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A Game Changer in Neuro-modulation: The Power of Sphenopalatine Ganglion From Autonomic Control to Therapeutic Potential

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Abstract
Inflammatory brain diseases of the central nervous system occurs for a variety of reasons. Primary processes are due to a malfunction of the immune system and / or neurogenic inflammation, such as what happens in vasculitis, multiple sclerosis, antibody-mediated inflammatory brain diseases, and acute disseminated encephalomyelitis. Secondary inflammatory diseases occur secondary to infection such as what happens in meningitis.
Inflammation of the brain can be presented with stroke, dizziness, headache, ataxia, parathesia, visual or speech impairment, memory loss, or decreased alertness. It can also be presented with changes in behavior, mood swings, or different psychiatric symptoms.
The sphenopalatine (SP) ganglion is considered one of the largest neuron collection in the head outside of the brain, being exposed to the environment via the nasal mucosa. It is the largest of the four parasympathetic gangliae associated with the trigeminal nerve. Over the years, pain management specialists have showed that cauterization, phenolization, or irrigation of the SP ganglion with lidocaine was effective in the treatment of headache or refractory facial pain. Although this ganglion is a very little-known region in the face, it is a very effective tool in the treatment of many conditions due to its particular anatomic place and its special nerve fibers, and because it has a peculiar connection with the higher centers of the brain.
The role of neurogenic inflammation in the pathogenesis of neurological diseases has gained increasing attention with a particular focus on its effects on modulation of the blood-brain barrier. The neuropeptide substance P has been shown to increase blood-brain barrier permeability and is associated with marked cerebral edema. Accordingly, blocking substance P transient receptor potential vanilloid type 1 ion channels may provide a novel alternative treatment to ameliorate the deleterious effects of neurogenic inflammation in the central nervous system.
Methods: *In this paper, irrigation of the SP ganglion with buffered dextrose in 5% concentration has been applied in order to treat many conditions such as depression, anxiety, stress, brain fogue, fibromyalgia, myasthenia gravis, multiple sclerosis, facial palsy, optic neuritis, optic nerve perineuritis, ocular pain, headache, migraine, trigeminal neuralgia, neck pain, shoulder pain, arm pain, gait problem and lower limbs weakness after neck surgery, epiphora, blepharospasm, allergic rhinitis, allergic*

conjunctivitis, and follicular conjunctivitis.
Conclusions: *Treating patients suffering from all of the above mentioned conditions with irrigation of the SP ganglion using buffered dextrose in 5% concentration has shown that this novel approach achieved a very good improvement, and that it was very effective regarding the signs and symptoms of all the patients. After the treatment, Optic nerve CT study became normal regarding the signs of optic nerve perineuritis, and MRI studies of the brain and cervical spine became normal regarding the signs of multiple sclerosis.*
Keywords: *Sweet nasal irrigation treatment, Lyftogt perineural injection treatment, inflammatory brain disease, optic neuritis, optic peri-neuritis, headache, migraine, multiple sclerosis, fibromyalgia, dextrose.*

Introduction

The sphenopalatine (SP) *"pterygopalatine"* ganglion of Meckel is the largest of the parasympathetic gangliae associated with the branches of the maxillary nerve, and it is deeply located in the pterygopalatine fossa behind the middle turbinate of the nose, close to the SP foramen. It is triangular or heart-shaped, of a reddish-gray color, and it is situated just below the maxillary nerve as it crosses the fossa[1].

SP ganglion receives a sensory, a parasympathetic and a sympathetic root. Its sensory root is derived from two sphenopalatine branches of the maxillary nerve; their fibers, for the most part, pass directly into the palatine nerves; a few, however, enter the ganglion, consisting its sensory root. Its parasympathetic pre-ganglionic nerve fibers come from the greater superficial petrosal nerve from the superior salivatory nucleus in the pons, which traverse via the nervous intermedius of the facial nerve. The post-ganglionic axons (vasodilator and secretory fibers) are distributed with the deep branches of the trigeminal nerve to the lacrimal gland, the glands of the mucosa of the nasal cavity, paranasal sinuses, hard and soft palate, tonsils, uvula, roof of the mouth, lips, gums and upper part of the pharynx. Its sympathetic post-ganglionic fibers come from T1 – T3, they synapse at the superior cervical sympathetic ganglion, then the post-ganglionic fibers, along the internal carotid artery, enter the skull as the deep petrosal nerve that traverses through the pterygoid canal as the Vidian nerve, and reaches the pterygopalatine fossa[2].

The SP ganglion has been associated with a wide variety of pain problems that range from pain in the head and neck - such as trigeminal neuralgia[3], temporomandibular joint pain[3], SP neuralgia, migraine headaches, cluster headaches, atypical facial pain[4], cancer pain of the head and neck, tongue pain, gum and mouth pain, teeth pain, Sluder's neuralgia[5], paroxysmal hemicranias[6], post-herpetic neuralgia[6], herpes zoster[7], vasomotor rhinitis, complex regional pain syndrome (CRPS), post-traumatic headache [8][9][10] - to low back pain[11].

Beginning with the early part of the 20th century, Sluder reported the first case of headache being relieved by SP ganglion block with local anesthetic. Patients with chronic recurring head and facial pain were treated with intranasal phenolization or cauterization of the SP ganglion for the treatment of Sluder's neuralgia with 90% relief from their pain[12][13].

The brain itself is not sensitive to pain, because it lacks pain receptors. However, several areas of the head and neck do have pain receptors and can thus sense pain. These include the extra-cranial arteries, middle meningeal artery, large veins, venous sinuses, cranial and spinal nerves, head and neck muscles, meninges, falx cerebri, parts of the brainstem, eyes, ears, teeth and lining of the mouth[14].

Headaches often result from traction to or irritation of the meninges or blood vessels. Blood vessels spasm, dilated blood vessels, inflammation or infection of the meninges and muscular tension can stimulate nociceptors and cause pain[15]. Once stimulated, a nociceptor sends a message up the

length of the nerve fiber to the nerve cells in the brain, signaling that a part hurts.

The sensory innervation of the meninges is primarily by meningeal branches of both the trigeminal and vagus nerves with a smaller contribution from the upper cervical spinal nerves[16][17][18].

Optic nerve is the second of twelve paired cranial nerves and is technically part of the central nervous system. The optic nerve is en-sheathed in all three meningeal layers (dura, arachnoid, and pia mater) rather than the epineurium, perineurium, and endoneurium found in peripheral nerves[19]. The reason for the optic neuritis[20] is unknown, but an explanation could be that sometimes the immune system attacks the fatty coating called myelin that covers and protects the optic nerve fibers. When the myelin is damaged or missing, the optic nerve can't send the right signals to the brain and this can lead to changes in the vision[21].

Optic nerve peri-neuritis is an uncommon variety of idiopathic orbital inflammatory disease in which the specific target tissue is the optic nerve sheath. It is distinct from demyelinating optic neuritis and it occasionally occurs as a manifestation of a specific infectious or inflammatory disorder, such as Wegener granulomatosis or giant cell arteritis[22].

The trigeminal nerve (the fifth cranial nerve) is a nerve responsible for sensation in the face and motor functions such as biting and chewing. It is the largest of the cranial nerves, as its name (tri = three, and geminal = twice or twinned). Each nerve has three major divisions: ophthalmic (V_1), maxillary (V_2), and mandibular (V_3). The ophthalmic and maxillary are purely sensory, while the mandibular division is a mixed nerve having motor as well as sensory functions[18].

The conjunctiva lines the inside of the eyelids and covers the sclera. It is highly vascular and its sensory innervations come from different branches of the ophthalmic and maxillary divisions of the trigeminal nerve [23].

In contrast to motor, sensory and autonomic nervous system, there exists another nervous system distributed all over the body, representing 50% of the somato-sensory system, and consists of the small nervi-nervorum which are responsible for the intero-ceptive sensation, and can at each instant detect, respond and equilibrate the homeostasis of the internal micro-environmental atmosphere. These nervi-nervorum carry the transient receptor potential vanilloid type 1 (TRPV1) ion channels which are trans-membrane, non-specific, polymodal channels capable of sensing the mechanical, thermal, metabolic and chemical variations in oxygen, glucose, pH, and osmolarity [24].

TRPV1 agonists lead to: (1) Influx of Na+ and efflux of K+, resulting in spike formation and propagation of action potential *"neuropathic pain"*. (2) Influx of Ca2+ which is toxic to mitochondria, and it also results in the release of pro-inflammatory neuro-peptides such as Calcitonin Gene Related Peptide (CGRP) and substance P from schwann cells, as well as Nitric Oxide (NO), Vasoactive Intestinal Polypeptide (VIP), Neurokinin A and 5-Hydroxytriptamine, while the release of the anti-inflammatory neuropeptides and growth factors such as galanin and somatostatin is inhibited *"neurogenic inflammation"*[24].

Substance P causes: (1) Vasodilatation of the post-capillary venules and tissue oedema, (2) Chemo-attraction and activation of the immune cells, (3) Mast cell degranulation, (4) Depression through its action on the amygdala, (5) Release of the corticotrophic releasing hormones in the hypothalamus and upregulates the hypothalamic axis stress response, (6) Exhaustion (depletion of dehydroepiandrosterone), (7) Sensitisation of TRPV1 in channels leading to allodynia and hyperalgesia.

CGRP causes: (1) Vasodilatation of the pre-capillary arterioles, (2) Up-regulation of the Vascular Endothelial Growth Factor (VEGF) causing neo-vascularisation and neo-angiogenesis, (3) Up-regulation of matrix metalloproteinase1 leading to collagenolysis, (4) Stimulation of osteoclasts leading to increase bone resorption, stress fractures and tissue calcification.

TRPV1 antagonists such as capsaicin and buffered dextrose (glucose) in low concentration (5% dextrose), inhibit and down-regulate the TRPV1 ion channels, thus treating the neurogenic inflammation and stopping the neuropathic pain.
Microglial activation is similar to that which occurs in peripheral macrophages during inflammatory attack, it was first demonstrated in Alzheimer's Disease (AD)[25].

Parkinson's Disease (PD) is the second most common central neuro-degenerative disorder among elderly population, and it is depicted by a progressive degeneration of the dopaminergic neurons in the midbrain [26].

Low-grade chronic inflammation of the brain seems to play a key role in mediating the interface between psychological stress, depressive symptomatology, altered intestinal microbiology, Major Depressive Disorder (MDD), and other psychiatric disorders with neuro-inflammatory components [27].

Patients and Methods

Optic neuritis: A 32 years old female suddenly developed severe migraine and visual impairment of her left eye (day 1).
Brain MRI and Visual Evoked Potential (VEP) studies revealed (day 29):

1. Normal brain MRI study.
2. VEP pattern according to ISCEVs standards revealed that both eyes showed well formed response with average implicit time on two different size stimuli with reduced amplitude in the left eye compared to the right eye (OD: 90,97ms and OS: 95,98ms), denoting affection of conduction in visual pathway. The impression was that the right eye was within normal optic nerve function and the left eye showed an attack of optic neuritis.

Irrigation treatment of the SP ganglion was done (day 30, 31, 32, 34), using the sweet solution of buffered dextrose in 5% concentration (buffered dextrose solution is obtained by adding 2.5 ml of 8.4% of sodium bicarbonate to a 500 ml bottle of dextrose 5% concentration). The treatment was performed as follows:

1. Patient lays down in supine position with a hyper-extended neck out of the bed, having the head resting on a small tabouret.
2. Instruct the patient to breath from the mouth (not from the nose).
3. Install 10 – 20 ml of dextrose solution in each nostril, and the patient stays in this position for 15 - 20 minutes.
4. Patient gets up with the head looking to the side, while leaning forward and downward.

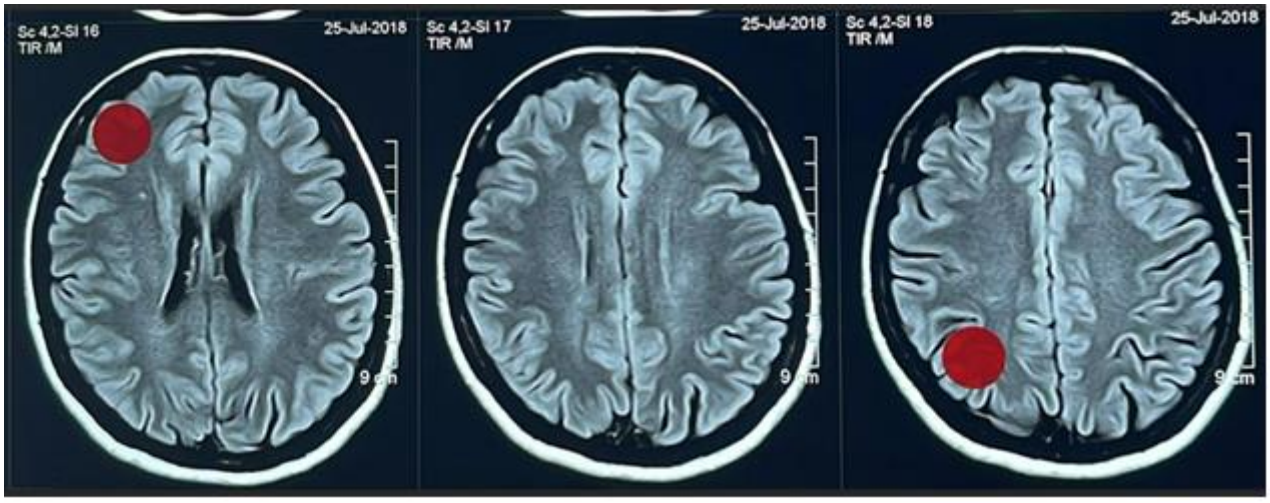
VEP was redone (day 34) at the same center, with the same person and same machine, and the VEP pattern according to ISCEVs standards revealed that the left eye showed well formed response with average implicit time on two different size stimuli (OS: 96,98ms), and improved amplitude compared to the first visit denoting good conduction in visual pathway. The impression was that the VEP response showed improved amplitude compared to the first visit returning to normal limits (resolved attack of optic neuritis).

Optic nerve peri-neuritis: in 2018, a 38 years old female suddenly developed a vision of a white cloud in the upper medial quadrant of the field of

vision of her right eye with occasional migraine and ocular pain (day 1).

Field of vision, optic nerve CT study, and MRI of the brain and cervical spine were done (day 7), they revealed:

1. Central 24-2 threshold test revealed a normal visual field finding.
2. Optic nerve CT (OCT) assessment of RNFL and Optic Nerve Head (ONH) was done. Optic disc scan 200 × 200 was performed and the impression was that the right eye showed a focal decrease of RNFL involving the nasal quadrant, with normal rim area and vertical C/D ratio = 0.31 within normal GCL analysis in all quadrants.
3. MRI of the brain and cervical spine was performed on a high field MR unit, and multiple pulse sequences were obtained before and after IV contrast injection. Findings revealed few subtle small sub-centimetric lesions within the deep cerebral white matter particularly on the right side, best seen on the FLAIR sequence, and with no corresponding post contrast enhancement to suggest activity by this criteria (red tags as representative).



4. As regards the cervical spine, and particularly the cervical spinal cord, findings revealed a suspected tiny similar lesion opposite C4 – C5 disc (red tag as representative), with otherwise, no similar cord lesions to suggest other demyelinating plaques at the scanned part of the cord.

The overall data was suggesting mild form or primary demyelinating disease with special attention to multiple sclerosis.

The patient was treated with the same treatment as described before (day 9, 17, 18, 19, 22, 23, 24).

OCT of RNFL and ONH was redone (day 25), at the same hospital and with the same machine. Optic disc scan 200 × 200 was performed and the impression was that the right eye showed normal RNFL thickness in all the quadrants with normal rim area and vertical C/D ratio = 0.34, temporal RNFL increased by 8um as compared to the previous scans.

MRI of the brain and cervical spine was redone after two years, in 2020, at the same hospital and with the same machine, and the study showed that there were no changes regarding the signs of multiple sclerosis, the findings in MRI of the brain and cervical spine were same as those found in 2018. The patient repeated again the same treatment of SP ganglion irrigation with buffered dextrose (treatment was done once a week for two months, then treatment was repeated once a month for six months). MRI of the brain and cervical spine was redone in 2024, at the same hospital and with the same machine, and the study revealed normal MRI of the brain and cervical spine, with no signs of multiple sclerosis.

Same method of SP irrigation using buffered dextrose in 5% concentration was applied once a week for patients with different conditions, and they reported:

Blepharospasm: One patient with idiopathic eye lid tremors started noticing a decrease in the frequency and intensity of the tremors in her eye lid after the first treatment, till they almost disappeared after 9 treatments.

Allergic conjunctivitis: Two patients with red itchy eyes started having non-itchy eyes with white sclera after 2 – 3 treatments.

Epiphora and Allergic Rhinitis: Two patients with increased eye lacrimation and tearing started noticing a decrease in their symptoms after the

first treatment. One of them had allergic rhinitis and she used to sneeze a lot, she started noticing a decrease in her symptoms regarding the itchiness in her nose, and she started having a less runny nose and less sneezing time after 3 treatments.

Ocular pain: Two patients with ocular pain reported a decrease in their pain level after 2 – 3 treatments.

Headache: Three patients suffering from headache (1 with and 2 without facial pain), reported no headache and no facial pain after 1- 3 treatments.

Migraine: Four patients with migraine, after 1 – 4 treatments, reported no migraine for three out of four patients. The forth patient, after the 4th treatment, reported one very mild short attack of migraine which resolved with a 1000 mg of acetaminophen.

Conclusion

Irrigation of SP ganglion is a very effective treatment and gives marvelous results for patients suffering from optic neuritis, optic nerve perineuritis, fibromyalgia, and multiple sclerosis. It is also a very strong and effective treatment for patients with headaches, migraines, facial pain, chronic sinusitis, snoring, ear tinnitus, eye lacrimation and dizziness. It is very promising in the treatment of neck, shoulder and arm problems.

SP irrigation is the challenging ease that solved the unsolved gait, back and lower limbs problems secondary to neck problems.

Irrigation of the SP ganglion is a very powerful technique in the treatment of the hard and serious problems that were not treated completely in the past. It is very promising in the Regenerative Medicine and therefore more research work is needed in the treatment field of the high cognitive functions of the brain, strokes, memory problems, mood stabilization, dementia, ataxia, Parkinson's, Alzhimer's and psychiatric diseases.

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