

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedure consultation document

# Implanting a baroreceptor stimulation device for resistant hypertension

Hypertension (or high blood pressure) raises the risk of having a heart attack or stroke, which can lead to early death. Resistant hypertension is when blood pressure stays high despite drug treatment. In this procedure, a small device is implanted beside the carotid artery in the neck. It sends signals to baroreceptors (sensors that measure blood pressure) that are in the carotid artery, which activate the body's blood pressure control system to lower blood pressure.

The National Institute for Health and Care Excellence (NICE) is examining implanting a baroreceptor stimulation device for resistant hypertension and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about implanting a baroreceptor stimulation device for resistant hypertension.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 25 February 2015

Target date for publication of guidance: 27 May 2015

## **1 Provisional recommendations**

- 1.1 Current evidence on the safety and efficacy of implanting a baroreceptor stimulation device for resistant hypertension is inadequate. Therefore, this procedure should only be used in the context of research.
- 1.2 Further research on implanting a baroreceptor stimulation device for resistant hypertension should document patient selection in detail and should specify the devices and techniques used. It should describe the changes in blood pressure that are considered to result from baroreceptor stimulation, and those that might be due to other factors. Outcomes should include the duration of effect of baroreceptor stimulation; device durability; and the complications of hypertension, such as myocardial infarction and stroke.

## **2 Indications and current treatments**

- 2.1 Hypertension is usually asymptomatic, but it is a common and preventable cause of premature morbidity and death. It is a major, but modifiable, risk factor for cardiovascular disease (including stroke and myocardial infarction) and chronic kidney disease. The cause of primary hypertension, which is the most common form, is not fully understood. However, it is likely to involve multiple factors including an increase in sodium retention and a reduction in renal blood flow mediated by the sympathetic nervous system. Secondary hypertension, which is less common, is caused by conditions affecting the kidneys, arteries, heart or endocrine system.
- 2.2 First-line treatment of hypertension includes lifestyle changes, such as diet and exercise. Antihypertensive medications are used if high blood pressure persists. The NICE guideline on [hypertension](#) defines resistant hypertension as blood pressure that remains higher than 140/90 mmHg after treatment with the optimal or best tolerated doses of an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin-II receptor blocker (ARB) plus a calcium-channel blocker (CCB) plus a diuretic.

## **3 The procedure**

- 3.1 Implanting a baroreceptor stimulation device for resistant hypertension aims to lower blood pressure by electrically stimulating the carotid baroreflex, which controls blood pressure by regulating autonomic nervous activity. The device consists of an electrode placed on 1 or both carotid sinuses and a battery-powered implantable generator, which is inserted under the skin near the clavicle. Device programming allows the frequency and amplitude of stimulation to be adjusted and it is programmable by time of day.

- 3.2 The procedure is usually done with the patient under general anaesthesia or conscious sedation. The exact technique varies according to the type of device being implanted. The following technique is used for a device that has bilateral leads with electrical contacts, which are wrapped around the carotid sinuses. The location of carotid bifurcation is marked on each side of the patient's neck using ultrasound guidance. The surgical procedure involves exposure of the carotid bifurcation; carotid sinus mapping and electrode positioning at the location with the highest density of baroreceptors; subcutaneous lead tunnelling to the pulse generator; and implanting the pulse generator under the skin near the clavicle.
- 3.3 A recent adaptation uses a smaller device with a single button electrode rather than leads. This procedure needs the carotid sinus to be exposed only on 1 side of the patient's neck. The internal carotid artery is dissected without surgical exposure of the external carotid artery. The electrode is sutured to the carotid sinus, rather than being wrapped around it.
- 3.4 The device is usually activated about a month after implantation. Clinic staff adjust therapy settings, such as the frequency and amplitude of stimulation, using wireless communication when the patient attends hospital for follow-up appointments. The device can be turned off by clinic staff if necessary.

## **4 Efficacy**

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 A randomised controlled trial of 265 patients treated by implantation of a baroreceptor stimulation device that was either turned on

1 month after implantation (immediate stimulation) or turned on after 6 months (deferred stimulation) was carried out. Response rates at 6 months (defined as a 10 mmHg or more drop in systolic blood pressure at month 6 compared with blood pressure obtained 1 month after implantation) were 54% and 46%, respectively ( $p=0.97$ ). Of those patients who responded to active therapy at 6 months, 88% maintained a response at 12 months ( $p<0.001$ ). The mean decreases in systolic blood pressure at 6 months were  $16\pm 29$  mmHg and  $9\pm 29$  mmHg respectively ( $p=0.08$ ). The proportion of patients with systolic blood pressure of 140 mmHg or less at 6 months was 42% for immediate stimulation and 24% for deferred stimulation ( $p=0.005$ ).

- 4.2 A cohort study of 322 patients, which was an open-label follow-up of the randomised controlled trial described in section 4.1 (including all patients who had a device implanted regardless of whether they were subsequently randomised), reported a mean decrease in blood pressure of 35/16 mmHg compared with pre-implantation, after a mean follow-up of 28 months. Among the 244 patients who had a response (defined as a 10 mmHg or more drop in systolic blood pressure at month 6 compared with blood pressure obtained 1 month after implantation) 55% reached goal pressures (less than 140 mmHg or less than 130 mmHg in patients with diabetes or kidney disease) throughout follow-up. A case series of 45 patients reported that mean blood pressure decreased by 21/12 mmHg in 37 evaluable patients after 3 months of baroreceptor stimulation ( $p=0.001$ ). The mean reduction after 2 years of follow-up was 33/22 mmHg ( $n=17$ ,  $p=0.001$  for systolic blood pressure and  $p=0.002$  for diastolic blood pressure).
- 4.3 The cohort study of 322 patients reported that the mean number of prescribed medications fell significantly between pre-implantation and month 12 in those patients who had a response ( $n=244$ ).

These reduced from  $5.3 \pm 1.9$  to  $4.7 \pm 2.1$  and remained lower after a mean follow-up of 28 months ( $p < 0.05$ ).

- 4.4 The specialist advisers listed key efficacy outcomes as reduction in blood pressure at 6 and 12 months, reduction in blood pressure variability, reduction in heart rate, and reduction in left ventricular hypertrophy.

## 5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Nerve injury with residual deficit was reported in 5% (13/265) of patients and transient nerve injury in 5% (12/265) of patients in a randomised controlled trial of 265 patients (no further details given). Tongue paresis, most likely due to intraoperative injury to the hypoglossal nerve, was reported in 1 patient in a case series of 45 patients.
- 5.2 Hypertension-related stroke was reported in 2% (6/265) of patients in the randomised controlled trial of 265 patients (timing and study group not reported). Perioperative stroke with minimal residual effects was reported in 1 patient in the case series of 45 patients.
- 5.3 Hypertensive crisis was reported in 5% (9/181) of patients treated by immediate baroreceptor stimulation and 8% (7/84) of patients treated by deferred stimulation in the randomised controlled trial of 265 patients.
- 5.4 Device removal before activation because of infection was reported in 7% (3/42) of patients in the case series of 45 patients. In 1 patient, the leads were left in and a new device was implanted 12 months later. Infection needing device removal was reported in

1 patient in a case series of 10 patients; the infection occurred after the 4-month follow-up visit.

- 5.5 Device pocket haematoma 3 days after device implantation was reported in 1 patient in a case series of 30 patients; the patient recovered with no residual effects. Wound complication (not otherwise described) after device implantation was reported in 3% (7/265) of patients in the randomised controlled trial of 265 patients. A self-inflicted wound complication was reported in 1 patient in the case series of 30 patients; the patient recovered with no residual effects.
- 5.6 Respiratory complication (not otherwise described) after device implantation was reported in 3% (7/265) of patients in the randomised controlled trial of 265 patients.
- 5.7 Movement of the implantable pulse generator, needing further surgery to reposition it, was reported in 1 patient in the case series of 45 patients.
- 5.8 Intermittent pain lateral to the device system was reported within 30 days of device implantation in 1 patient in the case series of 30 patients; this resolved without intervention.
- 5.9 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers considered that the following were theoretical adverse events: traumatic injury to the carotid artery or major neck veins; bleeding; cerebral embolisation causing stroke; wound dehiscence; late damage to the carotid artery; bradycardia; bradypnoea; excessive lowering of blood pressure; orthostatic hypotension; and device failure.

## **6 Committee comments**

- 6.1 In reviewing the evidence on implanting a baroreceptor stimulation device for resistant hypertension the Committee noted that there had been reductions in blood pressure before stimulation began. It also noted that most of the available evidence was related to bilateral stimulation, but that the technology has evolved and unilateral stimulation is now used. These issues complicated the Committee's consideration of the evidence and formed the basis for some of the specific recommendations about further research.

## **7 Further information**

- 7.1 For related NICE guidance, see the [NICE website](#).

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