

# Drug-resistant Headache and Cranio-facial Pain: Rationale for Greater Occipital Nerve Stimulation

Lavano Angelo\*, Della Torre Attilio, Valente Vinicio, Lavano Francesco and Guzzi Giusy

Department of Neurosurgery, University Hospital of Germaneto, Campus "Salvatore Venuta", Catanzaro, Italy

## Introduction

Despite the advances in the management of headache disorders, many patients suffering from chronic migraine are refractory to current treatments. New treatments backed by good evidence are therefore in great need. Electrical stimulation of peripheral nerves is used to treat various painful conditions including headache disorders. More recently it has been reported good outcome in these painful conditions with subcutaneous placement of leads at the level of C1 and stimulation of the greater occipital nerve: This procedure is named Occipital Nerve Stimulation (ONS) [1-5]. The clinical conditions treated with ONS include occipital neuralgia, Trigeminal Autonomic Cephalalgias (TACs), migraine and transformed migraine.

The surgical procedure is divided in two steps. In the first step, with the patient in prone position under local anaesthesia, a vertical incision of 2 cm is made in posterior cervical region in the midline on the external occipital protuberance. Under fluoroscopy control, a Tuohy needle is passed transversely in the subcutaneous space across the base of the greater occipital nerve at the level of C1 starting from the midline incision towards the mastoid process and following the trajectory of the nuchal line. A quadripolar wire lead is introduced into the Touhy needle by medial to lateral direction; under fluoroscopy control the needle is withdrawn and the lead is connected to an external cable for intraoperative testing with an external stimulator. The stimulation parameters are chosen to obtain paraesthesias in the innervation territory of the greater occipital nerve. The lead is then sutured to the underlying fascia with a silicone fastener and a silk sutures. In some cases, according to Franzini lead fixation techniques [6]. Pisces Quad lead may be fixed to the lateral portion of the superficial fascia transfixing the plastic tip of the lead with a suture needle through a vertical incision of 4 cm lateral to the external occipital protuberance. After a 7-15 days trial period of external stimulation, if the patient reported at least 50% decrease in headache intensity and/or frequency associated with a decrease headache medication use, a permanent implant of a single channel IPG or a dual-channel IPG is then performed under general anesthesia. The parameters used for chronic stimulation are usually: Frequency 30-60 Hz, Pulse Width 90-400 microsec, Amplitude 1.5-9.0 Volts, bipolar stimulation configuration, cyclic mode.

Weiner and Reed first described a percutaneous approach for Occipital Nerve Stimulation (ONS) in presumed occipital neuralgia [7]. Greater occipital nerve electrical stimulation could have effects on pain both in the area directly innervated by this nerve and in regions innervated by the trigeminal nerve. The greater occipital nerve is a medial branch of the posterior ramus of C2 spinal root and lies in the subcutaneous tissue. C2 dorsal horn converges with trigeminal nerve in the "trigemino-cervical complex" that is a neuronal column extending from trigeminal nucleus caudalis up to C3 level [8].

Convergence of trigeminal nerve and occipital nerve in the "trigemino-cervical complex" may explain how nociception activation at either end of this structure may result in both anterior and posterior pain: thus occipital nerve stimulation could have effects on pain not only

in regions directly innervated by the occipital nerve but also in the areas innervated by the trigeminal nerve. The exact mechanism by which ONS produces analgesia is still incompletely understood: electrical stimulation of occipital nerve has both peripheral and central nervous system effects that may modulate nociception. Stimulation could give rise to depolarization blockade of the small diameter afferent fibers A $\delta$  and C. Alternately stimulation of the large diameter A $\beta$  afferent fibers may have an antinociceptive effect due to suppression of activity in C fibers and A $\delta$  fibers at the level of the spinal dorsal horn (gate control theory). ONS may influence supraspinal structures involved in central nociceptive trafficking, such the dorsal pons. PET study demonstrated, as a result of electrical stimulation of occipital nerve, an activation of this region that may be involved in descending pathways that control pain via stimulation of the trigemino-vascular system at the level of upper cervical pain [3,8]. Finally ONS may influence the pulvinar nucleus of the thalamus and the anterior cingulate cortex that are involved in the affective dimension of pain [9].

Use of ONS is reported in occipital neuralgia, cervicogenic headache, migraine, transformed migraine and also in trigeminal autonomic cephalalgias (TACs). TACs is a group of primary headache disorders recognised in the 2<sup>th</sup> edition of the International Headache Society classification [10]. It is characterized by unilateral trigeminal distribution pain that occurs in association with prominent ipsilateral cranial autonomic features. The group comprises: Chronic Cluster Headache (CCH), Chronic Paroxysmal Headache (CPH), Continuous Headache (CH) and Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT syndrome).

Deep Brain Stimulation of posterior hypothalamus is showed to be effective in TACs, mainly in Chronic Cluster Headache and SUNCT [11]. Anyway because of possible cerebral hemorrhagic complications (1-2%), hypothalamic implantation should be used with caution. ONS in refractory chronic migraine patients was studied in 2 multi-centre randomized trials. In PRISM trial 125 drug-refractory chronic migraine patients were treated with ONS or sham, without any significant improvement [12]. In ONSTIM trial 39% of patients treated with active ONS during 3 months had at least 50% reduction in headache frequency and/or a 3-point intensity scale decrease, while there was no improvement in the non-stimulated or ineffectively stimulated groups

\*Corresponding author: Lavano Angelo, Department of Neurosurgery, University Hospital of Germaneto, Campus "Salvatore Venuta", Viale Europa, Catanzaro 88100, Italy, Tel: +39 09613647389; Fax: +39 09613647092; E-mail: [lavano@unicz.it](mailto:lavano@unicz.it)

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[13]. Lead migration/dislodgement is the common complication due to the wide range of neck movements and the distance from the anchoring area to the IPG pocket [2]. Leads and technique of implantation evolved over time to minimize lead displacements: The transfixation by a needle of the plastic tip of the Pisces Quad lead and the suturing of it to the superficial fascia with a non-absorbable suture proposed by Franzini has proven to be effective in preventing this complication [6]. Reported infection rates range from 4% to 30% with varied length of follow-up [14]. A case of subcutaneous tissue change at implant site and another case of reduction or loss of musculoskeletal control were reported in Silberstein et al. [15].

ONS may require an early replacement of the IPG because of power loss/battery failure. This is due to the high voltage needed to effectively stimulate the nerve which is not in anatomical contact with the lead; besides some type of TACs, as chronic cluster headache, need higher amplitude of stimulation for obtain benefits.

## Conclusions

Subcutaneous Occipital Nerve Stimulation offers significantly effective prospect to attend patients suffering from severe headaches and cranio-facial pain syndromes resistant to medications and others conservative therapies. ONS is well a tolerated and safe procedure if compared with other invasive modality of treatment and with Deep Brain Stimulation. Further development of ONS and other similar techniques and validation of their effectiveness require both continuous improvement of clinical evidence and further studies on migraine pathophysiology and its responses to various forms of neuromodulation. Meanwhile, individual preferences of the patient and improvement in the evidence base by RCT can guide the application of ONS.

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