

Treatment of Trigeminal Neuralgia Utilizing Neural Prolotherapy: A Case Report

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ABSTRACT

Neural prolotherapy, as developed by Jon Lyftogt, has been found to be an effective treatment for neurogenic pain syndromes. We report a case of trigeminal neuralgia successfully treated with neural prolotherapy. The patient is a 70-year-old man with a 15-year history of trigeminal neuralgia refractory to pharmacologic treatment. After one treatment of neural prolotherapy the patient reported 5 months of complete resolution of his symptoms. A second treatment was performed affording him another 10 months of relief. Neural prolotherapy may have an important role in treating trigeminal neuralgia. It can be a safe and effective treatment for those experiencing side effects from medications, contraindications to surgery, or less than favorable improvement from traditional treatments.

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KEYWORDS: facial pain, allodynia, chronic constriction injury, lyftogt perineural injection treatment, tic douloureux, trigeminal neuralgia, neural prolotherapy, neuralgia, neurogenic inflammation, TRPV1, 5% dextrose.

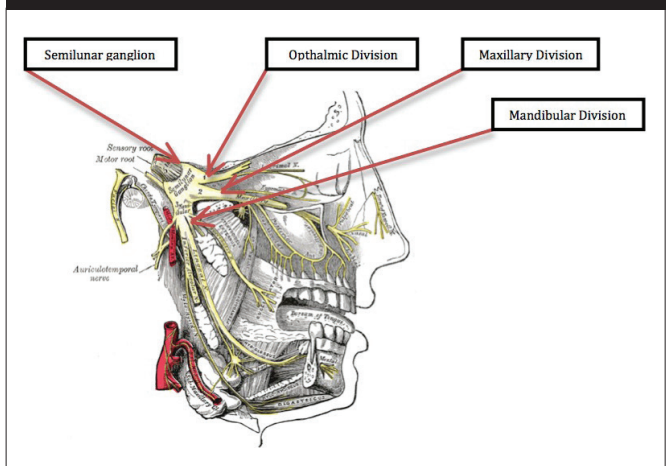
Background

Neural prolotherapy, as developed by Jon Lyftogt, has been found to be an effective treatment for neurogenic pain syndromes. Neural prolotherapy, now known as Lyftogt Perineural Injection Treatment™, involves injecting a 5% dextrose or mannitol solution around subcutaneous nerves.¹ The procedure is typically performed with a 27 gauge 1/2 inch needle. Approximately 1-2cc of solution is injected into each site. The number of injections varies with the area and symptoms to be treated. The theory behind the effectiveness of this treatment involves the effect of glucose on the capsaicin receptor TRPV1. When activated, the TRPV1 receptor mediates the release of inflammatory chemicals from the neuron. It has been hypothesized that glucose and mannitol bind to the TRPV1 receptor, inhibit its function, and restore normal nerve function.¹⁻⁴

Anatomy of the Trigeminal Nerve

The trigeminal nerve is the largest cranial nerve. It primarily supplies sensory information to the face and motor control to the muscles of mastication. The nerve forms the semilunar ganglion in a cavity of the dura mater near the apex of the petrous part of the temporal bone. The nerve then divides into three major components named the ophthalmic, maxillary, and mandibular divisions. The ophthalmic division supplies sensory information to the mucous membrane of the nasal cavity, skin of the eyelids, eyebrow, forehead and nose. The maxillary division supplies the mid-face, maxillary teeth, lower eyelid and upper lip. The mandibular division supplies the teeth and gums of the mandible, the skin of the temporal region, the skin of the outer ear, lower lip, lower part of the face, mucous membrane of the anterior two thirds of the tongue, and the muscles of mastication.

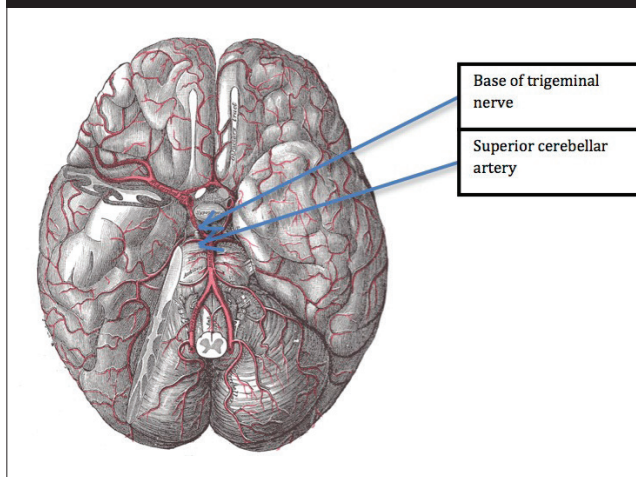
Figure 1. Anatomy of the trigeminal nerve and its division into its 3 major branches.⁵



Pathophysiology of Trigeminal Neuralgia

Trigeminal Neuralgia is divided into 2 categories, classic and symptomatic. The classic form, which is considered idiopathic, includes cases due to a normal artery present in contact with the nerve. The artery may compress the nerve resulting in focal trigeminal nerve demyelination.⁶ The symptomatic form can be due to aneurysms, tumors and chronic meningeal inflammation. An abnormal vascular course of the superior cerebellar artery is often cited as the cause.⁶

Figure 2. Notice the location of the superior cerebellar artery in relation to the trigeminal nerve. An elongated loop of the artery may compress the nerve leading to the symptoms of trigeminal neuralgia. Surgical microvascular decompression may relieve compression of the nerve in this area.⁷



Trigeminal Neuralgia and TRPV1

In a study by Urano et al., rats were subjected to partial infraorbital nerve ligation to mimic the nerve damage seen in trigeminal neuralgia. The goal was to induce heat and mechanical sensitivity and evaluate the effectiveness of a TRPV1 antagonist in reducing this sensitivity. This study found that heat hyperalgesia was decreased with TRPV1 antagonism and that TRPV1 expression in large neurons in the trigeminal ganglia was increased. They concluded that these findings may play

an important role in developing and maintaining heat hyperalgesia induced by trigeminal neuropathic pain.⁸ It is hypothesized that TRPV1 expression mediates the release of pro-inflammatory chemicals seen in neurogenic inflammation. These include CGRP and Substance P. In a study conducted by Meng et al., it was found that TRPV1 stimulation mediated the release of CGRP. Another study by Murata found that TRPV1 of corneal neurons in mice works in close relationship to Substance P and CGRP both in the cornea and CNS for healing and nociceptive transduction.⁹

Symptoms of Trigeminal Neuralgia

Trigeminal Neuralgia is characterized by several symptoms. The condition is severely painful. The IASP (International Association for the Study of Pain) defines trigeminal neuralgia utilizing the characteristics seen in *Table 1*. Patients typically complain of unilateral, sharp, stabbing, burning, superficial pain. The pain is brief lasting seconds to 2 minutes. Allodynia and trigger zones may be seen. Behaviors such as eating talking, washing the face, brushing teeth and smoking may provoke symptoms. Interestingly, sensation to the face typically remains intact.

Table 1. IASP definition of Trigeminal Neuralgia.²

	IASP definition of Trigeminal Neuralgia
Site	Unilateral
Quality of pain	Sharp, stabbing, burning, superficial
Duration of pain	Brief
Duration of paroxysms	Seconds to 2 minutes
Refractory period	Yes
Continuous pain	No
Allodynia	Limited trigger zones
Associated features	Slight flush
Radiation	None outside affected division
Provoking factors	Eating, talking, washing face, brushing teeth, smoking
Variability of pain	Stereotyped
Sensory loss	None
Pain behavior	Not discussed
Course of pain	Spontaneous remissions

Case Presentation

HISTORY:

A 70-year-old male presented to our PM&R clinic referred by his allergist for evaluation and treatment of trigeminal neuralgia. The patient was first seen in our clinic in January 2012. He reported a history of facial bone fractures in 1983 with no subsequent symptoms of trigeminal neuralgia. He reported having root canals complicated by infections several years prior to the onset of trigeminal neuralgia. His diagnosis of trigeminal neuralgia was made by a neurologist prior to being seen in our clinic. At the time of his initial visit, the patient was being treated with carbamazepine and lamictal. The patient complained of severe, sharp, stabbing pains on the right side of his face involving the mandibular, maxillary and ophthalmic branches of the trigeminal nerve. He also noted severe pain when trying to brush his teeth.

PHYSICAL:

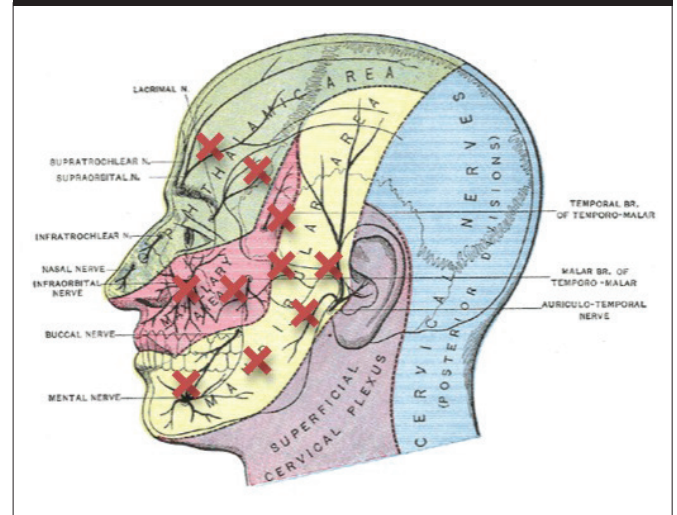
Examination showed no focal neurologic deficits. There were dysesthesias and allodynia along the maxillary and ophthalmic branches of the trigeminal nerve. Throughout the visit the patient did have a characteristic “tic” every 1-2 minutes due to the lancinating pain of trigeminal neuralgia. We elected to proceed with a neural prolotherapy treatment. Prior to the procedure the patient was given a cotton swab to rub against his gums and teeth to reproduce some of his pain and sensitivity. This was done to obtain a baseline of his pain prior to the procedure.

TREATMENT:

The patient was then placed in the left lateral decubitus position and the right side of the face was treated utilizing a neural prolotherapy technique. Approximately 15 injections were provided to the distribution of the 3 involved branches of the trigeminal nerve. A 27 gauge 1/2 inch needle was used to inject a 5% dextrose solution into the subcutaneous tissues. Approximately 1-2cc was injected in each area. After the procedure, the patient was instructed to utilize the cotton swab to try and reproduce his symptoms. The patient was unable to reproduce any of the pain and sensitivity that was present prior to the procedure. The patient was observed in the clinic for 15 minutes and had no “tics” from trigeminal neuralgia. The

patient was instructed to follow up in 1 week however the patient did not return until 6 months later.

Figure 3. Approximate sites of injection performed on the patient described in this case report. Each injection site is depicted by a red X.⁵



SIX MONTH FOLLOW UP:

At this visit, the patient reported that the neural prolotherapy treatment provided him with 5 months of complete resolution of his symptoms. He stated that his symptoms only returned after hitting his head when exiting his car. His complaints at this time involved severe, sharp stabbing pain in the right forehead, right eyeball, periorbital region and right temple. He complained of pain when getting a haircut, he found that just simply touching his hair and scalp caused him severe pain.

TREATMENT #2:

The patient was given a second treatment of neural prolotherapy along the course of the trigeminal nerve. The same technique as the first treatment was utilized. The patient again noted immediate complete resolution of his pain. The patient was again instructed to follow up in 1 week however the patient did not return until 10 months later.

FOLLOW UP AT 10 MONTHS POST 2ND INJECTION:

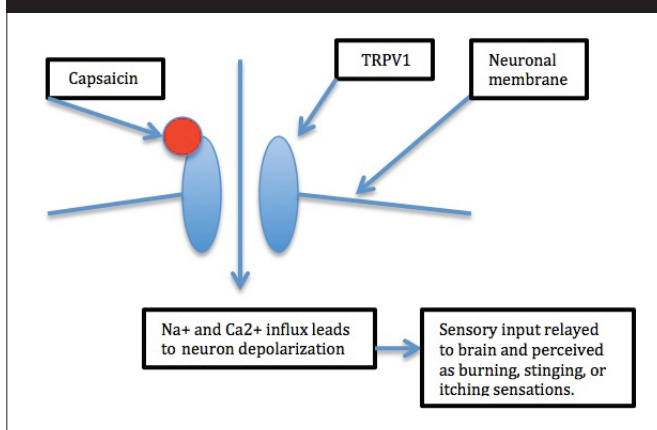
At this visit the patient reported relief of his symptoms during the 10 month time period. Unfortunately, at this visit he returned due to another head injury that aggravated his symptoms. This head injury was more

concerning than in the past and the patient had suffered a concussion. The treatment was modified at this point and the patient received an ultrasound guided occipital nerve block. The relief was short lived however, lasting only a couple of days. The patient had resumed follow up with his neurologist who referred him to a neurosurgeon. Once evaluated by the neurosurgeon it was decided that microvascular decompression of the trigeminal nerve be performed. After this procedure, the patient noted complete resolution of his trigeminal neuralgia. I was able to see the patient at the time of writing this case report, about 2 years post-op, and he was able to confirm that he has not had any recurrence of symptoms to date.

Discussion

The concept of neurogenic inflammation and its relationship with TRPV1, CGRP and substance P has been researched.^{2,10,11} The article titled, The Concept of Neurogenic Inflammation, in BJU International explores the connection between TRPV1, CGRP and substance P in neurogenic inflammation. It is primarily understood that inflammatory mediators are released from afferent neurons. Some of these inflammatory mediators include substance P and Calcitonin Gene-Related Peptide (CGRP).²

Figure 4. Capsaicin is shown to be an activator of TRPV1. Notice that TRPV1 is located on the neuronal membrane. Once activated, sensory input is relayed to the brain where it is perceived as burning, stinging, or itching sensations.¹²

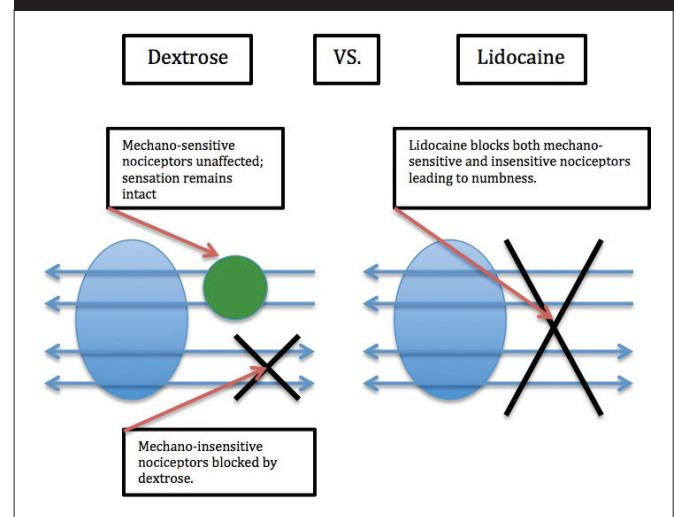


A research study performed by Jansco in 1967 provided evidence for neurogenic inflammation. The study found that antidromic electrical stimulation of sensory nerves (saphenous or trigeminal) of rats elicited signs of an

inflammatory response. These included vasodilatation, enhancement of vascular permeability, protein exudation, fixation of injected colloidal silver onto the walls of venules and, later, their storage in histiocytes. They also found that capsaicin did not evoke inflammation after degeneration of the sensory nerve. In addition to this, capsaicin desensitization inhibited the signs of inflammation induced both by antidromic stimulation of the sensory nerve and by orthodromic stimulation of pain sensitive nerve terminals with irritants.¹¹

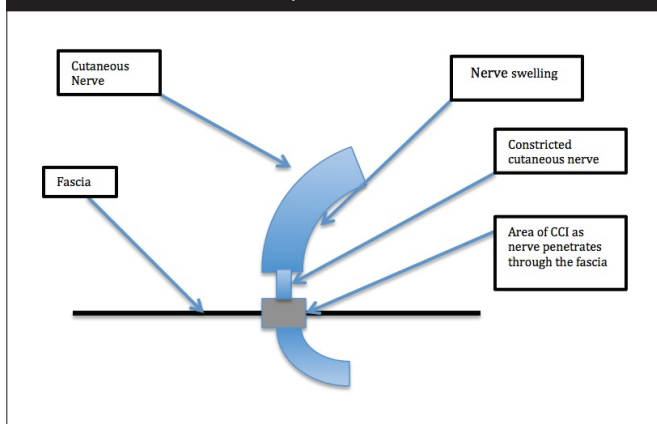
Another study, by Simone et al., found that intradermal injections of capsaicin in humans resulted in primary hyperalgesia to heat and mechanical stimuli.¹⁰ This study shows a direct connection between capsaicin TRPV1 agonism and hyperalgesia. This suggests that antagonism of TRPV1 with neural prolotherapy may reduce symptoms of hyperalgesia and/or nociception. The proposed theory also states that dextrose may down regulate TRPV1 receptors.

Figure 5. On the left: Effect of dextrose on TRPV1 receptor. Notice that dextrose blocks nociceptive pain. Sensation to touch remains intact as opposed to lidocaine. On the right: Effect of lidocaine on the TRPV1 receptor. All pathways are blocked by lidocaine leading to numbness.¹³



In addition to neurogenic inflammation, a localized injury to cutaneous nerves can occur at points where cutaneous nerves pass through fascial layers. These are referred to as chronic constriction injury points (CCIs). CCIs occur due to the fact that the nerve may become constricted at certain points along its course. The points are thought to inhibit the flow of nerve growth factor. It is essential for nerve health to have proper flow of nerve growth factor.³

Figure 6. Simple depiction of a CCI. Notice the constriction of the cutaneous nerve as it penetrates the fascia.³



Neural Prolotherapy is hypothesized to be effective for treating neurogenic inflammation. It is also thought to be effective in relieving the constriction of nerves at CCIs. Its effects seem to be appreciated quite rapidly. In the case above immediate resolution of neurogenic pain was seen after each treatment.

Similar reports of substantial relief of trigeminal neuralgia have been seen. This was explained in a case report by Eileen Conaway, DO and Brian Browning, DO titled Neural Prolotherapy for Neuralgia published in the *Journal of Prolotherapy*. Their case involved a 63 year old female with 13 years of burning facial pain involving the forehead and scalp. She was treated with neural prolotherapy. The first 2 injections were performed 1 week apart and the third injection 12 weeks later. They found her pain progressively reduced after each treatment. After 3 treatments she had complete resolution of her pain. They also found that at 1 year post injection the patient continued to have no symptoms.⁴

While there are well-accepted pharmacologic and surgical treatments for trigeminal neuralgia, neural prolotherapy may be of benefit in certain circumstances. Many of the medications used in the treatment of trigeminal neuralgia cause significant side effects. Neural prolotherapy may serve as a stand alone or adjunctive treatment to either reduce or eliminate the need for medications. Further, some patients may wish to avoid surgery and pursue less invasive treatment. Other patients may be high-risk surgical candidates or have contraindications to surgery. For those with some of the above described issues, neural prolotherapy may prove to be a safe and effective treatment option for trigeminal neuralgia. ■

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