ORIGINAL ARTICLE

Outcomes of Occipital Nerve Stimulation for Craniofacial Pain Syndromes

Philippe Magown, Werner J Becker, Zelma HT Kiss

ABSTRACT: ***Objectives:*** Occipital nerve regional stimulation (ONS) is reported to improve pain in several studies. We examined long-term pain and functional outcomes of ONS in an open-label prospective study. ***Methods:*** Patients with medically refractory and disabling craniofacial pain were prospectively selected for ONS. Primary outcome was a change in mean daily pain intensity on the numeric pain rating scale (NPRS) at 6 months. Secondary outcomes included changes in NPRS, Headache Impact Test-6 (HIT-6), Migraine Disability Assessment (MIDAS), Pain Disability Index (PDI), Center for Epidemiologic Studies Depression Scale – Revised (CESD-R), and Short Form-36 version 2 (SF36) at last follow-up. ***Results:*** Thirteen patients (mean age 49.7 ± 8.4) diagnosed with occipital neuralgia (6), hemicrania continua (2), persistent idiopathic facial pain (2), post-traumatic facial pain (1), cluster headache (1), and chronic migraine (1) were enrolled. Mean NPRS improved by 2.1 ± 2.1 at 6 months and 2.1 ± 1.9 at last follow-up (23.5 ± 18.1 months). HIT-6 decreased by 8.7 ± 8.8, MIDAS decreased by 61.3 ± 71.6, and PDI decreased by 17.9 ± 18. SF36 physical functioning, bodily pain, and social functioning improved by 16.4 ± 19.6, 18.0 ± 31.6, and 26.1 ± 37.3, respectively. Moderate to severe headache days (defined as ≥50% of baseline mean NPRS) were reduced by 8.9 ± 10.2 days per month with ONS. ***Conclusion:*** ONS reduced the long-term NPRS and moderate–severe monthly headache days by 30% and improved functional outcomes and quality of life. A prospective registry for ONS would be helpful in accumulating a larger cohort with longer follow-up in order to improve the use of ONS.

RÉSUMÉ : Résultats de la stimulation nerveuse occipital pour syndromes de douleur cranio-faciale. ***Objectifs :*** La stimulation nerveuse occipitale (SNO) a été rapportée de soulager la douleur. Nous avons examiné le soulagement de la douleur à long terme et les bienfaits fonctionnels de la SNO de part une étude prospective à indications ouvertes. ***Méthodes :*** Des patients souffrant de douleur cranio-faciales médicalement réfractaires et invalidantes ont été sélectionnés pour la SNO. L'objectif principal était de déterminer un changement de l'intensité moyenne de douleur quotidienne à 6 mois, mesuré sur l'échelle numérique de l'intensité de la douleur (numeric pain rating scale, NPRS). Les objectifs secondaires étaient de quantifier, au dernier suivi médical, le changement au niveau du NPRS, du questionnaire sur l'impact des céphalées (Headache Impact Test-6, HIT-6), du questionnaire MIDAS (Migraine Disability Assessment), de l'index d'incapacité reliée à la douleur (Pain Disability Index, PDI), de l'échelle CESD-R (Center for Epidemiologic Studies Depression Scale Revised), et du questionnaire sur l'état de santé SF36 (Short Form-36 version 2). ***Résultats :*** Treize patients (âge moyen 49.7 ± 8.4) avec les diagnostiques suivants : névralgie occipitale (6), hémicrânie continue (2), douleur faciales idiopathiques persistantes (2), douleurs faciales post-traumatiques (1), céphalée vasculaire de Horton (1), et migraine chronique (1) ont été enrôlés. Le NPRS moyen s'est amélioré de 2.1 ± 2.1 à 6 mois et de 2.1 ± 1.9 au dernier suivi médical (23.5 ± 18.1 mois). Le HIT-6, MIDAS, et PDI ont diminué respectivement de 8.7 ± 8.8 points, 61.3 ± 71.6 points, et de 17.9 ± 18 points. La capacité physique fonctionnelle, les douleurs corporelles, et le fonctionnement social du SF36 se sont améliorés respectivement de 16.4 ± 19.6 points, de 18.0 ± 31.6 points, et de 26.1 ± 37.3 points. Le nombre de jours avec céphalées modérées à sévères, soit des douleurs plus sévères ou égales à 50% du NPRS initial, ont diminué de 8.9 ± 10.2 jours par mois avec la SNO. ***Conclusion :*** La SNO a réduit l'intensité des céphalées à long terme et le nombre de jours par mois avec céphalées modérées à sévère par 30%. La SNO a aussi amélioré l'état de santé et la qualité de vie des patients. Cela étant, un registre prospectif pour la SNO serait primordial afin d'assembler une cohorte plus substantielle et des périodes de suivi plus longues pour améliorer l'utilisation de la SNO.

Keywords: Occipital nerve stimulation, Headache, Occipital neuralgia, Neuromodulation

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Introduction

Peripheral occipital nerve stimulation (ONS) can reduce pain in patients suffering from occipital neuralgia,[1] chronic migraine,[2,3] cluster headaches,[4] hemicrania continua,[5] and craniofacial pain syndromes.[6] Several small patient series have reported good outcomes independent of diagnosis, yet randomized controlled trials for ONS have shown conflicting outcomes with a prominent placebo effect.[7–9] Highly variable outcomes among trials, and equipoise between neuromodulation and placebo in randomized controlled trials have made it less likely that large-scale trials will be funded (although one randomized controlled trial is ongoing[10]). Despite this, ONS has seen a wide clinical

From the University of Calgary, Department of Clinical Neurosciences and Hotchkiss Brain Institute, Calgary, Alberta, Canada (PM, WJB, ZHTK); and Section of Neurosurgery, Health Sciences Centre, Winnipeg, Manitoba, Canada (PM)

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Correspondence to: Zelma HT. Kiss, Hotchkiss Brain Institute, University of Calgary, Cumming School of Medicine, HRIC 1AC58, 3280 Hospital Drive NW, Calgary, AB T2N 4N1, Canada. Email: zkiss@ucalgary.ca

uptake mostly as a minimally invasive and low-risk surgical procedure.

While several studies report outcomes based on pain intensity or frequency (either ≥ 30% or ≥ 50% improvement) or numbers of moderate–severe headache days (days with pain intensity of 4 or greater, lasting 4 h or longer) or number of headache days (days with any headache lasting more than 4 h), few studies have investigated functional outcomes and quality of life with ONS.[11] We designed this open-label prospective single-center study to address the efficacy of ONS on pain and quality of life in various headache and craniofacial pain syndromes. In order to objectively evaluate pain levels, functional status, and quality of life, nine standardized questionnaires were administered.

Method

Patients who were referred for ONS for chronic headaches and craniofacial pain and deemed refractory to medical, psychological, and physical therapies, as determined by a multidisciplinary team and a headache neurologist (WJB) were prospectively enrolled in a study approved by the University of Calgary ethics committee. All referrals were evaluated and optimized by a single multidisciplinary chronic pain group specializing in headache disorders led by a single headache neurologist (WJB) prior to enrolment. Inclusion criteria were age 18–65 years, diagnosis of occipital neuralgia, or persistent idiopathic facial pain, or cluster headache, or hemicrania continua, or post-traumatic headache, or chronic migraine (based on the International Classification of Headache Disorders),[12] completion of a multidisciplinary pain treatment program, pain severity of at least 5 out of 10 on the numeric pain rating scale (NPRS) for at least 20 days per month, and demonstrated significant disability. Patients completed a three times per day headache diary over 1 month (28 days) using the NPRS (0–10 scale). Baseline questionnaires included the Brief Pain Inventory (BPI), Pain Catastrophizing Scale (PCS), and General Anxiety Disorder 7 (GAD-7). Outcome questionnaires included the Headache Impact Test-6 (HIT-6), Migraine Disability Assessment (MIDAS),[13] Center for Epidemiologic Studies Depression Scale – Revised (CESD-R),[14] Pain Disability Index (PDI),[15] and Short Form Health Survey 36 version 2 (SF36).

The HIT-6 is a six-item questionnaire with a score of 36–78 developed to assess headache severity and impact on life.[16] The minimally important change is between −2.5 and −6.[16,17] HIT-6 can be categorized into four severity stages: little or no impact (49 or less), some impact (50–55), substantial impact (56–59), and severe impact (60–78).[18]

The MIDAS is a five-item questionnaire designed to assess headache-related disability over 3 months focusing on employment, household work, and nonwork activities. The score is the sum of days of missed activities or substantially reduced activities.[19,20] The MIDAS score can be categorized into five grades of headache-related disability: grade 1, little or no disability (score 0–5), grade 2, mild disability (score 6–10), grade 3, moderate disability (score 11–20), grade 4A, severe disability (score 21–40), and grade 4B, very severe disability (score 41–270).[20] For analysis purposes, we plotted grade 4A as grade 4, and grade 4B as grade 5.

The CESD-R is a 20-item self-reported questionnaire focusing on symptoms of depression and is an accurate and valid measure of depression among the general population.[21] The CESD-R total scores were adjusted to reflect the original score range of the CESD where the top two values were given the same points as follows: not at all or less than 1 day was 0 point, 1–2 days was 1 point, 3–4 days was 2 points, 5–7 days was 3 points, and nearly every day for 2 weeks was 3 points.

The PDI consists of 7 questions, rated 0–10, used to evaluate the degree of daily life disruption by chronic pain. It has been validated across different patient populations to measure pain-related disability.[22] The minimal improvement change is 17.9 points, but has also been shown to be baseline dependent in some populations.[23]

Twenty-eight-day headache diaries and these outcome questionnaires were administered at the following time points: baseline, 6, 12, 24, 36, and 48 months post-ONS surgery.

Exclusion criteria consisted of inability to comply with planned follow-up, uncontrolled psychiatric comorbidity, and significant medical comorbidities increasing surgical risk.

All subjects underwent a blinded nerve blocks (lidocaine, bupivacaine, and saline) administered in a random order at least 1 week apart. The best response within 2 h for lidocaine, and within 8 h for bupivacaine and saline, were utilized for analysis.

A temporary ONS trial was performed to confirm benefit prior to undergoing permanent implantation in all patients except the one with cluster headache. Occipital nerve stimulators were surgically implanted using a midline incision as previously described.[24] Either percutaneous (PISCES QUAD, Medtronic, Minneapolis, MN, USA) or paddle leads (Resume, Medtronic, Minneapolis, MN, USA) were implanted in the vicinity of the greater occipital nerve (GON) or directly on the nerve.[25] Bilateral electrodes were implanted in those with bilateral pain, and unilateral electrodes for those with unilateral pain. For those patients undergoing awake implantation, intraoperative testing required paresthesia to cover most of the GON territories before securing the electrodes in place and implanting the lead extensions and pulse generator in an infraclavicular pocket. In the patients in whom leads were implanted directly on the GON, this was performed under general anesthesia and the paddle lead was sutured to the periosteum around the nerve.

Parameters were modified to optimize coverage, including adding additional contacts and different polarities to modulate the stimulation field. Once optimal paresthesia coverage was obtained to cover either the GON territory or the region of pain, cycling stimulation was initiated to conserve battery power and prevent tolerance.

The primary outcome measure was the change in mean daily pain intensity averaged over 1 month from baseline to 6 month follow-up. Secondary outcomes included change in mean daily pain intensity, SF36, PDI, CESD-R, MIDAS, and HIT-6, calculated at the last follow-up available. The monthly averaged baseline NPRS was used as baseline pain intensity. Responders were defined as patients demonstrating 50% or greater pain reduction on the average monthly NPRS at the last follow-up. Moderate–severe headache days were defined as days on which the averaged NPRS was above 50% of baseline NPRS mean. At baseline, no patient reported a day with pain intensity lower or equal to 50% of their baseline NPRS mean. Moderate–severe headaches days per month were transformed into percentages by dividing the number of moderate–severe headache days by the total number of days scored in the pain diary as some pain diaries included less than 28 days.

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Table 1: Patient demographics

Patients	Age	Gender	Diagnosis	Last follow-up (month)
1	50	M	Persistent idiopathic facial pain	48
2	50	F	Occipital neuralgia[§]	48
3	60	M	Cluster headache	12*
4	39	F	Post-traumatic facial pain	48
5	45	M	Occipital neuralgia	36
6	45	M	Occipital neuralgia	48
7	47	M	Persistent idiopathic facial pain	0*
8	32	M	Occipital neuralgia	36
9	50	M	Hemicrania continua	12
10	58	F	Hemicrania continua	12
11	55	M	Occipital neuralgia	24
12	62	M	Occipital neuralgia	24
13	54	F	Chronic migraine	12
Mean ± SD	49.7 ± 8.4	9 M/4 F		27.7 ± 17.2

Demographics of patients implanted with an ONS. *Explanted ONS: patient 1 was explanted at 39 months for infection and reimplanted at 45 months; patient 3 was explanted at 20 months for therapy failure and converted to a hypothalamic deep brain stimulator, follow-up data were available up to 12 months; patient 7 was explanted at 11 months secondary to an infection, no follow-up data were available. [§]Atypical clinical presentation due to predominant temporal pain.

Results are shown as mean ± standard deviation (SD). All implanted patients were included in baseline characteristics but only patients with follow-up data were included in each outcome. Data were analyzed using paired Student's *t*-tests at 6 months and at last follow-up compared to baseline. We opted not to carry forward previous data points. Time points with missing data were excluded, thus preventing the use of alternative statistical tests. Categorical data were analyzed with a Fischer's exact test while a Wilcoxon-matched pairs signed-rank test was used for ordinal data (HIT-6 stages and MIDAS stages). A Mann–Whitney test was used for contingency analysis. A p-value of 0.05 was considered significant.

Results

Thirty-two patients were referred for ONS between 2008 and 2016. Sixteen patients were deemed candidates for this study and consented to undergo a percutaneous stimulation trial. Thirteen moved forward to permanent implantation. Clinical characteristics are shown in Table 1. Patient 2 was classified as having occipital neuralgia according to the International Classification of Headache Disorders, although it was atypical with predominant temporal pain. This patient had a past history of occipital neuralgia and had undergone a previous neurectomy. Patient 1 was revised at 35 months for a migrated lead. The lead was revised again 2 months later and was explanted 2 months later due to an infection. A new lead was implanted 6 months later. At that time, the patient had been enrolled for 45 months. Patient 3 underwent lead revision at 3 months and was explanted at 20 months for therapy failure. A hypothalamic deep brain stimulator was implanted instead. Patient 5 lead was revised at 3 months. Patient 7 was explanted at 11 months after a lead erosion and never reimplanted. Follow-up data at 6 and 12 months had not been acquired. Among patients with occipital neuralgia, five were unilateral and one was bilateral.

Stimulation parameters used ranged from 30 to 110 Hz, 330 to 450 μs pulse width, and 0.8 to 6.3 V. One patient had a percutaneous quadripolar lead (PISCES, Medtronic, Minneapolis, MN, USA) and all others had paddle leads (Resume TL, Medtronic, Minneapolis, MN, USA) implanted either in the region of the occipital nerves or directly on the occipital nerve to achieve adequate paresthesia coverage. Stimulation parameters are shown in Supplementary Table S1.

Baseline characteristics and pain ratings were similar among patients (Table 2, Figure 1). Patients showed no statistically significant difference between occipital nerve block performed with lidocaine, bupivacaine, or saline (Figure 1D).

Table 2 shows all values at baseline, 6 months, and last follow-up. Daily headache NPRS significantly decreased by 2.1 ± 2.1 at 6 months ($p = 0.02$). At the last follow-up, the NPRS showed a similar decrease ($p = 0.004$; Figure 2A). Patient 6 did not have baseline NPRS, thus follow-up NPRS scores were excluded. We classified patients as "responders" if they reported a 50% or more reduction in pain intensity over 1 month.[26] Three ON patients and one chronic migraine patient were responders (Figure 2B). Mean monthly moderate–severe headache days expressed in percentages decreased from 100 ± 0% at baseline to 68.1 ± 36.5% at last follow-up (23.5 ± 18.1 months, $p = 0.02$; Figure 2C) equivalent to a decrease of 8.9 ± 10.2 days per month. ON patients reduced their average moderate–severe headache days by 13.5 days per month while the patients with other diagnoses reduced by 5.1 days per month; this difference was not statistically significant.

HIT-6 improved by 8.7 ± 8.8 at the last follow-up ($p = 0.008$, Figure 3A, B). HIT-6 stages[18] showed five patients improving: three from stage 4 (severe impact) to stage 1 (little to no impact) and one from stage 4 to stage 3 (substantial impact). The MIDAS scores improved significantly at the last follow-up decreasing by 61.3 ± 71.6 ($p = 0.02$, $n = 11$, Figure 3C). Six patients improved on the MIDAS stages: from stage 4B (very severe) to stage 1 (little to no impact, $n = 1$), stage 2 (mild, $n = 2$), stage 3 (moderate, $n = 1$), and stage 4A (severe, $n = 1$), and from stage 4A to stage 3 ($n = 1$, Figure 3D). This change was statistically significant ($p = 0.03$). Data from patient 8 was excluded as the MIDAS questions did not apply to his living situation. Being not employed and not attending school, headaches were not interfering with these activities resulting in a score of 5 (stage of 1) despite daily severe headaches. The PDI statistically improved by 17.9 ± 18.0 at the last follow-up ($p = 0.006$, Figure 3E). While the CESD-R questionnaire did not show a statistically significant improvement (−12.5 ± 23.2, $p = 0.09$), scores did improve although not enough for most patients to change class: most remained in either the normal ($n = 6$) or subthreshold ($n = 7$) depression group. Patient 1 went from probable major depressive episode to subthreshold after ONS.

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Table 2: Outcomes

	Baseline		6 months		Last follow-up		
	Mean ± SD	*(n)*	*Mean ± SD*	*(n)*	*Mean ± SD*	*(n)*	*Months*
NPRS	6.1 ± 1.3	12	**4.2 ± 2.3***	9	**4.1 ± 1.9****	11	23.5 ± 18.1
BPI	42.5 ± 12.2	13	–		–		–
PCS	19.5 ± 14.6	13	–		–		–
GAD-7	4.6 ± 3.6	9	–		–		–
HIT-6	67.6 ± 3.0	11	**58.1 ± 8.0****	8	**58.9 ± 9.0****	11	27.8 ± 16.2
HIT-6 stages	4.0 ± 0.0	11	3.1 ± 1.1	8	3.1 ± 1.4	11	27.8 ± 16.2
MIDAS	115.2 ± 76.4	12	**58.9 ± 42.5***	9	**63.9 ± 62.4***	11	16.4 ± 7.6
MIDAS stages (1–4)	3.8 ± 0.9	12	3.4 ± 1.1	9	3.2 ± 1.1	11	16.4 ± 7.6
MIDAS stages (1–4B)	4.9 ± 0.3	12	4.1 ± 1.5	9	**3.6 ± 1.5**[§]	11	16.4 ± 7.6
PDI	42.8 ± 7.3	13	**24.1 ± 14.8****	8	**25.0 ± 17.3****	12	27.5 ± 15.5
CESD-R	24.9 ± 18.8	13	16.2 ± 14.4	10	17.0 ± 14.3	12	27.5 ± 15.5
SF36							
Physical functioning	61.3 ± 17.6	12	**82.5 ± 9.8***	10	**80.4 ± 15.6***	12	27.5 ± 15.5
Role – physical	26.0 ± 27.2	12	56.3 ± 32.0	10	60.0 ± 40.0	12	26.5 ± 15.2
Bodily pain	31.2 ± 16.6	12	**50.1 ± 21.4****	10	47.8 ± 26.5	12	27.5 ± 15.5
Social functioning	39.6 ± 19.1	12	60.0 ± 31.6	10	**62.5 ± 31.5***	12	27.5 ± 15.5
Mental health	59.7 ± 13.7	12	59.6 ± 20.4	10	62.7 ± 19.4	12	27.5 ± 15.5
Role –emotional	72.9 ± 21.9	12	74.2 ± 29.3	10	71.5 ± 25.5	12	27.5 ± 15.5
Vitality	38.3 ± 11.2	12	42.5 ± 20.6	10	49.2 ± 20.4	12	27.5 ± 15.5
General health	63.8 ± 23.3	12	57.7 ± 20.0	9	61.9 ± 22.4	12	27.5 ± 15.5

BPI=Brief Pain Inventory; CESD-R=Center for Epidemiologic Studies Depression Scale – Revised; GAD-7=General Anxiety Disorder 7; HIT-6=Headache Impact Test 6; MIDAS=Migraine Disability Assessment; (n)=number of patients; NPRS=Numerical Pain Rating Scale; PDI=Pain Disability Index. Questionnaire data at baseline, 6 months, and last follow-up. Values are presented as mean ± standard deviation. [†]MIDAS stages are also presented as stages 1–4B where stage 4 is subdivided into 4A and 4B[20]. For graphic representation and statistical purposes, stage 4A was represented as stage 4 and stage 4B as stage 5. [§]$p<0.05$ by Wilcoxon-matched pairs signed-rank test compared to baseline; *$p < 0.05$, **$p<0.01$ by paired Student's *t*-test compared to baseline.

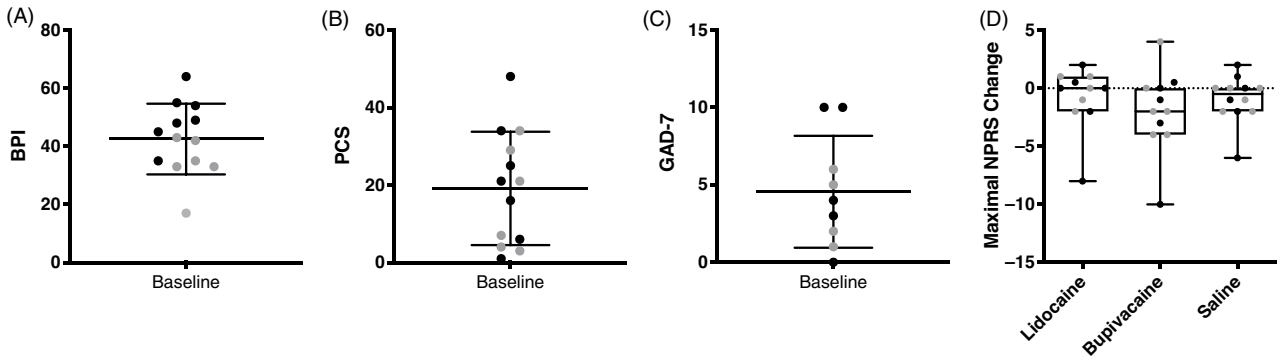

Figure 1: *Baseline characteristics. (A) Baseline Brief Pain Inventory (BPI), (B) Baseline Pain Catastrophizing Scale (PCS), and (C) Baseline Generalized Anxiety Disorder 7 (GAD-7) scores. (D) Numerical Pain Rating Scale (NPRS) change after single-blinded randomly administered nerve block with lidocaine, bupivacaine, or saline, showing no significant differences between any injection. Gray circles: occipital neuralgia patients; black circles: other diagnoses.*

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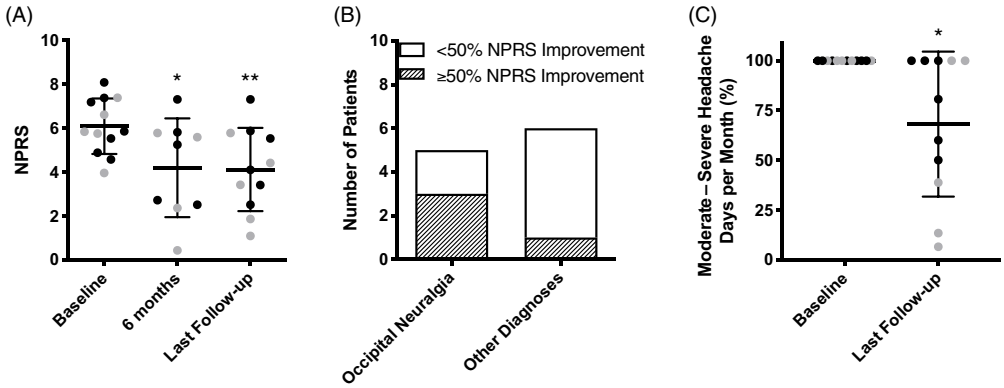

Figure 2: *Pain and moderate–severe headache days outcomes. (A) Headache diary NPRS cumulated as means from three times per day headache rating over 1 month obtained at baseline and at 6 months and at last follow-up. NPRS decreased by 2.1 ± 2.1 at 6 months (*p = 0.02) and similarly at the last follow-up (2.1 ± 2.1, 23.5 months, **p = 0.004). (B) Number of patients with 50% or more NPRS improvement grouped in occipital neuralgia versus other diagnoses (post-traumatic facial pain, persistent idiopathic facial pain, cluster headache, hemicrania continua, and chronic migraine, p = 0.2 by Fischer's exact test). (C) Percentage of moderate–severe headache days per month at baseline versus last follow-up (100 ± 0% vs. 68.1 ± 36.5%, respectively, 23.5 ± 18.1 months, *p = 0.02. These percentages are equivalent to 28 ± 0.0 days at baseline and 19.1 ± 10.2 days at last follow-up). Moderate–severe headache days were defined as days on which the NPRS was greater than 50% of the mean baseline NPRS. Gray circles: occipital neuralgia patients; black circles: other diagnoses.*

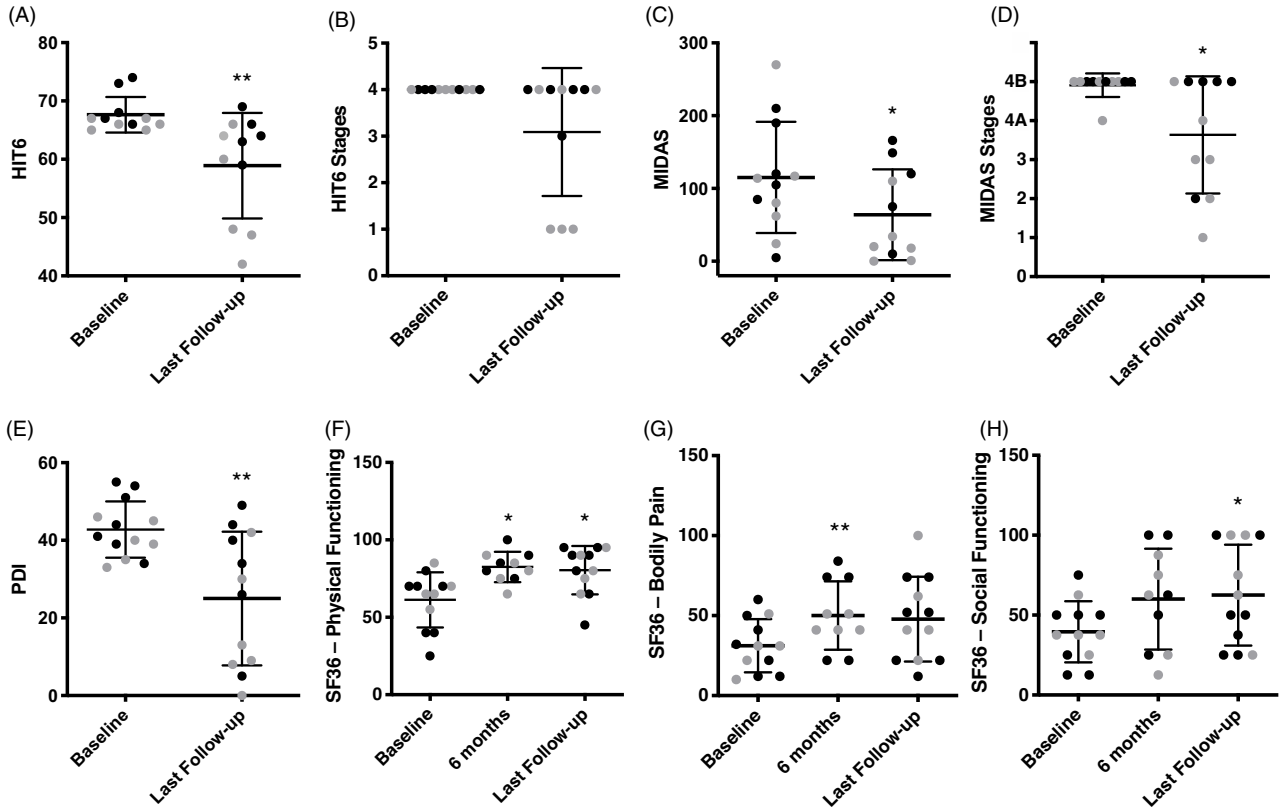

Figure 3: *Functional outcomes and quality of life outcomes at last follow-up. (A) HIT-6 decreased by 8.7 ± 8.8 at last follow-up (27.8 ± 16.2 months, **p = 0.008). (B) HIT-6 stages improved for four patients. (C) MIDAS score decreased significantly by 61.3 ± 71.6 at last follow-up (16.4 ± 7.6 months, *p = 0.02). (D) MIDAS stages, scored from 1 to 4B, where stage 4 is subdivided into 4A and 4B, decreased for six patients (p = 0.03 by Wilcoxon-matched pairs signed-rank test). (E) PDI significantly decreased by 17.9 ± 18.0 at last follow-up (27.5 ± 15.5 months, **p = 0.006). Quality of life was assessed with the SF36 and is shown at baseline, 6 months, and at last follow-up (27.5 ± 15.5 months). (F) SF36 physical functioning significantly improved at 6 months and last follow-up (15.5 ± 17.2 and 16.4 ± 19.6, 6 months and last follow-up, *p = 0.02). (G) SF36 bodily pain improved significantly at 6 months by 21.8 ± 20.9, **p = 0.01. (H) SF36 social functioning improved significantly at last follow-up by 26.1 ± 37.3, *p = 0.04. Gray circles: occipital neuralgia; black circles: other diagnoses.*

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Statistically significant improvement on the SF36 was seen for the physical functioning, bodily pain, and social functioning subgroups. Physical functioning improved by 15.5 ± 17.2 ($p = 0.02$) at 6 months and 16.4 ± 19.6 ($p = 0.02$) at the last follow-up (Figure 3F). Bodily pain improved significantly at 6 months by 21.8 ± 20.9 ($p = 0.001$), but not at the last follow-up with an improvement of 18.0 ± 31.6 ($p = 0.09$, Figure 3G). Social functioning was significantly improved at the last follow-up by 26.1 ± 37.3 ($p = 0.04$), but not at 6 months. (Figure 3H).

A Pearson correlation matrix was used to identify functional outcomes correlating with a reduction in the NPRS at the last follow-up time point where complete data were available. Complete data sets were only available from 7 patients (patients 2, 3, 4, 8, 10, 11, 13). At an average follow-up of 12 ± 6 months, an improvement in the NPRS was correlated with an improvement in the HIT-6 ($r = 0.77$, $p = 0.04$), MIDAS ($r = 0.83$, $p = 0.02$), CESDR ($r = 0.93$, $p = 0.003$), SF36 bodily pain ($r = -0.95$, $p = 0.004$), and SF36 social functioning ($r = -0.92$, $p = 0.009$) scores. This suggests that pain severity correlated with functional outcomes and quality of life.

Discussion

ONS provides significant pain and functional improvement as measured by nine standardized questionnaires addressing pain intensity, level of disability, and quality of life, in a mixed cohort of patients with medically refractory disabling craniofacial pain. NPRS decreased by 2.1, HIT-6 by 8.7, MIDAS by 61.3, PDI by 17.9, and SF36 scores displayed an improvement in physical functioning of 16.4, bodily pain of 18.0, and social functioning of 26.1 at last follow-up. Furthermore, MIDAS stages improved in half of the patients.

The degree of these changes is considered clinically important. A clinically significant change in pain rating requires it to be at least 2 points on a 10-point scale.[27] Despite a clinically significant decrease in NPRS of 2.1, only 4 of the 12 patients were responders, decreasing their monthly NPRS mean by 50% or more, and also substantially reducing their number of moderate–severe headache days per month.

The within-person minimally important change for HIT-6 is between −2.5 and −6 points, and the between-group minimally important difference is −1.5.[16] Eight patients had a change of −2.5 or more at the last follow-up and 5 had a change of −6 or more. Although the HIT-6 decreased more for occipital neuralgia patients than for other diagnoses (−11.5 vs. −5.4 points), the same number of patients fulfilled the −2.5 to −6 within-person minimal change, irrespective of diagnosis. Change found in patients with other diagnoses is similar to those reported in the PREEMPT Botox trial, which was also considered clinically significant.[28,29] Despite HIT-6 stages having been developed to address the clinical significance of the HIT-6 score,[18] in our study, HIT-6 stages did not improve in the majority of patients.

A change in PDI of 17.9 points is considered the smallest clinically significant detectable change based on three musculoskeletal pain populations.[22] Our patient population reached this clinically significant change mostly due to six patients, of which four were ONS responders.

Among the eight dimensions of the SF36, our patients improved significantly on three dimensions. Furthermore, physical functioning improved to be very close to population norms[30] (80.4 ± 15.6 patients vs. 85.8 ± 20 population). Bodily pain and social functioning improved by more than 50%, but remained below Canadian population norms which have reported values of 75.6 ± 15.3 for bodily pain and 86.2 ± 19.8 for social functioning.[30]

While we expected that nerve blocks might provide a method to predict responders, and rule out placebo responders, similar to Schwedt et al.,[31] we were unable to show a statistical difference between short-acting, long-acting, and placebo nerve blocks, suggesting that a successful nerve block may not be a good predictor ONS outcome.

Four randomized controlled trials of ONS for different chronic headache diagnosis have been published with mixed results ranging from 59.5% responders (≥ 30% pain reduction in either intensity or number of days),[32] to 39% responders,[8] to no difference from placebo.[7,9] Pooled results from three trials showed a reduction of 2.59 headache days, but the different definitions of "responder" prevented conclusive results.[2] On the other hand, a randomized crossover trial for chronic migraine showed a response rate of 97% based on at least a 50% reduction in pain severity or frequency.[33] Together, the above randomized controlled trials point toward an important placebo effect unavoidable and uncontrollable without proper blinding. It also emphasizes the need for standardized definitions of ONS responder, and consistency in outcomes used to study ONS.

Few publications have looked at the functional quality of life improvement after ONS.[11,34–38] Of these, four showed a link between pain reduction and functional improvement.[11,35,36,38] Our study adds to this literature on the use of ONS for functional and quality of life improvement. In our study, we correlated a decrease in NPRS with improvement on HIT-6, MIDAS, CESD-R, and SF36. However, the correlation was run using data from only half the patients; incomplete data sets from the other patients prevented complete analysis. Despite showing a correlation between pain intensity and functional outcome questionnaires, and improvement on questionnaires, these changes might not directly relate to improvement of daily life functionality. We did not design this study to include personal functional goals and to follow these through the study. In further studies, personalized clinical outcome assessments might provide a patient-centered method of evaluating the effectiveness of neuromodulation that is clinically meaningful to each individual patient.

Our study has several limitations mainly based on numbers: small number of screened patients, low enrollment, and few implanted stimulators. Because patients were being routed through a multidisciplinary chronic headache program, many improved before assessment for neuromodulation. Furthermore, if patients were not part of the headache program, they had to proceed through it before becoming eligible for the study. Long wait times to be seen in the multidisciplinary chronic pain center may have turned patients away. Two patients out of 14 (14%) implanted patients developed an infection (one early, one delayed) requiring hardware to be explanted. Two patients required lead repositioning at 3 months (patients 3 and 5) and one at 3 years (patient 1). Data loss at follow-up was high, averaging 21%. One patient's data at 6 months was not collected prior to explant of the stimulator at 11 months. One patient's baseline functional data was lost to flooding of the pain center while another patient's baseline headache diary was lost. The

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burden imposed by a series of nine questionnaires and a month-long headache diary rated three times per day might have also contributed to poor compliance. Finally, the heterogeneity of our selected population may have confounded the results.

ONS is a technology used for the treatment of different headache etiologies. With equivocal randomized controlled trial results, further studies are unlikely to be funded without a significant technological advancement in therapy, better patient selection criteria, or understanding of the mechanisms responsible for benefit. Furthermore, recruiting a patient population large enough to provide results with adequate statistical power might take too long for a single institution. While not achieving statistical significance, patients with ON had the best functional outcomes. We propose that a patient registry, able to collect a larger data set, might be a more valuable tool to study outcomes of ONS.

Conclusion

In a highly selected medically refractory patient population with disabling craniofacial pain, who had previously failed multidisciplinary conservative pain approaches, ONS treatment reduced the NPRS by almost 30% at the last follow-up, decreased the HIT-6 by 13%, decreased the MIDAS by 53%, decreased the PDI by 42%, increased the SF36 physical functioning by 26% nearly normalizing this value to population levels, improved the SF36 bodily pain by 59%, and increased the SF36 social functioning by 68%. Patients who showed a positive response based on 50% or more improvement on the NPRS after ONS implantation also showed an improvement in their functional and quality of life outcomes. Our study is limited by the small number of patients, similar to other publications. Considering the small number of occipital nerve stimulators implanted yearly per institution in general, data might be better acquired through an ONS registry. Finally, personalized clinical outcomes might be valuable outcomes to study as they may better reflect expectations and functional improvement of individual patients.

Disclosures

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Statement of Authorship

WB and ZK designed the study and collected the data. PM performed the data analysis. All authors contributed to the interpretation of the analysis and the manuscript drafting, revisions, and final approval.

Supplementary Material

To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2020.259.

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