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| Subject: Occipital Nerve Block Therapy for Treatment of Headaches and Occipital Neuralgia | Original Effective Date: 4/23/20 |
| Policy Number: MCP-355 | Revision Date(s): 6/17/20; 2/8/21 |
| Review Date: 6/17/20, 2/8/21 | |
| MCPC Approval Date: 4/23/20; 6/17/20; 2/8/21 | |

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DISCLAIMER

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RECOMMENDATION

This policy addresses ONB as a therapy for treatment of various headache syndromes and occipital neuralgia.

Occipital nerve block (ONB) therapy involves injection of a local anesthetic with or without steroid around the greater and lesser occipital nerves located in the back of the head just above the neck area.

Occipital nerve block therapy is considered experimental, investigational or unproven for the treatment of headache or occipital neuralgia including, but not limited to:

► **Diagnostic Occipital Nerve Blocks**

Occipital nerve blocks have been used as a diagnostic test for cervicogenic headache (CGH) and occipital neuralgia; however, the standardization of diagnostic nerve blocks in the diagnosis of CGH remains to be defined. There is no high-quality evidence and well-designed clinical trials indicating that injection of occipital nerves should be used as a specific diagnostic test for headaches and occipital neuralgia.

► **Therapeutic Occipital Nerve Blocks**

- **Cervicogenic headache**
- **Cluster headache**
- **Migraine headache**
- **Neck pain**
- **Tension headache**

DESCRIPTION OF PROCEDURE/SERVICE/PHARMACEUTICAL

Peripheral Nerve Blocks (PNBs)

PNBs have been employed in the treatment of a variety of headache disorders for many years. PNBs involve injections of local anesthetic agents around peripheral nerve branches. The most widely used target for PNBs is the greater occipital nerve (GON). Other commonly targeted nerves are the lesser occipital nerve (LON) and several branches of the trigeminal nerve: the supratrochlear (STN), supraorbital (SON) and auriculotemporal (ATN) nerves (Robbins and Blumenfeld, 2017).

- The rationale for using GONB in headache treatment comes from evidence for convergence of sensory input to trigeminal nucleus caudalis neurons from both cervical and trigeminal fibers. Injecting this region with local anesthetic and corticosteroids decreases sensory input to the trigeminal nucleus caudalis.
- A GON injection involves injecting a small dose of local anesthetic alone or with corticosteroids around the greater occipital nerve, which is located at the back of the head, at the top of the neck. These injections can be performed unilaterally or bilaterally. Although there is no standardized procedure, the nerve is usually infiltrated with a local anesthetic (e.g., lidocaine, bupivacaine, or both) with or without a corticosteroid (e.g. such as methylprednisolone, dexamethasone, or triamcinolone) during GONBs.

Greater Occipital Nerve Block (GONB)

GONB or nerve block therapy has been suggested as a treatment of medically intractable chronic headache types, including migraine, cluster, cervicogenic and occipital neuralgia, using locally injected anesthetics with or without the addition of corticosteroid preparations. However, the published evidence regarding the use of occipital nerve therapy as a treatment option for chronic headache syndromes, including occipital neuralgia, has been largely limited to case series and individual case reports at single institutions and headache centers.

The use of occipital nerve block therapy as a treatment for occipital neuralgia and chronic headaches have shown some improvement in pain management for some individuals in some preliminary studies ranging from no relief to hours or weeks/months of pain relief; however additional randomized, placebo-controlled studies with larger test populations and longer follow-up periods are needed before conclusions regarding the safety and efficacy of this technique can be reached.

U.S. Food and Drug Administration (FDA)

Greater occipital nerve block (GONB) is a procedure and is not subjected to FDA regulation; however, any medical devices, drugs, biologics, or tests used as a part of this procedure may be subject to FDA regulation.

SUMMARY OF MEDICAL EVIDENCE

Cervicogenic Headache

Different treatment modalities have been used in cervicogenic headaches; however, none have been proven effective. An UpToDate peer review notes that ‘Greater and lesser occipital nerve blockade may provide temporary pain relief in some cases, but the benefit of this treatment is not specific for cervicogenic headache. In addition, there is no anatomic rationale for greater occipital nerve blockade in the diagnosis or treatment of cervicogenic headache.’ (Watson 2020)

A Hayes assessment on the use of anesthetic-based injections for patients with cervicogenic headache found overall low-quality body of evidence suggesting that anesthetic-based injections provide superior pain relief compared with placebo and similar pain relief compared with more invasive treatments (Hayes, December 2019). A rating of C was assigned for the use of anesthetic-based injections for patients with cervicogenic headache and the report concluded that there “remains uncertainty regarding the duration of pain relief, the optimal formulation of anesthetic-based injections, the comparative effectiveness and safety versus conservative treatments, and patient selection criteria.”

Gross et al. (2013) conducted a systematic review of 12 RCTs of patients treated with injection therapies for mechanical neck disorders, including cervicogenic headache and concluded that there is insufficient evidence to confirm the efficacy of anesthetic-based nerve blocks for pain relief in cervicogenic headache.

National Institute for Health and Care Excellence (NICE): Cervicogenic headaches and occipital neuralgia were not addressed in a guideline for the diagnosis and management of headaches updated in 2015 ([NICE Clinical Guidance \[CG150\]](#)).

Cluster Headache

To date there is insufficient high-level evidence for the efficacy of GON block in the acute or preventive treatment of headache. Current evidence of benefit of GONB in the management of cluster headache is limited to case series showing only temporary symptomatic relief and from non-controlled studies which suggested efficacy of GONB in the treatment of migraine, cluster headache, and chronic daily headache. There are few well-designed controlled, blinded studies to assess the role of GONB in headache treatment which is needed to determine the patient populations who would benefit the most from this procedure, and to establish the optimal drug combination to use for nerve blockade. Results of case series varied in terms of frequency, intensity and duration of headache relief (Gantenbein, 2012; Peres, 2002). Controlled studies are required to better assess the role of GON block in the treatment of migraine and other headaches.

Occipital Neuralgia

Occipital neuralgia is a distinct type of headache characterized by piercing, throbbing, or electric-shock-like chronic pain in the upper neck, back of the head, and behind the ears, usually on one side of the head. Typically, the pain of occipital neuralgia begins in the neck and then spreads upwards. Some individuals will also experience pain in the scalp, forehead, and behind the eyes. Their scalp may also be tender to the touch, and their eyes especially sensitive to light. The location of pain is related to the areas supplied by the greater and lesser occipital nerves, which run from the area where the spinal column meets the neck, up to the scalp at the back of the head. The pain is caused by irritation or injury to the nerves, which can be the result of trauma to the back of the head, pinching of the nerves by overly tight neck muscles, compression of the nerve as it leaves the spine due to osteoarthritis, or tumors or other types of lesions in the neck. Treatment is generally symptomatic and includes massage and rest. In some cases, antidepressants may be used when the pain is particularly severe. Other treatments may include local nerve blocks and injections of steroids directly into the affected area.

According to Hayes (2019), the current evidence for local injection therapy for cervicogenic headache or occipital neuralgia is limited by small sample sizes, short-to-intermediate follow-up periods, a lack of data regarding optimal patient selection, and a lack of comparisons with conservative treatment approaches. Additional studies are needed to address optimal use of injection therapy for nerve blockade in occipital neuralgia. Hayes (2019) cited the evidence as very-low-quality and insufficient to evaluate the efficacy of injections for outcomes since the outcomes, including QOL, headache frequency, or complication rates were reported by a single study (Cohen et al., 2015). The efficacy of injections (anesthetic with or without steroids) versus placebo was not assessed for patients with occipital neuralgia (Hayes, December 2019).

A Hayes report assigned a rating of D2 for the use of anesthetic-based injections in patients with occipital neuralgia due to the very-low-quality body of evidence suggesting that anesthetics plus steroid injections provide inferior pain relief compared with more invasive treatments. (Hayes, December 2019).

Migraine Headache

Migraine is a chronic neurologic disease that is recurrent in nature and classically presents as moderate-to-severe head pain lasting on average from 4 to 72 hours. It is typically unilateral with a pulsating quality, accompanied by nausea, vomiting, photophobia, and/or phonophobia, and may be preceded by aura that consists of sensory, motor, or language symptoms. The involvement of the trigeminovascular system (TVS) is broadly accepted, however the pathophysiology of migraine, both episodic and chronic, is not fully understood.

According to the *International Classification of Headache Disorders (ICHD)*, 3rd edition (beta version) chronic migraine is defined as headache occurring on 15 or more days/month for more than 3 months, which, on at least 8 days/month, has the features of migraine headache.

- Chronic migraine is the most commonly used term to indicate a progression from or complication of migraine; however, the ICHD-3 definition of chronic migraine is more indicative of migraine that retains its clinical characteristics but with an increase in the number of headache days.
- First-line prophylactic agents are propranolol, amitriptyline, and topiramate; valproic acid and its derivatives are first line for men and for women who do not have childbearing potential. The choice among migraine prophylactic agents depends upon individual patient factors and comorbid conditions. For patients with chronic migraine who have failed treatment with first-line agents, second-line pharmacologic agents include: onabotulinumtoxinA injections, CGRP antagonists (subcutaneous erenumab, fremanezumab, or galcanezumab), or verapamil, other beta blockers, gabapentin, magnesium, riboflavin, candesartan, and other tricyclic antidepressants (AHS, 2019).⁸
- Alternatives for those who fail treatment with first and second-line agents: Third-line agents include feverfew, tizanidine, memantine, pregabalin, cyproheptadine, and zonisamide.
- Treatments for patients refractory to conventional treatment (e.g., management of lifestyle and headache triggers or acute or preventive migraine medication) include neuromodulatory therapies, such as GONB, occipital or vagal nerve stimulation, transcranial magnetic stimulation, and surgical decompression of the GON (Weatherall, 2015; Su and Yu, 2018). At the present time, there are no migraine-related standardization of GONB treatment protocols (Hayes, Dec 2020).

Greater Occipital Nerve Blocks (GONB)

GONBs are frequently used to treat migraine headaches even though a paucity of supporting clinical evidence exists. Despite some favorable clinical experience reported, there is a lack of high-quality published evidence and clinical trials supporting in the efficacy of GONB in migraine treatment:

The efficacy of GONB therapy for the treatment of occipital neuralgia has been demonstrated in observational and cohort studies and series of small numbers with only short-term outcomes data. There is no conclusive evidence of the durable therapeutic effect of GONB in occipital neuralgia, further study is needed to confirm its benefits when closely balanced with risk, before a widespread use of GONB can be recommended. Therefore, the use of GONB for prophylaxis and treatment of migraine headache, including for the prevention of debilitating symptoms of chronic migraine and for the prevention of debilitating symptoms of episodic migraine or transformed migraine in adult patients, are considered experimental, investigational and unproven due to insufficient evidence in the peer-reviewed medical literature that have not established long term safety, efficacy and effect on net health outcomes.

- Although studies have been conducted and reported variable results and conclusions, there is heterogeneity in treatment and migraine types across studies due to the lack of standardization of GONB treatment protocols. Considerable variability exists regarding the technique, injection site(s), drug/agent used (type of anesthetic, addition of corticosteroid to local anesthetic i.e. lidocaine, bupivacaine, or both) with or without corticosteroids, patient selection criteria, dosages, and frequency of administration. This gap in consensus and professional society recommendations to guide practice supports the need for further research in this area to improve the outcome and safety of this treatment modality.
- Standard treatment protocols, and larger, well-designed controlled trials with longer follow-up are required to establish long-term safety, efficacy and effect on net health outcomes of GONB.
- Comparative efficacy studies of GONB and standard treatments such as onabotulinumtoxinA (Botox-A) (the only FDA-approved therapy for prevention of headaches in adults with chronic migraine) are lacking currently.
- Currently there are no clinical guidelines or consensus released by major U.S.-based headache or neurology organizations addressing GONB in the treatment of migraine and to establish the patient populations who benefit the most from this procedure, and optimal drug combination to use for nerve blockade.

Systematic Review and Meta-Analysis

A recent meta-analysis and systematic review was conducted to analyze the role of greater occipital nerve block (GONB) in chronic migraine headaches (Shauly et al. 2019). Nine randomized control trials were pooled and the results were analyzed. The mean number of headache days per month were reported in both the intervention and control groups of 440 participants (intervention, n=224; control, n=216).

- 8 studies that were analyzed reported the mean headache days per month in both intervention and control groups. A pooled mean difference of -3.6 headache days (95% CI, -1.39 to -5.81 headache days; $p < 0.00001$) in a total of 417 patients studied. Pooled mean difference in pain scores of -2.2 (95% CI, -1.56 to -2.84) demonstrated a decrease in headache severity compared with controls ($p < 0.0121$).
- 7 studies assessed reported mean visual analogue scale pain scores. Pooled mean difference in pain scores of -2.2 (95% CI, -1.56 to -2.84; $p = 0.0121$).
- 2 studies also reported patients that experienced a greater than 50% reduction in headache frequency. Risk ratios were calculated in these two studies, and the average risk ratio was found to be 0.76 (95% CI, 0.97 to 0.55; $p < 0.00001$).
- The authors concluded that 'greater occipital nerve blocking should be recommended for use in migraine patients, particularly those that may require future surgical intervention. The block may act as stepping stone for patients experiencing migraine headache because of its usefulness for potentially assessing surgical candidates for nerve decompression.'
- Limitations of the meta-analysis and systematic review stem from the studies that were pooled (Khansa, I. et al. 2019).
 - **The studies evaluated do not perform the same comparisons and results in variations between the control and intervention groups:** 3 studies compared local anesthetic with saline (bupivacaine or lidocaine) versus local anesthetic and corticosteroid while 6 studies compared local anesthetic (bupivacaine or lidocaine) versus saline injection. A critical review noted that it is 'very difficult to reach meaningful conclusions by pooling studies that have such different study and control group.
 - **Another limitation of meta-analysis and systematic review is heterogeneity of the data from the inclusion of other headache patients (e.g. cervicogenic headache and medication overuse headache).** One study did not examine patients with classic migraine headache but included patients with triptan-overuse headaches experiencing abrupt medication withdrawal (Karadas et al.) and another study that included more than half patients who received blocks in the facial area in addition to GONB which (Naja et al.)

Chowdhury et al. 2020, in a critical review, analyzed the evidence of the efficacy and safety of greater occipital nerve block (GONB) for the preventive treatment of chronic migraine (CM). The lack of rigorous scientific assessment of GONB and use in headache centers as a preventive treatment for CM despite a lack robust evidence base and standardized method of use is discussed. It is also noted that while few reviews in the past have examined the role of GONB in various headache disorders including migraine, none have focused exclusively on CM.

- The review evaluated 9 open-label and 4 placebo-controlled trials for the role of GONB prevention of CM.
- The open-label trials reported positive results with a reduction of headache severity and frequency in 35–68% of patients and the beneficial effect of a single block lasted up to 4 weeks; however, the randomized controlled trials (RCTs) used heterogeneous methodology and techniques of GONB and the outcomes were reported at different time points. A single RCT showed a beneficial effect of the GON block at 1 week. However, the GON block was found to be safe and well-tolerated.
- **According to the review, GONB may be beneficial in CM patients but larger well-devised RCTs are needed due to the limitations and the uncertainties, such as blocking technique, local anesthetic type, concentration, dose, combinations and frequency of administration. In addition, the ‘long-term efficacy of GONB for CM requires further well-designed RCTs using standardized methodology.’**
- **Two meta-analyses evaluated the role of GONB in reducing the severity and frequency of headache in migraine, however not specifically in chronic migraine (Tang et al. 2017; Zhang H, et al. 2018).**

Tang et al. (2017) conducted a systematic review and meta-analysis of 6 randomized controlled trials (RCTs) to assess the efficacy of GONB compared with control intervention of GON placebo (saline) injection in 279 patients diagnosed with migraine:

- GONB consisted of bupivacaine alone in 3 trials, bupivacaine plus methylprednisolone in 1 trial, bupivacaine plus triamcinolone in 1 trial, and lidocaine plus triamcinolone in 1 trial
- 4 trials included only patients with chronic migraine; 2 trials included patients with episodic or chronic migraine
- All trials had < 40 patients per treatment group; 4 trials had < 25 patients per treatment group
- Compared to placebo injection, GONB associated with:
 - Moderate reductions in:
 - Number of days/month with headache (standardized mean difference [SMD] -0.68, 95% CI -1.02 to -0.35) in analysis of 3 trials with 145 patients (all with chronic migraine)
 - Headache pain (SMD -0.51, 95% CI -0.81 to -0.21) in analysis of 4 trials with 180 patients (chronic migraine in 3 trials, episodic or chronic migraine in 1 trial)
 - Small reduction in acute medication use (SMD -0.35, 95% CI -0.67 to -0.02) in analysis of 3 trials with 145 patients (chronic migraine in 1 trial, episodic or chronic migraine in 2 trials)

- No serious adverse events reported; quantitative analysis on any adverse events not reported, but authors describe rate as "very few"
- Compared with control intervention in migraine patients, GONB intervention was found to significantly reduce pain score, number of headache days, and medication consumption but demonstrated no influence on duration of headache per four weeks.
- The authors concluded that compared with control intervention in migraine patients, GONB intervention was found to significantly reduce pain score, number of headache days, and medication consumption but demonstrated no influence on duration of headache per four weeks.
- The short-term follow-up did not allow for assessment of intermediate and long-term outcomes.

Zhang H, et al. (2018) performed a systematic review of seven RCTs and a meta-analysis investigated the impact of GONB on pain management of migraine. The primary outcome was pain intensity. GONB reported to reduce pain intensity and analgesic use and headache frequency outcomes not reported.

- The authors concluded that compared with control intervention in migraine patients, GONB intervention can significantly reduce pain intensity and analgesic medication consumption, however, has no remarkable impact on headache duration and adverse events.
- The analysis was based on only seven RCTs, the same 6 trials (Tang et al. 2017) plus 1 additional small trial, with relatively small sample size ($n < 100$) and short follow-up time.

Yang et al. (2016) conducted a systematic review to evaluate the clinical efficacy and safety of occipital nerve stimulation (ONS) for treating migraine. Five randomized controlled trials, 4 retrospective studies, and one prospective study met the inclusion criteria. Improvement was noted in the migraine disability assessment (MIDAS) score and SF-36 score at follow-up. The mean complication incidence of ONS was 66% for the reviewed studies.

- The authors concluded that results from the retrospective studies and case series indicated that ONS significantly reduced the pain intensity and the number of days with headache in patients with migraine. The evidence of ONS efficacy established by randomized controlled trials was limited.
- The authors recommended that future clinical studies should optimize and standardize the ONS intervention process and identify the relationship among the surgical process, efficacy, and complications resulting from the procedure.

Clinical Studies

GONB appears to improve migraine headache measures over the short term, however the follow-up times in the reviewed studies were inadequate (usually 3 months or less) to demonstrate long-term efficacy of GONB for treatment of migraine. Evidence is lacking from RCTs regarding the benefit of GONB in patients who receive recurrent injections over a more extended period.

According to the critical review conducted by Chowdhury et al. (2020), 'It is difficult to make a composite outcome assessment based on the four RCTs because of inherent methodological heterogeneity. Further, they differed significantly in terms of quality. Of the four RCTs, one study evaluated the short-term outcome at 1 week following a single GON block (Cuadrado et al. 2017). This was a well-conducted RCT that showed a significant reduction in moderate to severe headache days and any headache days in CM patients receiving GON block. Two other RCTs used identical frequency of initial GON block (once a week for 4 weeks) (Inan et al. 2015; Gul et al. 2017). Of these, only one study found a significant difference in favor of active treatment at the end of 1 month (Inan et al. 2015). The other one did not find any significant difference as compared to placebo at 1 month although on repeat GON block monthly for the next 2 months, a significant reduction in VAS score and headache days in the active arm was found at the end of the second and third month (Gul et al. 2017). One RCT reported no difference between active and placebo arms in terms of headache severity at 1 month (Palamar et al. 2015). The review concludes 'Based on these results, the efficacy of the GON block in CM remains a suspect although there is a fair suggestion that GON block probably works well as a short-term preventive at 1 week. In both open-label and RCTs, the headache duration in CM did not decrease with the GON block. Further, not enough data are available regarding predictive factors for favorable outcomes following GON block in CM as open-label studies reported conflicting results.'

GONB with Local Anesthetic vs Placebo Saline

Cuadrado et al. (2017) evaluated the short-term outcome at 1 week following a single GONB. The randomized, double-blind, placebo-controlled included 36 women with chronic migraine

- Women aged 18-65 were treated either with bilateral GON block with bupivacaine 0.5% (n=18) or a sham procedure with normal saline (n=18). Headache frequency was recorded a week after and before the procedure.
- The effect of the GON block on pressure pain thresholds (PPTs) in different territories were also analyzed. The assessment was done 1 week before and 1 h and 1 week after the GON block.
- The study demonstrated an absolute reduction in the number of headache calendar days with the use of GON block with bupivacaine.
- The authors noted that the GON anesthetic blocks appear to be effective in the short-term in chronic migraine, as measured by a reduction in the number of days with moderate-to-severe headache or any headache during the week following injection. GONB is followed by an increase in PPTs in the trigeminal area, suggesting an effect on central sensitization at the trigeminal nucleus caudalis.
- **Cuadrado et al. concluded that anesthetic GON block may be useful as a bridging therapy in the short-term treatment of chronic migraines; however, RCTs are still required to**

confirm these results since the study was limited by its heterogeneous patient population and small sample size. ClinicalTrials.gov (NCT02188394).

Gul et al. (2017) evaluated the efficacy of GON blockade in patients with chronic migraine in a randomized, double-blind, placebo-controlled study involving 44 chronic migraine patients

- Randomized into two groups; group A (bupivacaine) and group B (placebo)
- GONB was administered four times (once per week) with bupivacaine or saline. After 4 weeks of treatment, patients were followed up for 3 months, and findings were recorded once every month for comparing each month's values with the pretreatment values.
- The primary endpoint was the difference in the frequency of headache (headache days/month). The Visual Analogue Scale (VAS) pain scores were also recorded. No severe adverse effects were reported.
- The mean number of headache days and VAS scores were significantly lower as compared to pretreatment in the active group at the first, second, and third months, whereas in the control group, they became nonsignificant after the second and third months:
 - Group A (bupivacaine) showed a significant decrease in the frequency of headache and VAS scores at the first, second, and third months of follow-up
 - Group B (placebo) showed a significant decrease in the frequency of headache and VAS scores at the first month of follow-up, but second and third months of follow-up showed no significant difference
- This study concluded that the GON block with bupivacaine not only was superior to placebo in the **treatment of chronic migraine but also had long-lasting effects of up to 3 months.**
- **Additional studies are required to better define the safety and cost-effectiveness of GONB in chronic migraine.**

Inan et al. (2015) reported the first randomized, multicenter, double-blind, and placebo-controlled study that evaluated the safety and efficacy of unilateral GONB in a multicenter, double-blind, randomized placebo-controlled crossover trial of 84 patients with chronic migraine at 1, 2, and 3-month follow-up.

- 84 patients were randomized to bupivacaine (n=42) or placebo group saline (n=42):
 - The intervention group received GONB with injections of 0.5% bupivacaine (n = 42), while the placebo group received 2.5 mL saline (n = 42) once a week for 4 weeks
 - After 4 weeks of treatment, blinding was removed; in group A, GON blockade was achieved using bupivacaine, while group B continued to receive bupivacaine, and blockade was administered once per month, then followed for 2 months
 - Primary endpoint was the difference in number of headache days, duration of headache, and pain scores
 - 72 out of 84 patients completed the study and 14.3% dropped out. Reasons for dropout were not provided.
- After 1 month of treatment, the number of headache days and headache severity decreased significantly in the bupivacaine group. After changing the placebo group with bupivacaine, both

the groups showed a similar significant decrease in outcome parameters in the second and third months.

- The authors stated the evidence suggests that GONB with bupivacaine relieves migraine headache symptoms and reduces the frequency of the attacks compared with a placebo (confirmed when the placebo patients crossed over to active treatment and experienced significant symptom relief).
- **Although treatment with bupivacaine reduced the number of headache days per month, it did not reduce the duration of headaches compared with placebo.**
- **The study was also limited by its small sample size, with only 72 of the 84 subjects completing the study (n=33 placebo; n=39 bupivacaine). Other limitations included a short duration of the double-blind phase; which was limited to only 1 month of actual blinding and a short follow-up of 3 months.**

Özer et al. (2018) evaluated the efficacy of GONB and supraorbital nerve block (SONB) with local anesthetics for the preventive treatment of migraine without aura in a single-blind, randomized, placebo-controlled study

- 87 adult patients diagnosed with migraine without aura were included in the study and patients were divided randomly. One group was injected with 1% lidocaine (n=44), the other group was injected with 0.9% saline (n=43). GON and SON injections were done bilaterally. The injections were repeated weekly for 3 weeks. Patients were followed up for 2 months to assess clinical response.
- 71 patients completed the study; lidocaine (n=43) and placebo 0.9% saline (n=28). Patients kept HA diary for 1 month prior to and 2 months following injection and assessed at clinic visits for 2 months after injection.
- Özer et al. concluded that GONB and SONB with lidocaine reduced pain severity but not HA frequency in patients with chronic migraine compared with placebo, although patients with episodic migraine improved. HA frequency and pain severity statistically significant improved in the GONB/SONB groups compared with placebo. No major adverse effects occurred.
- **The limitations of this study includes the lack of a double blind trial and high attrition rate (16 patients withdrew from study before completion; 15 (34.9%) patients in placebo group due to continued pain and loss to follow-up and 1 patient was lost to follow-up in GONB group) which lead to an imbalance in group sizes and loss of statistical power. The study was also limited due to short follow-up period of only 2 months.**

Adding Corticosteroid or Saline (placebo) to Local Anesthetic

Dilli et al. (2015) evaluated the role of GONB (local anesthetic and corticosteroid) for preventive treatment in migraine in adults with chronic migraine in randomized, double-blind placebo-controlled study.

- 70 patients between 18 and 75 years old with ICHD-defined episodic (> 1 attack per week) or chronic migraine were randomized to receive either with local anesthetic and corticosteroid:
 - 35 patients received local anesthetic and corticosteroid: 2.5 ml 0.5% bupivacaine plus 0.5 ml (20 mg) methylprednisolone over the ipsilateral (unilateral headache) or bilateral (bilateral headache) occipital nerve (ON), or
 - 35 patients received placebo treatment: 2.75 ml normal saline plus 0.25 ml 1% lidocaine without epinephrine (placebo arm)
- Due to the missing data of 7 patients (2 patients missing f/u data in the active steroid group and 5 in placebo group) the full analysis of 33 patients in the active and 30 patients in the placebo group was analyzed for efficacy. In the active and placebo groups respectively, the mean frequency of at least moderate (mean 9.8 versus 9.5) and severe (3.6 versus 4.3) migraine days and acute medication days (7.9 versus 10.0) were not substantially different at baseline. The percentage of patients with at least a 50% reduction in the frequency of moderate or severe headache days was 30% for both groups.
- Patients completed a one-month headache diary prior to and after the double-blind injection.
- The primary outcome measure was defined as a 50% or greater reduction in the frequency of days with moderate or severe migraine headache in the four-week post-injection compared to the four-week pre-injection baseline period.
- An evaluation 4 weeks after the procedure did not find any significant changes in the frequency of moderate to severe headache days in either group with respect to its baseline data.
- **The authors concluded that GONB with local anesthetic (bupivacaine) and corticosteroid (methylprednisolone) does not result in improved HA outcomes compared with control (lidocaine and saline) in patients with episodic migraine or chronic migraine.** The GONB evaluated does not reduce the frequency of moderate to severe migraine days in individuals with episodic or chronic migraine compared to placebo.
- Limitation of the study: The study was underpowered to make any useful inference of the efficacy of the GONB in chronic migraine specifically and was excluded (only six patients in the active group and three patients in the control group had moderate to severe migraine of ≥ 15 days per 4 weeks, thereby qualifying as CM). Another limiting factor to consider is that the study did not evaluate the onset or duration of benefit of the GONB; it also did not evaluate the acute response to the injection. In addition, not every participant was experiencing headache pain at the time of injection. The authors acknowledged the need for a placebo-controlled trial to evaluate GONB for acute relief of migraine pain. The study had a small sample size and the procedure was performed once, compared to the multiple times in other studies. This study's placebo treatment included a small amount of anesthetic.

An UpToDate review on chronic migraine (Garza 2020) notes: “There are inconsistent data from small randomized trials regarding the benefit of occipital nerve stimulation for the treatment of chronic migraine [Saper JR et al. (2011); Silberstein SD et al. (2012)]. In the largest trial, there was no significant difference at 12 weeks for the primary endpoint, the percentage of patients that had a ≥ 50 percent reduction in mean daily pain score in the active compared with the control group [Silberstein SD et al. (2012)]. However, there were statistically significant if modest improvements with active stimulation for a number of secondary endpoints, including the percentage of patients with a ≥ 30 percent reduction in mean daily pain score, and reduction in the mean number of headache days and migraine-related disability. The findings from these reports are limited by concerns about blinding in the control (sham treatment) groups, given that active treatment causes paresthesia, and relatively high rates of complications, including lead migration in 14 to 24 percent of subjects [Saper JR et al. (2011); Silberstein SD et al. (2012); Schwedt TJ (2011); Diener HC (2012)].”

Professional Society Guidelines/Consensus Statements

No consensus or professional U.S. society guidelines addressing greater occipital nerve block (GONB) for the treatment of migraine headache has been published resulting in a lack of standardization of GONB treatment protocols and heterogeneity in treatment and migraine types across studies (Hayes 2020).

Hayes

GONB for the prevention of debilitating symptoms of chronic migraine (CM) in adult patients who do not respond adequately to standard therapy

Hayes concluded potential but unproven benefit (Rating C): ‘Some published evidence suggests that safety and impact on health outcomes are at least comparable to standard treatment/testing. However, substantial uncertainty remains about safety and/or impact on health outcomes because of poor-quality studies, sparse data, conflicting study results, and/or other concerns’

GONB for the prevention of debilitating symptoms of episodic migraine (EM) or transformed migraine in adult patients who do not respond adequately to standard therapy

Hayes concluded that there is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management (Rating: D2)

According to NICE Clinical Guidance on Occipital Nerve Stimulation for Intractable Chronic Migraine (2013): “The evidence on occipital nerve stimulation (ONS) for intractable chronic migraine shows some efficacy in the short term but there is very little evidence about long-term outcomes. With regard to safety, there is a risk of complications, needing further surgery.”

DEFINITIONS

Cervicogenic headache: A secondary headache, caused by another illness or underlying condition, such as neck injuries, infections, or severe high blood pressure. The pain caused by a cervicogenic headache begins in the neck and the back of the head and radiates towards the front of the head. Numerous pain-sensitive structures

exist in the cervical (upper neck) and occipital (back of head) regions. Cervicogenic headache presents as unilateral pain that starts in the neck. (American Migraine Foundation, 2019)

Cluster headache: A primary headache disorder and that occur in occurring in "bouts" or "clusters" of frequencies. During a cluster cycle, brief, excruciatingly severe headache attacks recur between 1-8 times per day. Cluster cycles can last for weeks or months and are usually separated by remission periods, or periods of headache freedom, which usually last months or years. (American Migraine Foundation, 2019)

Occipital Neuralgia: A primary or secondary headache caused by irritation or injury to the greater or lesser occipital nerves; a secondary condition is associated with an underlying disease or as a result of injury or irritation of these nerves. Occipital Neuralgia is a condition in which the occipital nerves, the nerves that run through the scalp, are injured or inflamed. This causes headaches that feel like severe piercing, throbbing or shock-like pain in the upper neck, back of the head or behind the ears.

CODING INFORMATION *The codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is covered or non-covered. coverage is determined by the benefit document. this list of codes may not be all inclusive.*

| CPT | Description |
|-------|--|
| 64405 | Injection, anesthetic agent; greater occipital nerve [when specified as a therapeutic nerve block] |
| 64450 | Injection(s), anesthetic agent(s) and/or steroid; other peripheral nerve or branch [when specified as a therapeutic nerve block of lesser occipital nerve] |

| HPCS | Description |
|------|-------------|
| | N/A |

| ICD-10 | Description |
|-----------------|-----------------------------|
| G43.001-G43.919 | Range of codes for Migraine |
| G44.001-G44.89 | Other headache syndromes |
| M54.81 | Occipital neuralgia |
| R51 | Headache |

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| Policy History | Approval |
|--|----------|
| <p><u>Policy Developed</u></p> <p>Policy created as “Greater Occipital Nerve Block for Treatment of Migraine Headache”</p> <p>Peer review: Advanced Medical Review. Practicing Physician. Board certified in Neurology. 12/29/19. Additional reference cited by reviewer:</p> <ul style="list-style-type: none"> • Shauly O, Gould DJ, Sahai-Srivastava S, Patel KM. Greater Occipital Nerve Block for the Treatment of Chronic Migraine Headaches: A Systematic Review and Meta-Analysis. Plast Reconstr Surg. 2019;144:943-952. | 4/23/20 |

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|--|----------------|
| <p><u>Policy Revision</u></p> <p>Revised policy from ‘Greater Occipital Nerve Block for Treatment of Migraine Headache’ to ‘Occipital Nerve Block Therapy for Treatment of Headache and Occipital Neuralgia’ to include occipital neuralgia treatment of various headache syndromes and occipital neuralgia.</p> <p>Peer Review: Advanced Medical Review. Practicing Physician. Board certified in Neurology. 5/8/2020. Additional reference cited by reviewer:</p> <ul style="list-style-type: none"> • Blumenfeld A, Ashkenazi A, Evans RW. Occipital and trigeminal nerve blocks for migraine. Headache. 2015;55:682-689. • Fernandes L, Khan N, Dobson J, Randall M, Idrovo L. Multiple Cranial Nerve Blocks as an Alternative Preventative Therapy for Chronic Migraine. Headache. 2020;60:981-987. | <p>6/17/20</p> |
| <p><u>Policy Revision</u></p> <p>Peer review: Advanced Medical Review. Practicing Physician. Board certified in Neurology with Special Qualification in Child, Sleep Medicine. 1/13/2021.</p> <p>Notable revisions include:</p> <ul style="list-style-type: none"> • Addressed the limitations of the meta-analysis and systematic review from the studies in Shaully et al. (2019) • Added a critical review (Chowdhury et al. 2020) which analyzed the evidence of the efficacy and safety of greater occipital nerve block for the preventive treatment of chronic migraine • Added an UptoDate review on chronic migraine (Garza 2020) • Updated ‘Professional Society Guidelines/Consensus Statements’ section with Hayes review | <p>2/8/21</p> |

**Annual Review and Policy Revisions: All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections were reviewed and revised with the most recent medical literature and available evidence. Coverage criteria for Initial and Continuation of Therapy were revised/updated as appropriate.*