Occipital Nerve Stimulation for the Treatment of Refractory Headache Disorders in Adults: A Narrative Review

Van Stighel G.[1,2], Van Buyten J-P.[1], Vanhonacker D.[2]

[1]*Multidisciplinary Pain Centre, VITAZ, Sint-Niklaas, Belgium;* [2]*Department of Anesthesia and Perioperative Medicine, University Hospital of Brussels, Jette, Belgium.*

Corresponding author: Gregory Van Stighel, Multidisciplinary Pain Centre, VITAZ, Moerlandstraat 1, 9100 Sint-Niklaas, Belgium. E-mail: Gregory.vanstighel@telenet.be

Abstract

Background: **Subcutaneous occipital nerve stimulation (ONS) has emerged as a neuromodulatory option for patients with chronic, medically intractable headache disorders, yet its clinical effectiveness and safety remain debated.**
Methods: **A narrative, non-systematic review (PubMed, Embase, Cochrane Library; search date 21 April 2025) was performed using combined terms for “occipital nerve stimulation” and refractory headache entities. After duplicate removal and staged screening, 77 peer-reviewed human studies were retained for qualitative synthesis.**
Results: **Across study designs, ONS produced clinically meaningful improvement in 35.7–100 % of patients, with a pooled responder rate of 57.3 % in chronic cluster headache and sustained benefit in >40 % of chronic migraine cases over ≥4 years. In occipital neuralgia and short-lasting unilateral neuralgiform attacks, 63–100 % response was observed. Randomised data show an additional mean reduction of 2.6 moderate-to-severe headache days per month versus sham in chronic migraine, and comparable efficacy at both high- and low-intensity stimulation in cluster headache. Despite therapeutic gains, adverse events were frequent: overall complication rates reached 66 %, driven by lead migration (2–60 %), infection (2–24 %) and premature battery depletion (up to 70 %), often necessitating revision surgery. Long-horizon modelling nevertheless suggests ONS can become cost-effective within one year for refractory cluster headache owing to reduced drug use and productivity loss.**
Conclusions: **Current evidence supports ONS as a valuable, albeit invasive, symptomatic therapy for selected patients with refractory headache syndromes. High hardware-related morbidity underscores the need for purpose-built implants, standardised surgical protocols and robust, blinded trials to refine patient selection and define long-term risk–benefit and cost-utility profiles.**

Keywords: **Headache Disorders, Chronic Pain; Neurostimulation, Electric Stimulation Therapy, Occipital nerve stimulation.**

Introduction

Headaches are a common symptom for a wide range of diseases, with the first descriptions of it dating back to ancient times[1]. The lifelong incidence of headache is reported to be as high as 96%, with females being more affected than males[2,3].

Some people, however, suffer from chronic headaches. The International Classification of Headache Disorders (ICHD) describes the different chronic headache syndromes as persistent for more than three months or with remissions periods of less than three months[4]. Although chronic daily headache itself is not listed in the ICHD-3, it is commonly used as an umbrella term for chronic headache disorders[5] and is described as having 15 or more headache episodes per month for at least three months[4,6]. The prevalence of chronic daily headache has been reported to be

This manuscript has not been a part of any (poster) presentation nor has it been communicated at any kind of meeting.

in a range of 3% to 5% worldwide[2],representing a significant burden to both patients and healthcare systems.

The treatment of chronic headache disorders depends on the specific type of headache disorder and their etiology. Different lifestyle changes, like minimizing or avoiding triggers and stressors, should always be the first step in managing these disorders. To abort an acute headache attack, different analgesics like paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, triptans, ergotamine derivatives or even steroids can be used, with or without antiemetics. Prophylactic medication can consist of beta-blockers, anticonvulsants, antidepressants, botulinum toxin A injections, monoclonal antibodies targeting the calcitonine gene-related peptide (CGRP) or their receptors, calciumantagonists or indomethacin. Other possible add-on therapies are psychotherapy, behavioural therapy, physiotherapy, manual therapy or muscle relaxants[2,5,6]. Some patients, however, suffer from refractory forms of chronic headache disorders, where effective treatment options are limited. In these cases, interventional pain therapies, such as subcutaneous occipital nerve stimulation (ONS), where one or two electrodes are implanted subcutaneously and near the greater and lesser occipital nerve (LON), have emerged as a potential alternative therapeutic strategy.

This narrative review aims to summarize the current understanding of ONS in the treatment of the different chronic refractory headache disorders, with emphasis on mechanisms, indications, clinical outcomes, and safety considerations.

Methods

A non-systematic literature review was conducted using three major databases, more specifically Medline (PubMed), Embase and the Cochrane library. The initial literature search was conducted on the 21st of April 2025, containing the following keywords: “occipital”, “nerve”, “stimulation”, “occipital nerve”, “nerve stimulation” and “occipital nerve stimulation” together with “headache”, “chronic headache”, “refractory headache”, “intractable headache”, “migraine”, “cluster headache” and “hemicrania continua”. The exact search terms with the use of the Boolean operators are listed in Table I.

Results

1507 articles were retrieved from the initial search. Additional filters were applied to the search, limiting the results to studies written in English conducted in humans and aged 18 years and older. It must be noted, however, that for the search in the Cochrane Library the filter for studies in humans aged 18 years and older could not be applicated. Using these filters, 903 articles were excluded, resulting in 604 articles that were retrieved. Another 148 duplicate articles were identified by automated screening tools and removed, resulting in 456 articles that were eligible for further screening.

After screening the articles on title and abstract, 301 were excluded for various reasons including: studies with a “Terminated” status on ClinicalTrials.gov, studies with no link to published article on ClinicalTrials.gov, completed studies on ClinicalTrials.gov linking to an already included article, studies with inconclusive titles and missing abstracts and studies with abstracts deemed out-of-scope for this review. This included 11 Cochrane reviews and 2 Cochrane protocols that revealed to be out-of-scope. This resulted in 155 articles remaining for full article screening.

Another 48 articles were excluded after this full article screening round. Reasons for exclusion were: conference articles or abstracts without any link toward a later published article, unavailability of a full article, double articles missed by automated processes in the previous screenings and articles that were deemed out-of-scope for this review. During this process, 6 cross referenced articles not retrieved from the aforementioned search in the major databases were included, resulting in 113 articles that were eligible for final inclusion.

Given the large amount of articles that were still eligible for inclusion and analysis, a more focussed approach on recent articles was deemed appropriate. Case reports of single cases were excluded unless they provided information on a new or different surgical technique, off-label usage of ONS, possible new indications for ONS or a rare or unique side effect. Ultimately, 77 articles were included in this narrative review.

Clinical background & indications of ONS

Indications

The concept of peripheral nerve stimulation for pain management dates back to Wall and Sweet in 1967[7], though early methods were highly invasive[8]. In 1999, a significant shift occurred when Weiner and Reed introduced a minimally invasive percutaneous method as a surgical treatment for intractable occipital neuralgia (ON)[9]. Since then, the indications for ONS have expanded greatly. To this day, ONS is still used as a therapy for refractory ON[10]. However, the most researched

Table I. — All used search terms in the different databases including the Boolian operators.

Embase
('occipital' AND 'nerve' AND 'stimulation' OR ('occipital nerve' AND 'stimulation') OR ('occipital' AND 'nerve stimulation') OR 'occipital nerve stimulation') AND ('headache' OR 'chronic headache' OR 'migraine' OR 'cluster headache' OR 'hemicrania continua' OR 'refractory headache' OR 'Intractable headache')
Medline (Pubmed)
(("Occipital"[Text Word] AND "Nerve"[Text Word] AND "Stimulation"[Text Word]) OR ("occipital nerve"[Text Word] AND "Stimulation"[Text Word]) OR "Occipital"[Text Word]) AND ("Nerve stimulation"[Text Word] OR "occipital nerve stimulation"[Text Word]) AND ("Headache"[MeSH Terms] OR "headache disorders"[MeSH Terms] OR "Headache"[Text Word] OR "chronic headache"[Text Word] OR "Migraine"[Text Word] OR "cluster headache"[Text Word] OR "hemicrania continua"[Text Word] OR "refractory headache"[Text Word] OR "Intractable headache"[Text Word])
Cochrane Library
((("occipital") AND ("nerve") AND ("stimulation")) OR (("occipital nerve") AND ("stimulation")) OR (("occipital" AND ("nerve stimulation")) OR ("occipital nerve stimulation")) AND ((MeSH descriptor: [headache] explode all trees) OR (MeSH descriptor: [headache Disorders] explode all trees) OR ("headache") OR (chronic headache) OR ("migraine") OR ("cluster headache") OR ("hemicrania continua") OR (refractory headache) OR (Intractable headache))

indications for ONS in recent days are chronic cluster headache and chronic migraine. Other than that, ONS has also been used in the treatment of several trigeminal autonomic cephalalgias, more specifically in short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA)[10–12], and hemicrania continua[13]. Reports have been published on the treatment of cervicogenic headache[14,15], post-traumatic headache[14], postherpetic neuralgia of the occipital nerves[16], post-chemotherapy headache[17], trigeminal neuralgia (TN)[18], persistent headaches in idiopathic intracranial hypertension following shunt-procedures[19], chronic refractory hypnic headache[20], persistent occipital pain in patients with Chiari I malformation[21], and even fibromyalgia[8] with ONS. Unlike some medications, the use of ONS in chronic cluster headache during pregnancy seems safe. It is suggested that ONS could be used as an alternative preventive treatment for women with medically intractable cluster headache and a possible wish to become pregnant[22], although this claim is made on a single case-study. Further research on the treatment with ONS during pregnancy and lactation is warranted. The concurrent use of ONS and implantable electric medical device, like a pace-maker, does not seem to induce any interference between both devices, given that precautions are taken and that the devices are being checked periodically. However, to this date there are no published trials that evaluate the degree of interference between medical devices[23].

Mechanisms of action of ONS

It has been shown that weak electrical currents can modulate the nervous system. This principle underlies electrical neuromodulation, where electrodes are implanted in proximity to nerve structures[24]. For ONS, the targetted nerves are the occipital nerves[9,25]. Despite the increasing use of ONS, its precise mechanisms of action remain largely unknown[25–29]. Several neuroimaging studies, however, have provided insights into potential underlying processes[26,30].

The prevailing hypothesis is that ONS modulates neural activity within the trigeminocervical complex (TCC) and interconnected brain regions involved in pain processing[25,26]. The occipital nerves, while not directly connecting with cortical structures, form a continuous neural network with the trigeminal system, converging on second-order neurons in the TCC where trigeminal and cervical nociceptive inputs integrate[14,15,26,29,31–34]. Evidence that ONS can relieve TN, despite its distinct pathophysiology, suggests a common and nonspecific modulatory mechanism[18]. Convergence of cervical nociceptive projections to the trigeminal nuclei has been supported by recent research[35].

ONS is believed to inhibit nociceptive transmission within the TCC and related brainstem circuits, in part through modulation of excitatory glutamatergic interneurons[25,27,31]. Functional studies demonstrate reciprocal influences between trigeminal and occipital systems: stimulation of one dermatome alters pain thresholds in the other, consistent with segmental inhibition at the brainstem level[33,36]. This connectivity explains why occipital interventions, such as nerve blocks, can suppress trigeminally mediated responses.

Beyond the TCC, ONS influences supraspinal regions implicated in pain regulation, including the periaqueductal gray matter, nucleus raphe magnus, and rostroventral medulla[15,25]. Functional imaging has shown changes in brain and brainstem activation, as well as altered cerebral blood flow in areas associated with chronic pain[25–28]. The thalamus, particularly the nucleus reticularis, may act as a critical inhibitory gate, while activation of the anterior cingulate cortex in ONS responders suggests involvement of descending opioid-mediated pathways[26,30].

The etiology of many headache disorders is a disrupted balance between peripheral and central nociception[37]. ONS significantly reduces the orbicularis oculi reflex, a protective antinociceptive mechanism of the eye mediated by the trigeminal nerve, when dynamically triggered by a standardized air flow. This reduction indicates that ONS can directly counteract trigeminally mediated central sensitization in chronic migraine. Importantly, this effect appears to require active stimulation, as the reflex response significantly increases shortly after ONS deactivation, suggesting that continuous stimulation is necessary for achieving therapeutic goals. This aligns with clinical observations that ONS typically becomes effective after several weeks of continuous active stimulation, and its effect rapidly diminishes if stimulation is stopped or battery levels are low. By modulating nociceptive input to the TCC, ONS reduces the effects of aversive peripheral stimulation. In patients with chronic headache, including migraine, ONS has been observed to lead to a normalization of the conditioned pain modulation response, suggesting a reduction in central sensitization. Increased afferent input to the TCC, coupled with peripheral sensitization and generalized central sensitization of trigemino-spinal or second-order trigeminal neurons, can contribute to chronic headache development. ONS helps reduce this reflex response to trigeminally mediated aversive irritation, indicating a direct therapeutic effect on the TCC[25].

The theorized mechanism by which neurostimulation works on pain reduction is also grounded in Melzack and Wall's gate-control theory[38]. This theory posits that the electrical stimulation of large C2-C3 nerve fibers effectively decreases activity in smaller-diameter nociceptive fibers, thereby "closing the gate" to pain signals. This peripheral modulation at the level of the spinal dorsal horn may suppress Aδ- and C-fibers[15,39].

In summary, ONS seems to induce slow neuroplastic changes within nonspecific pain-control systems. These mechanisms explain its observed efficacy across different headache disorders, while highlighting that ONS remains a symptomatic rather than curative treatment[40].

'Voltage tuners'

A notable patient behavior observed in chronic cluster headache (CH) patients treated with ONS is "voltage tuning", where patients manually adjust the amplitude of their stimulator using a remote control, often at the onset of an attack. This behavior is suggested to help cease or terminate CH attacks, and research on it may provide insights into ONS as an acute attack treatment. To this day, the mechanism behind voltage tuning is still unclear. It is proposed that it may operate by increasing diffuse noxious inhibitory control, thereby hindering remaining CH attacks that would not be prevented by regular stimulation. This is hypothesized to involve overcoming a neurophysiological "threshold" that is dynamic and may depend on attack intensity and neuropeptide. Additionally, behavioral factors like reduced anxiety and an enhanced sense of self-control of CH attacks may contribute to the perceived benefit of voltage tuning[41].

Predicting factors for ONS failure or succes

ONS has emerged as a therapeutic option for refractory headache syndromes, including chronic migraine (CM) and ON[10]. However, its variable response rates, costs and invasive nature underscore the need reliable predictors of treatment success or failure[31,42,4]3. Research has explored various clinical, psychological, and technical elements to understand ONS outcomes, presenting both consistent findings and areas of ongoing debate.

A. Pre-implantation assessments

The predictive value of trial stimulation and nerve blocks remains debated. Temporary percutaneous ONS trials show questionable utility for predicting long-term outcomes[10,44,45]. While an initial high trial success rate was observed in one study, a substantial portion of permanently implanted systems were later removed due to inefficacy[10]. Benefits seen in brief trials may reflect placebo responses, as neuromodulatory effects typically develop over weeks[10,45]. Even longer, semi-permanent trials of one month have not consistently predicted success in CM[10]. Some evidence suggests higher responder rates when implantation is performed without a trial[44]. The PRISM-study[46] found no significant benefit of active ONS over sham stimulation, although trial response moderately predicted 12-week outcomes. It should be noted, however, that the PRISM-study is only available as a conference abstract article. Consequently, some suggest that trials introduce additional risks and economic burden without reliably selecting long-term responders[10].

Similarly, the predictive value of an occipital nerve block (ONB) prior to ONS is inconclusive[11,42,43,45,47–49]. Studies have explicitly demonstrated that analgesic response to ONB is not useful in predicting the therapeutic effect of ONS. One cohort found that many ONB non-responders benefit from ONS, while not all ONB responders do[49]. This may reflect ONB's short-term, segmental action compared with ONS's broader and slower neuromodulatory effects[45]. Presurgical percutaneous nerve field stimulation (PENS) also failed to reliably identify responders[45]. Conversely, a positive preoperative response to transcutaneous electrical nerve stimulation (TENS) has been associated with better ONS outcomes[43,50].

B. Headache phenotype and clinical features

Headache phenotype and clinical characteristics are crucial predictive factors. Certain headache types appear to respond more favorably to ONS[10,45]. In ON, for instance, ONS consistently shows a high success rate, with all patients reporting more than 50% reduction in pain intensity and/or frequency at long-term follow-up in one review10. Patients with SUNCT and chronic CH also respond more favorably than those with CM[42,43,51]. A systematic review reported a pooled ONS response rate of 57.3% in chronic CH[31], while hemicrania continua may also be highly responsive to it[49]. In contrast, CM generally shows lower response rates and slower therapeutic onset[45].

Within refractory chronic CH, certain specific clinical features predicts ONS failure. This includes an earlier headache onset age, a higher smoking rate, and the presence of seasonal or nocturnal exacerbations. This observation may suggest that ONS is less effective for headaches involving a permanent hypothalamic dysfunction or those highly influenced by environmental factors like light or nicotine. Conversely, chronic CH patients whose headache course presents without significant fluctuations tend to benefit most from ONS[31]. Notably, occipital pain itself is a negative predictor, reducing the likelihood of success by approximately 73 to 74%, contradicting its historical role as an inclusion criterion in ONS studies and possibly relating to intolerance of painful stimulation effects[42,43].

C. Psychological and behavioral factors

Psychological comorbidities significantly affects ONS outcomes. Severe anxiety or depression is consistently associated with poorer responses[42,43]. Broader pain literature also suggests that pain catastrophizing, personality disorders, a history of abuse, and significant cognitive deficits are negative predictors[10]. The lower response rates in patients with mood disorders may have a neurochemical basis, impacting anti-nociceptive processing in higher pain centers[42]. On the other hand, one study demonstrated the beneficial impact of neuromodulation on depression, catastrophic thinking, disability, and pain[52]. Comprehensive psychological assessment and multidisciplinary care, involving a headache specialist, a pain physician with neuromodulation expertise, and a psychologist, are therefore essential to optimize patient selection and outcomes[10,39,45].

Furthermore, medication overuse headache (MOH) and opioid use are further negative predictors[39,45,53]. Patients with MOH at follow-up experience significantly less pain relief, highlighting the importance of withdrawal before implantation[39].

D. Technical considerations

Technical and hardware-related complications, although not predictors of initial response, critically affect long-term outcomes and cost-effectiveness[43]. Early ONS systems were not designed for subcutaneous use, resulting in frequent complications such as lead migration, breakage, and skin erosion[10,39,43]. Despite advances in surgical technique, these remain a significant limitation[53]. Interestingly, sensory responses such as unpleasant paresthesias (buzzing, vibrating, pinching, throbbing) have been more frequent among responders than non-responders, suggesting they may indicate effective stimulation[44].

In summary, ONS outcomes are shaped by headache phenotype, clinical features, psychological comorbidities, and technical factors. Pre-implantation trials and nerve blocks offer limited predictive value, while psychiatric evaluation, management of medication overuse, and careful patient selection remain essential.

Evidence and Clinical Effectiveness of ONS

The reported overall response rate for ONS varies considerably by headache type, ranging from 35.7% to 100% for CH, 17% to 100% for CM, and 63% to 100% for ON. Long-term studies indicate that between 41.6% and 88.0% of patients maintain a response after an average of 18.3 months[54].

Chronic Migraine

For CM, the evidence presents mixed results across studies. A meta-analysis of three multicenter randomized controlled trials (RCTs) demonstrated that ONS was associated with an average additional reduction of 2.59 days per month of prolonged moderate or severe headache after three months, compared to sham stimulation[55]. While the ONSTIM feasibility study showed a promising responder rate of 39% for adjustable stimulation versus 6% for preset stimulation[53,56,57], larger sham-controlled studies, such as PRISM, often did not achieve statistically significant differences in primary outcome measures[46,47,53]. However, secondary outcomes in these studies frequently suggested a benefit, for instance, showing a significant difference when evaluating a 30% reduction in pain severity or headache frequency[47,53,58]. Long-term open-label studies have reported sustained clinical benefit in over 40% of patients with highly intractable CM after a mean follow-up of four years, with reports of continuous treatment leading to a stable effectiveness over a seven-year follow-up period[47,59]. Additionally, some studies have found that 48.9% of stimulation intervals were reported as effective by patients[44]. Patient-centered outcomes, such as quality of life and disability, also show improvement[53,60]. A key finding is that ONS can provide consistent and reproducible results for medically intractable migraine, and that paresthesia is not required for pain reduction, although suprathreshold stimulation may yield better results[61]. In a systematic review by Barad et al., implantable stimulation, including ONS, receives a weak recommendation for the prevention of CM[62].

Chronic Cluster Headache

ONS is considered an effective treatment option for medically intractable chronic CH[48]. A meta-analysis reported a pooled response rate of 57.3% for ONS in chronic CH51. Long-term follow-up studies, some with a median duration exceeding six years, show that approximately 66.7% of patients achieve a reduction of at least 50% in daily attack frequency63. In a large multicenter prospective registry, 69% of patients experienced a reduction of over 50% in attack frequency after ONS, leading to a decrease in mean weekly attack frequency from 22.5 at baseline to 9.9. These patients also demonstrated significant improvements in functional impact, anxiety, and quality of life[64]. The ICON study, a randomized, electrically dose-controlled trial, revealed that both 100% and 30% ONS intensities resulted in a comparably rapid and sustained halving of attack frequency. Half of the participants even achieved a reduction of over 50% in attack frequency[48,65]. This suggests that ONS can be effective even at lower intensities[65]. The effects of ONS often manifest within months, and pain typically returns upon deactivation of the device, arguing against a sole placebo effect[64,66–68]. Furthermore, "voltage tuning" has shown promise in ceasing or preventing attacks, suggesting a potential role for ONS as an acute attack treatment[41]. More than 80% of patients have been reported to respond to ONS for chronic CH, experiencing substantial relief in attack frequency, intensity, and duration[69]. This sustained effectiveness has been confirmed in long-term follow-up studies[67,70].

Trigeminal neuralgia

A retrospective study of patients with refractory TN without occipital pain, who had failed numerous medical and surgical treatments, found that all seven included patients reported improvement after ONS implantation. The average BNI pain score at last follow-up was IIIa, with a mean pain relief of 58.0%. While not validated for this indication, ONS may offer sustained long-term benefits for recurrent TN[29]. It is suggested that ONS could serve as a "salvage treatment" when other surgical options have failed or are contraindicated, or as a less invasive alternative. The interaction between trigeminal and occipital systems is hypothesized to be a key factor[18,29].

Occipital Headaches (Occipital Neuralgia, Cervicogenic Headache, Occipital Migraine)

In a large series of 60 patients with intractable occipital headaches, ONS reduced the mean VAS score from 8.4 to 2.8 on a scale from 0 to 10 (corresponding to a 72.2% reduction) after one year, with 76% achieving at least a 50% decrease. The effectiveness appears linked to a local effect on neurons in the posterior fossa or posterior scalp[50]. Long-term benefits for ON have also been suggested[71].

Short-lasting Unilateral Neuralgiform Headache Attacks

ONS is a promising treatment for medically intractable SUNCT and SUNA. A review reported that 33 of 41 (80.5%) SUNCT/SUNA patients responded to ONS, with 24.4% becoming pain-free and discontinuing concomitant medications after a mean follow-up of 42.5 months[11,37]. Significant improvements were observed in headache-specific disability and quality of life[12].

Cost Aspects

ONS is an expensive procedure with initial costs estimated at approximately €28,186 per treated case in certain contexts[31,51,69]. However, cost-effectiveness studies emphasize the importance of the time horizon for evaluation. For refractory chronic CH, while the incremental cost-effectiveness ratio (ICER) after three months was reported at €109,676 per Quality-Adjusted Life-Year (QALY) gained, which is typically not considered cost-effective. A one-year extrapolation indicated an ICER of €-4846 per QALY gained, suggesting that ONS can become "dominant" (more effective and less costly) compared to conventional treatment over the long term[72].

This long-term cost-effectiveness is attributed to several factors. The first factor is reduced healthcare resource utilization. Successful ONS leads to a decrease in the need for acute medications[67,69], and potentially other healthcare services. The significant reduction in acute medication consumption in successful ONS patients helps justify the initial investment[72]. Secondly, ONS can lead to improved QALYs, with an added gain of 0.28 QALYs over one year[72]. Lastly, ONS leads to a reduction in indirect costs[72]. The impact of chronic headaches on patient activity, such as sick leave and disability leave, is substantial[69,72]. The high direct and indirect societal burden of severe chronic headache disorders means that long-term savings can offset the initial high costs[68,72].

While the initial investment for ONS is considerable, it is argued that for severely disabled patients with refractory chronic CH, it can be a cost-effective therapy, justifying its wider acceptance and reimbursement[72]. Comparisons with other neurological disorders with similar prevalence show that ONS's initial costs, when viewed over a long observation period and considering ongoing therapeutic success, may decrease favorably in terms of annual individual treatment costs[69].

Rechargeable vs non-rechargeable implantable pulse generators

A recent study investigated patient satisfaction with rechargeable ONS systems for medically intractable chronic CH. A large patient survey involving 92 individuals revealed high levels of satisfaction, with 74% finding recharging convenient and 88% deeming the associated inconvenience acceptable given the therapeutic benefits. Notably, 84% of patients who previously used a non-rechargeable device preferred the current rechargeable system due to its smaller size and extended lifespan. These findings suggest that ONS with a rechargeable IPG may be considered the system of choice, offering advantages such as longer overall lifespan, reduced need for replacement surgeries, and enhanced cost-effectiveness. This preference is further supported by the significant cost savings over a 10-year period compared to non-rechargeable devices, despite a higher initial cost[73].

Surgical techniques

Weiner and Reed introduced a minimally invasive percutaneous method for ONS in 19999, which involves placing an electrode near the greater occipital nerve (GON) using a Tuohy needle[8,74]. This technique, however, is prone to complications, with lead migration being the most common, often necessitating revision surgery[8,16,74–78]. Revision rates in literature have been reported as high as 10-60%, with some studies noting up to 60% migration after two years[8,77,78].

Other than patient selection and a multidisciplinary team approach, the success of ONS heavily relies on meticulous surgical technique[28,75,77]. Various methods and considerations have been described to optimize lead placement and minimize complications, and are supposed to be entirely reversible[16].

Patient positioning

Patients are typically positioned prone, often with their head resting on a horseshoe headrest, creating a mild flexion of the cervical spine[8,75,77]. For unilateral lead placement, a lateral decubitus position might be preferred for easier airway management[75]. Optimal head fixation during ONS can be achieved using equipment like the Mayfield holder, molded cushions, or a radiolucent frame. The head should ideally be in line with the thorax, at a 180-degree alignment, which may require an infusion bag under the head or thorax for sufficient flexion[28].

Surgical approach

A common approach involves a midline incision, often made at the C1 or T1 level, just underneath the occipital protuberance[8,77,79,80]. This midline incision, though it may necessitate two electrodes for bilateral stimulation, is believed to allow for more effective and easier placement, along with better anchoring and greater coverage compared to lateral incisions[77]. The skin and subcutaneous tissue along the needle's trajectory are typically anesthetized with local anesthetic, sometimes mixed with epinephrine for vasoconstriction[16,78].

Lead insertion

The insertion of stimulator leads involves advancing a Tuohy needle subcutaneously, typically just above the periost, to guide the electrode[8,78,80]. The electrodes are designed to cross the branches of the occipital nerve, primarily the GON and LON28. Optimal depth placement of the leads is critical to avoid complications. Superficial leads can lead to scalp dysesthesias, skin erosion, ulceration, or infection. Conversely, leads placed too deep can cause "flowover stimulation," resulting in uncomfortable muscle contractions or spasms, which may worsen headaches[75,76,78,80]. In smaller patients, appropriate contact programming on the leads should be considered, as lateral contacts can cause noxious stimulation of the mastoid process and ears[75].

Anatomical considerations

The anatomical location of the occipital nerve branches can be highly variable[28,43]. The GON, originating from the C2 spinal nerve, typically provides sensory innervation to a large portion of the posterior scalp[28]. While the classic technique involved placing leads transversely at the C1 or C1-2 level[76], this approach has been supplanted by placement at the nuchal ridge, which is superior due to its closer proximity to the GON and a higher probability of capturing fewer lesser occipital nerve fields[75]. Lead placement at or above the nuchal line has been shown to provide good paresthesias without causing neck muscle spasms[76]. Some studies suggest reproducible stimulation of the GON can be achieved by placing electrodes parallel to the atlas, approximately 30mm below the external occipital protuberance. This position typically targets the region where the GON penetrates the trapezius muscle[80]. The placement of electrodes just underneath the inion is also important, as this region is likely to result in the stimulation of the main branches of the occipital nerve while preventing muscle spasms[8].

Minimizing the risk of lead migration

Lead migration is a significant problem, and several techniques are proposed to prevent it. These include anchoring the lead with or without anchoring devices, and the application of strain relief loops. Anchoring can involve a nonresorbable stitch or commercially produced anchoring devices[8,75,77,78]. Suitable solid tissue for anchoring, such as the periost and fascia, is critical but can be difficult to find in the high cervical area[8]. The use of an additional strain relief loop through a separate incision, particularly at the cervical-thoracic junction, has been shown to dramatically reduce lead migration and revision rates. For instance, one study reported a 10% revision rate with a second strain relief loop compared to 62.5% without it[77]. In some surgical techniques, a subcutaneous pocket is created at the midcervical area to provide space for a strain relief loop, especially given the high mobility of this region[8,75]. A dual anchor-lead complex with a tension-relief loop of approximately 5 cm between the anchors has also been advocated to lessen tensile force on the proximal anchor and potentially reduce lead migration. This technique has been associated with an unprecedentedly lower complication rate of lead migration[78].

Use of fluoroscopy and ultrasonography

Fluoroscopy is a popular modality for guiding both trial and permanent lead placement in ONS[28,75,77]. It allows for proper alignment with bony landmarks, such as the C1 vertebral body and the occipital protuberance. However, fluoroscopy alone does not provide information about the depth of insertion or the surrounding tissue planes[78,80,81]. Ultrasonography (US) can provide valuable real-time information regarding depth perspective, the precise location of the GON, and visualization of scar tissue, mesh implants, or aberrant vasculature, which is particularly helpful in revision surgeries or elderly patients where anatomical considerations may be altered[16,28,75,78,79]. While the use of US itself is not definitively associated with reduced lead migration rates, it can improve the efficacy of lead placement by ensuring the lead is in the adequate tissue plane, more precisely between the subcutaneous fat and the paravertebral muscle, thereby potentially prolonging implantable pulse generator (IPG) battery life and improving programming efficacy[75,78]. Some studies, however, found insufficient evidence to suggest that the addition of ultrasonography to fluoroscopy significantly improves lead survival rates or times[81]. A more recent cadaveric study suggested that an X-ray tube angle of 10° provides the best representation of electrode placement in relation to the GON and mastoid[28].

Permanent implantable pulse generator implantation

For permanent implantation, an IPG is connected to the leads. The IPG is typically placed in a subcutaneous pocket created at the gluteal area, chest wall, or abdomen, with patient preference and cosmetic/aesthetic considerations influencing the choice[8,75,77]. IPG placement in the abdomen has been suggested to be better tolerated by patients compared to the buttock[77]. Additional strain relief loops are created at the midscapular area and midcervical area before tunneling the extension lead to the IPG, due to the high mobility of these regions[8]. Some cases also use external IPGs, which can make the ONS procedure significantly less invasive by avoiding the need for tunneling and internal IPG implantation, reducing trauma and discomfort.

Adverse Events and Complications in ONS

The widespread adoption of ONS has been challenged by a consistently reported high rate of adverse events (AEs) and complications[43,50,53,82–88]. These complications are a significant concern for both patients and physicians, often necessitating additional surgical interventions[8,31,53,57,63,64,86–88].

Adverse events associated with ONS are generally categorized into three main types: hardware-related, biological, and stimulation-related. In large studies, up to 71% of implanted patients experienced one or more adverse events over a 52-week follow-up period[84,87]. The overall mean incidence of total complications has been reported as high as 66%, with ranges varying widely across studies[88]. Notably, a substantial proportion of these AEs required additional surgery[43,53,57,87]. Hospitalization was required in approximately 8.6% of cases[43,53].

Hardware-Related Adverse Events

Hardware-related AEs involve issues with the device components, including leads, extensions, or IPGs[84,87]. Lead migration and fracture are consistently cited as the most frequent and significant hardware complication[8,14,16,31,37,43,50,54,57,63,64,67,70,84,87,88]. Incidence rates for lead migration range widely, from 2% to 60% across different studies[8,16,37,37,43,50,53,54,57,67,83,87,88]. Lead fracture rates are typically reported between 4.5% and 15%[37,54,64,67,87,88]. Lead migration and fracture often necessitate lead revision surgeries[8,43,64,87,89]. Premature IPG battery depletion is another very common AE, occurring in up to 64-70% of patients due to the high amplitude voltage required for continuous stimulation[34,43,57,63,67,70,84,86,87,89]. Device malfunction, including disconnection, is reported in 4.5-6.3% of cases[84,87]. Erosion of electrodes through the skin or insulation damage mimicking lead migration have also been reported, with incidences around 2.0-3.9%[67,86–88]. complication[8,14,16,31,37,43,50,54,57,63,64,67,70,84,87,88]. Incidence rates for lead migration range widely, from 2% to 60% across different studies[8,16,37,37,43,50,53,54,57,67,83,87,88]. Lead fracture rates are typically reported between 4.5% and 15%[37,54,64,67,87,88]. Lead migration and fracture often necessitate lead revision surgeries[8,43,64,87,89]. Premature IPG battery depletion is another very common AE, occurring in up to 64-70% of patients due to the high amplitude voltage required for continuous stimulation[34,43,57,63,67,70,84,86,87,89]. Device malfunction, including disconnection, is reported in 4.5-6.3% of cases[84,87]. Erosion of electrodes through the skin or insulation damage mimicking lead migration have also been reported, with incidences around 2.0-3.9%67,86–88. complication[8,14,16,31,37,43,50,54,57,63,64,67,70,84,87,88]. Incidence rates for lead migration range widely, from 2% to 60% across different studies[8,16,37,37,43,50,53,54,57,67,83,87,88]. Lead fracture rates are typically reported between 4.5% and 15%[37,54,64,67,87,88]. Lead migration and fracture often necessitate lead revision surgeries[8,43,64,87,89]. Premature IPG battery depletion is another very common AE, occurring in up to 64-70% of patients due to the high amplitude voltage required for continuous stimulation[34,43,57,63,67,70,84,86,87,89]. Device malfunction, including disconnection, is reported in 4.5-6.3% of cases[84,87]. Erosion of electrodes through the skin or insulation damage mimicking lead migration have also been reported, with incidences around 2.0-3.9%[67,86–88].

Biological Adverse Events

Biological AEs are surgical-procedure-related complications or reactions to the device[84,87]. Infection at the implant site is a persistent concern, with rates ranging from 2% to 24% and almost always requires lead removal or revision surgery[8,31,37,43,50,57,64,67,70,82,83,86–88,90]. Persistent pain, discomfort, or numbness at the IPG or lead site is common, reported in 5.9-17.8% of patients. These issues may require additional surgical intervention[54,64,67,82,87,88]. Although rather rare, changes in subcutaneous tissue at the implant site and rare allergic reactions to surgical materials or device components have been documented[8,16,84,87,91].

Stimulation-Related Adverse Events

Stimulation-related AEs consists of complications caused by the stimulation itself[84,87]. Perceptible paresthesia in the scalp area innervated by the occipital nerve is a common effect of conventional tonic ONS. While often intended for therapeutic effect, it can be bothersome for some patients, limiting therapy and potentially affecting sleep[31,34,43,63,70,90,92]. Undesirable stimulation effects, including unintended changes in headache, muscle spasms, muscle cramping or undesirable changes in stimulation quality, are reported to occur. Such effects may necessitate lead repositioning or reprogramming[8,53,67,76,84,85,87]. Some patients experience a reduction or complete loss of therapeutic effect over time. This can lead to device explantation if not remedied by reprogramming[31,53,67,70,84,86–88]. It has been reported that in a subset of patients, the headache pain may shift to the contralateral side or present as non-painful autonomic attacks[43,64,70].

Factors Contributing to Complications

There are several factors that contribute to the high rate of complications in ONS. First of all there is the hardware design. The hardware, including leads, anchors, and extensions, was often not specifically designed for use in the highly mobile neck region, but rather adapted from spinal cord stimulation technology[85]. This leads to issues like lead migration due to constant head movement, and rapid battery depletion from high voltage requirements[16,63,70,87,89]. Secondly, there is the variation in surgical techniques. Lack of standardized surgical techniques across centers contributes to varying complication rates[28,50,77,83,88].

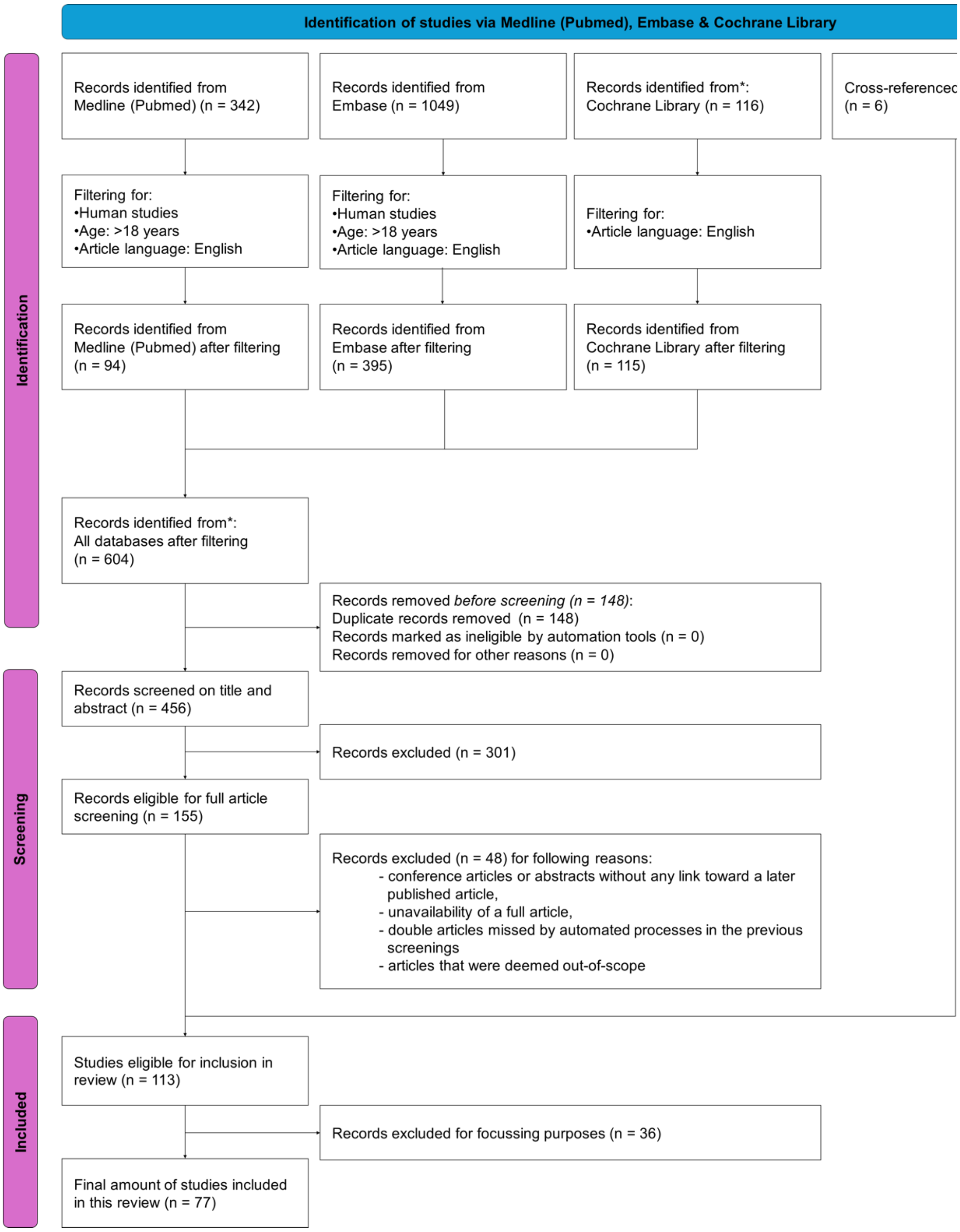

Fig. 1 — Modified PRISMA-flowchart for study inclusion.

Factors like anchoring strategy, strain relief loops, and IPG placement location play a crucial role[53,57,77,87–89]. Direct suturing of leads, while common, is not always recommended by manufacturers and can damage insulation[85]. Implanting a lead positioning too superficial or too deep can lead to skin erosion or painful muscle spasms respectively[8,76,87]. Thirdly, the experience and skill of the implanter significantly influence the incidence of device- and procedure-related AEs. It has been shown that higher case volumes are associated with lower complication rates[14,50,82,87]. Lastly, certain patient factors, such as a history of medication overuse headache, severe anxiety or depression, or specific headache may predict a poorer response to ONS or higher complication rates[14,31,43,86,89]. Patients who fluctuate with circadian or seasonal patterns, or are exposed to nicotine, may also have less effective outcomes[31,87]. Allergic disease history is important for rare allergic reactions[91].

Prevention and Mitigation Strategies

Addressing the high complication rates is crucial for improving ONS outcomes. First of all, the development of ONS-dedicated hardware, including smaller, rechargeable IPGs, low-profile anchors, and leads that are less prone to migration or fracture in the mobile cervical region, is greatly needed and advocated for in multiple studies. Rechargeable batteries can significantly reduce the need for repeat battery replacement surgeries[14,34,37,63,67,70,83–85,87,89,90]. Secondly, standardization and refinement of surgical techniques are essential[28,53,83,84,87]. This includes the consistent use of strain-relief loops and appropriate anchoring techniques to minimize lead migration. Proper lead placement is also critical[8,53,57,87,88,93]. Using techniques like tunnelling leads at a 45-degree angle without anchoring has shown promise in reducing migration. The use of self-anchoring tined leads may also decrease the incidence of lead migration. Ultrasound guidance can improve precision and safety during lead placement[16]. Thirdly, careful patient selection using a multi-specialist approach is paramount. As mentioned earlier, screening tools to identify patients most likely to benefit and avoid those prone to complications or non-response are still under research. Fourthly, strict adherence to infection prevention measures throughout the surgical procedure, including prophylactic antibiotics and optimal operating room environments, can reduce infection rates[53]. Lastly, while traditional ONS produces paresthesias, newer stimulation paradigms like burst ONS are paresthesia-free and may offer comparable efficacy[34,90].

Future Directions and Emerging Developments

Despite promising results in managing intractable headaches, the evidence for ONS remains debateable due to inherent challenges in trial methodology and patient selection variability[55]. As such, ONS remains a field ripe for further research and development. Several critical areas require attention to optimize outcomes, reduce complications, and broaden the applicability of this neuromodulatory therapy.

Standardization of Surgical Techniques and Hardware

A significant challenge in ONS is the wide variability in anatomical landmarks, patient positioning, imaging techniques, and electrode placement across different centers and surgeons. This lack of standardization makes it difficult to combine and compare data, hindering the precise evaluation of ONS efficacy. There is a pronounced need for a standardized surgical protocol to ensure consistent data collection and improve patient management. Recent proposals, including specific electrode insertion points and patient positioning aim to provide such a standardized approach[28].

The choice of imaging modality is also under investigation. While fluoroscopy is widely used for lead placement, ultrasonography could potentially improve lead placement and reducing complications, although one study found no statistically significant difference in lead survival rates or times with the addition of ultrasound guidance[81]. This, however, highlights the need for further investigation into its benefits, including impact on lead migration, revision rates, and operative time.

Furthermore, as aforementioned, current ONS hardware was often not originally designed for subcutaneous occipital use, leading to frequent complications necessitating repeat operations, which increases healthcare costs and patient burden. Future research should focus on developing ONS-specific hardware that is more flexible, resistant to migration and fracture, and better suited for the high-mobility cervical region. The recent introduction of self-anchoring tined leads is a perfect example of this. The use of rechargeable IPGs could also reduce the frequency of battery replacements and associated surgeries.

Optimization of Stimulation Protocols and New Paradigms

Despite all current research, the exact mode of action of ONS is not yet fully elucidated, and further studies are crucial to fully unravel the precise details of its central mechanisms. Future research should also focus on elucidating the pathophysiology of the different headache disorders and their responses to neuromodulation.

New stimulation paradigms are emerging to improve patient comfort and efficacy. Burst stimulation delivers paresthesia-free impulses, mimicking natural neuronal firing patterns. This allows for blinded, placebo-controlled trials, which are challenging with conventional tonic stimulation that evokes noticeable paresthesia. Initial studies suggest burst ONS may be as effective as tonic stimulation for chronic CH.

Furthermore, voltage tuning suggests that ONS could have a role in acute attack treatment of chronic CH. Research into voltage tuning could provide insights into optimizing ONS use and possibly reducing reliance on acute medications. High-frequency stimulation and closed-loop systems, similar to those in spinal cord stimulation, are also being explored for their potential benefits in intractable headache syndromes.

Patient Selection and Outcome Predictors

Identifying patients most likely to benefit from ONS is crucial due to its invasive nature and cost. Future research should aim to validate predicting factors, identify other clinical or stimulation-related factors, refine patient selection criteria and optimize clinical pathways within a multidisciplinary framework to improve ONS outcomes for patients with refractory chronic headaches.

Long-term Efficacy and Robust Clinical Trials

While ONS has shown long-term benefit in some studies, overall response rates vary. There is a critical need for high-quality, well-designed, large placebo-controlled trials with long-term follow-up to definitively establish the efficacy, safety, and risk-benefit ratio, as well as to clarify the cost-effectiveness of ONS. With the advancements in paresthesia-free stimulation modes, double-blinded, randomized, placebo-controlled trials, like the HortONS study[24], should become possible and more easily applicable. Future trials should be aiming to provide definitive evidence for ONS in medically intractable headache disorders. Furthermore, multi-center, prospective registries are vital for accumulating real-world clinical evidence and should be implemented.

Limitations

Any narrative review must acknowledge the inherent limitations within both the review methodology itself and the studies it encompasses. Understanding these limitations is crucial for interpreting the current evidence base and guiding future research.

Limitations of This Narrative Review

Firstly, a significant limitation of this review stems from its search strategy, which was restricted to specific databases (PubMed, Embase and the Cochrane library). This approach may have inadvertently omitted relevant articles published elsewhere, potentially affecting the comprehensiveness of the included literature. Secondly, by the very nature of these types of studies, a publication bias is likely skewed toward positive outcomes. While efforts were made to include negative outcomes in this review, this inherent bias in published literature remains a consideration. Thirdly, this review aimed to evaluate the effect of ONS across various headache syndromes. However, the majority of available research has focused primarily on CM and chronic CH. Consequently, the applicability of this narrative review to other headache disorders may be limited. Lastly, this review specifically focused on ONS as a sole modality, yet other articles investigating combinations of different therapeutic modalities might yield superior results compared to ONS alone, representing a limitation in the scope of this review.

Limitations of Included Studies on ONS

A major weakness consistently observed across many ONS studies is the lack of placebo or blinded stimulation. Blinding with ONS is particularly challenging, as occipital paresthesia often appears to be a prerequisite for achieving a clinical effect11. While acknowledging the undoubted presence of a placebo effect in headache treatment, several observations strongly argue against the findings being solely attributable to a placebo response or natural history. These include the intractable nature of the patient cohorts, a delayed clinical response consistent with other trigeminal autonomic cephalalgia cohorts, the demonstration of stable long-term responses and sustained long-term improvement, and the rapid return of attacks when stimulation is stopped or deterioration/recovery after technical failures11,12. Moreover, reported placebo response rates for ONS in migraine are notably low12, and there is no evidence to suggest a different placebo response in other headache conditions. Additional arguments against a pure placebo or natural history effect include a protracted preceding chronic phase, the lack of response to numerous other treatments prior to ONS, and the relatively robust response rate observed.
Another significant limitation arises from the variability in outcome measures and their definitions across different studies. Studies evaluated pain intensity using diverse tools such as the Numerical Rating Scale (NRS), VAS, subjective pain severity, and patient complaints, often on a 0-to-10 scale. Other outcomes included the number of days with headache, Migraine Disability Assessment Scale (MIDAS), and SF-36 scores[88]. This lack of standardization in outcome assessment and differing definitions for response rates introduced a risk of bias in evaluating the efficacy of ONS. Furthermore, follow-up periods varied widely, ranging from as short as 1 week to as long as several years.

Finally, a notable clinical discordance was observed between objective primary outcomes and more subjective measures of patient improvement. In one study, for instance, some long-term responders reported only low-to-moderate levels of satisfaction despite significant improvements in headache frequency following neurostimulation. Conversely, a surprising six out of ten non-responders in terms of frequency at three years expressed high levels of satisfaction, with three even able to return to work post-implantation[15]. Reasons for this discordance might be attributed to varying patient expectations and resilience levels, and the potentially difficult-to-qualitativelyevaluate therapeutic benefit of long-term care provided by a specialized team.

Conclusion

Occipital nerve stimulation (ONS) represents a valuable symptomatic intervention for selected patients with medically intractable chronic headache disorders, including chronic migraine, chronic cluster headache, and occipital neuralgia. In a substantial proportion of patients, ONS reduces attack frequency and intensity, improves quality of life, and decreases the need for prophylactic medication. Patient satisfaction is frequently high, with many indicating they would choose to undergo the procedure again.

These therapeutic benefits, however, must be weighed against a persistently high rate of adverse events and complications. Across studies, up to two-thirds of patients experience hardware- or procedure-related problems, including lead migration, fracture, premature battery depletion, and infection. Many of these events require revision surgery, explantation, or prolonged hospitalization, while stimulation-related side effects such as intolerable paresthesias, muscle spasms, or diminishing efficacy further limit long-term outcomes. Such complications not only place a considerable burden on patients but also impact the cost-effectiveness of ONS in routine practice.

Future progress will depend on reducing this morbidity. Priorities include the development of ONS-specific hardware optimized for the mobile cervical region, refinement and standardization of surgical techniques, and robust patient selection protocols. Moreover, new stimulation paradigms such as burst ONS may improve tolerability and trial methodology. Ultimately, large-scale, double-blinded randomized controlled trials with long-term follow-up are essential to clarify both the therapeutic potential and the full risk–benefit profile of ONS in refractory headache management.

Author contributions: GVS contributed to the concept of the article, drafting of the manuscript and final revision of the manuscript. JPVB contributed to the concept of article, critical revision of the manuscript, final approval of the manuscript and direct supervision of the writing progress. DV contributed to the critical revision of the manuscript, final approval of the manuscript and general supervision of the writing progress.

Acknowledgements: The authors acknowledge the use of ChatGPT-4o (OpenAI, San Francisco, California, USA) and NotebookLM (Google LLC, Mountain View, California, USA) as Large-Language Model AI tools that supported the drafting and refinement of this manuscript. These tools were used to enhance clarity, structure, and language precision. The output of these tools has been manually double-checked and final responsibility for the content rests solely with the authors.

Conflict of interests: GVS declares no conflict of interests.

JPVB declares to have done scientific research for Nevro Corporation, Medtronic, Abbott, Mainstay Medical, Man & Science. JPVB is also on the speaker's bureau of Nevro Corporation, Medtronic, and Mainstay. Lastly, JPVB is a shareholder in Man&Science and BrainM.

DV declares to have received funding from BD and Aguetant.

However, both JPVB and DV declare no specific conflict of interests nor other financial disclosures related to this article.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Magiorkinis E, Diamantis A, Mitsikostas DD, Androutsos G. Headaches in antiquity and during the early scientific era. J Neurol. 2009 Aug;256(8):1215–20.
2. Rizzoli P, Mullally WJ. Headache. Am J Med. 2018 Jan 1;131(1):17–24.
3. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The Global Burden of Headache: A Documentation of Headache Prevalence and Disability Worldwide. Cephalalgia. 2007 Mar 1;27(3):193–210.
4. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia Int J Headache. 2018 Jan;38(1):1–211.
5. Garza I, Schwedt TJ. Chronic daily headache: Associated syndromes, evaluation, and management [Internet]. UpToDate - Wolters Kluwer; [cited 2025 Apr 22]. Available from: https://www.uptodate.com/contents/chronic-daily-headache-associated-syndromes-evaluation-and-management
6. Murphy C, Hameed S. Chronic Headaches. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Apr 22]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK559083/
7. Wall PD, Sweet WH. Temporary Abolition of Pain in Man. Science. 1967 Jan 6;155(3758):108–9.
8. Plazier M, Camp TV, Mevnosky T, Ost J, De Ridder D, Vanneste S. A Simple Technique for Surgical Placement of Occipital Nerve Stimulators without Anchoring the Lead. J Neurol Surg Part Cent Eur Neurosurg. 2016 Sep;77(5):441–6.
9. Weiner RL, Reed KL. Peripheral Neurostimulation for Control of Intractable Occipital Neuralgia. Neuromodulation Technol Neural Interface. 1999;2(3):217–21.
10. Palmisani S, Al-Kaisy A, Arcioni R, Smith T, Negro A, Lambru G, et al. A six year retrospective review of occipital nerve stimulation practice--controversies and challenges of an emerging technique for treating refractory headache syndromes. J Headache Pain. 2013 Aug 6;14(1):67.
11. Lambru G, Shanahan P, Watkins L, Matharu MS. Occipital nerve stimulation in the treatment of medically intractable SUNCT and SUNA. Pain Physician. 2014;17(1):29–41.
12. Miller S, Watkins L, Matharu M. Long-term follow up of intractable chronic short lasting unilateral neuralgiform

headache disorders treated with occipital nerve stimulation. Cephalalgia Int J Headache. 2018 Apr;38(5):933–42.
13. Miller S, Watkins L, Matharu MS. Treatment of intractable hemicrania continua by occipital nerve stimulation. J Neurol Neurosurg Psychiatry. 2017 Sep;88(9):805–6.
14. Joswig H, Abdallat M, Karapetyan V, MacDougall KW, Cooper PE, Parrent AG. Long-Term Experience with Occipital and Supraorbital Nerve Stimulation for the Various Headache Disorders-A Retrospective Institutional Case Series of 96 Patients. World Neurosurg. 2021 Jul;151:e472–83.
15. Eghtesadi M, Leroux E, Fournier-Gosselin MP, Lespérance P, Marchand L, Pim H, et al. Neurostimulation for Refractory Cervicogenic Headache: A Three-Year Retrospective Study. Neuromodulation Technol Neural Interface. 2018;21(3):302–9.
16. Eshraghi Y, Khan R, Stern H, Gelter M, Guirguis M. Peripheral Nerve Stimulation of the Occipital Nerve to Treat Postherpetic Neuralgia. Pain Manag Case Rep. 2020 Nov 1;193–7.
17. Abd-Elsayed A, Pahapill N. Successful Treatment of Chemotherapy-Induced Headaches With Occipital Nerve Stimulation: A Case Report. Neuromodulation Technol Neural Interface. 2020;23(6):881–2.
18. Fontaine D, Bozzolo E, Chivoret N, Paquis P, Lanteri-Minet M. Salvage treatment of trigeminal neuralgia by occipital nerve stimulation. Cephalalgia Int J Headache. 2014 Apr;34(4):307–10.
19. Shaw AB, Sharma M, Shaikhouni A, Marlin ES, Ikeda DS, McGregor JM, et al. Neuromodulation as a last resort option in the treatment of chronic daily headaches in patients with idiopathic intracranial hypertension. Neurol India. 2015 Oct;63(5):707.
20. Son B chul, Yang SH, Hong JT, Lee SW. Occipital Nerve Stimulation for Medically Refractory Hypnic Headache. Neuromodulation Technol Neural Interface. 2012;15(4):381–6.
21. Vadivelu S, Bolognese P, Milhorat TH, Mogilner AY. Occipital nerve stimulation for refractory headache in the Chiari malformation population. Neurosurgery. 2012 Jun;70(6):1430–6; discussion 1436-1437.
22. De Coo IF, Wilbrink LA, Haan J. Effective occipital nerve stimulation during pregnancy in a cluster headache patient. Cephalalgia. 2016 Jan;36(1):98–9.
23. Chaiban G, Tolba R, Eissa H, Lirette LS, Almualim M, Malaty A, et al. Successful treatment of occipital neuralgia with implantable peripheral nerve stimulation in a pacemaker-dependent patient. Ochsner J. 2014;14(1):119–22.
24. Fogh-Andersen IS, Sørensen JCH, Petersen AS, Jensen RH, Meier K. The HortONS study. Treatment of chronic cluster headache with transcutaneous electrical nerve stimulation and occipital nerve stimulation: study protocol for a prospective, investigator-initiated, double-blinded, randomized, placebo-controlled trial. BMC Neurol. 2023 Dec;23(1):1–11.
25. Göbel CH, Heinze A, Karstedt S, Clasen S, Göbel H. Effect of Occipital Nerve Stimulation (ONS) on the Orbicularis Oculi Reflex Triggered by a Standardized Air Flow in Patients with Chronic Migraine—A Prospective, Randomized, Interventional Study. Pain Ther. 2021 Jun 1;10(1):567–76.
26. Kovacs S, Peeters R, De Ridder D, Plazier M, Menovsky T, Sunaert S. Central Effects of Occipital Nerve Electrical Stimulation Studied by Functional Magnetic Resonance Imaging. Neuromodulation Technol Neural Interface. 2011;14(1):46–57.
27. Veilleux C, Khousakoun D, Kwon CS, Amoozegar F, Girgis F. Efficacy of Occipital Nerve Stimulation in Trigeminal Autonomic Cephalalgias: A Systematic Review. Neurosurgery. 2023 Oct 1;93(4):755–63.
28. Kurt E, Kollenburg L, van Dongen R, Volkers R, Mulleners W, Vinke S. The Untold Story of Occipital Nerve Stimulation in Patients With Cluster Headache: Surgical Technique in Relation to Clinical Efficacy. Neuromodulation J Int Neuromodulation Soc. 2024 Jan;27(1):22–35.
29. Balossier A, Donnet A, Régis J, Leplus A, Lantéri-Minet M, Fontaine D. Occipital Nerve Stimulation for Recurrent Trigeminal Neuralgia Without Occipital Pain. Neuromodulation J Int Neuromodulation Soc. 2023 Dec;26(8):1795–801.
30. Magis D, Bruno MA, Fumal A, Gérardy PY, Hustinx R, Laureys S, et al. Central modulation in cluster headache patients treated with occipital nerve stimulation: an FDG-PET study. BMC Neurol. 2011 Dec;11(1):1–9.
31. Membrilla JA, Cuadrado ML, González-García N, Porta-Etessam J, Sánchez-Soblechero A, Lozano Ros A, et al. Clinical predictors of therapeutic failure of occipital nerve stimulation in refractory chronic cluster headache. Cephalalgia. 2024 May 1;44(5):03331024241254078.
32. Reindl C, Seifert F, Nickel F, Maihöfner C. Neuromodulation of Electrically Induced Hyperalgesia in the Trigeminocervical System. Pain Pract. 2016;16(6):712–9.
33. Busch V, Jakob W, Juergens T, Schulte-Mattler W, Kaube H, May A. Occipital nerve blockade in chronic cluster headache patients and functional connectivity between trigeminal and occipital nerves. Cephalalgia. 2007;27(11):1206–14.
34. Fogh-Andersen IS, Sørensen JCH, Jensen RH, Knudsen AL, Meier K. Treatment of chronic cluster headache with burst and tonic occipital nerve stimulation: A case series. Headache. 2023 Sep;63(8):1145–53.
35. Piovesan E, Kowacs P, Tatsui C, Lange M, Ribas L, Werneck L. Referred pain after painful stimulation of the greater occipital nerve in humans: evidence of convergence of cervical afferences on trigeminal nuclei. Cephalalgia. 2001;21(2):107–9.
36. Basedau H, Nielsen T, Asmussen K, Gloss K, Mehnert J, Jensen RH, et al. Experimental evidence of a functional relationship within the brainstem trigeminocervical complex in humans. Pain. 2022 Apr 1;163(4):729–34.
37. Smit RD, Mouchtouris N, Kang K, Reyes M, Sathe A, Collopy S, et al. Short-lasting unilateral neuralgiform headache attacks (SUNCT/SUNA): a narrative review of interventional therapies. J Neurol Neurosurg Psychiatry. 2023 Jan;94(1):49–56.
38. Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965 Nov 19;150(3699):971–9.
39. Paemeleire K, Van Buyten JP, Van Buynder M, Alicino D, Van Maele G, Smet I, et al. Phenotype of patients responsive to occipital nerve stimulation for refractory head pain. Cephalalgia Int J Headache. 2010 Jun;30(6):662–73.
40. Magis D, Gérard P, Schoenen J. Invasive occipital nerve stimulation for refractory chronic cluster headache: what evolution at long-term? Strengths and weaknesses of the method. J Headache Pain. 2016 Dec;17(1):1–5.
41. Kollenburg L, Arnts H, Heitkamp M, Geerts S, Robinson C, Dominguez M, et al. Occipital nerve stimulation for cluster headache: lessons to learn from the ‘voltage tuners.’ J Headache Pain. 2024 Dec;25(1):1–8.
42. Miller S, Watkins L, Matharu M. Predictors of response to occipital nerve stimulation in refractory chronic headache. Cephalalgia Int J Headache. 2018 Jun;38(7):1267–75.
43. Vukovic Cvetkovic V, Jensen RH. Neurostimulation for the treatment of chronic migraine and cluster headache. Acta Neurol Scand. 2019;139(1):4–17.
44. Göbel CH, Göbel A, Niederberger U, Heinze A, Heinze-Kuhn K, Meinecke C, et al. Occipital Nerve Stimulation in Chronic Migraine: The Relationship Between Perceived Sensory Quality, Perceived Sensory Location, and Clinical Efficacy—A Prospective, Observational, Non-Interventional Study. Pain Ther. 2020 Dec 1;9(2):615–26.

45. Kinfe TM, Pintea B, Roeske S, Güresir Á, Güresir E, Vatter H. Percutaneous nerve field stimulation (PENS) of the occipital region as a possible predictor for occipital nerve stimulation (ONS) responsiveness in refractory headache disorders? A feasibility study. Cephalalgia Int J Headache. 2016 Jul;36(8):779–89.
46. Lipton RB, Goadsby PJ, Cady RK, Aurora SK, Grosberg BM, Freitag FG, et al. PRISM study: occipital nerve stimulation for treatment-refractory migraine. CEPHALALGIA. 2009 Oct;29:30–30.
47. Miller S, Watkins L, Matharu M. Long-term outcomes of occipital nerve stimulation for chronic migraine: a cohort of 53 patients. J Headache Pain. 2016 Dec;17(1):68.
48. Brandt RB, Wilbrink LA, de Coo IF, Haan J, Mulleners WM, Huygen FJPM, et al. A prospective open label 2-8 year extension of the randomised controlled ICON trial on the long-term efficacy and safety of occipital nerve stimulation in medically intractable chronic cluster headache. EBioMedicine. 2023 Dec;98:104895.
49. Schwedt TJ, Dodick DW, Trentman TL, Zimmerman RS. Response to occipital nerve block is not useful in predicting efficacy of occipital nerve stimulation. Cephalalgia Int J Headache. 2007 Mar;27(3):271–4.
50. Raoul S, Nguyen JM, Kuhn E, de Chauvigny E, Lejczak S, Nguyen JP, et al. Efficacy of Occipital Nerve Stimulation to Treat Refractory Occipital Headaches: A Single-Institution Study of 60 Patients. Neuromodulation Technol Neural Interface. 2020;23(6):789–95.
51. Membrilla JA, Roa J, Díaz-de-Terán J. Preventive treatment of refractory chronic cluster headache: systematic review and meta-analysis. J Neurol. 2023 Feb;270(2):689–710.
52. Ramineni T, Prusik J, De La Cruz P, Gee L, Kumar V, Wilock ME, et al. The Impact of Peripheral Nerve Stimulation on Disability and Depression. Neuromodulation J Int Neuromodulation Soc. 2016 Apr;19(3):306–10.
53. Dodick DW, Silberstein SD, Reed KL, Deer TR, Slavin KV, Huh B, et al. Safety and efficacy of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: long-term results from a randomized, multicenter, double-blinded, controlled study. Cephalalgia Int J Headache. 2015 Apr;35(4):344–58.
54. Kollenburg L, Kurt E, Mulleners W, Abd-Elsayed A, Yazdi C, Schatman ME, et al. Four Decades of Occipital Nerve Stimulation for Headache Disorders: A Systematic Review. Curr Pain Headache Rep. 2024 Oct;28(10):1015–34.
55. Chen YF, Bramley G, Unwin G, Hanu-Cernat D, Dretzke J, Moore D, et al. Occipital Nerve Stimulation for Chronic Migraine—A Systematic Review and Meta-Analysis. Sommer C, editor. PLOS ONE. 2015 Mar 20;10(3):e0116786.
56. Robbins MS, Lipton RB. Transcutaneous and Percutaneous Neurostimulation for Headache Disorders. Headache. 2017 Apr;57 Suppl 1:4–13.
57. Saper JR, Dodick DW, Silberstein SD, McCarville S, Sun M, Goadsby PJ. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. Cephalalgia. 2011 Feb;31(3):271–85.
58. Silberstein SD, Dodick DW, Saper J, Huh B, Slavin KV, Sharan A, et al. Safety and efficacy of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: results from a randomized, multicenter, double-blinded, controlled study. Cephalalgia Int J Headache. 2012 Dec;32(16):1165–79.
59. Rodrigo D, Acin P, Bermejo P. Occipital Nerve Stimulation for RefractoryChronic Migraine: Results of a Long-TermProspective Study. Pain Physician. 2017 Jan 14;1(21;1):E151–9.
60. Mekhail NA, Estemalik E, Azer G, Davis K, Tepper SJ. Safety and Efficacy of Occipital Nerves Stimulation for the Treatment of Chronic Migraines: Randomized, Double-blind, Controlled Single-center Experience. Pain Pract Off J World Inst Pain. 2017 Jun;17(5):669–77.
61. Slotty P, Bara G, Kowatz L, Gendolla A, Wille C, Schu S, et al. Occipital nerve stimulation for chronic migraine: A randomized trial on subthreshold stimulation. Cephalalgia. 2015 Jan;35(1):73–8.
62. Barad M, Ailani J, Hakim SM, Kissoon NR, Schuster NM. Percutaneous Interventional Strategies for Migraine Prevention: A Systematic Review and Practice Guideline. Pain Med Malden Mass. 2022 Jan 3;23(1):164–88.
63. Leone M, Proietti Cecchini A, Messina G, Franzini A. Long-term occipital nerve stimulation for drug-resistant chronic cluster headache. Cephalalgia Int J Headache. 2017 Jul;37(8):756–63.
64. Leplus A, Fontaine D, Donnet A, Regis J, Lucas C, Buisset N, et al. Long-Term Efficacy of Occipital Nerve Stimulation for Medically Intractable Cluster Headache. Neurosurgery. 2021 Jan 13;88(2):375–83.
65. Wilbrink LA, de Coo IF, Doesborg PGG, Mulleners WM, Teernstra OPM, Bartels EC, et al. Safety and efficacy of occipital nerve stimulation for attack prevention in medically intractable chronic cluster headache (ICON): a randomised, double-blind, multicentre, phase 3, electrical dose-controlled trial. Lancet Neurol. 2021 Jul;20(7):515–25.
66. Burns B, Watkins L, Goadsby PJ. Treatment of intractable chronic cluster headache by occipital nerve stimulation in 14 patients. Neurology. 2009 Jan 27;72(4):341–5.
67. Miller S, Watkins L, Matharu M. Treatment of intractable chronic cluster headache by occipital nerve stimulation: a cohort of 51 patients. Eur J Neurol. 2017;24(2):381–90.
68. Burns B, Watkins L, Goadsby PJ. Treatment of medically intractable cluster headache by occipital nerve stimulation: long-term follow-up of eight patients. The Lancet. 2007 Mar 31;369(9567):1099–106.
69. Mueller O, Diener HC, Dammann P, Rabe K, Hagel V, Sure U, et al. Occipital nerve stimulation for intractable chronic cluster headache or migraine: A critical analysis of direct treatment costs and complications. Cephalalgia. 2013 Dec;33(16):1283–91.
70. Magis D, Gerardy PY, Remacle JM, Schoenen J. Sustained effectiveness of occipital nerve stimulation in drug-resistant chronic cluster headache. Headache. 2011 Sep;51(8):1191–201.
71. Copeland R, Nwankwo A, Husu E. Temporary Peripheral Nerve Stimulation for the Treatment of Greater Occipital Neuralgia. Pain Med Case Rep. 2024 Apr 30;8(3):115–8.
72. Bulsei J, Leplus A, Donnet A, Regis J, Lucas C, Buisset N, et al. Occipital Nerve Stimulation for Refractory Chronic Cluster Headache: A Cost-Effectiveness Study. Neuromodulation Technol Neural Interface. 2021;24(6):1083–92.
73. Sciacca S, Smith JS, Akram H, Asim A, Matharu M, Watkins L. Rechargeable occipital nerve stimulator systems: a patient satisfaction study. Br J Neurosurg. 2014 Oct;28(5):645–9.
74. Craig JA, Fisicaro MD, Zhou L. Revision of a superficially migrated percutaneous occipital nerve stimulator electrode using a minimally invasive technique. Neuromodulation J Int Neuromodulation Soc. 2009 Jul;12(3):250–3.
75. Rajneesh KF. Occipital Nerve Stimulation and Sphenopalatine Ganglion Stimulation for Treatment of Intractable Headache Syndromes. Neurol India. 2020 Dec;68(Suppl 2):S231.
76. Hayek SM, Jasper JF, Deer TR, Narouze SN. Occipital neurostimulation-induced muscle spasms: implications for lead placement. Pain Physician. 2009;12(5):867–76.
77. Falowski S, Wang D, Sabesan A, Sharan A. Occipital nerve stimulator systems: review of complications and surgical techniques. Neuromodulation J Int Neuromodulation Soc. 2010 Apr;13(2):121–5.

78. Pittelkow TP, Pagani-Estevez GL, Landry B, Pingree MJ, Eldrige JS. Occipital Neuromodulation: A Surgical Technique with Reduced Complications. Pain Physician. 2016;19(7):E1005-1012.
79. Kim S, Hosseini M, Elsharkawy H. Peripheral Nerve Stimulation for Occipital Neuralgia: A Parallel Approach. Pain Med Case Rep. 2024;8(7):243–7.
80. Mueller O, Hagel V, Wrede K, Schlamann M, Hohn HP, Sure U, et al. Stimulation of the greater occipital nerve: anatomical considerations and clinical implications. Pain Physician. 2013;16(3):E181-189.
81. Jones JH, Brown A, Moyse D, Qi W, Roy L. Survival Analysis of Occipital Nerve Stimulator Leads Placed under Fluoroscopic Guidance with and without Ultrasonography. Pain Physician. 2017 Nov;20(7):E1115–21.
82. Díaz-de-Terán J, Membrilla JA, Paz-Solís J, de Lorenzo I, Roa J, Lara-Lara M, et al. Occipital Nerve Stimulation for Pain Modulation in Drug-Resistant Chronic Cluster Headache. Brain Sci. 2021 Feb;11(2):236.
83. Fontaine D, Blond S, Lucas C, Regis J, Donnet A, Derrey S, et al. Occipital nerve stimulation improves the quality of life in medically-intractable chronic cluster headache: Results of an observational prospective study. Cephalalgia. 2017 Oct;37(12):1173–9.
84. Ashkan K, Sokratous G, Göbel H, Mehta V, Gendolla A, Dowson A, et al. Peripheral nerve stimulation registry for intractable migraine headache (RELIEF): a real-life perspective on the utility of occipital nerve stimulation for chronic migraine. Acta Neurochir (Wien). 2020 Dec;162(12):3201–11.
85. Clarke C, Azari P, Huh B. Damaged Insulation Mimicked Symptoms of Occipital Stimulator Lead Migration. Neuromodulation Technol Neural Interface. 2011;14(6):539–41.
86. Lagrata S, Cheema S, Watkins L, Matharu M. Long-Term Outcomes of Occipital Nerve Stimulation for New Daily Persistent Headache With Migrainous Features. Neuromodulation Technol Neural Interface. 2021;24(6):1093–9.
87. Sharan A, Huh B, Narouze S, Trentman T, Mogilner A, Vaisman J, et al. Analysis of Adverse Events in the Management of Chronic Migraine by Peripheral Nerve Stimulation. Neuromodulation Technol Neural Interface. 2015;18(4):305–12.
88. Yang Y, Song M, Fan Y, Ma K. Occipital Nerve Stimulation for Migraine: A Systematic Review. Pain Pract. 2016;16(4):509–17.
89. Brewer AC, Trentman TL, Ivancic MG, Vargas BB, Rebecca AM, Zimmerman RS, et al. Long-term outcome in occipital nerve stimulation patients with medically intractable primary headache disorders. Neuromodulation J Int Neuromodulation Soc. 2013;16(6):557–62; discussion 563-564.
90. Garcia-Ortega R, Edwards T, Moir L, Aziz TZ, Green AL, FitzGerald JJ. Burst Occipital Nerve Stimulation for Chronic Migraine and Chronic Cluster Headache. Neuromodulation Technol Neural Interface. 2019;22(5):638–44.
91. Zhou L, Lee A, Schaffner R, Dworkin G. Allergic Reaction to Peripheral Nerve Stimulator. Open Neurosurg J. 2012 May 8;5(1):12–5.
92. Trentman TL, Zimmerman RS, Seth N, Hentz JG, Dodick DW. Stimulation Ranges, Usage Ranges, and Paresthesia Mapping During Occipital Nerve Stimulation. Neuromodulation Technol Neural Interface. 2008;11(1):56–61.
93. Fontaine D, Christophe Sol J, Raoul S, Fabre N, Geraud G, Magne C, et al. Treatment of refractory chronic cluster headache by chronic occipital nerve stimulation. Cephalalgia Int J Headache. 2011 Jul;31(10):1101–5.

doi.org/10.56126/76.S.18