Treatment of intractable chronic cluster headache by occipital nerve stimulation in 14 patients

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ABSTRACT

Background: Cluster headache is a primary headache involving repeated attacks of excruciatingly severe headache usually occurring several times a day. Most patients with chronic cluster headache (CCH) have an unremitting illness requiring daily preventive therapy for years.

Objective: To describe the clinical outcome of occipital nerve stimulation (ONS) for 14 patients with intractable CCH.

Methods: Fourteen patients with medically intractable CCH were implanted with bilateral electrodes in the suboccipital region for ONS and a retrospective assessment of their clinical outcome obtained.

Results: At a median follow-up of 17.5 months (range 4–35 months), 10 of 14 patients reported improvement and 9 of these recommend ONS. Three patients noticed a marked improvement of 90% or better (90%, 90%, and 95%), 3 a moderate improvement of 40% or better (40%, 50%, and 60%), and 4 a mild improvement of 20–30% (20%, 20%, 25%, and 30%). Improvement occurred within days to weeks for those who responded most and patients consistently reported their attacks returned within hours to days when the device was off. One patient found that ONS helped abort acute attacks. Adverse events of concern were lead migrations and battery depletion.

Conclusion: Intractable chronic cluster headache (CCH) is a devastating, disabling condition that has traditionally been treated with cranially invasive or neurally destructive procedures. ONS offers a safe, effective option for some patients with CCH. More work is required to evaluate and understand this novel therapy. ***Neurology***® **2009;72:341–345**

GLOSSARY

CCH = chronic cluster headache; **DBS** = deep brain stimulation; **DHE** = dihydroergotamine; **ONS** = occipital nerve stimulation.

Cluster headache is a form of primary headache characterized by bouts during which patients experience many attacks of very severe headache. Chronic cluster headache (CCH) is defined as having a break of no more than a month in every 12 months, unless there is some form of treatment.[1] A proportion of patients with CCH are refractory to medical management, although it is unclear how large this problem is since guidelines have only recently defined such patients.[2]

Destructive surgery for CCH, such as trigeminal nerve root section, has been reported to be useful after long-term follow-up despite serious side effects, including death, corneal anesthesia, anesthesia dolorosa, and jaw deviation.[3] Although this surgery is performed for those with strictly unilateral attacks, there is a risk of attacks swapping sides or persisting on the same side despite trigeminal nerve root section.[3]

Neurostimulation involves central or peripheral nervous system targets. Central neurostimulation has been used for medically intractable cluster headache and utilizes deep brain stimulation (DBS) of the posterior hypothalamus but carries a small risk of fatal hemorrhage.[4] Peripheral stimulation of the occipital nerve has been used in a number of open label trials and

Supplemental data at www.neurology.org

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Table 1 Patients' estimates of cluster frequency, severity, and duration of attacks before and after use of stimulator

	Frequency		Severity (peak/average)*		Duration, min			
					Before		After	
Patient no.	Before	After	Before	After	Without abortive	After using SSC 6 mg	Without abortive	After using SSC 6 mg
1	2/d	2–3/d	10/No data	10/8	240	No data	240	No data
2	10–20/d	Same	10/9	10/8	120	15	60–70	Same
3	1–6/d	Same	10/No data	10/No data	120	10	120	10
4	8–12/d	1–4/mo	10/8	10/10	15–90	N/A	15–90	N/A
5	3/d	Same	10/8	10/8	15–30	<30	<30	No data
6	2–3/d	4–5/wk	8/6–7	7–8/6–7	120	20	N/A	8–15
7	1–2/d	0–1/d	10/10	10/9	60–600	60–120	180	60
8	2–12/d	0–8	10/5	10/5	30–90	5–20	30–60	Same
9	4–5/d	2–3/d	10/9	5–10/7–8	180–240	20	N/A	20
10	3–4/d	1–6/wk	10/6–10	10/6–10	30–180	<30	N/A	<15
11	6–8/d	Same	10/9	10/8	60–180	90*	N/A	60*
12	0–2/d	1/wk–2/d	10/8	10/7	180–240	30	Same	Same
13	2–8/d	3–5/d	10/8	5/5	40–120	10	15–30	10
14	0–4/d	Same	10/9	10/9	180–240	Inconsistent	Same	Using DHE

No. 11: Triptan changed from rizatriptan wafer to SSC after implant. No. 14: Does not use abortive as on IM DHE. No. 13: Values for bilateral electrodes only.
*Values based on verbal rating scale out of 10.
SSC = subcutaneous sumatriptan; N/A = not applicable, always uses abortive; DHE = dihydroergotamine.

series for several primary headaches[5] but more information on the long-term outcome for medically intractable CCH is required. This report of occipital nerve stimulation (ONS) for CCH follows our initial report for eight patients[6] with extended follow-up and a further six patients.

METHODS **Patient selection.** Patients with medically refractory CCH from outpatients at the National Hospital, Queen Square, London, UK, were offered ONS. Patients were offered the choice of a destructive trigeminal nerve procedure or DBS as alternatives and the first 14 such patients all opted for ONS and were implanted over a 40-month period from 2003 to 2006. Patients fulfilled the standard criteria for CCH,[1] with the exceptions of one who had long attacks (case 1) and two who had a high frequency of attacks (cases 2 and 4) whose lack of an indomethacin response ruled out chronic paroxysmal hemicrania.[1]

Occipital nerve block using lidocaine and corticosteroid and a trial of ONS did not form part of the selection criteria.

Patients were implanted on compassionate grounds and the study was an audit of outcome and, as such under UK guidelines, does not require ethics committee approval.

Surgical technique. Bilateral ONS electrodes, leads, and battery were implanted after informed consent was obtained (L.W.). In brief, a single stage procedure with two parts was used to allow an intraoperative trial of stimulation. The first part was performed under local anesthetic and gentle sedation, with care taken to avoid anesthetizing the occipital nerves. The patient was placed in the lateral position and a sterile field was established. A midline posterior cervical incision was made and bilateral cylindrical style, quad electrodes (Medtronic, Inc., Minneapolis, MN) were introduced with curved Tuohy needles using an image intensifier to aid position. A dual program pulse generator (Medtronic Synergy from Medtronic, Inc.) was then used to test stimulation and confirm paresthesia was felt bilaterally. The second part of the insertion was performed under a general anesthetic. The electrodes were looped and anchored to the cervical fascia then tunneled to a lateral cervical or subclavicular skin crease intermediate incision. A left/right subclavicular or abdominal incision was made (according to patient preference) to form a pocket to implant the pulse generator. Electrodes were tunneled to the intermediate incision and a pair of extensions lead (Medtronic, Inc.) attached. Silicone sheaths were used to protect the lead connections. Topical antibiotic cover with gentamicin was introduced around the pocket. The incisions were closed.

Patients were provided with and instructed how to use remote controls to communicate with the implanted pulse generators. It was possible for patients to adjust their stimulator settings if they chose to by using the remote control although the pulse generators were programmed to provide continuous stimulation. Patients could turn the stimulator on/off or vary the pulse width, frequency, or amplitude, although most patients tended only to vary the amplitude. The polarity of the electrodes was adjusted during follow-up visits to achieve comfortable bilateral paresthesia in the occipital region. Patients remained in hospital for several days after implantation.

Follow-up and data collection. Data were collected from patient records, outpatient visits, and mail and telephone by one investigator (B.B.). Patients retrospectively compared their attacks before and after the procedure; patient diaries were not

Table 2 Follow-up for main outcomes

Patient no.	Months since implantation at follow-up	Patients' overall view of outcome since implantation	Patients' estimate of % change in cluster headache since implantation	Triptan use before vs after implantation	Would patient recommend use of stimulator?
1	31	Same	0	Same	No
2	6	Improved	20	Same	Yes
3	35	Same	0	Same	Yes
4	10	Improved	90	Not using	Yes
5	19	Improved	95	Less	Yes
6	25	Improved	60	Less	Yes
7	14	Improved	50	Less	Yes
8	9	Improved	25	Same	Not sure
9	35	Improved	20	Same	Yes
10	16	Improved	90	Less	Yes
11	19	Same	0	Same	Yes
12	11	Improved	30	Less	Yes
13*	32 (23)	Improved	40	Less	Yes
14	4	Same	0	Not using†	Not sure
Summary	17.5 (4–35)	10 Improved	3 at ≥90%	6 Less	11 Yes
		4 The same	3 at 40–60%	6 Same	1 No
			4 at 20–30%	2 Not using	2 Not sure
			4 at 0%		

*Value for left electrode (bilateral electrodes). Median (ranges for bilateral electrodes).
†Using IM dihydroergotamine.
No. 2: Improvement mainly due to reduction in background pain. No. 8: Improvement could be accounted for by patient using intermittent steroids. No. 11: Not achieving consistent stimulation for 7–8 months and feels he is no better than before implant although previously reported 25% improvement. No. 12: Improvement in both background headache and frequency of attacks. No. 13: Patient did not have stimulator on since 23 months after bilateral electrodes (40% improvement occurred in first 12 months).

used. Triptan use was similarly assessed and the following question was asked: Would you recommend the procedure to a fellow cluster headache sufferer? Additionally, patients' opinion as to how long it took before minimal and maximal improvement and if deteriorated occurred when their device was switched off, together with the time taken for this and recovery.

RESULTS

Patient demographics. Ten men and four women with a median age of 44 years (range 31–58 years) were implanted. Median duration of CCH at the time of operation was 6 years (range 2–17). Seven had secondary CCH, the chronic form evolved from an episodic form, and seven had primary CCH, i.e., chronic since the beginning.

Previous therapies. All patients were intractable according to a recent definition,[2] having tried and failed or being unable to tolerate at least four of the most commonly used preventive medications.

Baseline headache pattern. Table 1 provides the cluster headache frequency, duration, and severities prior to ONS.

Follow-up and overall outcome. Median follow-up for bilateral electrodes was 17.5 months (range 4–35; table 2). Ten of 14 (71%) patients improved. Eleven patients recommended ONS to others. No patient became pain free. Improvement occurred in frequency, severity, or duration but a reduction in frequency was most apparent.

Change in attacks. Of the 10 patients who improved, 3 improved by 90% or better, 3 by 40% or better, and 4 by 20–30% (table 2). Some patients noticed a reduction in background pain (see notes for table 2). Patients who improved did so without the addition of new therapy, other than patient 8, who occasionally used intermittent dexamethasone.

Triptan use. With regards to triptans, one patient stopped use, five reduced use, six did not alter use, and two were not using triptans for other reasons (table 2).

Time to effect and time to reappearance. Five patients (cases 4, 5, 6, 7, 10) who benefited by 50% or more improved within weeks (table 3). Slower improvement occurred for those with less benefit (cases 2, 8, 12, and 13), with the exception of case 9, who improved quickly. When a technical fault developed, patients reported an immediate (hours or days) worsening of their headache in five cases (cases 2, 4, 6, 7,

Table 3 Patient estimates of time taken to improve and response to stopping and restarting occipital nerve stimulation

Patient no.	Time to improvement?		Cluster response to stopping occipital nerve stimulation?		Cluster response to restarting occipital nerve stimulation?	
	Minimal	Maximal	Worse	Time taken	Improved	Time taken
1	N/A					
2	6 mo	Don't know	Yes	Few hours	Waiting battery	
3	N/A					
4	48 h (50%)	4 wk (60–70%), 6 mo (90%)	Yes	1 h	Yes	3 d
5	Immediate	Immediate	No	N/A		
6	3–7 d	3–7 d	Yes	Immediate	Yes	2 d
7	Immediate	5 mo	Yes	Few hours	Yes	Few hours
8	4 mo	6 mo	Not been off	N/A		
9	Next day	2 wk	Yes	3 wk	Yes	Next day
10	2–3 wk	3–4 wk	Yes	Immediate	Yes	Immediate
11	N/A					
12	6 mo	Improving	Not been off	N/A		
13	3 mo	18 mo	Not been off	N/A		
14	N/A					

N/A = not applicable.

10), but over 3 weeks for a sixth (case 9). After fixing faults, all patients rapidly improved within 3 days (see table 3).

Technical issues. Twelve patients used continuous, two used intermittent stimulation. A wide range of stimulator settings were used (table e-1 on the *Neurology*® Web site at www.neurology.org). As a group, the range for amplitude was 0–10.5 volts, pulse width 60–450 μsec, and frequency 3–130 Hz.

Complications. Complications are listed in table e-2. Occipital paresthesia was considered a reassuring marker of activity, although one patient (case 5) found this unpleasant and only used stimulation intermittently. The mean battery life was 15.1 months and as a result, the most common "complication" was battery depletion requiring replacement for 6 of the 14 patients (43%). Four patients required new electrodes/leads (29%). Muscle recruitment, neck stiffness, skin discomfort, superficial infections, and painful overstimulation were also seen.

DISCUSSION ONS for CCH was initially abstracted for two cases and was safe and effective.[7] Larger series have followed[6,8] and the general outcome seems to be positive for a significant proportion of otherwise highly disabled patients.

Although response rates are better for DBS, with over two-thirds of patients reported as completely pain free in the largest study to date,[9] one might conclude that ONS should be tried first, since its side effect profile is modest. Interestingly, it has been reported in abstract that five of six patients with drug-resistant CCH who failed to respond to ONS had a 60% or better response to hypothalamic DBS.

In our initial description,[6] the time to improvement was months, in keeping with other data.[8] Retrospective exploration of this issue (table 3) appears to show two groups, the first being patients with quick improvement within weeks going on to report most benefit (cases 4, 5, 6, 7, 10) and the second being those gradually improving over months reporting less substantial benefit (cases 2, 8, 12, and 13). The exception is case 9.

A limitation of this study is the absence of a control group. This is of particular concern as there is little doubt placebo effects are seen in cluster headache and the natural history of cluster headache is to fluctuate. Blinding with ONS is a particular challenge since it seems paraesthesia is a requirement for the clinical effect. Two main observations in this report suggest more than natural history or a placebo effect: the preceding duration of chronicity for this patient group was a median of 6 years (range 2–17 years) and the rapid deterioration and recovery after technical failures, which appears a consistent finding in other similar series.[8] Randomized controlled trials are now ongoing in migraine (PRISM NCT00286078 and ONSTIM), with provisional results for ONSTIM suggesting effectiveness over sham stimulation.[10] Taken together, our data and current studies suggest at least an

open mind and more careful prospective work is required.

Neither we nor others[11] have so far been able to identify a favorable set of stimulator settings or paresthesia to predict or improve efficacy.

For the future, electrode migration needs to be minimized and although battery depletion is not strictly a complication it did require further surgery. However, with the recent availability of rechargeable batteries this issue will probably become a historic one.

The outcome of this study provides hope for patients whose lives have been devastated and an opportunity to understand the biology of primary headache syndromes.

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