NICE guidance

Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine

Interventional procedures guidance
Published: 23 March 2016

www.nice.org.uk/guidance/ipg552

1 Recommendations

1.1 Current evidence on the safety of transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine raises no major concerns. The evidence on efficacy is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine should:

- Inform the clinical governance leads in their NHS trusts.

- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.

- Audit and review clinical outcomes of all patients having transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine (see section 7.2).

1.3 NICE encourages further research on transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine. Studies should describe whether the procedure is used for treatment or prevention, and whether it is used for cluster headache or migraine. Clinicians should clearly document details of patient selection and the treatment regimen. Outcome measures should include changes in the number and severity of cluster headache or migraine episodes, medication use, quality of life in the short and long term, side effects, acceptability, and device durability. NICE may update this guidance on publication of further evidence.

2 Indications and current treatments

2.1 Cluster headaches are characterised by episodes of unilateral periorbital pain, conjunctival injection, lacrimation and rhinorrhoea. Attacks can last from a few minutes to several hours and can occur many times a day, for several days, weeks, months or years. Migraines are severe headaches that may last for hours, days or longer, often accompanied by nausea, photophobia, phonophobia and the perception of unpleasant odours. In some people migraines may be accompanied by an aura, characterised by the focal neurological symptoms that usually precede or sometimes accompany the headache. The International Headache Society's International Classification of Headache Disorders classifies migraine types.

2.2 The usual treatment option for patients with cluster headache or migraine is medical therapy, either to stop or prevent attacks. Treatments for acute cluster headache attacks include oxygen inhalation and medications such as triptans. Corticosteroids and verapamil may be used to prevent or reduce the frequency of cluster headaches. Treatments for

acute migraine attacks include analgesics, triptans and anti-emetics (as recommended in NICE's guideline on headaches in over 12s). Beta-blockers, tricyclic antidepressants and antiepileptics (topiramate, sodium valproate) may be used to prevent or reduce the frequency of migraine attacks.

2.3 Invasive treatments are reserved for patients with distressing symptoms that are refractory to medical treatments. For patients with chronic cluster headache, these include deep brain stimulation to modulate central processing of pain signals. For patients with chronic migraine, these include treatments such as nerve blocks, botulinum toxin (see NICE's technology appraisal guidance on botulinum toxin type A for the prevention of headaches in adults with chronic migraine), acupuncture or nerve stimulation.

3 The procedure

3.1 Transcutaneous vagus nerve stimulation uses low-voltage electrical currents to stimulate the cervical branch of the vagus nerve. The aim is to relieve pain and reduce the frequency of attacks for both cluster headaches and migraine.

3.2 Therapy is administered by the patient, using a handheld device the size of a mobile phone. The patient places the device on the side of the neck, over the cervical branch of the vagus nerve, positioning its 2 smooth metal stimulation surfaces in front of the sternocleidomastoid muscle, over the carotid artery. The patient slowly increases the stimulation strength until small muscle contractions are felt under the skin; stimulation is then applied for approximately 90 seconds. The device can be used to treat acute attacks, and as prophylaxis between attacks.

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.

Efficacy of transcutaneous stimulation of the cervical branch of the vagus nerve for treating cluster headache

4.1 In a randomised controlled trial of 97 patients with cluster headache treated by standard care plus transcutaneous vagus nerve stimulation (tVNS; n=48) or standard care alone (n=49), the mean number of cluster headache attacks per week decreased by 5.9 attacks in the standard care plus tVNS group and by 2.1 attacks in the standard care alone group at 4-week follow-up (p value between groups=0.02). Baseline measurements were not reported. During the extension phase of the study, patients from both groups received adjunctive tVNS for 4 additional weeks. In this period, the mean number of cluster headache attacks per week decreased from 9.6 to 7.6 in patients who were initially in the standard care plus tVNS group (n=30; p<0.001) and from 15.7 to 12.4 in patients initially in the standard care alone group (n=41; p<0.001).

4.2 In a case series of 19 patients with cluster headache, complete resolution of pain was achieved in 47% of cluster headache attacks within a mean of 11 minutes of starting neurostimulation.

4.3 In the randomised controlled trial of 97 patients with cluster headache treated by standard care plus tVNS or standard care alone, the mean number of times subcutaneous sumatriptan was used decreased from 7.2 to 2.8 in the standard care plus tVNS group (n=32; p=0.007) and increased from 6.8 to 7.5 in the standard care alone group (n=42; not significant), during the last 2 weeks of the 4-week follow-up period. In the same study, the mean number of times inhaled oxygen was used decreased from 17.3 to 6.5 in the standard care plus tVNS group (n=32; p=0.02) and from 12.6 to 10.8 in the standard care alone group (n=42; not significant) during the last 2 weeks of the 4-week follow-up period.

4.4 In the randomised controlled trial of 97 patients with cluster headache treated by standard care plus tVNS or standard care alone, mean EQ-5D scores (ranging from 0 to 100 with higher scores indicating better quality of life) increased from baseline by 9.20 and 0.27 points respectively at

4-week follow-up (p=0.039). During the extension phase of the study, patients from both groups received adjunctive tVNS for 4 additional weeks. In this period, mean EQ-5D scores increased from baseline by 10.79 points in patients who were initially in the standard care plus tVNS group and by 4.36 points in patients initially in the standard care alone group (p value not reported).

Efficacy of transcutaneous stimulation of the cervical branch of the vagus nerve for treating migraine

4.5 In a case series of 50 patients with high-frequency episodic migraine or chronic migraine, pain relief (defined as more than a 50% improvement in visual analogue scale scores for pain) was reported in 38% (50/131) of attacks, 1 hour after neurostimulation. Complete resolution of pain was reported in 18% (23/131) of attacks, 1 hour after neurostimulation. Pain relief and complete resolution of pain were reported in 51% (67/131) and 23% (30/131) of attacks respectively, 2 hours after neurostimulation.

4.6 In a case series of 30 patients with migraine, relief of nausea was reported in 38% (11/29) of attacks accompanied by nausea. In the same study, relief of photophobia was reported in 30% (16/53) of attacks accompanied by photophobia. Relief of phonophobia was reported in 52% (17/33) of attacks accompanied by phonophobia.

4.7 In the case series of 50 patients with high-frequency episodic migraine or chronic migraine, complete recovery from functional disability was reported in 35% (46/131) of attacks 2 hours after neurostimulation.

4.8 In the case series of 50 patients with high-frequency episodic migraine or chronic migraine, rescue medication was needed in 53% (70/131) of attacks 2 hours after neurostimulation.

4.9 Specialist advisers listed key efficacy outcomes as complete resolution of pain, reduction in the frequency, duration and severity of headache episodes, use of rescue medication, and improvements in quality of life.

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 In a randomised controlled trial of 97 patients with cluster headache, transcutaneous vagus nerve stimulation (tVNS) was judged to cause cluster headache in 2% (1/48) of patients in the standard care plus tVNS group and 10% (5/49) of patients initially in the standard care alone group but who then received adjunctive tVNS in a 4-week extension phase. In the same study, headaches that were not cluster headaches were reported in 8% (4/48) of patients in the standard care plus tVNS group and 2% (1/49) of patients initially in the standard care alone group.

5.2 Dizziness was reported in 6% (3/48) of patients in the standard care plus tVNS group and 6% (3/49) of patients in the standard care alone group in the randomised controlled trial of 97 patients with chronic cluster headache (no further details on timing in relation to tVNS provided).

5.3 Oropharyngeal pain was reported in 6% (3/48) of patients in the standard care plus tVNS group and 2% (1/49) of patients in the standard care alone group in the randomised controlled trial of 97 patients with chronic cluster headache.

5.4 Moderate shoulder pain or spasm was reported in 7% (2/28) of patients in a case series of 30 patients with migraine (no further details on timing in relation to tVNS provided).

5.5 Mild lip or facial drooping was reported in 7% (2/28) of patients in the case series of 30 patients with migraine (no further details on timing in relation to tVNS provided).

5.6 Neck stiffness was reported in 18% (5/28) of patients in the case series of 30 patients with migraine (no further details on timing in relation to tVNS provided).

5.7 Reddening of the skin around the treatment site was reported in 7% (2/

28) of patients in the case series of 30 patients with migraine.

5.8 In the randomised controlled trial of 97 patients with chronic cluster headache treated by standard care plus tVNS or standard care alone, 1 or more of the following device-related adverse events were reported in 27% (13/48) of patients in the standard care plus tVNS group: depressed mood, malaise, oropharyngeal pain, induced cluster headache, muscle twitching, muscle spasms, hot flushes, acne, pain, throat tightness, dizziness, hyperhidrosis, toothache, decreased appetite and skin irritation. One or more of the following device-related adverse events were reported in 14% (7/49) of patients initially in the standard care alone group: erythema, facial oedema, induced cluster headache, chest pain, fatigue, depressed mood, pruritus, musculoskeletal stiffness and parosmia. All adverse events occurred during the extension phase of the study when these patients received adjunctive tVNS.

5.9 A single occurrence of the following adverse events was reported in the case series of 30 patients with migraine: mild confusion that lasted for 2 hours after neurostimulation, joint pain, mild twitching of neck muscles, mild swelling of the neck, tinnitus in 1 ear, fever (39ºC), a raspy voice, fatigue, coughing and sneezing.

5.10 Palpitations were reported in 1 patient in a case series (conference abstract) of 18 patients with various primary headache disorders. In the same study, tonic muscle contraction was reported in 17% (3/18) of patients and cervical muscle spasm was reported in 1 patient.

5.11 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 listed the following anecdotal adverse events: shortness of breath and changes in blood pressure. They considered that cardiac arrhythmia and interaction with pacemaker devices were theoretical adverse events.

6 Committee comments

6.1 The committee noted that migraine is a very common condition and therefore good evidence of efficacy is particularly important. This consideration contributed to the recommendation for further research.

6.2 The committee noted that cluster headache is a rare condition and that few effective treatment options exist for it.

6.3 The committee noted that the evidence for the efficacy of transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache was better than for migraine.

6.4 In its interpretation of the evidence, the committee noted the potential for a placebo response and the relapsing and remitting course of cluster headaches and migraine.

6.5 The committee noted that further evidence is likely to become available from a number of current trials.

6.6 The committee noted patient commentary and the number of positive comments received from patients during public consultation, much of which was favourable.

7 Further information

7.1 For related NICE guidance, see the NICE website.

7.2 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

Information for patients

NICE has produced information on this procedure for patients and carers (information for the public). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

ISBN: 978-1-4731-1771-6

Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation