NHS England

Clinical Commissioning Policy Proposition: Deep Brain Stimulation for Central Post Stroke Pain

First published:

Prepared by NHS England Specialised Services Clinical Reference Group for Specialised Pain Services

Published by NHS England, in electronic format only.

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1 Executive Summary

Policy Statement

NHS England proposes to not routinely commission deep brain stimulation (DBS) for the treatment of Central Post-Stroke Pain (CPSP) in accordance with the criteria outlined in this document.

In creating this policy proposition NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Plain Language Summary

Central post-stroke pain (CPSP) has been defined by the International Association for the study of Pain as “chronic neuropathic pain caused by cerebrovascular lesions of the central somatosensory nervous system”. It is often chronic (i.e. long term) and the response to treatment with medication may be poor. A proportion of patients

require very large doses of pain medicines which provides limited benefit and side effects, particularly cognitive impairment, are almost universal.
Deep brain stimulation (DBS) involves the implantation of a device that delivers small electrical pulses to specific parts of the brain that are involved in pain perception, with the aim of masking the pain by producing other sensations such as buzzing or warmth in the painful area. The device is somewhat like a heart pacemaker except that the wires, rather than running into the heart, go into the brain through small holes in the skull. In highly selected patients this procedure provides pain relief and reduced requirement for systemic medications.

2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission deep brain stimulation for central post-stroke pain.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

3 Proposed Intervention and Clinical Indication

This policy considers the use of Deep Brain Stimulation (DBS) for Central post-stroke pain (CPSP) and states the commissioning position for the funding of this intervention by the NHS.

CPSP is a type of chronic neuropathic pain. This is long-term pain resulting from damage to the somatosensory nervous system as a result of a stroke, usually along the spinothalamocortical tract (Henry et al 2008). The location of pain is associated with the area of stroke lesion. Symptom severity and duration are often greater than for other types of pain, and pharmacological treatment is refractory for many patients, either because it is ineffective or because the side effects are intolerable. There have been no significant breakthroughs in the therapeutic options for patients with chronic neuropathic pain. There is an urgent (due to risk to self-harm) unmet clinical need for additional effective treatment, as CPSP has significant implications

on quality of life, sleep, ability to work, and mood, sometimes leading to such extreme distress that patients contemplate, and may even commit, suicide.

DBS presents an alternative option, or at least adjunct, for patients who fail all conventional management, as it is more specific in inducing analgesia without the associated risks of pharmacotherapy. There may also be significant long-term benefits to the health system and economy of using DBS to treat medication refractory CPSP, as medication usage is likely to fall substantially and patients may be enabled to return to greater independence and employment.

DBS is a surgical treatment involving the implantation of a medical device acting like a 'brain pacemaker', which sends electrical impulses to specific parts of the brain. By targeting specific areas (typically in the thalamus and periventricular grey matter) that play a part in pain perception, or related limbic areas that mediate the unpleasantness of pain, this treatment has been used in the UK between May 1999 and April 2013 for chronic pain with success in selected patients, including those with CPSP and was funded by CCGs/PCTs.

4 Definitions

Central Post-Stroke Pain: is a chronic neuropathic pain caused by cerebrovascular lesions of the central somatosensory nervous system. Breaking down this definition further, chronic pain is defined as 'pain that persists for more than 6 months' and neuropathic pain is defined as 'pain in the corresponding area of the body that is caused by a lesion or disease of the somatosensory nervous system'.

Deep Brain Stimulation (DBS) involves the surgical implantation of a medical device like a 'brain pacemaker', which sends small electrical impulses to specific parts of the brain. DBS leads are placed in the brain in precise locations that depend on the type of symptoms to be addressed.

5 Aims and Objectives

This policy proposition aims to define NHS England's commissioning position on

deep brain stimulation for central post stroke pain (CPSP).

The objectives were to improve patients' quality of life through DBS in those cases in which CPSP has not responded to other treatments.

6 Epidemiology and Needs Assessment

Central post-stroke pain (CPSP) has been defined by the International Association for the study of Pain as "chronic neuropathic pain caused by cerebrovascular lesions of the central somatosensory nervous system" (IASP 2014). CPSP prevalence amongst stroke patients ranges between 1 and 12% according to different estimates (Hosomi et al 2015). The wide range of the estimated prevalence arises as a result of different populations of patient studied and different tools for assessing pain severity.

1. An observational descriptive study of the epidemiology and treatment of stroke in a UK general population conducted in 2013 assessed the burden of central post-stroke pain in the UK and the numbers of patients likely to be eligible for DBS for CPSP annually. There are approximately 142,000 strokes in the UK/year and around 50,000 stroke victims die shortly afterwards. Of the 92,000 who survive, 30% (27,600) make full recovery, 65% (60,000) are disabled, and 5% (4,600) develop CPSP (source: The Parliamentary Office of Science and Technology, 2014; Stroke Association 2013). This estimate is supported by findings in other published studies (e.g. Andersen et al 1995). Of the 4,600 with CPSP, around 80% will fail best medical therapy, leaving 3,680 who could potentially benefit from DBS. However, of these, at least 30% (1100) are expected to be medically unfit for surgery, giving an estimate of 2,500 potentially fit for referral for DBS annually in the UK. Some of these patients would not consider their medically refractory pain sufficiently severe to undergo surgery and a significant proportion of those fit for surgery will remain on best alternative therapies and refuse surgery because of the risk of the operation. Further patients would be excluded due to contraindications picked up during the assessment process including psychological and cognitive factors which might prevent their ability to safely use the DBS system and inability to comply with long

term follow up.

2. To put these numbers into the context of the Oxford experience, from 1999-2013 (funding for pain DBS was stopped in April 2013), the Oxford functional neurosurgery department was referred about four patients per week for pain DBS. Of the patients referred, one in three was accepted for consideration of DBS and one in three of those assessed went on to have DBS implanted. Approximately a third of the total Oxford cohort who received DBS for chronic pain had CPSP, although if CPSP had been the only indication for referral it is probable that more CPSP cases would have been accepted.

Based on the natural disease progression and epidemiology (point 1, above) combined with our understanding of how many patients are excluded from DBS *after referral* during the process of screening referrals and patient assessment (point 2, above) we would estimate that around 100 patients nationally each year would have both a clinical indication for DBS surgery, be willing to undergo the treatment and would have no medical or psychosocial contraindications to the procedure.

DBS has provided therapeutic benefits for otherwise treatment resistant movement disorders including Parkinson's disease, dystonia, and tremor, where it is currently routinely commissioned. In England there are 12 centers that perform DBS, but only one is using it for the management of pain, the other centers use it for other indications as above thus historical experience in Oxford is likely to predict future surgical numbers. However, it is anticipated that the prevalence of stroke will increase due to expected demographic changes and with a reduction in mortality the number of people requiring DBS for CPSP is anticipated to increase.

The patients with CPSP who are considered for DBS are those who have tried and failed, are inappropriate for or are having significant side effects with all other standard interventions. As such it is a complex group of patients with pain having a major impact on their function, quality of life and requirement for social and healthcare support. Relatively small improvements in pain may have a life-changing

impact in this patient group which may be better reflected by changes in self-reported quality of life scores rather than pain assessment scales.

7 Evidence Base

NHS England has concluded that there is insufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.

The reference baseline for this policy was the NICE (IPG 382) guidance published in March 2011. NICE in 2011, endorsed that DBS for refractory chronic pain syndromes could be used in patients selected by a specialised pain MDT, when other treatments had failed to control their pain, provided informed consent, clinical governance, patient information and audit arrangements were in place. The evidence available to support routine commissioning is limited due to the small number of patients suitable for this intervention and the limited number of centers involved.

A further review was carried out within the functional neurosurgery department in Oxford by Sethi, Roy, Aziz et al looking only at studies published after the NICE review. It identified smaller case series that provide positive evidence about the efficacy of DBS for CPSP (Rezaei-Haddad et al 2015, Alves et al 2011, Mallory et al 2012, Hunsche et al 2013) as well as a large study finding positive quality of life outcomes after DBS for pain which included patients with CPSP (Gray et al 2014). These additional studies add new evidence in relation to quality of life or cognitive outcomes. The two noteworthy trials identified in this review are described below:

The first reported a perspective case series of 18 patients with neuropathic pain (Gray et al.), which included patients with CPSP (27.7% of the sample). Although the sample size was small due to the nature of these conditions and the supportive medications accompanying DBS were not recorded, significant improvements following DBS of the periventricular/periaqueductal grey area and sensory thalamus were observed with a; 44.7% mean reduction in subjective pain intensity (MPQ), 25.8% reduction in total disability score (FLP), 20.8% reduction in HADS depression and anxiety score at 6 months following surgery. Although post-surgery

scores on all cognitive measures were not significantly different to pre-surgery levels, DBS in PVG/PAG was observed to be associated with a deterioration in executive function (spatial working memory) particularly among those reporting the greatest pain alleviation (39% of the sample reported a 50% reduction in pain). The second was a case series of 4 patients with intractable pharmaceutical therapy resistant thalamic pain affecting the whole hemi-body, lasting more than 2 years (Hunsche et al). 3 of these patients had post-stroke pain. Patients were assessed at 3, 6 and 12 months. 3 / 4 patients achieved long-lasting pain relief of more than 40%, at 3, 6 and 12 months of follow-up post DBS.

The conclusions of the Gray and Hunsche papers may differ because the approach of the two groups is different in some key aspects. For example, the Gray et al paper reports outcomes from a group where drug reduction is not insisted upon after DBS for pain, whereas drug reduction is typical in the management of patients reported by the Hunsche group. Also, Hunsche et al set a limit of 40% reduction in VAS score to signify significant reduction in pain, and this was the main outcome measure they assessed. The Gray et al group used a greater number and range of outcome measures and did not set a fixed percentage change as a threshold for success.

SUMMARY FROM SPH EVIDENCE REVIEW:

Clinical Effectiveness

- We found one systematic review. It included an earlier systematic review and meta analysis which may have been misreported and contained an important methodological limitation. It suggested an overall success rate for DBS in CPSP of 31%. The only other studies included in this systematic review are described below.
- We found four uncontrolled studies with ten or more participants:

  - The first reported a series of 15 people with CPCP treated with DBS in Oxford. Three noticed no improvement and their electrodes were removed. The remaining twelve reported a mean improvement of 49% in their pain.

Pain ratings improved by 38%. Seven participants stopped all analgesics and five others stopped regular opiates.

- The same research group reported a series of 18 people with CPSP. Six noticed no improvement after DBS and their electrodes were removed, and three were lost to follow-up. Pain severity in the remaining nine participants showed mean improvement of 49%; the significance of this result was not reported. Four of the nine reported improvement in pain severity of at least 50%. The participants in this study may have also been reported in the first study.
- The third study reported a series of 31 people with CPSP treated with DBS. This study was also from the same research group in Oxford and apparently included all the participants in the earlier two studies. Results were similar: four patients did not benefit from DBS and the electrodes were removed, sixteen reported an improvement in their health status and in their pain, seven had permanent electrodes but no improvement in health and the remaining four were lost to follow-up.
- Rasche et al reported a separate set of eleven patients treated in Germany. Nine of the eleven participants experienced no pain improvement and had their electrodes removed. Patients' quality of life did not improve because of "persistent chronic burning pain component and intermittent lancinating pain attacks."

Cost Effectiveness

- We found no health economic evaluations of DBS for CPSP.

Safety

Complications were not widely reported in the studies that we found. NICE's guidance refers to the risks of intracranial haemorrhage, massive cerebral oedema and haematoma in the basal ganglia, infection, ventriculitis, subgaleal infection, subdural empyema and erosion of hardware.

8 Proposed Criteria for Commissioning

NHS England concluded that there was not sufficient evidence to support the routine commissioning of this treatment for the indication. In the interests of transparency the evidence base that was described and considered is set out in Appendix A of this policy.

9 Proposed Patient Pathway

Not applicable

10 Proposed Governance Arrangements

Not applicable

11 Proposed Mechanism for Funding

NHE England has found insufficient evidence to consider the routine commission of this intervention therefore, Deep Brain Stimulation for central post-stroke pain will not be routinely commissioned by NHS England.

12 Proposed Audit Requirements

Not applicable

13 Documents That Have Informed This Policy Proposition

NICE GUIDELINES - Deep brain stimulation for refractory chronic pain syndromes (excluding headache) (IPG382)

Policies in closely related areas include:
NHSCB/D03/P/b: Deep Brain Stimulation for movement disorders
TA159 (NICE): Spinal Cord Stimulation for Chronic Pain of Neuropathic or Ischaemic origin

14 Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned.

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