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Review

GLOSSOPHARYNGEAL NERVE AS A SOURCE OF OROFACIAL PAIN - DIAGNOSTIC AND THERAPEUTIC CHALLENGES

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ABSTRACT – Chronic neuropathic orofacial pain along with physical suffering can cause emotional, psychological and social difficulties, which significantly affects the quality of life of patients. Pain in the area of glossopharyngeal nerve innervation, especially chronic neuropathic, is relatively rare, but is significant because of the great suffering it causes to sufferers. It can be life threatening, due to the cardiac arrhythmia, syncope or convulsions it can cause. Drug treatment is often of limited effectiveness and can be fraught with side effects. It is necessary to look for the etiology of the underlying disease, and if possible, to take adequate causal treatment. This review article discusses the etiology, clinical features, differential diagnosis, and treatment modalities of neuropathic pain in the area of glossopharyngeal nerve innervation.

Keywords: *orofacial pain, glossopharyngeal nerve, vago-glossopharyngeal neuralgia, glossopharyngeal block*

Introduction

The head area is extremely well sensory innervated, due to overlap of visceral and somatic innervation, pain syndromes manifest some specifics, which we do not find in other body areas. Most of the orofacial region is innervated by the trigeminal nerve. Its fibers form anastomoses with the fibers of other nerves in the area and pain syndromes often share a similar clinical appearance (1), thus diagnosis and treatment can be difficult. Painful conditions in the glossopharyngeal nerve innervation area are not common, but are significant due to anatomical and functional specificity, as well as due to the great suffering they cause to patients. Vagoglossopharyngeal neuralgia may be accompanied by asystole, convulsions or syncope, which should be considered in the treatment process as well as in differential diagnostics.

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Anatomy

The orofacial region encompasses the facial area between the orbitomeatal line and the neck to the front of the ears and includes structures of the oral cavity. The largest cranial nerve, the trigeminal nerve, innervates most of the orofacial region with its three branches. Therefore, orofacial pain can be defined as both pain and dysfunction involving motor and sensory transmission

in the trigeminal system. The trigeminal tract in the brainstem, in addition to the afferent fibers from the trigeminal ganglion, receives afferent fibers from intermedius nerve, branch of the facial nerve (n.VII), glossopharyngeus (n.IX) and vagus nerve (n. X) and upper cervical roots (2). The glossopharyngeal nerve contains motor, sensory, and parasympathetic fibers. Motor fibers originate from the nucleus in the medulla oblongata, which is common to glossopharyngeus, vagus, and accessory nerve, innervating soft palate and pharyngeal musculature. Somatosensory fibers conduct impulses from the oropharynx, posterior third of the tongue, soft palate, epiglottis, Eustachian tube, middle ear, and mastoid. They also conduct a taste sensation from the back third of the tongue. Some neurons transmit afferent impulses from chemoreceptors and baroreceptors located around the bifurcation of the common carotid artery (n. IX) and the aortic arch and its branches (n. X) centrally (3) and thus participate in reflex respiratory and circulatory activity, which explains arrhythmogenicity in some glossopharyngeal neuralgia cases. Sensory fibers innervate the pia and the arachnoid, while the brain parenchyma does not receive sensory innervation (1). The glossopharyngeal nerve innervates the stylopharyngeus muscle by motor fibers and the parotid gland with secretomotor parasympathetic fibers. The back of the scalp and the skin of the entire neck are innervated by the cervical spinal nerves.

Painful conditions in the glossopharyngeal nerve innervation area

Orofacial pain can be classified according to anatomical structures or pathophysiological mechanism, and the first comprehensive classification was made in 2020 (4). Considering the pathophysiological mechanism, we distinguish between nociceptive, neuropathic, nociplastic and mixed pain. Orofacial pain can be odontogenic and nonodontogenic, localized and referred to, acute and chronic, episodic (paroxysmal) and continuous. Distinguishing these categories is important because of the different therapeutic approaches. Chronic neuropathic nonodontogenic orofacial pain is one of the biggest therapeutic and diagnostic challenges in this area. Typical and most common clinical entity is trigeminal neuralgia. Glossopharyngeal neuralgia is significantly less common, but these two disorders may coexist.

Clinical appearance

Glossopharyngeal neuralgia is an infrequent disorder (approximately 0.8 per 100,000), most commonly manifested as paroxysmal pain in the innervation area of the glossopharyngeal and the vagus nerve (5, 6). It is thought to be related to compression of the glossopharyngeal or the upper parts of the vagus nerve. Suspicion of the involvement of these nerves is raised by asymmetry in the movement of the soft palate and uvula or the absence of the emetic reflex (7). The pain can encompass the pharynx, the base of the tongue, the area inferior to the angle of the mandible and the ear. It can spread to the eye, nose, chin or shoulder area. It can be so severe that the patient avoids eating, which can cause weight loss. The pain is most often caused by chewing, swallowing, speaking, coughing, yawning, abrupt head turning, or outer ear area touching. The pain is usually one-sided, sudden, strong and sharp, sometimes like a lightning strike. It is often accompanied by paresthesia, a burning sensation and / or lightning. It lasts from a few seconds to a few minutes and then disappears and does not appear until the next attack. In some people with a long history of pain, pain is continuously present between paroxysms. In general, it can be said that the incidence increases with age. Unlike trigeminal neuralgia, the left side of the face is more commonly affected. Bilateral pain is possible, and according to some studies, it occurs in about 12% of patients (8).

Pain may also be present in the innervation area of the auricular and pharyngeal branches of the vagus nerve. In rare cases, pain attacks may be associated with vagal symptoms such as coughing, hoarseness, syncope, and / or bradycardia (9). Neuralgia of the upper laryngeal nerve, n. X branch, may present with identical symptoms, and it may be clinically difficult to distinguish the two entities. Therefore, some authors suggest a distinction between pharyngeal, otalgic and vagal forms of neuralgia, and the use of the term vagoglossopharyngeal neuralgia, when pain is accompanied by asystole, convulsions or syncope (10). In the weeks before the onset of a specific clinical appearance of glossopharyngeal neuralgia, unpleasant sensations may be present in the affected area. The course of the disease is unpredictable. Episodes can last for weeks or months, followed by pain-free periods. Pain attacks usually return after some time, and in some patients, symptoms may show a tendency to decrease. It is the only cranial neuralgia in which painful afferent

impulses can precipitate cardioinhibitory reflexes of the vagus nerve with consequent bradycardia / asystole or syncope (8, 11).

Diagnostic approach

As with trigeminal neuralgia, we distinguish the so-called classical, primary, and secondary form of glossopharyngeal neuralgia. The International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria are listed in Table 1. The classic form is caused by compression of the nerve root the following uncommon disorders are considered in differential diagnostics: optic neuritis, headache due to ipsilateral ischemic lesion of oculomotor nerves (III, IV or VI), Tolosa Hunt syndrome, Raeder's syndrome, recurrent painful ophthalmologic neuropathy, superior laryngeal nerve neuralgia, burning mouth syndrome, persistent facial pain, temporal arteritis, and carotidynia. Short paroxysms of pain deep in the ear canal can be caused by intermedius nerve neuralgia, a branch of the facial nerve (geniculate or Hunt's neuralgia). Occipital neuralgia can be the cause of

Table 1 ICHD-3 Diagnostic criteria for glossopharyngeal neuralgia (5)

ICHD-3 Diagnostic criteria for glossopharyngeal neuralgia	Classical	Secondary	Idiopathic
A. Recurring paroxysmal attacks of unilateral pain in the distribution of the glossopharyngeal nerve (posterior part of the tongue, tonsillar fossa, pharynx or angle of the lower jaw and/or in the ear) and fulfilling criterion B	Yes	Yes	Yes
B. Pain has all of the following characteristics: - lasting from a few seconds to 2 minutes - severe intensity - electric shock-like, shooting, stabbing or sharp in quality - precipitated by swallowing, coughing, talking or yawning	Yes	Yes	Yes
C. Not better accounted for by another ICHD-3 diagnosis	Yes	Yes	Yes
D. Demonstration on MRI or during surgery of neurovascular compression of the glossopharyngeal nerve root.	Yes	No	No
E. An underlying disease has been demonstrated known to be able to cause, and explaining, the neuralgia.	No	Yes	No

by an aberrant loop of one of the nearby arteries or veins, which can be proven by imaging methods. In most cases, the pain is tympanic and retrotonsillar. Glossopharyngeal neuralgia due to compression of some other cause is classified as secondary. Secondary neuralgia can occur because of trauma, surgery, or radiotherapy in the area. It can occur due to demyelinating lesion, pontocerebellar tumor, oropharyngeal tumor, meningioma, epidermoid cyst, carotid artery aneurysm, AV malformation or Chiari I malformation. It may be part of the clinical appearance of peritonsillar abscess and Eagle's syndrome (12, 13, 14).

Pain in the orofacial area may also be a reflection of heart pain, part of the clinical appearance of sickle cell anemia, or some distant neoplasm. It can also be of psychogenic origin. In addition to trigeminal neuralgia, headaches in the occipital region. It usually occurs as a stabbing pain in the innervation area of the greater, lesser, or third occipital nerve. Pain in the innervation area of the glossopharyngeal nerve may be part of the clinical appearance of primary headaches with autonomic symptoms (cluster headache, paroxysmal hemicrania, short lasting unilateral neuralgiform headache with conjunctival injection and tearing) which include lacrimation, ptosis, nasal congestion, and eyelid edema (15).

Multiple factors contribute to the diagnostic and therapeutic challenges related to orofacial pain (16). Pain may arise from a variety of tissues making a multidisciplinary approach essential to the diagnosis and treatment of orofacial pain. Rational procedure should primarily include starting from the

simplest, i.e. history and examination by a dentist and determining whether it is odontogenic or non-odontogenic neuropathic pain. If dental disease is not found to be the cause of neuralgia, modern imaging methods should determine whether it is primary or symptomatic neuralgia.

Magnetic resonance imaging (MRI) or Multi Slice Computed Tomography (MSCT) of the brainstem may show vascular compression, tumor, or demyelinating lesion involving the glossopharyngeal nerve. MSCT or MRI of the neck may show a prolonged styloid process of the temporal bone suggestive of Eagle syndrome. A local anesthetic injected into the trigger point area reduces pain and can help with diagnosis. The diagnosis is confirmed by cessation of pain after nerve block through the jugular foramen or after topical pharyngeal anesthesia. Ultimately, nerve stimulation during surgery can also help to confirm the diagnosis.

Standardized screening questionnaires, such as The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Neuropathic Pain Diagnostic Questionnaire (DN4), Neuropathic Pain Questionnaire (NPQ), painDETECT and others can help identify the neuropathic component of pain (6, 7).

To assess the intensity of pain as well as to assess the effectiveness of therapy, we use a visual analog scale (VAS) or numerical rating scale (NRS). It should be noted that questionnaires are screening tools, not a tool for diagnosis. The gold standard in diagnosis remains the history of the disease, and clinical and neurological examination, supplemented by modern imaging methods and electrophysiological diagnostics. This applies in particular to laboratory blood tests, serological tests, magnetic resonance imaging, and electrophysiological testing of trigeminal reflexes (8, 17, 18).

Treatment

Due to the complexity of the biopsychosocial components of pain, treatment is often of limited effectiveness. Non-invasive (pharmacological, psychological and complementary) and invasive (surgical) methods are available (8). The choice depends on whether it is idiopathic or symptomatic neuralgia, the effectiveness of drug prescribed and the side effects profile. In addition, for the success of treatment, it is necessary to explain to the patient the possibilities and limitations of the drugs prescribed, especially when one could expect the onset of analgesic action. As a first line of treatment, carbamazepine is recommended at an initial dose of 100 to 200 mg twice daily, with a gradual increase in dose. In most cases, doses of 300 to 400 mg twice daily are effective, and in some cases a maximum dose of 1200 mg per day is required (12, 13). In case of carbamazepine intolerance, oxcarbazepine may be tried. For most patients, with gradual titration, a dose of 300 mg twice a day is effective. In case of intolerance or pain refractory to the previous medication, baclofen or lamotrigine may be tried as adjunctive therapy, with gradual dose titration. Despite the insufficient number of adequate clinical studies, in practice, pregabalin 300 to 600 mg and gabapentin 900 to 1800 mg have shown good results in some patients. Although without a base in clinical studies, we sometimes choose to use low-dose opioid analgesics in cases of acute pain exacerbation lasting several days or weeks, or in the initial phase of anticonvulsant therapy titration. In some patients, tricyclic antidepressants or serotonin and norepinephrine reuptake inhibitors (SNRIs, duloxetine and venlafaxine) may be helpful. In the symptomatic treatment of chronic neuropathic pain, acupuncture is beneficial to a large number of patients, as it alleviates the intensity of pain and reduces the frequency of pain attacks (19).

Invasive procedures for orofacial pain treatment caused by glossopharyngeal neuralgia include glossopharyngeal block, or even more invasive, surgical procedures. Glossopharyngeal blocks have important therapeutic as well as diagnostic value in distinguishing the cause of a painful condition. A glossopharyngeal block can be carried out intra-orally (the premolar approach) or using a peristyloid technique. When applying the intraoral approach, care should be taken due to the proximity of the glossopharyngeal nerve to the internal carotid artery. Ultrasound-guided peristyloid technique of the glossopharyngeal nerve block is recommended as a safer method. Sometimes it is necessary to do a few dozen nerve blockages to get a more lasting result (20).

In case of therapeutic failure of conservative therapy and nerve blocks, it is recommended to consider the optimal options for surgical treatment. Microvascular decompression is a treatment option for medically intractable glossopharyngeal neuralgia (21). Intracranial techniques include rhizotomy or an intracranial root resection of the glossopharyngeal nerve and / or vagus nerves (22). For patient who cannot tolerate open intracranial procedures extracranial

neurotomy, percutaneous radiofrequency rhizotomy and stereotactic radiosurgery with gamma knife surgery are indicated (23). In secondary glossopharyngeal neuralgia it is necessary to treat the underlying pathology: stilectomy due to Eagle's syndrome, tumor resection, posterior fossa decompression in Arnold-Chiari malformation, embolization of an arteriovenous malformation and coagulation of choroid plexus overgrowth (23).

Conclusion

The orofacial region is important for speaking, chewing, swallowing, communicating, and expressing one's personality. Pain in the innervation area of the glossopharyngeal nerve, especially chronic neuropathic, is a relatively rare in occurrence, but is significant because of the great suffering it causes. At the same time, it can be life-threatening, due to the cardiac arrhythmia it can cause. Drug treatment is often of limited effectiveness and may be fraught with side effects. It is necessary to look for the etiology of the disorder, and if necessary, undertake adequate surgical treatment. Chronic neuropathic orofacial pain in addition to physical suffering can cause emotional, psychological and social difficulties, which significantly affects the quality of life of those affected.

References

1. Bičanić I, Hladnik A, Džaja D, Petanjek Z. The Anatomy of Orofacial innervation. Acta Clin Croat. 2019 Jun;58(Suppl 1):35-42. doi: 10.20471/acc.2019.58.s1.05. PMID: 31741557; PMCID: PMC6813484.
2. Usunoff KG, Marani E, Schoen JH. The Trigeminal system in man. Adv Anat Embryol Cell Biol. 1977; 136:I-X, 1-126.
3. Jannig W. Integrative Action of The Autonomic Nervous System Neurobiology of Homeostasis. 2006, Cambridge: Cambridge University Press.
4. International Classification of Orofacial Pain, 1st edition (ICOP) Cephalalgia, 2020, Vol. 40(2) 129–221. International Headache Society 2020. DOI: 10.1177/0333102419893823
5. Headache Classification Committee of the International Headache Society (HIS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. (2018) 38:1–211. 10.1177/0333102417738202 - DOI - PubMed
6. Rozen TD. Trigeminal neuralgia and glossopharyngeal neuralgia. Neurol Clin. 2004;22:185.
7. Horowitz M, Horowitz M, Ochs M, Carrau M, Kassam A. Trigeminal neuralgia and glossopharyngeal neuralgia: Two orofacial pain syndromes encountered by dentists, J Am Dent Assoc, 2004;135(10):1427-33.
8. Rushton JG, Stevens JC, Miller RH. Glossopharyngeal (vagoglossopharyngeal) neuralgia: a study of 217 cases. Arch Neurol. 1981;38:201.
9. Nieuwenhuys R, Voogd J, Huijzen C. The human central nervous system. 2008, Berlin; New York: Springer.
10. Kandan SR, Khan S, Jeyaretna DS, Lhatoo S, Patel NK, Coakham HB. Neuralgia of the glossopharyngeal and vagal nerves: long-term outcome following surgical treatment and literature review. Br J Neurosurg. 2010;24(4):441—6. doi:10.3109/02688697.2010.487131. Review.
11. Elias J, Kuniyoshi R, Carloni WV, et al. Glossopharyngeal neuralgia associated with cardiac syncope. Arq Bras Cardiol. 2002;78:510.
12. Fini G, Gasparini G, Filippini F, et al. The long styloid process syndrome or Eagle's syndrome. J Craniomaxillofac Surg. 2000;28:123
13. Soh KB. The glossopharyngeal nerve, glossopharyngeal neuralgia and the Eagle's syndrome- current concepts and management. Singapore Med J. 1999;40:659.
14. Kim E, Hansen K, Frizzi J. Eagle syndrome: case report and review of the literature. Ear Nose Throat J. 2008;87:631.
15. May A. Update on the diagnosis and management of trigemino-autonomic headaches. J Neurol. 2006;253(12):1525-32.
16. Šklebar D, Šklebar I, Cesarik M, Barada A, Maletić A. Neuropathic orofacial pain – diagnostic and therapeutic challenges. Periodicum biologorum. 2015;117(2):231-237.
17. Bruynn GW. Glossopharyngeal neuralgia. Cephalalgia.1983;3:143
18. American Academy of Orofacial Pain. In: Orofacial Pain: Guidelines for Assesment, Diagnosis and Management, 4th ed. de Leeuw R, editor. Chicago; Quintessence Publishing; 2008.
19. Šklebar D, Šklebar I. Bolna neuropatija lingvalnog živca. Acta medica Croatica. 2019;73(Suplement 1):83-86.
20. Liu Q, Zhong Q, Tang G, He G. Ultrasound-guided glossopharyngeal nerve block via the styloid process for glossopharyngeal neuralgia: a retrospective study. J Pain Res. 2019 Aug 8;12:2503-2510. doi: 10.2147/JPR.S214596. PMID: 31496791; PMCID: PMC6690851.
21. Sampson JH, Grossi PM, Asaoka K, Fukushima T. Microvascular decompression for glossopharyngeal neuralgia: long-term effectiveness and complication avoidance. Neurosurgery. 2004 Apr;54(4):884-9; discussion 889-90. doi: 10.1227/01.neu.0000114142.98655.cc. PMID: 15046654.
22. Shah RJ, Padalia D. Glossopharyngeal Neuralgia. 2022 Feb 17. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 31082085.
23. Singh PM, Kaur M, Trikha A. An uncommonly common: Glossopharyngeal neuralgia. Ann Indian Acad Neurol. 2013 Jan;16(1):1-8. doi: 10.4103/0972-2327.107662. PMID: 23661955; PMCID: PMC3644765.

Sažetak

INERVACIJSKO PODRUČJE GLOSOFARINGEALNOG ŽIVCA KAO ISHODIŠTE OROFACIJALNE BOLI- DIJAGNOSTIČKI I TERAPIJSKI IZAZOV

D. Šklebar, L. Vučemilo i T. Šklebar

Kronična neuropatska orofacijalna bol uz fizičku patnju može uzrokovati emocionalne, psihičke i socijalne poteškoće, što značajno utječe na kvalitetu života bolesnika. Bol u inervacionom području glosofaringealnog živca, osobito kronična neuropatska, relativno je rijetka, ali je značajna zbog velike patnje koju može uzrokovati oboljelima. Istodobno, može biti životno ugrožavajuća, zbog srčane aritmije, sinkope ili konvulzija koje može uzrokovati. Medikamentno liječenje je često ograničene učinkovitosti i može biti opterećeno nuspojavama. Neophodno je tragati za etiologijom poremećaja, te po mogućnosti poduzeti adekvatno kauzalno liječenje. Ovaj pregledni članak govori o etiologiji, kliničkim značajkama, diferencijalnoj dijagnostici i modalitetima liječenja kronične neuropatske boli koja potječe iz inervacionog područja glosofaringealnog živca.

Ključne riječi: *orofacijalna bol, glosofaringealni živac, vagoglosofaringealna neuralgija, glosofaringealni blok*