Pain Physician 2014; 17:E369-E374 • ISSN 2150-1149

Case Report

The Effects of Peripheral Occipital Nerve Stimulation for the Treatment of Patients Suffering from Chronic Migraine: A Single Center Experience

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 06-25-2013
Revised manuscript received: 01-08-2014
Accepted for publication: 01-28-2014

Free full manuscript: www.painphysicianjournal.com

About 1% of patients suffering from chronic migraine do not respond to medications and require more invasive treatments. Occipital nerve stimulation (ONS) is one of these new therapeutic options. The aim of this data review is to evaluate the clinical impact of ONS and whether the neuropsychological aspects of anxiety and depression can be considered as predictors of therapeutic effects.

Seventeen migraine patients, according to the ICHD-II classification, were treated with ONS. At baseline all patients were assessed by numeric rating scale (NRS), Migraine Disability Assessment (MIDAS), SF-36 Health Survey (SF-36), Beck Depression Inventory II (BDI II), and Beck Anxiety Inventory (BAI) questionnaires. MIDAS and NRS were re-assessed at 3 and 12 month follow-up visits, while SF-36 was evaluated after 12 months of stimulation. The population was divided in 2 subgroups based on MIDAS improvement, and BDI II and BAI scores in the 2 subpopulations were compared to investigate whether anxiety and depression can be considered as predictive factors of clinical outcomes. MIDAS showed a significant reduction both at 3 and 12 month visits and NRS scale showed the same trend. The SF-36 questionnaire showed a significant improvement not only in Physical Component Summary (PCS) and Mental Component Summary (MCS) indices, but also in sub-dimensions. Patients who reported a MIDAS improvement ≤ 40% showed a significant difference in BDI-II test at baseline.

Significant clinical improvements were obtained already after 3 months of treatment and stayed stable throughout the first year after the procedure. ONS seems to be an effective and safe treatment for chronic migraine. The effects of ONS can be optimized by a multidisciplinary diagnostic and therapeutic approach, especially for the importance of the psychological factors in pain perception and their correlation with a good therapeutic outcome. Our experience highlighted that a multidisciplinary team which includes psychological support and psychosocial rehabilitation is essential for the success of this therapy.

Key words: Peripheral nerve stimulation, PNS, chronic migraine, ONS, occipital nerve stimulation, intractable migraine, stimulation

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Despite the efforts made by research in the field of the treatment of migraine, about 1% of patients suffer with a form that does not respond to medications and requires other treatments (1-3). Occipital nerve stimulation (ONS), one of these techniques, significantly reduces the frequency of attacks and disability related to migraine (4,5). The severity and long-term continuity of chronic migraine may have a strong psychological impact, leading patients to lose their social roles both within the family and in the workplace (6-8). Reactive symptoms of anxiety and depression as well as relational

difficulties may arise leading to a consequent increase in avoidance behaviors (5-8). For a comprehensive treatment protocol it is important to include in the flow chart an operative program offering psychological support and psychosocial rehabilitation which supports the patient toward the restructuring of the self and the re-acquisition of a social identity. The goal of our data review is to evaluate the clinical impact of occipital neurostimulation for the treatment of chronic migraine. We also evaluated whether the state of anxiety and depression at baseline can be considered as a predictor of therapeutic effects and influence the perception of clinical outcomes.

Methods

Seventeen patients treated with ONS at our Department of Pain Medicine of Cà Granda Hospital (Italy) between 2008 and 2011 have been included in this data review. All patients met these inclusion criteria: (i) diagnosis of chronic migraine according to the ICHD-II (9), (ii) failure of previous drug therapies, positive surgical evaluation, (iii) Migraine Disability Assessment (MIDAS) scale score > 21, (iv) numeric rating scale (NRS) score > 5, (v) absence of a primary diagnosis of psychiatric condition (with exception for the presence of anxious-depressive symptoms of the reactive type related to pain), (vi) high compliance, adequacy of expectations of efficacy, absence or limited expectations of efficacy also on the comorbidities related to the migraine.

For all patients, the diagnosis of chronic intractable migraine was made by Italian headache centers. The clinical assessment of patients has been carried out according to the Eurpoean Federation of Neurological Societies (EFNS) (10) international guideline by a multidisciplinary team including anesthetists, pain specialists, neurologists, surgeons, psychiatrists, and psychologists. All surgical procedures were performed by the same surgical team. All patients were assessed by NRS, MIDAS at baseline and 3 and 12 months after the implant of a neurostimolator, SF-36 questionnaire was evaluated before the implant and after 12 months of stimulation. Beck Depression Inventory II (BDI II) was used to assess the depressive framework before surgery and the Beck Anxiety Inventory (BAI) was used for the assessment of anxiety symptoms at baseline. Clinical and psychological interviews were run in order to explore the general functioning of the patient at the psychosocial level, the motivations for surgery, and the expectations for improvement and compliance.

To assess whether there was a different psychological profile that could influence the perception of clinical outcomes obtained after the implant, the patient population was divided into 2 groups according to the percentage of improvement recorded after 12 months of treatment with the MIDAS scale (group 1 MIDAS improvement $\leq$ 40%; group 2 MIDAS improvement > 40%). This data review was approved by IRB of this institution and all patients gave their informed consent before being included.

Surgical Technique

ONS takes place in 2 stages. In the first stage one percutaneous octopolar lead (Octad, St. Jude Neuromodulation, Plano, TX) is placed subcutaneously under local anesthesia and minimal sedation (anxiolysis) with continuous monitoring and assistance of the anesthesiologist. The lead is placed using a lateral (or retromastoid) approach.

Sterile preparation of the surgical field is used and, to prevent infections, a short-term antibiotic prophylaxis was given after the lead insertion. The patient is placed in a prone decubitus position. A retromastoid incision is made in correspondence of the lateral side of the suboccipital triangle. A Tuohy needle is inserted subcutaneously and transversally in this entry point, and then the octopolar electrode is inserted through the needle and placed perpendicularly to the occipital region, above the peripheral branches of the occipital nerves at C2 level, to intercept the main nerve afferents of the great and lesser occipital nerves (GON and LON) bilaterally.

Through this lateral approach, the single octopolar electrode is inserted across the midline, in order to provide bilateral stimulation coverage. Intraoperative fluoroscopy is routinely used before the lead insertion to identify anatomic landmarks (C2 and mastoid process), during the lead insertion to verify the correct direction and orientation of the lead, and after the lead implantation to verify the final electrode location (Fig. 1). The correct paresthesia coverage of the painful area was tested intraoperatively. In correspondence of the incision a small subcutaneous pocket is made to leave a stress relief loop and to fix the lead to the fascia with absorbable suture. No anchor system is used to fix leads, in order to avoid skin erosion or pain in correspondence of the anchor's site. Then the subcutaneous lead is tunneled and connected via an extension cable to an external stimulator (Trial Stimulator, St. Jude Neuromodulation, Plano, TX). The connection between lead and

external cable is placed in a small subcutaneous pocket close to the midline at C7/T1 level in the periscapular area controlaterally to the side of the entry point of the lead. With this approach, the pathway of the lead creates a sharp angle (like a 7 inverted) to prevent lead migration. Before being connected to the extension cable, the lead is looped.

The stimulation test lasts for about 3 – 4 weeks after which the patients underwent an assessment to define the real effectiveness of the procedure. In addition, the trial period was useful to assess the real compliance of the patient in managing the stimulation, and tolerability and expectations of patients regarding the treatment. During the trial phase patients can experience the parasthesias related to the ONS and verify whether it is tolerable or not, and clinicians can further understand whether patients' expectations are realistic or not. The patients underwent the second phase of implant if (i) a reduction in the number of migraine attacks was > 40%, (ii) a reduction in the intensity of the crisis was > 40%, (iii) an adequate functional recovery and a reduction of perceived discomfort in everyday life had been reached (6), or (iv) patients were able tolerate the pareshesia, manage the system, and not have unrealistic expectations regarding the treatment (6-8).

The second phase of surgery consists of creating a subcutaneous pocket in the abdominal wall to lodge the Implantable Pulse Generator (IPG) (Genesis St. Jude Neuromodulation, Plano, TX). The IPG is connected with the previously placed lead. The external connection was removed and the permanent one is tunneled through a periscapular to a low abdominal pathway. The connection is placed in the same small pocket used for the temporary connection. To prevent infection a short-term prophylaxis was given after the IPG implantation. The stimulation parameters are determined according to the patient report. However the patients can adjust the stimulation parameters by themselves according to their needs, via an external remote control.

Statistical Analysis

Continuous data are presented as mean ± SD. A general linear model for repeated measures was used to compare the scores of MIDAS and NRS administrated over time. Differences between SF-36 indexes [Physical Component Summary (PCS) and Mental Component Summary (MCS) indices] and sub items at the 2 follow-up controls were evaluated by means of non-parametric matched pairs Mann-Whitney test. Comparisons between groups were carried out by one-way analysis of variance (ANOVA) using MIDAS improvement at 12 months follow-up as an independent variable. All 2-tailed P values < 0.05 were considered statistically significant. The SPSS version 9.0 statistical package was used for the analysis.

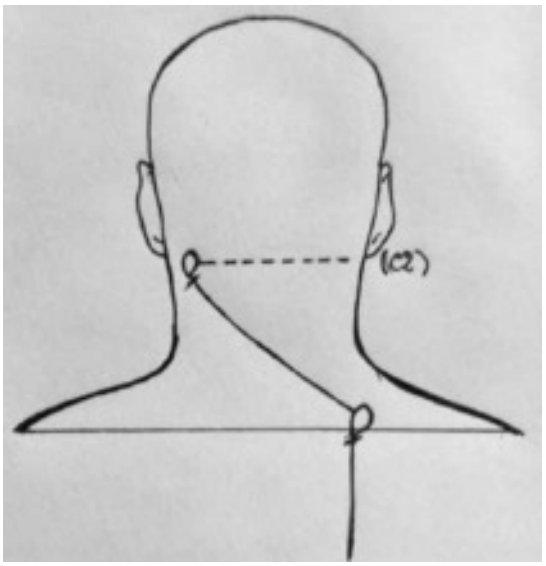

Fig. 1. *Illustration showing proper lead placement.*

Results

Demographic data are shown in Table 1. All patients underwent definitive implant.

The MIDAS questionnaire showed a significant reduction both at 3 and 12 month visits compared to the basal values (Table 2), with an improvement of 42% (± 9.7) and 46% (± 28.2), respectively.

The NRS scale showed the trend (Table 2), with an improvement of 49% (± 16.7) at 3 months and 40% (± 30.5) at 12 months.

The SF-36 questionnaire showed a significant improvement both in PCS and MCS indices. After 12 months of the stimulation all the sub-dimensions significantly improved (Fig. 2).

A migration of the lead occurred in 5 patients and all migrations occurred in the first 2 months after the implant. All migrated leads were repositioned in the following days without further complications for the patients. All lead migrations were related to repeated lead and extension traction events due to the high mobility of the implanted area. Three IPGs were removed after an average of 8 months from surgery. Two ex-

Table 1. *Demographic characteristics and basal scores.*

Variables (N = 17 pts) Minimum Maximum Mean Std.	Minimum	Maximum	Mean	Standard Deviation
Age	31	77	51.12	13.233
Gender	15 Females (88%); 2 Males (12%)			
Midas basal	22	68	45.29	13.810
NRS basal	8	10	9.76	.664
BDI total basal	50	99	86.53	17.547
BDI Cognitive. basal	40	99	88.59	17.582
BDI Affective. basatl	40	99	83.59	18.745
BAI basal	40	99	82.82	17.296
BAI (num)	3.00	32.00	16.1176	7.95206
PCS basal	**20.99**	**34.97**	**29.8154**	**3.03496**
MCS basal	**12.41**	**40.28**	**26.5498**	**6.62911**

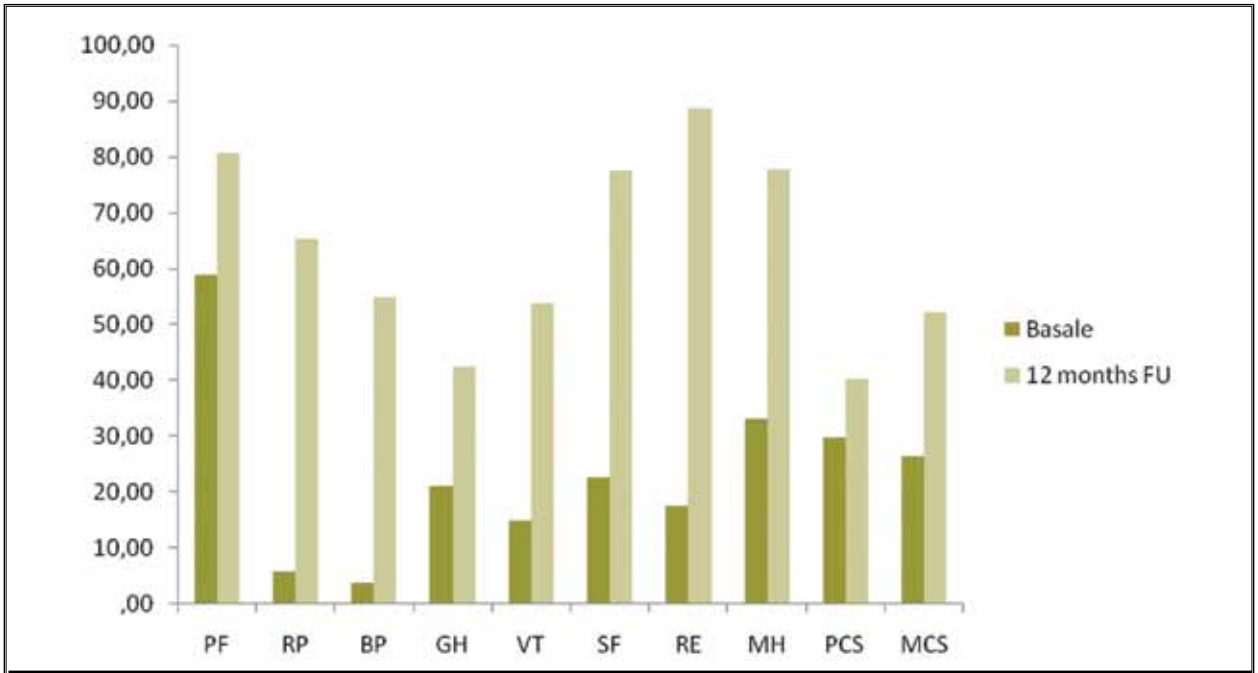

Fig. 2. *SF-36 mean score at the baseline and at 12 months after implant.*
PF = Physical Functioning, RP = Role Physical, BP = Bodily Pain, GH = General Health, VT = Vitality, SF = Social Function, RE = Role Emotional, MH = Mental Health, PCS = Physical Component Summary, MCS = Mental Component Summary. The PCS and MCS increased from a mean of 29.8 ±3 and 26.5 ± 6.6 at the baseline to 40.3 ± 7 and 52.3 ± 6.7 at 12-months after implant respectively ($P = 0.001$).

Table 2. *Scores of rating scales at baseline, 3 and 12 months FU (Mean ± SD).*

Assessment (N = 17 pts)	Baseline	3 Months Follow-up	12 Months Follow-up
MIDAS	45.3 ± 13.8	26.2 ± 8.1*	22.1 ± 9.74*
NRS	9.8 ± 0.7	5.0 ± 1.6*	5.7 ± 2.6*
PCS	29.8 ± 3		40.3 ± 7*
MSC	26.5 ± 6.6		52.3 ± 6.7*

* the asterisk indicates statistically significant value ($P < 0.05$)

plants occurred following a specific request from the patient because of a loss of effectiveness of the therapy. In one case the explant was due to the onset of a disturbing abdominal pain perceived in the area of the subcutaneous pocket.

The 2 groups, obtained on the basis of clinical improvement, were respectively formed of 8 (group 1) and 9 patients (group 2). The comparison of basal psychological tests showed a significant difference in BDI-II (90.6 ± 16.9 in group 1, 82.9 ± 18.3 in group 2; $P = 0.043$).

Discussion

The results showed the efficacy of ONS in the treatment of chronic migraine (4-5). Significant improvement in the scales was obtained after 3 months of treatment and stayed stable throughout the first year after the procedure. Clinical improvements were highlighted also by psychological interviews during follow-up assessments. Anxiety and depression seemed to be important factors in overall morbidity and should be well investigated in patients eligible for ONS. To investigate the impact of these psychological factors on the clinical outcomes, we divided the whole population into 2 subgroups on the basis of MIDAS improvement reached after 12 months of treatment. The minor pain relief reached in one of these subgroups seemed to be linked directly to different and more severe states of depression. This finding is consistent with the results reported for patients affected by other chronic pain conditions. In fact, the presence of moderate to severe depression has been identified as one of the most important negative predictive factors of efficacy in patients affected by chronic pain and treated by spinal cord stimulation (14). Although the anxious-depressive symptoms were not so severe as to be considered a contraindication to the procedure, it is possible to assume their impact on the level of well-being reported. Patients who reported less benefit from therapy have shown, during the follow-up interviews, a communicative tendency to dramatization, to negative coping, unrealistic expectations of healing, and more uncertain motivation to treatment.

In addition, post-operative psychological interviews revealed the difficulty of some of these patients in adapting to the new conditions of life in which a better pain relief and partial functional recovery had led to the breakdown of interpersonal balances and relational dynamics consolidated over time, forcing the patient to implement a sudden restructuring of self.

In our population the migration of the lead was the most frequent adverse event. The percentage of migration observed in our sample is comparable to that of recent published studies (4-5). All lead migrations were related to extension traction events due to the high mobility of neck and waist areas, where the components of the system are placed. To avoid electrode migration, both after lead and IPG implantation, we advise patients to avoid sudden and extreme neck movements and to minimize flexion and lateral rotation at the waist in the first 60 post implant days. All lead migrations occurred in those patients who did not follow these suggestions. IPG implantation site seemed to be an important factor to keep in mind in order to avoid lead migrations (7). In order to minimize the risk of lead migration we also chose the low abdominal IPG site, because the retromastoid to low abdomen pathway seemed to be associated with one of the least electrode pathway length change during patient movements (7,14).

Conclusion

In conclusion, our experience seems to confirm that the ONS is an effective and safe procedure in the treatment of chronic migraine. The effects of this procedure can be optimized by a multidisciplinary diagnostic and therapeutic approach, especially for the importance of the psychological factors in pain perception and their correlation with a good therapeutic outcome. The presence of coping styles, lower levels of motivation, and poor compliance are aspects that can adversely affect the outcome, interfering and reducing the well-being state perceived by the patient (11-13).

All patients undergoing a procedure of nerve stimulation must be adequately informed about the treatment and consequences, including side effects, so as to facilitate the construction of realistic expectations with respect to outcome. Of course, factors such as a good doctor-patient relationship, an adequate backing from the family, and the presence of social support, can foster a sense of confidence in the patients, functional to the perception of an improvement of their health condition.

The observation of a strong psychological component in our series of patients with migraine led us to design an innovative therapeutic pathway including psycho-social rehabilitation programs which could give the patients the right tools to correctly evaluate clinical outcomes reached.

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