The Safety and Efficacy of Peripheral Nerve Stimulation of the Occipital Nerve for the Management of Chronic Migraine

Stephen Silberstein, MD, Jefferson Headache Center, Philadelphia, PA; David Dodick, MD, Mayo Clinic Hospital, Phoenix, AZ; Joel Saper, MD, Michigan Head Pain & Neurological Institute, Ann Arbor, MI; Billy Huh, MD, PhD, Duke Pain & Palliative Clinic, Durham, NC; Ken Reed, MD, Ascendant Neuro, Dallas, TX; Samer Narouze, MD, Summa Western Reserve Hospital, Cuyahoga Falls, OH; Donald Bacon, MD, Consultants in Pain Medicine, San Antonio, TX; Alon Mogilner, MD, PhD, Northshore-LIJ Health System, Dept of Neurological Surgery, Great Neck, NY; James Banks, MD, Mercy Health Research, Ryan Headache Center, St Louis, MO; Roger Cady, MD, Headache Care Center, Springfield, MO; Stuart Black, MD, Baylor Neuroscience Center Headache and Movement Disorders, Dallas, TX; Konstantin Slavin, MD, University of Illinois/Chicago, Department of Neurosurgery, Chicago, IL; Jerome Goldstein, MD, San Francisco Headache Clinic, San Francisco, CA; Herbert Markley, MD, New England Regional Headache Center, Worcester, MA; Tim Deer, MD, The Center for Pain Relief, Charleston, WV; Robert Levy, MD, PhD, Northwestern University, Department of Neurological Surgery, Chicago, IL; Nagy Mekhail, MD, PhD, Cleveland Clinic, Cleveland, OH

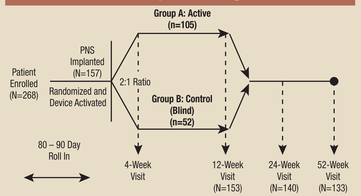
Introduction

Chronic migraine is a debilitating disorder with few treatment options. Peripheral nerve stimulation (PNS) of the occipital nerve is emerging as a potentially promising therapy for chronic migraine patients. We conducted a clinical trial to assess the safety and efficacy of PNS of the occipital nerve for the management of headache pain and disability associated with chronic migraine.

Methods

In this prospective, multicenter, double-blind, controlled study, 157 patients were implanted with a neurostimulation system (St. Jude Medical Neuromodulation Division, Plano, TX) and randomized to an Active (n=105) or Control group (n=52) for 12 weeks. Patients then continued in an open-label phase with 24-, 48-, and 52-week evaluations. Outcome measures included headache days recorded through a patient diary, the Migraine Disability Assessment (MIDAS), Visual Analog Scale (VAS), patient-reported headache relief, the Zung Pain and Distress (PAD) Scale, satisfaction, quality of life (QoL), patient assessment of procedure, and adverse event rates.

Study Design



Patient Characteristics

	Control Group (n=52)	Active Group (n=105)
History and Prevalence		
Mean (±std) Number of Years Suffering from Migraine Headache	24.6 (± 13.3)	21.9 (± 14.9)
Mean (+std) Number of Headache Days per Month at Baseline	16.2 (± 8.4)	19.9 (± 7.9)
Headache Type		
Unilateral	15 (28.8%)	35 (33.3%)
Bilateral	37 (71.2%)	70 (66.7%)
Headache Episode Length		
0-2 hours	1 (1.9%)	2 (1.9%)
3-5 hours	5 (9.6%)	3 (2.9%)
6-9 hours	6 (11.5%)	5 (4.8%)
10-12 hours	1 (1.9%)	11 (10.5%)
> 12 hours	39 (75.0%)	84 (80.0%)
Patient Disability		
Mean (±std) MIDAS Score at Baseline	152.7 (± 77.1)	158.4 (± 76.8)
Headache Inhibits Daily Activity	51 (98.1%)	101 (96.2%)

Table 1. Patients tried an average of 5.2 therapies (range 1–8) . Overall, there were no significant differences in demographics between the Active and Control groups.

Patient Population

Chronic Migraine Criteria

- A migraine headache that occurs 15 or more days per month for more than 3 months without **medication overuse**
- Not attributed to any other disorder
- Has at least two of the following diagnostic characteristics:
  - — Unilateral location
  - — Pulsating quality
  - — Moderate or severe pain intensity
  - — Capability to be aggravated by routine physical activity or to cause avoidance of these activities
- Additionally, at least one of the following occurs during the headache:
  - — Nausea
  - — Vomiting
  - — Aversion to light and loud noises

Intractable Chronic Migraine Criteria

- 15 or more days per month with headache lasting at least 4 hours per day
- Failure of three or more preventive drugs
- At least moderate disability determined using a validated migraine disability instrument (e.g., MIDAS or HIT-6)

Inclusion/Exclusion

Inclusion Criteria

- Diagnosed with chronic migraine headache or probable migraine with ≥15 headache days/mo
- Has tried at least two migraine specific acute medications, and at least two different classes of prophylactic medications and found to be refractory
- VAS score of 6 cm (or greater) on a 10 cm line
- Headache pain is posterior head pain or pain originating in the cervical region

Exclusion Criteria

- Patients who have undergone a destructive procedure affecting C2/C3/occipital distribution
- Patients who within 8 weeks prior to initial baseline started new medications or therapy to treat headache
- Botox within 6 months prior to initial baseline

Results: 12-Week Controlled Phase

Patient Diary: Headache Days

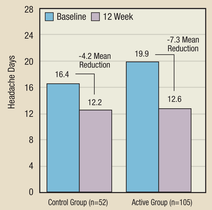


Figure 1. In an intent-to-treat analysis of all 157 patients, the patients in the Active group reported a decrease of 7.3 headache days from a mean of 19.9 days at baseline, a 36.6% reduction. The Control group reported a decrease of 4.2 headache days from a mean of 16.4 days at baseline, a reduction of 25.6%. The difference in the decrease of headache days between groups (3.1 days) was significant (p=0.015).

Migraine Disability Index (MIDAS)

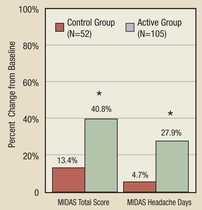


Figure 2. Mean (±std) Total scores at baseline were 158.4 (±76.8) for the Active group and 152.7 (±77.1) for the Control group. Mean (±std) headache days at baseline were 80.7 (±18.2) for the Active group and 72.3 (±23.5) for the Control group. The difference between groups at 12 weeks was statistically significant for Total scores and MIDAS headache days (both p<0.001).

Patients Achieving Various Levels of Relief

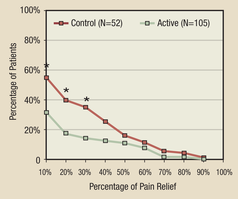


Figure 3. This continuous proportion responder analysis was based on mean daily average pain intensity VAS measurements in patients with no increase in average headache frequency or duration. Statistically significant group differences were noted for the percentage of patients achieving a 10%, 20% and 30% reduction in pain (all p<0.05).

Headache Pain Relief

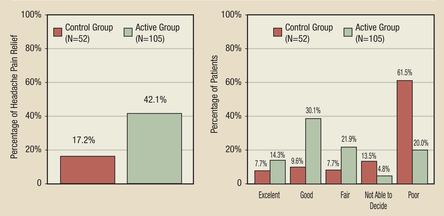


Figure 4. The difference in patient-reported headache pain relief (left) between the Active and Control groups was statistically significant (p<0.001) as was headache pain relief category (right) as analyzed by the Cochran Mantel Haenszel procedure (p<0.001).

Zung Pain and Distress (PAD) Scale

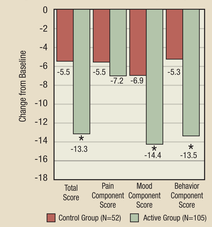


Figure 5. Mean (±std) Total scores at baseline were 67.5 (±13.0) for the Active group and 66.4 (±14.1) for the Control group. The difference between groups at 12 weeks was statistically significant for Total, Mood Component, and Behavior Component Scores (all p<0.001).

Results: 52-Week Open-Label Phase

Patient Diary: Headache Days

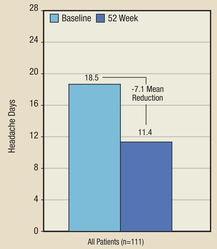


Figure 6. In an intent-to-treat analysis of all 157 patients at the end of the study (52 weeks post-implant), all patients who completed the study reported a mean of 11.4 headache days per month, a statistically significant decrease of 7.1 days from baseline (p<0.001).

Headache Pain Relief

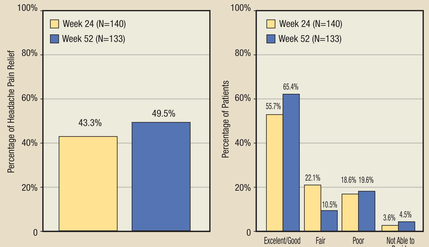


Figure 7. Patient-reported headache pain relief was assessed at 24 and 52 weeks post-implant (left) as was headache pain relief category (right). On average, patients reported 43.3% and 49.5% headache pain relief at 24 and 52 weeks post-implant, respectively, and the majority of patients rated their headache pain relief as excellent or good.

Satisfaction and Quality of Life

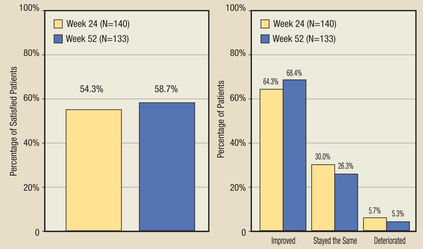


Figure 8. Patient satisfaction with headache pain relief (left) and quality of life (right) were assessed at 24 and 52 weeks post-implant. The majority of patients were satisfied with the amount of headache pain relief and indicated improved quality of life at both 24 and 52 weeks post-implant.

Patient Assessment of Procedure

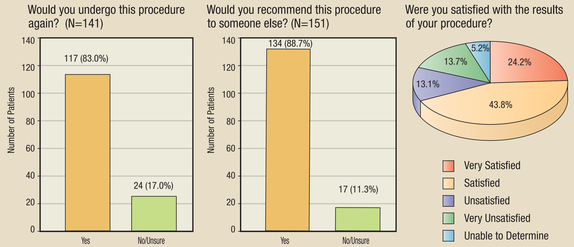


Figure 9. At the end of the study, the majority of patients indicated that they would undergo the procedure again (83.0%), would recommend the procedure to someone else (88.7%), and were satisfied or very satisfied with the results of the procedure (68.0%).

Summary and Conclusions

- Most patients (153/157) completed the 12-week visit
- During the 12-week Control phase, there were significant group differences in the reduction of headache days, as well as on the MIDAS, headache relief assessments and Zung PAD
- In the Active group, 35.2% of patients achieved a 30% reduction on the VAS, whereas only 17.3% of patients in the Control group achieved the same
- Statistical significance was not observed on the primary endpoint as established by the U.S. Food and Drug Administration. This was defined as a significant difference between patients in the Active and Control group who reported a 50% or greater reduction in pain as measured on the VAS
- Patients reported 43.3% and 49.5% headache relief at 24 and 52 weeks post-implant, respectively, and the majority of patients rated their headache relief as excellent or good
- The majority of patients were satisfied with the amount of headache relief and indicated improved quality of life at both 24 and 52 weeks post-implant. They also indicated that they would undergo the procedure again (83.0%), would recommend the procedure to someone else (88.7%), and were satisfied or very satisfied with the results of the procedure (68%)
- Overall, the rate of serious device or procedure-related events was 1.0%
- The results of this study provide evidence to support safety and effectiveness of PNS of the occipital nerve for the management of headache pain and disability associated with chronic migraine

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