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Factors contributing to intense and chronic pain in Occipital Neuralgia: A review

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Abstract:
Introduction: *Occipital neuralgia is a common headache disorder described in the territory of the greater/lesser occipital nerve with radiation to the territory innervated by the trigeminal nerve. The pain usually described as severe and sometimes as moderate.* ***Goals:*** *Review the current literature about occipital neuralgia and describe factors responsible more intense pain and chronification of this disorder.* ***Methods:*** *A series of descriptors including occipital neuralgia, headache, diagnosis, medication, neuropathic pain, convergence and sensitization were entered into www.google.com in order to evaluate papers on interest to carry out this study.* ***Outcome:*** *Sixty papers related to different aspects of intense and chronic occipital neuralgia were retrieved. However, because of insufficient information and/or papers written in other languages, 31 papers were discarded and only 29 papers were evaluated, summarized and used in the current study.*
Conclusion: *A number of factors contribute to more intense and chronic occipital neuralgia including failed use of over the counter medication, diagnostic difficulties and confusion with other headache disorders, convergence of nociceptive information to the trigeminocervical complex, sensitization, wind up, and the fact that occipital neuralgia is a true neuropathic pain.*
Key Words: *Occipital Neuralgia. Intense Pain. Sensitization. Nerve Damage. Diagnosis. Neuropathic.*

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I. Introduction

Headaches accounts for millions of outpatients visits per year in the United States and is one of the most common complains of patients at initial consultation for pain disorders. In general, headache is currently considered as a major health problem both in the general population and in medical practice[1]. Unremitting, severe and refractory headache is a common experience in Orofacial Pain (OFP) and headache medicine[2] usually associated with both diagnostic and treatment challenges. A major difficulty in the diagnosis and treatment of Occipital Neuralgia (ON) is that many times it mimics many headache disorders including tension-type headache (TTH), migraine (MIG), cervicogenic headache (CGH) and sometimes cluster headache (CHA). Despite many advances in imaging methods, researchers believe that the differential diagnosis and treatment for headaches including ON, the complex mechanisms involved with severity, pain referral and refractoriness to medications, constitute a challenge for clinicians and specialists in the field of headache. Because of many difficulties with the diagnosis and treatment of ON, patients usually present with chronic signs and symptoms as a result of subtle changes in the central nervous system neurons properties associated with sensitization, wind-up, convergence and frequent changes in membrane excitability[3].

Anatomy of the Greater Occipital Nerve (GON)

The GON originates from the medial or internal aspect of the dorsal ramus of C2 spinal nerve, from which receives many sensory fibers. The GON also receives some contribution of nerve fibers from the third cervical nerve[4]. From C2, the GON branches out to become the largest pure sensory nerve in the body. The GON receives sensory fibers from the C2 nerve root and the lesser occipital nerve (LON) receives fibers from the C2 and C3 nerve roots[5]. From its origin in C2, the GON travels downward and laterally bending around the inferior oblique muscle[5]. After traversing the inferior oblique muscle, such nerve travels between the inferior oblique and the deep surface of the semispinalis capitis muscle. When the nerve turns upward, it pierces the semispinalis muscle inferior to the inion and then turns superiorly and laterally and pierces the aponeurotic fibrous attachment of the trapezius and sternocleidomastoid muscles, where it exits and travels through multiple superficial branches to supply the integument of the scalp, overlying the posterior skull to the vertex[5]. At the exit site, the occipital artery and the GON are closely associated[6]. The GON innervates the occipital skin (medial branches) and the region behind the pinna (lateral branches)[6].

Definition of ON

ON also known as C2 neuralgia is **a common but frequently unrecognized form of** headache that involves the posterior occiput in the GON or LON distribution. ON is defined by the International Headache Society as **headache characterized by paroxysmal, non-throbbing**, shooting or stabbing neuropathic pain in the distribution of the GON and/or LON that many times responds favorably to occipital nerve blocks[7]. **ON is a very specific headache disorder** characterized by pain restricted to the sensory fields of the greater and/or lesser occipital nerves[8]. ON is a very specific and severe type of headache that describes the irritation of the GON and the signs and symptoms associated with that disorder[9] ON and cervicogenic headache (CGH) are secondary headache disorders with occipital pain as key element[5] ON is currently considered as a neuropathic pain headache due to nerve entrapment, whiplash injuries of the neck, tumor infiltration or a consequence of neurosurgery[4].

Clinical Description of ON

ON is a bilateral or unilateral pain disorder usually described as intermittent or continuous episodes of aching, burning and throbbing, shocking, shooting pain[5]. The pain is also described as paroxysmal episodes of intense pain with diminished sensation or disesthesia in the affected anatomic area[10]. Most frequently ON is reported by patients in the posterior part of the scalp, in the distribution of the greater, lesser and/or third occipital nerves sometimes accompanied by diminished sensation in the affected area and intense tenderness over the affected nerve[11]. Lee and Son[12] reported a clinical case of a 67-year-old woman with ON in the left side of the head, which she described as intense and intermittent, mild to moderate and as a disesthesic aching pain associated with mild tenderness over the left occipital area. Because ON usually becomes chronic which translates into different descriptions at different times, such pain is described using different terms by many patients. Thus, in the clinical case reported by Lee and Son[12], some months later, the patient described her pain as ill-defined, continuous, burning and as a tingling sensation in the left malar, periorbital and left upper lip.

Patterns of pain radiation in ON

Pain in ON usually originates in the suboccipital area but radiates to the posterior and/or lateral scalp. Pain mal also radiate or be referred behind the eye on the affected side, over the neck, temple and/or frontal regions[5]. Pain in ON radiates over the vertex in the dermatomes of greater occipital nervus in 90% or minor in 10% and both in 8.7% of the cases[4]. Clinicians report many difficulties in differentiating ON from other types of headaches. ON patients suffer from a shooting or stabbing pain in the neck that radiates over the cranium to the retro-orbital area and also above the orbit[6]. Pain may also be perceived over the neck, temple and frontal regions usually triggered by strong neck movements[5]. These patterns of pain radiation are due to complex interneural connections in the trigeminal spinal nuclei through the trigeminocervical (TCC) complex[5] Lee and Son[12] presented a clinical case of 67-year-old woman who described her pain as repeated attacks of sudden aching pain radiating from the occipital area to her left cheek and temple. Molina and associates[9] evaluated subjects presenting with ON, tension-type headache (TTH) and migraine (MIG). They found that ON subjects reported a higher frequency of ON pain referred to the teeth as compared to MIG and TTH subjects. Severe pain in ON usually initiates in the occipital area but soon radiates to the posterior or lateral scalp[5]. Continuous neuropathic OFP originates in neural structures and manifests as constant, ongoing and unremitting pain. Patients usually report varying intensities of pain that is frequently perceived in dental structures usually diagnosed as atypical odontalgia or phantom toothache[13]

Patterns of pain radiation in ON are probably proportional to the level of excitability of the nerve. With more intense pain and higher levels of central and peripheral sensitization, more severe damage to the nerve, and higher levels of excitability are observed, then, each pain episode is more likely to induce pain very far from the original source of the pain.

Etiology of Occipital neuralgia

ON may be a consequence of a known underlying irritant to the occipital nerve. Etiological factors should be considered in the context of the clinical presentation (signs and symptoms) and suspected underlying disorder. Tumors, fractures, infections, cervical spondylosis, osteochondritis and rheumatoid arthritis of the spine may be the cause of cervicogenic and/or ON in certain individuals[5]. ON is a disease that may be caused by multiple disorders or conditions including local trauma, fracture, hematoma, Chiari´s malformation, compression sensitivity, fibromyalgia, neuroma, osteochondroma, multiple myeloma and degenerative changes in the region of C2 and C1[14]. Because the precise etiology of ON remains unclear, both diagnosis and treatment are very difficult. Muscular entrapment, structural lesions or secondary diseases such as multiple sclerosis and myelitis may also be etiologic agents for ON[15].

Clinical case reports have demonstrated that although a number of pathological conditions may be associated with ON, nerve entrapment, local and general trauma, and rheumatoid arthritis are the most

common etiological elements[11]. Neoplasms, aneuryisms affecting the involved nerve, injury to the head, direct occipital nerve trauma, compression of upper cervical roots, degenerative changes like in osteoarthritis and congenital factors may also result in ON[5]. The C2 ramus could be compressed by intra or extracranial vessels and/or by tendinous and muscular structures between the posterior arch of the C1 nerve and the lamina of the C2 nerve, but the nerve is not especially vulnerable at this location[16]. The ON nerve is very vulnerable to a pathologic vascular contact which leads to moderate local inflammation and this has been reported widely in the current literature[12]. Giant cell arteriritis, callus formation following vertebral fractures, schwannoma and other mass occupying lesions may be other sources of compression on the ON[7]. Compression of the GON by degenerative cervical spinal changes and cervical disc disease, are also currently accepted etiological factors for ON[5]. Some researchers and clinicians believe that the development of ON symptoms has a biomechanical origin. A postural alteration that has as consequence the nervous and venous compression of the root of the C2 vertebra, is also considered an etiological factor for ON[14]

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Clinical features in ON

Even though **ON** is currently considered a very complex neurophysiological and clinical disorder usually associated with **diagnostic and treatment difficulties,** this disorder is considered as a neuropathic alteration. Thus, to a certain extent, its richness of descriptors used by patients is correlated with its neuropathic nature and at the same time such ON characteristics facilitates the evaluation and diagnostic process. Because ON is a clinical entity in which the neural components of the GON are subjected to pressure resulting in damage to the nerve, pain in this disorder is described as **very severe, lancinating**, shooting and unbearable. Thus, it is a common observation that patients report previous hospitalizations during the initial interview for diagnosis and treatment. Because the diagnostic and treatment of the disorder are very difficult, patients usually recounts a history of **multiple diagnosis and treatments**. Thus, when he or she is examined the patient reports pain **of longer duration** as compared to other headache conditions.

Because pain in ON is the result of direct damage or lesion to different nerve structures in which fibers carry a set of different sensations including pain and temperature, pain in ON is described using multiple descriptors including severe, lancinating, shooting, stabbing, burning, shocking, electric-like and radiating to distant areas innervated by the trigeminal nerve[5]. The type of nerve fibers may also be responsible for some clinical characteristicof ON including a description of **intermittent** and stabbing combined with a persistent or constant **dull aching** pain over the occipital nerve territory[17].

From a clinical and diagnostic viewpoint ON is usually described as pain that is most frequently reported in three anatomic zones: The neck, upper part of the cervical structures and the face, orbits and teeth. One common behavioral characteristics of ON patients is the self-reported excessive use of medications most frequently pain killers and muscle relaxants, but opioids and antidepressants are also reported frequently. From a diagnostic and clinical standpoint, ON should be considered as a neuropathic pain disorder[11]. As such, the pain is described as very severe, lancinating, paroxistic, shooting or stabbing, electric shock-like, burning, sudden and intermittent. Clinically, ON presents with a richness of ear disorders including dizziness, vertigo, hearing deficiency, ear stuffiness and tinnitus, rarely observed in other clinical disorders. Such disorders occur much more frequently as compared to subjects with Craniomandibular Disorders.

Another clinical feature of ON is that it responds readily to one or more superficial anesthetic block to the GON. If repeated blocks are used in a certain patient, the pain may be relieved during weeks or even months. This is so, as repeated anesthetic blocks inhibits nerve excitability and the vicious cycle of damage>>>>increased nerve excitability>>>>pain>>>damage. ON is also characterized by repeated and sudden attacks of severe pain that increases the probability of patients being taken to emergency treatment at the hospital. In fact, many ON patients report a history of hospitalization associated with intense ON. Paraesthesia or a numbness or tingling sensation in ON is reported in the upper cervical area (vertex), exactly in the area innervated by the GON, thus providing a diagnostic clue to the examiner. One useful diagnostic feature of ON is excessive use of over - the counter medication. Patients usually report a history of having used large amounts of pain killers that with time became ineffective. In this situation, the patient is encouraged to use another group of analgesics and muscle relaxants which again, become ineffective with time. In a third stage the patient seek medical attention and starts using more powerful pain killers including opiates, anti-anxiety drugs and antidepressants. Because of their undesirable side effects, opiates are no frequently used by patients.

Mechanisms

ON is considered by most clinicians and researchers as a form of **neuropathic disorder.** This translates into persistent and severe pain and many difficulties to treat or manage the disorder. In line with this point of view, one investigation[11] indicates that ON is a neuropathic disorder arising from the LON, GON and/or third occipital nerves. ON is now considered as 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 that may

be unilateral or bilateral being the unilateral form, the most frequently reported. Neuropathic pain involves the presence of severe structural changes in the nerve. Damage nerves usually bombard the SNC with unremitting nociceptive information. In line with this point of view, one investigation[13] indicates that a number of complex peripheral and central mechanism are involved in the initiation and maintenance of pain and that those changes in the neural system occur as a consequence of mechanical trauma inducing nerve damage which is a characteristic of neuropathic pain disorder.

ON is caused by chronic compression and adhesion of the occipital artery on the GON the GON and constriction by the aponeurotic fibrous aperture of the trapezius muscle[12]. This mechanism generates **chronic nerve stimulation** and maintained nerve excitability. Both mechanisms operate in any form of neuropathic pain, thus rendering treatment unsatisfactory for both the patient and the professional. In line with these observations Bond and Kinslow[15], describe a clinical case of a woman presenting with signs and symptoms of ON. The patient reported a number of previous different modes of treatment including manipulation, an occlusal splint and different types of medication. However, none of these approaches or intervention brought complete or lasting resolution of her pain. Additional support for these considerations comes from one study[7] reporting that subjects with ON are characterized by previous and multiple failed conservative modes of therapy. ON patients are also subjected to interventional treatment modalities that may result in treatment failures. Many ON patients seek non-pharmacological treatment modalities for headache due to failed responses to first-line therapy[18]. As long as some therapies for ON fail, the result is a pain condition that becomes more chronic and thus, more refractory to pharmacological treatment[18].

Chronic noxious afferent input from the GON or LON may cause amplification of pain in the TCC and central and peripheral sensitization causing referred pain[12] to anatomic structures innervated by the fifth cranial nerve. Thus, with longer duration of ON (chronification), pain tends to become more frequent, severer and long lasting. These considerations are echoed by one investigation[17] indicating that interneural connections in the trigeminal spinal nucleus (subnucleus caudalis) through the TCC facilitates the development of more severe pain and pain referral to ipsilateral, temporal, frontal or orbital areas. Referred pain can be interpreted as " excessive stimulation from the TCC that has to be spread to distant anatomic areas". Supporting these considerations, one investigation[5] asserts that pain in ON originates in the suboccipital area but because of amplification in the TCC, pain radiates to posterior and/or lateral scalp, behind the eye, neck, temple and frontal regions.

Clinical experience demonstrates that in the process of chronification, some types of headache including ON, MIG and TTH become very similar[19]. Such phenomenon is caused by shared neurophysiological changes responsible for more chronic pain. Additional support to the theory of chronification as a mechanism in ON comes from one investigation[20] indicating that most patients receiving corticoid infiltration experience pain recurrence while prolonged pain relief is observed in a small group of patients. At the same time, the quality of life worsens and medication becomes less effective. Amplification of pain in the TCC, the phenomenon of chronic maintained pain and unresponsiveness to pharmacological therapy are neurophysiologic changes closely associated with the development of a lower threshold for pain. This point of view is congruent with one study[21] indicating that a general state of pain sensitivity is closely associated with lower threshold for pain which in turn is correlated with altered sensory processing and other psychopathological phenomena.

Interneural connections of the GON and LON may explain some neurophysiological phenomena including referred pain, paraesthesia distant from the original source of pain and even a set of ear disorders reported frequently by ON patients. These observations are congruent with studies indicating that "due to interconnections of the GON and LON with vestibulocochlear nerve (VIII), glossopharyingeal nerve (IX) and vagus nerve (X), symptoms such as dizziness, tinnitus and nausea, may be observed frequently in clinical cases of ON[17].

II. Factors contributing to intense and chronic pain

I.Diagnostic Difficulties

The diagnosis of ON is quite difficult. ON may be confused with other headaches and cervical disorders including CGH, TTH, MIG and even CHA. Further, regarding signs and symptoms, there may be significant overlap when some signs and symptoms of ON, TTH, MIG and CGH are compared. Pericranial tenderness is a common sign among all these types of headache. ON and MIG are more frequently described as severe as compared to TTH and CGH. Neck pain may be reported by patients presenting with characteristic of this four types of headache. TTH is usually bilateral whereas migraine, ON and cervicogenic headache are more frequently reported as unilateral. Overlap of signs and symptoms between ON and other clinical entities including CHA, paroxysmal hemicranias and other types of headaches has been reported recently[22].

Anesthetic blocks are diagnostically more useful in TTH and ON than in migraine and cervicogenic headache. Sometimes is very difficult to differentiate signs and symptoms of migraine from those reported in ON. Magnetic resonance imaging is the most important instrument in the diagnosis of ON as it allows clear

visualization of the surrounding cervical and occipital soft tissues[6]. When some symptoms for instance photophobia, phonophobia and nausea are included in ON diagnostic criteria, this inclusion may lead to the misdiagnosis of migraine[17] as such symptoms are reported frequently by MIG patients, rarely by TTH subjects and they are not specific for ON.

2.Excessive consumption of ineffective drugs

Most patients presenting with signs and symptoms of ON report that they have used large amounts of different medications when they present for another interview for their signs and symptoms. By far, muscle relaxants and pain killers are the most frequently used medications. Under the impression of migraine, trigeminal neuralgia or a cervical disorder, the pain specialists is encouraged to prescribe gabapentin, carbamazepine, tramadol and other less effective analgesics to abolish pain. Many patients report a history of previous use of anti-anxiety and antidepressant drugs. Of all these drugs, over-the-counter analgesics and anti-inflammatory drugs are the less effective. Some pain specialists use a combination of anesthetic block to the GON, oral diazepam 10mg and diclofenac 75 mg to alleviate pain[4]. Ineffective drugs specially over the counter analgesics, anti-inflammatory and muscle relaxants, contribute to chronification and severer pain as they condition the patient to believe that "next drugs may also be ineffective".

4.The fact that the disorder is neuropathic and damage to the nerve cause intense and maintained pain: The combination of damage to the nerve, convergence of constant nociceptive information to the TCC, central, peripheral sensitization and other neurophysiologic disturbances, make the treatment of ON very difficult. Experimental studies in animals[23] have demonstrated that significant structural damage to A beta, A delta and C nociceptive fibers is capable of altering transduction and transmission of peripheral information due to altered ion channel function. These changes induce functional alterations in the spinal cord including excess of excitation and a loss of inhibition of ascending nociceptive information. For these reasons, sometimes aggressive surgery is used by many pain specialists[6]. Because pain from nerve entrapment can be only temporarily alleviated, pain relief is not definitive as the pressure and damage to pain sensitive structures of the nerve, are not eliminated. Further, pain in ON may be aggravated by abnormal neck posture and/or movements, spasm of the trapezius and sternocleidomastoid muscle[11]. Because of the difficulties in treating ON using conservative methods, some surgical techniques including cryioneuroablation, neurectomy, peripheral nerve stimulation, neurolytic injections[11] and spinal manipulation therapy[17] have been recommended. Because there is evidence indicating more benefits using invasive therapeutic methods, in many cases, surgical methods are preferred over pharmacological interventions[17].

5.Convergence

Convergence is the phenomenon in which multiple nerves converge into a single shared neural pathway with the central nervous system which makes it difficult for the observer to differentiate the true source of the nociceptive stimulation[24]. The most classical example of convergence is the information that converges from cervical and trigeminal structures to a shared TCC complex.When nociceptive information is excessive and prolonged as in the case of chronic ON, the information converges into the TCC. However, such information frequently bombards the SCN and may be redirected to areas innervated by the trigeminal nerve thus, resulting in frontal, temporal, orbital and facial pain. The excessive information may also be discharged stimulating other nerves including the vagus, glossopharyngeal and vestibulocochlear thus, resulting in the development of ear disorders. In many patients presenting with ON, OFP in the distribution of the trigeminal nerve may result from chronic ON due to pathological vascular contact on the GON[12] .

The convergence of nociceptive afferents from cervical nerves to the TCC and the subsequent sensitization has enormous clinical significance in headache pathophysiology. For instance, increased sensitivity of neurons and dissemination of pain and pain referral[25] to adjacent anatomic areas, for instance the face, mandible and maxilla innervated by the trigeminal nerve (fifth cranial nerve) constitute clinical correlates of both convergence and sensitization.

6.Presence of wind-up

Wind-up is a progressive frequency-dependent increase in the excitability of trigeminal and spinal dorsal horn wide dynamic range nociceptive neurons evoked by repetitive stimulation of primary afferent nociceptive C-fibers[26]. Wind-up is closely related with temporal summation defined as an increase in pain perception to repetitive constant nociceptive stimulation[26]. Wind-up is linearly correlated to the stimulus intensity[26]. This observation indicates that wind-up, convergence and central sensitization are more likely to be observed in cases of chronic headache characterized by frequent and intense pain. Thus, wind-up may be observed more frequently in such types of pain as MIG, ON and CHA.

The wind-up phenomenon is also defined as the temporal summation of pain and it may be induced experimentally using the pinprick test applied repeatedly on a determined skin area[19]. The wind-up

phenomenon is observed ubiquitously in cases of central and peripheral sensitization. One characteristic of the wind-up phenomenon is the reduction of pressure pain threshold as observed in chronic headache states[19].

7.Central and peripheral sensitization

Sensitization is the process whereby the stimulus needed to generate a response decreases over time, while the amplitude of the response to any given stimulus increases[19]. Central sensitization is also defined as an amplification of neural signaling within the central nervous system that elicits pain hypersensitivity. In central sensitization neurons become hyper-excitable, resulting in hypersensitivity to both noxious and non-noxious stimulation[27]. Many factors may contribute to sensitization including constant and severe pain, failure of previous modes of treatment, depression, sensitization of nociceptive structures and deficiency of antinociceptive inhibitory descending mechanisms[19]. Chronic and continuous strong afferent input from peripheral receptors in ON caused by pathological vascular contact with the GON is a major factor causing sensitization and increased sensitivity to pain of second-order neurons in the TCC, a population of neurons in the C2 dorsal horn which receives frequent and convergent input from dural and cervical structures[25]
Sensitization of the central nociceptive neurons in the TCC occurs in .response to strong dural noxious inputs observed in secondary headache syndromes. Sensitization of these second-order neurons in the TCC is explained by the presence of increased afferent flow of nociceptive information from peripheral receptors or from pain modulatory influences in higher areas of the SNC which facilitate or disinhibit inflow of information to the TCC[25].

8.Decreased activation threshold in local nociceptors or pain receptors:

Decreased activation threshold in both cervical and trigeminal nociceptores is a phenomenon common to wind-up, central and peripheral sensitization, convergence and chronic and severer pain. In many cases, irreversible or invasive medical and dental procedures may cause additional damage to the nerve, thus increasing its excitability condition but decreasing the corresponding threshold for nociceptive information and pain[13]. Allodynia, a common phenomenon observed in MIG, chronic TTH and ON, is defined as pain resulting from innocuous stimulation and is considered a clinical correlate of chronic headache and central sensitization. Allodynia and lower threshold to evoke painful stimulation are the result of prolonged and intense stimulation[19] of peripheral nociceptors and is observed more frequently in chronic orofacial and headache disorders. In allodynia and lowered threshold for pain, peripheral nociceptors respond with pain even in the presence of innocuous stimuli, the one that in normal physiologic conditions does not produce stimulation in the nociceptive receptor.

XI. Evaluation and diagnosis

As mentioned before, the diagnosis of ON may be very difficult for the pain practitioner. ON usually occurs together with signs and symptoms of cervical disorders, other headache types and temporomandibular disorders (TMDs). This overlap of signs and symptoms makes ON diagnosis very difficult. The richness of symptoms especially those in the ear and face, is an additional element of confusion in the diagnostic treatment dyad. On the other hand, the variety of differentiated signs and symptoms in ON and clinician´s careful observations during evaluation facilitate the diagnosis process. However, the inclusion of some characteristics of other headaches, for instance, nausea, vomiting, photophobia and phonophobia which are commonly reported by MIG patients, creates confusion in the differentiation between ON and migraine.

A comprehensive diagnostic procedure such as the one indicated by Barmherzig and Kingston[17] is highly recommended and is summarized as follows: Detailed history of the chief complain, physical examination, biomechanical tests for the cervical spine including passive flexion, extension and rotation, and palpation of the cervical structures. The clinician should take into account the fact that ON is a neuropathic disorder. Thus, many characteristics of neuropathy are observed during careful questioning and gathering of information, for instance, pain descriptors listed as follows, are unique features of ON: shooting, stabbing, electric-shock-like, burning, intermittent, severe, pain superimposed on a dull aching low grade pain, referred pain to specific anatomic areas and presence of local and distant paraesthesia.

Patients with ON associated with compression or pressure on the GON or LON usually present a hyperalgesic pain generating zone which responds with moderate to severe pain on careful palpation inferiorly and medially to the external occipital protuberance. This area is extremely painful as there is a local perineural inflammation[2] which constitutes the basis for the formation of an extremely tender "pain generating zone" mentioned in some studies about ON. Summarizing the previous information about the diagnosis of ON and based on the examination of about 100 patients with ON, the following diagnostic information can be very useful to have an accurate diagnosis of the condition:

1.Pain in ON is frequently described as severe, shooting, lancinating, burning and stabbing;
2.Pain in ON is described mostly in two anatomic zones: posteriorly in the upper cervical area and anteriorly in the face corresponding to the frontal, orbital and malar areas.
3.ON is characterized by the presence of a very painful "pain generating zone" located inferiorly and medially to the occipital protuberance.
4.Facial paraesthesia occurs very frequently in patients presenting with ON signs and symptoms;
5.Ear symptoms are reported very frequently by ON patients
6.Nasal congestion and secretion are reported frequently by ON patients.

III. Treatment

A number of modalities of treatment and/or management have been indicated in the case of ON. For instance, Blake and Burstein[2] recommend the use of extracranial treatments including occipital nerve blocks, cervical trigger point injections, botulinum toxin and even monoclonal antibodies directed at calcitonin gene related peptide (CGRP) so as to get more substantial pain relief. Although decompression of the GON and/or LON from muscular and fascial compression has been indicated in many studies, Blake and Burstein´studies[2] indicate that the technique is only effective for some patients. A pharmacological approach in which indomethacin 50-150mg per day, lamotrigine, tricyclic antidepressants, and intramuscular tramadol, may be more effective alleviating pain as compared to other more known and conventional drugs[11]. Centrally acting agents that reduce neuronal excitability such as anti-convulsants and antidepressants are highly recommended. However, in cases when these anti-nociceptive agents are not so effective, the treatment may be complemented using occipital nerve blocks, trigger point injections and botulinum toxin[28].

Barmherzig and Kingston[17] claim that structural education, offering substantial support and creating a psychological environment of mutual patient-professional cooperation may have a substantial active role in the understanding and management of pain as it may assist patients to improve their skills to manage the adverse psychological and social effects of chronic pain. The dental practitioner and the specialist in endodontics should be extremely cautious in the diagnosis and treatment of dental pains in subjects presenting with signs and symptoms of ON and pain referred to the teeth[29]. The teeth should not be treated as such approach may lead to additional neuropathic pain, sensitization and sometimes the development of atypical facial pain. If the differentiation of pain from true dental pathology and that associated with referred mechanism from the GON and LON nerves, is previously established, unnecessary treatment may be prevented. Regarding other modalities of treatment Kulkarny[4] advocates the use of local anesthetic blocks of the occipital nerves, over the counter medication for pain (diclofenac) and inflammation, Botox injections, diazepan 5mg, Radio frequency, ablation of occipital nerves, or surgical intervention.

Ducic and associates[22] reviewed the literature on treatment of ON. Their study indicated that various modalities of treatment including nonsteroidal anti-inflammatory drugs and acetaminophen, narcotics, ergot derivatives and other drugs, provide unsatisfactory and transient positive results whereas local anesthetic injection, corticoids and Botox, demonstrate long-lasting pain relief for ON pain. Botox injections probably have very promising positive results in the treatment of ON. This is so as Botox mechanism of action is relatively well known and facilitates recovery of a severely damage nerve. It has been reported that Botox injection in the site of the nerve entrapment or irritation site may lead to direct local inhibition of neurogenic inflammation and decreased activity of dynamic range neurons, which in turn, indirectly inhibits central sensitization[29]. Further, because of the mechanism of action of Botox injection, its effects may be more lasting as compared to other pharmacological approaches including anesthetic injections.

Pharmacologic treatment for ON has not been systematically evaluated. Because the treatment of ON is very difficult, many drugs in different categories have been recommended. Many clinical reports have recommended the use of NSAIDS, tricyclic antidepressants such as amitriptyline, muscle relaxants such as baclofen, and anticonvulsants such as gabapentin and carbamazepine[17]. Given the lack of diagnostic consensus related to ON, it is very difficult to interpret the current literature regarding the efficacy of various treatment modalities. It is practically impossible to evaluate comparison studies assessing the efficacy of two or three pharmacological agents, when more than 20 pharmacological agents to treat ON pain have been mentioned in the current literature.

IV. Conclusion

ON is usually a chronic and recalcitrant severe pain condition presenting an enormous challenge for the practitioner regarding diagnosis and management. Many elements may contribute increasing intensity and chronicity of ON pain including:

Factor or element	Negative correlation
1.The diagnosis of ON is difficult. ON may be confused with other headache disorders.	The condition becomes more chronic Chronicity/severer pain may facilitate

	the development of anxiety/depression
2.Use of ineffective drugs may facilitate the development of chronic ON	The patient is conditioned to believe that drugs are not effective to treat his or her pain.
	Longer use of medication facilitates a state of chronic pain.
3.ON is a neuropathic pain disorder	The total recovery of a damaged nerve is very difficult to occur. Compensatory mechanism (neurochemical changes) worsens the clinical presentation of pain.
4.Convergence	Excessive/prolonged nociceptive Information results in more severe/chronic and referred pain.
5.Wind up	Increased excitability of trigeminal and spinal dorsal horn neurons.
6.Central/peripheral sensitization	Amplitude of nociceptive response (pain) increases with time.
7.Lower threshold for painful stimulation	Pain may occur in response to an innocuous stimulation.
8.Presence of depression and anxiety	Anxiety and depression may further contribute to lower pain threshold.

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