs, who have severe side effects from medication or who have severe fluctuations in response to drugs.

One of the surgical treatments available is deep brain stimulation of the subthalamic nucleus. This involves the delivery of an electric current to a targeted area of the brain from a pulse generator, usually implanted in the chest wall, via fine cables tunneled beneath the skin to electrodes placed in the brain.

**Current advice:** The NICE clinical guideline on Parkinson’s disease recommends that bilateral subthalamic nucleus stimulation may be used in people with Parkinson’s disease who:

- have motor complications that are refractory to best medical treatment,
- are biologically fit with no clinically significant active comorbidity,
- are levodopa responsive and
- have no clinically significant active mental health problems, for example, depression or dementia.

The NICE interventional procedure guidance on deep brain stimulation for Parkinson’s disease states that evidence on the safety and efficacy of the procedure appears adequate to support its use, provided that normal arrangements are in place for consent, audit and clinical governance. It recommends that patient selection should be made with the involvement of a multidisciplinary team, and that patients should be offered the procedure only when their disease has become refractory to best medical treatment.

**New evidence:** A randomised controlled trial (EARLYSTIM) compared deep brain stimulation plus medical therapy with medical therapy alone in 251 patients with Parkinson’s disease and recent onset of motor complications (Schuepbach et al. 2013). Patients aged 18–60 years, with Parkinson’s disease for at least 4 years and an on-medication disease severity rating below stage 3 on the Hoehn and Yahr scale, were included. Patients with dementia, major depression or acute psychosis were excluded. Patients were randomised to bilateral stimulation of the subthalamic nucleus plus medical therapy, or medical therapy alone. In all patients, adjustments to stimulation and medical therapy were in accordance with European Federation of Neurological Societies guidelines, and overseen by an independent expert panel. The primary outcome was quality of life, measured by mean change.
from baseline to 2 years in the Parkinson’s Disease Questionnaire-39 summary index score (range 0–100).

Quality of life score with stimulation improved by 7.8 points, but worsened by 0.2 points with medical therapy alone (between-group difference=8.0 points, p=0.002). Stimulation was also superior as measured by motor disability (p<0.001), activities of daily living (p<0.001), levodopa-induced motor complications (p<0.001), and time with good mobility and no dyskinesia (p=0.01). Serious adverse events were reported in 68 patients (54.8%) receiving stimulation (22 relating to surgical implantation or the stimulation device) and in 56 patients (44.1%) who received medical therapy alone.

Commentary: “The clinical implications of the EARLYSTIM study are unclear because this study included a highly selected group of patients with early Parkinson’s disease, which has potential for bias. However, the effects on motor symptoms and quality of life are important and may change our decisions about management of early-stage Parkinson’s disease.

“Whether best medical therapy was achieved for participants in this study is unclear: apomorphine or levodopa infusions may lead to similar benefits in these patients and may be preferable to many patients. Furthermore, the study reported no data on non-motor effects, which are a key determinant of quality of life. Long-term assessment is crucial to address the neuropsychological safety of early deep brain stimulation, which has been associated with worsening of cognitive function and depression.

“In terms of current guidelines, whether deep brain stimulation should be selected ahead of medical therapy in early Parkinson’s disease needs risk–benefit analysis for individual cases. Detailed information about the risks and benefits of all available treatments should be shared with patients. However, the cost to the NHS of increasing use of deep brain stimulation may be considerable, which also needs to be taken into account.” – Professor K Ray Chaudhuri, Clinical Director and Professor, National Parkinson Foundation International Centre of Excellence, King’s College Hospital and King’s College, London

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