NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

Cluster headaches are attacks of severe pain around the eye accompanied with reddening, eye-watering and a runny nose. Attacks can occur several times a day and last from minutes to hours. In this procedure a small device is implanted just above the gum. This device electrically stimulates a group of nerves at the base of the skull called the sphenopalatine ganglion. The aim is to relieve pain and reduce the number of headache attacks.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in September 2014.

Procedure name

- Implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

Specialist societies

- British Society for Stereotactic and Functional Neurosurgery (BSSFN)
- British Association for the Study of Headache

Description

Indications and current treatment

Cluster headaches are characterised by episodes of unilateral periorbital pain, conjunctival injection, lacrimation and rhinorrhoea. This form of neurovascular headache most commonly affects middle-aged men. Headache attacks can last from a few minutes to several hours and can occur many times a day, over several days. Chronic cluster headaches can be separated by headache-free periods of less than 1 month, or not separated at all.

The usual treatments for acute cluster headache attacks are oxygen inhalation and/or with or without medications such as triptans. Medications such as corticosteroids, verapamil and occipital nerve blocks are used to prevent or reduce the number of attacks. Surgical treatments are reserved for patients with distressing symptoms that are refractory to medical treatments. They include deep brain stimulation to modulate central processing of pain signals and radiofrequency ablation to interrupt trigeminal sensory or autonomic pathways.

What the procedure involves

It is believed that cluster headaches are caused by a trigeminal-autonomic reflex mediated through the sphenopalatine ganglion. This procedure aims to relieve pain and reduce the frequency of cluster headache attacks by implanting a device in the pterygopalatine fossa to stimulate the sphenopalatine ganglion with small electrical currents.

Implantation of the neurostimulator device is performed with the patient under general anaesthesia. A small incision is made in the mucogingival margin adjacent to the maximillary first or second molar on the affected side. Under X-ray control, the lead of the neurostimulator device is advanced subperiosteally along the posterior maxilla in order to place stimulating electrodes in the pterygopalatine fossa. Through the same incision in the mucogingival margin, the main body of the device is fixed medial to the zygoma by means of a small plate. After implantation, the device is tested to assess electrode functionality and the patient's physiological responses to stimulation.

When cluster headaches occur, the patient activates the neurostimulator (up to a pre-determined maximum dose) by placing a handheld control unit on their cheek, over the area where the main body of the device is implanted.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache. Searches were conducted of the following databases, covering the period from their commencement to 30 September 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with chronic cluster headache.
Intervention/test	Implantation of a sphenopalatine ganglion stimulation device
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 43 patients from 2 randomised controlled trials[1–2] and 1 case series[3].

Table 2 Summary of key efficacy and safety findings on implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

Study 1 Schoenen J 2013

Details

Study type	**Randomised sham-controlled crossover trial**
Country	Multicentre: Belgium, Denmark, France, Spain, Germany
Recruitment period	Not reported
Study population and number	Patients with chronic cluster headache n=**32** (All patients randomly received full stimulation, sub-perception stimulation or sham stimulation)
Age and sex	Mean age, 45 years; 84% (27/32) male
Patient selection criteria	Inclusion criteria: patients aged between 18 and 65 years with chronic cluster headache according to the 2004 International Headache Society criteria were included. All patients reported a minimum of 4 cluster headaches per week which were distinguishable from other types of headaches. Exclusion criteria: patients with osteomyelitis, malignancies of the face or significant pain problems that would confound observations were excluded. Patients who had undergone previous facial surgery in the area of the pterygopalatine fossa within 4 months of enrolment, had radiation therapy to the face within 6 months of enrolment, had undergone radiofrequency ablation of the ipsilateral sphenopalatine ganglion or had botulinum toxin injections to the head/neck within 3 months of enrolment or patients who had a change of in type or dosage of headache medications within 1 month of enrolment were also excluded.
Technique	The neurostimulator was implanted under general anaesthesia using a minimally invasive, trans-oral, gingival buccal technique. The device was implanted so that stimulating electrodes on the integral lead were positioned within the pterygopalatine fossa proximate to the sphenopalatine ganglion. Positioning was verified by X-ray imaging immediately after implantation. Patients randomly received 3 stimulation doses: full stimulation, sub-perception stimulation and sham stimulation. Stimulation doses were delivered randomly (1:1:1) using pre-specified randomisation sequences that were programmed into the remote controller. Patients and investigators were blinded to the type of stimulation dose applied at each attack. Patients logged the result of each treatment in headache diaries.
Follow-up	**1 year**
Conflict of interest/source of funding	The study was funded by the manufacturer. Furthermore, 3 of the authors were employed by the manufacturer

Analysis

Follow-up issues: for sham stimulation comparisons, patients were followed-up until 30 attacks had occurred or for a maximum of 2 months, whichever was more. 4 patients were excluded from sham stimulation assessments due to: failure to implant (n=1), device explantation due to lead migration (n=2) and pregnancy (n=1).

Study design issues: Patients were recruited from 6 centres across Europe. The primary efficacy endpoint was a reduction in pain at 15 minutes after the start of neurostimulation. Secondary endpoints included complete resolution of pain at 15 minutes, as well as a reduction in pain at 30, 60 and 90 minutes after the start of neurostimulation.

Study population issues: None identified

Other issues: Headache impact test (HIT)-6: scores range from 36 to 78 with lower scores indicating better quality of life

- Mental and physical component scores of the SF-36 questionnaire range from 0 to 100 with higher scores indicating better outcomes.
- Pain scores: ranged from 0 to 4 with 0 indicating no pain and 4 indicating very severe pain. A reduction in pain was classified by a reduction in scores from 2, 3 or 4 to 0 or 1.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **28**

Reduction in pain and complete resolution of pain at 15 minutes after neurostimulation (proportion of treatments)

Type of stimulation	Proportion that resulted in a reduction in pain (%) [n]	p value compared against sham	Proportion that resulted in complete resolution of pain (%) [n/N]	p value compared against sham
Full	67.1 [127/190]	<0.001	34.1 [65/190]	<0.001
Sub-perception	7.3 [14/184]	0.96	1.6 [3/184]	0.97
Sham	7.4 [15/192]	-	1.5 [3/192]	-

Reduction in pain at later time points after neurostimulation (proportion of treatments)

	Proportion of treatments that resulted in a reduction in pain **including** complete resolution of pain (%)		
Type of stimulation	30 minutes	60 minutes	90 minutes
Full	55.5	60.6	60.0
Sham	8.0	11.5	12.9

Significant differences were observed between stimulation settings at each time point (p values <0.001).

Results for sub perception stimulation not reported.

Proportion of attacks that required acute rescue medications

Type of stimulation	Proportion (%)	p value compared against sham
Full	31.0	<0.001
Sub-perception	78.4	0.68
Sham	77.4	-

Attack frequency

Mean attack frequency reduced from 17.4 attacks per week to 12.5 attacks per week at 2-month follow-up (p=0.005).

The frequency of headaches reduced by a minimum of 50% in 43% (12/28) of patients at 2-month follow-up: 3 additional patients experienced reductions in headache frequency but were not counted due to changes in medication use.

No reduction in headache frequency was reported in 46.4% (13/28) of patients at 2-month follow-up.

Quality of life

Mean headache impact test scores decreased by 6.8±10.2 points (from 66 to 59) at 2-month follow-up (p=0.002; results obtained from a graph).

Mean SF-36 physical function scores increased from 38 to 43.5 at 2-month follow-up (p=0.005; results obtained from a graph)

Mean SF-36 mental function scores increased from 34.5 to 39 at 2-month follow-up (p=0.02; results obtained from a graph).

Overall mean SF-36 scores improved in 75% (21/28) of patients. No further details were provided.

Safety

Number of patients analysed:**32**

	Within 30 days of implant procedure		**Between 30 days and 1 year after implant procedure**	
Adverse event	Proportion of patients %(n) [N=32]	Proportion of patients that resolved % (n/N)	Proportion of patients % (n) [N=32]	Proportion of patients that resolved % (n/N)
Sensory disturbances (includes localised loss of sensation, hypoaesthesia, paraesthesia dysaesthesia, allodynia)	81 (26)	58 (15/26)	16 (5)	60 (3/5)
Pain (face, cheek, gum, temporomandibular joint, nose, incision, site or periorbital)	38 (12)	100 (12/12)	19 (6)	50 (3/6)
Tooth pain/sensitivity	16 (5)	80 (4/5)	3 (1)	100 (1/1)
Swelling	22 (7)	86 (6/7)	-	-
Swelling and pain	9 (3)	100 (3/3)	-	-
Trismus	16 (5)	80 (4/5)	-	-
Headache (non-cluster headache)	9 (3)	100 (3/3)	9 (3)	33 (1/3)
Dry eye (xerophthalmia)	9 (3)	33 (1/3)	3 (1)	-
Haematoma	9 (3)	100 (3/3)	-	-
Mild paresis of the muscles around the nasolabial fold	6 (2)	50 (1/2)	-	-
Infection	6 (2)	100 (2/2)	3 (1)	100 (1/1)
Reduced autonomic symptoms (tearing, nose block) during cluster attacks	3 (1)	100 (1/1)	-	-
Epistaxis	3 (1)	100 (1/1)	-	-
Facial asymmetry	3 (1)	100 (1/1)	6 (2)	-
Tearing	3 (1)	100 (1/1)	-	-
Vomiting	3 (1)	100 (1/1)	-	-
Tenderness in cheek	3 (1)	-	-	-
Bites tongue	3 (1)	100 (1/1)	-	-
Failures to implant	3 (1)	100 (1/1)	-	-
Explant/lead revision	-	-	16 (5)	100 (5/5)
Lead migration	3 (1)	100 (1/1)	-	-
Maxillary sinus puncture	3 (1)	100 (1/1)	-	-
Conjunctivitis	-	-	3 (1)	100 (1/1)
Itching	-	-	3 (1)	100 (1/1)
Dry nose	-	-	3 (1)	100 (1/1)
Dry skin	-	-	3 (1)	100 (1/1)
Taste alterations	-	-	3 (1)	100 (1/1)
Sensation of implant	-	-	3 (1)	-
Depressed gag reflex	-	-	3 (1)	-
TMJ (no further details provided)	-	-	3 (1)	-
Increase in static electricity	-	-	3 (1)	100 (1/1)
Sensation in infratemporal fossa	-	-	3 (1)	100 (1/1)

NB: Adverse events are reported as stated by the authors. It is unclear if these adverse events were directly related to the surgical procedure or use of the neurostimulator.

Abbreviations used: TMJ, temporomandibular joint

Study 2 Schytz K 2013

Details

Study type	**Double-blind randomised crossover trial**
Country	Denmark
Recruitment period	Not reported
Study population and number	Patients with chronic cluster headache n=**7** (Patients randomly received low-frequency stimulation or high-frequency stimulation)
Age and sex	Mean age, 49 years; 71.4% (5/7) male
Patient selection criteria	Inclusion criteria: patients aged between 18 and 65 years with chronic cluster headache according to the 2004 International Headache Society criteria were included. All patients reported a minimum of 4 cluster headaches per week which were distinguishable from other types of headaches. Exclusion criteria: not reported
Technique	Not reported; however a description was obtained by another study (Schoenen 2013) by the same study group. The device was implanted so that stimulating electrodes on the integral lead were positioned within the pterygopalatine fossa proximate to the sphenopalatine ganglion. Positioning was verified by X-ray imaging immediately after implantation. Patients who were previously implanted with sphenopalatine ganglion neurostimulators (duration not reported) were randomly allocated to receive low-frequency stimulation or high-frequency stimulation for 3 minutes on 2 separate days. Both patients and investigators were blinded to neurostimulator settings. Stimulation was performed in hospital where patients were monitored for 1 hour. Patients were allowed to leave and asked to fill in a headache diary every hour for up to 12 hours.
Follow-up	**12 hours**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: One patient was excluded from analysis because of technical issues when applying stimulation.

Study design issues: Authors hypothesised that low-frequency neurostimulation induced cluster headache attacks and high-frequency neurostimulation prevented attacks. Patients were allowed to treat any subsequent headaches with neurostimulation and/or their typical acute therapy (oxygen inhalation, sumatriptan or over-the-counter rescue medication).

Study population issues: Overlap with patients recruited in Schoenen 2013. Four patients were receiving prophylactic cluster headache medication at the time of the study.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: 6
Headache frequency before and after implantation. NB: results were obtained <u>before the crossover trial</u>
<table>
<tr><th>Patient</th><th>Number of attack days per month before implantation</th><th>Number of attack days per month after implantation, but before the crossover trial</th></tr>
<tr><td>1</td><td>31</td><td>0</td></tr>
<tr><td>2</td><td>31</td><td>1</td></tr>
<tr><td>3</td><td>26</td><td>0</td></tr>
<tr><td>4</td><td>24</td><td>2</td></tr>
<tr><td>5</td><td>26</td><td>2</td></tr>
<tr><td>6</td><td>28</td><td>18</td></tr>
<tr><td>7</td><td>31</td><td>21</td></tr>
<tr><td>Mean</td><td>28</td><td>6</td></tr>
</table>
Low-frequency stimulation
Ipsilateral cluster headache-like attacks were reported in 67% (4/6) of patients after low-frequency stimulation.
Cluster headache-like attacks with autonomic features were reported in 50% (3/6) of patients within 30 minutes of low-frequency stimulation. These patients applied high-frequency stimulation to treat their cluster headaches: pain relief or complete resolution of pain was reported in all 3 patients within 10 minutes.
o Cluster headache-like attacks with autonomic features were reported in 50% (3/6) of patients within 4 hours of low-frequency stimulation. These patients applied high-frequency stimulation to treat their cluster headaches: pain relief or complete resolution of pain was reported in all 3 patients.
High-frequency stimulation
Ipsilateral cluster headache-like attacks were reported in 33% (2/6) of patients after high-frequency stimulation.
One patient experienced a cluster headache attack 7 minutes after stimulation. The patient was pain free without autonomic symptoms 10 minutes after onset.
Another patient experienced a cluster headache attack 120 minutes after stimulation. The patient was pain free without autonomic symptoms 15 minutes after onset.
Vital signs
The mean heart rate decreased by 6% after low-frequency stimulation and increased by 2.5% after high-frequency stimulation (results were obtained from a graph, no absolute values reported).
The mean end tidal CO_2 volume decreased by 1.5% after low-frequency stimulation and increased by 2.5% after high-frequency stimulation (results were obtained from a graph, no absolute values reported).
• The mean arterial blood pressure increased by 2% after low-frequency stimulation and by 1% after high-frequency stimulation (results were obtained from a graph, no absolute values reported).
</td><td>Investigators did not actively monitor the occurrence of adverse events.</td></tr>
</table>

Study 3 Ansarinia M 2010

Details

Study type	**Case series (feasibility study)**
Country	United States
Recruitment period	Not reported
Study population and number	Patients with refractory chronic cluster headache n=**5**
Age and sex	Mean age (of 5 patients), 43 years; 67% (4/6) male
Patient selection criteria	Inclusion criteria: not reported Exclusion criteria: not reported
Technique	The procedure was performed under local anaesthesia. **No permanent device was implanted.** Under fluoroscopic guidance, a percutaneous infrazygomatic approach was used to place a 20-gauge needle at the ipsilateral sphenopalatine ganglion. The needle stylet was removed and a temporary single contact stimulation electrode was inserted and advanced through the tip of the needle. Cluster headaches were induced and the patient was asked to rate their headache intensities, using a visual analogue scale. Electrical stimulation was applied for up to 1 hour once the cluster headache intensity was rated 8 or higher on the visual analogue scale.
Follow-up	**1 hour**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: One patient responded to sham stimulation, resulting in the relief of 2 cluster headaches; their results were excluded from the analyses.

Study design issues: Cluster headache attacks were induced by reducing preventative medication use and exposing patients to known triggers, including oral or intravenous nitroglycerin, alcohol ingestion, exposure to bright light and exposure to pungent scents.

Study population issues: None identified.

Other issues: None identified.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 5 patients (18 acute attacks) • Stimulation resulted in resolution of cluster headaches in 61% (11/18) of attacks. • A 50% reduction in VAS scores was reported in 17% (3/18) of attacks.	Investigators did not actively monitor the occurrence of adverse events. Severe persistent headache was reported in 1 patient. This was treated by a rescue procedure involving the use of an anaesthetic nerve block. Transient epistaxis, which resolved spontaneously, was reported in 1 patient.
Abbreviations used: VAS, visual analogue scale	

Efficacy

Pain relief

In a randomised sham-controlled crossover trial of 32 patients who randomly had full stimulation, sub-perception stimulation or sham stimulation during each cluster headache attack, a reduction in pain at 15 minutes after neurostimulation was reported in 67% (65/190) of attacks treated by full stimulation and 7% (15/192) of attacks treated by sham stimulation (p<0.001). A reduction in pain at 15 minutes after neurostimulation was reported in 7% (14/184) of attacks treated by sub-perception stimulation (p value against sham stimulation = 0.96). Complete resolution of pain at 15 minutes after neurostimulation was reported in 34% (65/190) of attacks treated by full stimulation and 2% (3/192) of attacks treated by sham stimulation (p<0.001). Complete resolution of pain at 15 minutes after neurostimulation was reported in 2% (3/184) of attacks treated by sub-perception stimulation (p value against sham stimulation = 0.97)[1].

In the randomised sham-controlled crossover trial of 32 patients, a reduction in pain at 90 minutes after neurostimulation was reported in 60% of cluster headache attacks treated by full stimulation and 13% of attacks treated by sham stimulation (p<0.001). Results for sub-perception stimulation were not reported[1].

Usage of acute rescue medication

In the randomised sham-controlled crossover trial of 32 patients, acute rescue medications were needed for 31% of attacks treated by full stimulation and 77% of attacks treated by sham stimulation (p<0.001). Acute rescue medications were needed for 78% of attacks treated by sub-perception stimulation (p value against sham stimulation = 0.68)[1].

Attack frequency

In the randomised sham-controlled crossover trial of 32 patients, the mean attack frequency reduced from 17.4 attacks per week to 12.5 attacks per week at 2-month follow-up for the 28 patients who completed the experimental period (p=0.005). The frequency of headaches reduced by a minimum of 50% in 43% (12/28) of patients: 3 additional patients experienced reductions in headache frequency but were not included due to changes in medication use. No reduction in headache frequency was reported in 46% (13/28) of patients at 2-month follow-up[1].

In a case series of 7 patients, the mean attack frequency reduced from 28 attack days per month to 6 attack days per month at follow-up: duration of follow-up not reported[2].

Quality of life

In the randomised sham-controlled crossover trial of 32 patients, mean headache impact test scores (scores range from 36 to 78 with lower scores indicating better

quality of life) decreased by 6.8±10.2 points (from 66 to 59) at 2-month follow-up for the 28 patients who completed the experimental period (p=0.002). In the same study, mean SF-36 physical function scores (scores range from 0 to 100 with higher scores indicating better outcomes) increased from 38 to 43.5 at 2-month follow-up (p=0.005). Mean SF-36 mental function scores increased from 34.5 to 39 (p=0.02)[1].

Safety

Lead revision

Lead revision or explantation of the device was needed for 16% (5/32) of patients, between 30 days and 1 year after the procedure, in a randomised sham-controlled crossover trial of 32 patients[1].

Sensory disturbances

Sensory disturbances (including localised loss of sensation, hypoaesthesia, paraesthesia, dysaesthesia and allodynia) were reported in 81% (26/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in 58% (15/26) of these patients. Sensory disturbances were reported in 16% (5/32) of patients between 30 days and 1 year after the procedure; symptoms resolved in 60% (3/5) of these patients[1].

Pain

Pain (facial, cheek, gum, temporomandibular joint, nose, incision site or periorbital) was reported in 38% (12/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients. Severity of pain was not described and symptoms resolved in all of these patients. Pain was reported in 19% (6/32) of patients between 30 days and 1 year after the procedure; symptoms resolved in 50% (3/6) of these patients[1].

Tooth pain/sensitivity

Tooth pain/sensitivity was reported in 16% (5/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in 80% (4/5) of these patients. Tooth pain/sensitivity was reported in 1 patient between 30 days and 1 year after the procedure; symptoms resolved in this patient[1].

Swelling

Unspecified swelling was reported in 22% (7/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in 86% (6/7) of these patients[1].

Trismus

Trismus was reported in 16% (5/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in 80% (4/5) of these patients[1].

Headaches (non-cluster headaches)

Headaches, that were not cluster headaches, were reported in 9% (3/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in all of these patients. Headaches, that were not cluster headaches, were reported in 9% (3/32) of patients between 30 days and 1 year after the procedure; symptoms resolved in 1 of these patients[1].

Dry eye (xerophthalmia)

Dry eye was reported in 9% (3/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial patients; symptoms resolved in 1 of these patients. Dry eye was reported in 1 patient between 30 days and 1 year after the procedure; no further details were provided[1].

Haematoma

Haematoma was reported in 9% (3/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in all of these patients[1].

Paresis

Mild paresis of the muscles around the nasolabial fold was reported in 6% (2/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in 1 of these patients[1].

Infection

Infection was reported in 6% (2/32) of patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in all patients following treatment with antibiotics. Infection was reported in 1 patient between 30 days and 1 year after the procedure; symptoms resolved following treatment with antibiotics [1]

Other adverse events

Epistaxis, facial asymmetry, lacrimation, vomiting, lead migration, and a maxillary sinus puncture (no details were provided) were each reported as occurring on single occasions in different patients within 30 days of device implantation in the randomised sham-controlled crossover trial of 32 patients; symptoms resolved in all patients[1].

Itching, dry nose, dry skin, taste alterations, a depressed gag reflex, and sensation in the infratemporal fossa (no details were provided) were each reported as occurring on single occasions in different patients, between 30 days and 1 year after the procedure, in the randomised sham-controlled crossover trial of 32 patients [1].

Validity and generalisability of the studies

- The majority of evidence on the efficacy and safety of implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache was obtained from 1 randomised controlled trial.
- The longest follow-up for efficacy outcome measures was 2 months, whereas safety was assessed for up to 1 year after device implantation[1].
- No studies were identified that compared the efficacy of implantation of a sphenopalatine ganglion stimulation device against acute medications, prophylactic treatments or other surgical interventions.
- A small number of conference abstracts were identified that assessed the safety and efficacy of the procedure; however, they reported no major safety concerns and were not included in this overview.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Deep brain stimulation for intractable trigeminal autonomic cephalalgias. NICE interventional procedure 381 (2011). Available from: http://www.nice.org.uk/guidance/IPG381

Clinical guidelines

- Headaches. NICE Clinical guidance 150 (2012). Available from http://www.nice.org.uk/guidance/CG150

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to where comments are considered voluminous, or publication would be unlawful or inappropriate. Six Specialist Advisor Questionnaires for implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache were submitted and can be found here; INSERT HYPER LINK TO MAIN IP PAGE.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

Ongoing trials

NCT01255813: Sphenopalatine Ganglion Stimulation for the Acute Treatment of Cluster Headache; Study type, multicentre randomised controlled trial; location, United States; estimated enrolment, 43; estimated completion date, April 2015

NCT02168764: Sphenopalatine Ganglion Stimulation for the Treatment of Chronic Cluster Headache; Study type, randomised controlled trial; location, United States; estimated enrolment, 120; estimated completion date, January 2019

References

1. Schoenen J, Jensen RH, Lantéri-Minet M, Láinez MJ, Gaul C, Goodman AM, Caparso A, May A. (2013) Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: a randomized, sham-controlled study. Cephalalgia. 33 (10):816-30. doi: 10.1177/0333102412473667.

2. Schytz HW, Barløse M, Guo S, Selb J, Caparso A, Jensen R, Ashina M. (2013) Experimental activation of the sphenopalatine ganglion provokes cluster-like attacks in humans. Cephalalgia. 33 (10):831-41. doi: 10.1177/0333102413476370

3. Ansarinia M, Rezai A, Tepper SJ, Steiner CP, Stump J, Stanton-Hicks M, Machado A, Narouze S. (2010) Electrical stimulation of sphenopalatine ganglion for acute treatment of cluster headaches. Headache. 50 (7):1164-74. doi: 10.1111/j.1526-4610.2010.01661

Appendix A: Additional papers on implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

There were no additional papers identified.

Appendix B: Related NICE guidance for implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

Guidance	Recommendations
Interventional procedures	**Deep brain stimulation for intractable trigeminal autonomic cephalalgias NICE interventional procedure 381 (2011).** 1.1 Current evidence on the efficacy of deep brain stimulation (DBS) for intractable trigeminal autonomic cephalalgias (TACs) is limited and inconsistent, and the evidence on safety shows that there are serious but well-known side effects. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake DBS for intractable TACs should take the following actions: • Inform the clinical governance leads in their Trusts. • Ensure that patients and their carers understand the uncertainty about the procedure's efficacy. They should be specifically informed that DBS may not control their headache symptoms and they should be fully informed about the possible risks associated with the procedure, including the small risk of death. Clinicians should provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended. • Audit and review clinical outcomes of all patients having DBS for intractable TACs (see section 3.1). 1.3 Patient selection for DBS for intractable TACs should be carried out by a multidisciplinary team specialising in pain management. 1.4 Further research studies should clearly define patient selection and report the intensity and duration of stimulation, medication use and quality of life, in addition to documenting the effects on headache symptoms as clearly as possible.

Clinical guidelines	**Headaches. NICE Clinical guidance 150 (2012)** **1.3 Management** **Cluster Acute treatment** 1.3.26 Discuss the need for neuroimaging for people with a first bout of cluster headache with a GP with a special interest in headache or a neurologist. 1.3.27 Offer oxygen and/or a subcutaneous [16] or nasal triptan [17] for the acute treatment of cluster headache. 1.3.28 When using oxygen for the acute treatment of cluster headache: • use 100% oxygen at a flow rate of at least 12 litres per minute with a non-rebreathing mask and a reservoir bag and • arrange provision of home and ambulatory oxygen. 1.3.29 When using a subcutaneous[16] or nasal triptan [17], ensure the person is offered an adequate supply of triptans calculated according to their history of cluster bouts, based on the manufacturer's maximum daily dose. 1.3.30 Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache. **Prophylactic treatment** 1.3.31 Consider verapamil [18]for prophylactic treatment during a bout of cluster headache. If unfamiliar with its use for cluster headache, seek specialist advice before starting verapamil, including advice on electrocardiogram monitoring. 1.3.32 Seek specialist advice for cluster headache that does not respond to verapamil [13]. 1.3.33 Seek specialist advice if treatment for cluster headache is needed during pregnancy.

Appendix C: Literature search for implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/09/14	Issue 9 of 12, September 2014
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	30/09/14	Issue 9 of 12, September 2014
HTA database (Cochrane Library)	30/09/14	Issue 9 of 12, September 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/09/14	Issue 9 of 12, September 2014
MEDLINE (Ovid)	29/09/14	1946 to September Week 3 2014
MEDLINE In-Process (Ovid)	29/09/14	September 26, 2014
EMBASE (Ovid)	29/09/14	1974 to 2014 Week 39
PubMed	30/09/14	-
BLIC	30/09/14/	-

Trial sources searched on 29/09/2014

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 29/09/2014

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 exp Cluster Headache/ (2169)

2 (clust* adj4 headach*).tw. (2400)

3 ((daily* or chron* or persist* or constant* or recur* or intract*) adj4 headach*).tw. (5907)

4 Trigeminal Autonomic Cephalalgias/ (114)

5 (Trigemin* adj4 Autonom* adj4 cephalalg*).tw. (171)

6 TACs.tw. (444)

7 exp Headache Disorders/ (26970)

8 (Headach* adj4 disord*).tw. (2369)

9 ((histamine or alarm clock or alarm-clock or horton* or suicid*) adj4 headach*).tw. (149)

10 ((migrainous or ciliary or petrosal) adj4 neuralgi*).tw. (45)

11 (Bing* adj4 erythroprosopalgi*).tw. (2)

12 or/1-11 (31465)

13 neurostimulati*.tw. (1102)

14 ((Sphenopalatin* or pterygopalat* or Meckel*) adj4 stimulat*).tw. (47)

15 Neuromodulat*.tw. (9405)

16 (implant* adj4 (stimulat* or electrod*)).tw. (11241)

17 Electric Stimulation Therapy/ (17468)

18 Elect* stimulat* therap*.tw. (131)

19 Electrodes, Implanted/ (17365)

20 (Electrod* adj4 implant*).tw. (8529)

21 or/13-20 (48640)

22 12 and 21 (377)

23 animals/ not humans/ (3919717)

24 22 not 23 (366)