



Acupuncture in Conjunction with Drug Therapy in the Treatment of Glossopharyngeal Neuralgia

Dominic P Lu^{1,2*}, Gabriel P Lu^{3,4}, and Ping-Shi Wu⁵

¹Clinical Professor of Oral Medicine, Course Director, Selective Program in Pain and Anxiety Control, School of Dental Medicine, University of Pennsylvania, USA

²President, American Society for the Advancement of Anesthesia in Dentistry, Teaching Staff, Saint Joseph's Regional Medical Center-New York Medical College, USA

³Professor of Clinical Anesthesiology, Albert Einstein College of Medicine, USA

⁴Director of Acupuncture Clinic, Montefiore Medical Center, USA

⁵Associate Professor of Biostatistics, Lehigh University, Bethlehem, USA

Abstract

In this study, 35 patients who suffered from glossopharyngeal neuralgia and received acupuncture with drug therapy were divided into 4 groups according to the medication they were prescribed to take. Those who took phenytoin were placed in Group I, those took gabapentin were in Group II, those who took carbamazepine were categorized as Group III, and those took amitriptyline and gabapentin belonged to Group IV. All patients received 4 sessions of acupuncture treatments. The clinical effect of combining acupuncture and drug therapy were biostatistically compared both pre- and post-operatively and between the acupuncture sessions. The authors found that the combination of drug therapy and acupuncture yielded a better clinical outcome than if acupuncture or drug therapy was solely used. Phenytoin, carbamazepine, gabapentin, and amitriptyline with gabapentin are usually the drugs of choice when treating the ailment of glossopharyngeal neuralgia. Phenytoin seemed to have better patients' acceptance perhaps because it has the advantage of keeping the patient relatively lucid after treatment. Drug therapy or acupuncture alone can benefit patients, but the success of the treatment outcome was shown to be limited. The treatment outcome using the combination regimen was much better, resulting in less recurrence and lower pain intensity during episodes of attack.

Keywords

Glossopharyngeal neuralgia, Acupuncture, Phenytoin, Carbamazepine, Gabapentin, Amitriptyline

Introduction

Combining acupuncture and drug therapy for the treatment of orofacial pain may result in significant reduction of pain [1]. Affecting the left side of the face more often than the right, glossopharyngeal neuralgia appears similar to Tic douloureux but mainly involves cranial nerve IX. The pain is excruciating, characterized by stabbing paroxysms, developing after the stimulation of a trigger zone located in the tonsil region or throat [2]. Swallowing may stimulate an attack. Pain evolves from the base of the tongue, or in the pharynx, and radiates outward to the ear. Other signs, such as coughing and even syncope, may appear during an attack [3].

The paroxysmal attacks are stimulated by chewing, swallowing, coughing, talking, yawning, or sneezing. The pain,

lasting seconds to a few minutes, usually begins in the tonsillar region or at the base of the tongue and may radiate to the ipsilateral ear. Occasionally, increased vagus

***Corresponding author:** Dominic P Lu, DDS, Clinical Professor of Oral Medicine, Course Director, Selective Program in Pain and Anxiety Control, School of Dental Medicine, University of Pennsylvania, USA; President, American Society for the Advancement of Anesthesia in Dentistry, Teaching Staff, Saint Joseph's Regional Medical Center-New York Medical College, USA, Tel: +610-298-8805, Fax: +610-395-8093, E-mail: dominicplu@gmail.com

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nerve activity causes sinus arrest with syncope; episodes may occur daily or once every few weeks [4].

Glossopharyngeal neuralgia is distinguished from other orofacial neuralgia by the location of the pain. Swallowing or touching the tonsils with an applicator tends to trigger pain, and applying lidocaine to the throat temporarily eliminates spontaneous or evoked pain.

Paroxysmal pain in the throat and the base of the tongue differentiates glossopharyngeal neuralgia from trigeminal and sphenopalatine neuralgias. Few organic lesions will cause paroxysms of pain; however, a thorough physical examination of the pharynx and hypo pharynx should be undertaken to rule out infection or neoplasm. The cocaine test is useful in making the diagnosis. Application of diluted (10 percent) cocaine to the site of pain almost invariably eliminates the symptoms in glossopharyngeal neuralgia. Patients seeking treatment should have ailments involving tonsillitis, burning mouth syndrome, and other diseases associated with the posterior region of the mouth ruled out to avoid confusion in the assessment of treatment outcomes [1,3].

Glossopharyngeal neuralgia affects mainly the 9th (glossopharyngeal nerve) and sometimes 10th (vagus) and occasionally 11th (accessory) cranial nerve distribution (posterior pharynx, tonsils, posterior tongue, middle ear, under the angle of the mandible), since those nerves extend to the muscles of palate, larynx, and pharynx. Glossopharyngeal neuralgia sometimes results from nerve compression caused by an aberrant, pulsating artery similar to that in trigeminal neuralgia and hemifacial spasms. The nerve may be compressed in the neck by an elongated styloid process (Eagle syndrome). Rarely, the cause is a tumor in the cerebellopontine angle or the neck, a peritonsillar abscess, a carotid aneurysm, or a demyelinating disorder. Often, no cause is identified [5,6]. The etiology may be attributed to injury, damage of the nerve, or deterioration of the protective sheath of the nerve, sending abnormal signals and disrupting the normal signaling of the nerve. Most often the damage is from a blood vessel compressing the nerve. Other causes include aging, multiple sclerosis, and nearby tumors [2,4].

Diagnosis of glossopharyngeal neuralgia is by MRI and clinical evaluation. MRI is done to exclude tonsillar, pharyngeal, and cerebellopontine angle tumors and metastatic lesions in the anterior cervical triangle. Local nerve blocks can help distinguish between carotidynia, superior laryngeal neuralgia, and pain caused by tumors. Anticonvulsants are usually the drugs of the choice for the treatment of glossopharyngeal neuralgia [4]. If oral drugs are ineffective, local anesthetics can provide relief. If pain is restricted to the pharynx, surgery can be restricted to the extracranial part of the nerve. If pain is widespread, surgery must involve the intracranial part of the nerve [7]. Glossopharyngeal neural-

gia is rare compared to other facial pain syndromes. Both genders are equally affected. Patients are usually middle age and older. When a person first experiences throat pain, a primary care physician or dentist is often consulted. If the pain requires further evaluation, a neurologist or a neurosurgeon may be required [3,4].

A variety of treatments including medication, surgery, needle procedures, and radiation is available, depending on the case. First-line treatment is usually medication [4]. When medications fail to control the pain or cause intolerable side effects, a neurosurgeon may be consulted if surgery is indicated [8]. However, over-the-counter drugs such as aspirin and ibuprofen are not effective against neuralgia pain.

Anticonvulsants, such as carbamazepine (Tegretol), gabapentin (Neurontin), and phenytoin (Dilantin), are mostly used to control pain. Sometimes other drugs administered include valproic acid, ethosuximide, barbiturates and benzodiazepine [9]. Side effects from these medications may include drowsiness, unsteadiness, nausea, skin rash, and blood disorders, etc. Therefore, patients are monitored with periodic blood tests to ensure that the drug levels remain safe. Multiple drug therapy may be necessary to control pain (e.g., Tegretol and amitriptyline). Phenytoin's first use in pain, for trigeminal neuralgia, was reported in 1942 by Bergouignan [1]. Since then, phenytoin has been useful for treating facial and head pain. Using phenytoin to treat glossopharyngeal neuralgia has shown some positive results but it would not usually cure the disease, and its chronic use often resulted in many undesirable side effects [10]. The combination of acupuncture therapy and phenytoin, or gabapentin (Neurotin), carbamazepine (Tegretol), or amitriptyline with gabapentin have shown promise for treating the illness [11].

This article is a clinical comparative study of effects about the combination of both acupuncture and the aforementioned drugs for treating glossopharyngeal neuralgia. Since the application of phenytoin and some other anticonvulsants for treating those oral and facial pain are considered "off-label" use, the clinician wishing to use these drugs should possess the fundamental knowledge of pharmacology of each drug so that serious consequence can be avoided for medico-legal reasons. Some of the drugs have a long list of significant toxicity and drug interactions, patients should be warned that they must inform their clinicians if they take other medication(s) that may interact with those anticonvulsants, resulting with adverse effect.

Material and Method

35 patients (18 males and 17 females, aged 31-68 most in middle age) were included in this study. Most of them had

been previously treated with traditional medicine by their neurologists or by their primary care physicians. They claimed the intensity and frequency of pain might have decreased in various degree but not to the degree they expected and the pain still persisted. Some of those patients (about 8) never had their illness treated before. They all wanted to try a treatment with the alternative and complementary medicine to find out if it would work for them. We also included the patients who had received acupuncture treatment previously from other acupuncturists because we found out the acupoints their previous acupuncturists used for treatment varied from one to another, and were not all the same acupoints we would use. For the sake of better control for our study, 16 patients were selected to receive acupuncture using the same identical acupoints for treatment so that we could make a better comparison of clinical outcome assessment. For precautions, since acupuncture therapy including Hoku Point (LI 4) and most anticonvulsants especially phenytoin and carbamazepine carry pregnancy risks and can also cause interdrug reaction, no pregnant women or patients taking medication(s) that would interact with anticonvulsant were included in our study. The patients were divided into 4 groups: (I) those who received acupuncture and phenytoin with dosage of 300 to 600 mg; (II) those who received acupuncture and gabapentin with dosage of 300 to 900 mg in 3 divided dose; (III) those who received acupuncture and carbamazepine with dosage of 400 to 800 mg in 2 divided dose for maintenance; and (IV) those with acupuncture and amitriptyline with dosage 25 to 100 mg at bed time and gabapentin with dosage 300 to 1200 mg at discretion of patient's physician. Other than Group (I) that we administered the phenytoin, the patients of the other 3 groups had already had their medication maintenance prescribed by their physicians when we saw them in our clinics. Patients' physicians were consulted before treatment. Since acupuncture does not introduce any medicine into the body, the physicians did not mind for the patient to receive acupuncture so far as the treatment would bring some beneficial results. In fact, most of those physicians possess some knowledge of acupuncture themselves.

The acupuncture points used for glossopharyngeal neuralgia were LI 4, LI 1, ST 44, PE 9, CV 22, and CV 23.

Not all the patients were enrolled in our program at the same time but they all underwent the same treatment program. All the patients underwent 8 sessions (two sessions each week) of treatment. The first 4 sessions only involved acupuncture therapy alone and the last 4 ses-

sions involved both acupuncture and phenytoin. How much phenytoin dosage was required for each patient was a matter of judgment based on the duration, frequency, and intensity of the pain attacks. For the patients to receive phenytoin, we prescribed the predetermined dosage to the patients to suit individual needs, generally ranged somewhere between 300 and 600 mg depending on our clinical judgment and the patient's condition. In the first 4 sessions, patients were not to take any medication (including phenytoin) so that we could compare the treatment outcome when acupuncture therapy was used alone on them.

Using the Visual Analogue Scale defining limits such as "no pain at all" and "pain as bad as it could be" as the two extremes, the patient was asked to mark the pain level they experienced on the line between the two endpoints. All patients were asked to rate pre-operatively (prior to our treatment session) the level of pain they experienced previously when neuralgia attacked, and also to rate the pain they experienced when attacks took place after our treatment. This was to determine any changes in pain intensity before and after our treatment for our clinical comparison of possible post-operative improvements following treatment. Patient were also asked to rate if they experienced 'great improvement', 'moderate improvement' or 'somewhat or no improvement' in their condition after therapy.

Results

Two tables of treatment outcomes, one with acupuncture alone and one with combination of acupuncture and phenytoin were listed below.

The result of sessions using acupuncture therapy alone is shown below in [Table 1](#).

Group I patients receiving the combination treatments of phenytoin and acupuncture therapies in the second half of the sessions (session 5-8) seemed to have a much better clinical results which is shown in [Table 2](#). Group II, III and IV patients also received same amount of four acupuncture sessions just as the Group I patients did.

Both Fisher's Exact and Likelihood Ratio Chi-Square test yield insignificant results (p -values at 0.8612 and 0.8512) against the null hypothesis where outcomes associates with treatment grouping, suggesting that outcome may be independent of the four treatments.

Table 1: Treatment results using acupuncture alone.

Disease entity	# of patients	Great improvement	Moderate improvement	Somewhat or no improvement
Glossopharyngeal neuralgia	16	3 (18.7%)	8 (50%)	5 (31.3%)

#: Number.

Table 2: Clinical comparison of combining acupuncture and various drug therapies.

Disease entity glossopharyngeal neuralgia	# of patients	Great improvement	Moderate improvement	Somewhat or no improvement
Group I with phenytoin	16	9 (56%)	5 (31%)	2 (13%)
Group II with gabapentin	7	3 (43%)	3 (43%)	1 (14%)
Group III with carbamazepine	8	2 (25%)	4 (50%)	2 (25%)
Group IV with amitriptyline & gabapentin	4	2 (50%)	1 (25%)	1 (25%)

#: Number.

Table 3: Cochran-mantel-haenszel statistics (based on table scores).

Statistic	Alternative hypothesis	DF	Value	Prob
1	Nonzero correlation	1	1.1101	0.2921
2	Row mean scores differ	3	1.8237	0.6098
3	General association	6	2.4874	0.8699

Moreover, Cochran-Mantel-Haenszel tests for testing “Zero correlation”, “Zero difference”, and “No General Association” renders *p*-values at 0.2921, 0.6098, and 0.8699 respectively, suggesting there is no any associations between outcomes and treatments. There seems no significant difference among outcomes of those four treatment groups (Table 3).

Generally speaking, overall treatment for those patients did not seem to eradicate the illness completely. Most patients reported that recurrent pain attacks had occurred to them less frequently, and they felt lesser degree of pain when comparing with traditional medical treatment (i.e. without acupuncture treatment) they had received before. Nevertheless, some patients reported that there were little improvement with our treatment but there were no harm or deterioration of their illness by acupuncture either. Those whose condition had improved reported that they could carry out daily activities more normally than before and the quality of life had improved. Our one year post-operative follow-up study after the treatment found that three patients (2 females and 1 male) remained symptom free. But the rest of the patients in the study had recurrent pain attacks but less frequently, and the degree of pain they experienced was much less and more tolerable than before treatment.

We also found that, compared to other anticonvulsants used in this study, phenytoin was therapeutically more beneficial for some dental patients afflicted with glossopharyngeal neuralgia. It seems to have rendered trigger zones less sensitive to dental manipulation and other operations involving the posterior quadrant of the arch. When combined with acupuncture, the results were even better.

Discussion

The treatment outcome and healing did not seem to favor any particular age group or gender. Onset, duration, and severity of a disease affected the outcome to a much greater degree. The prognosis and progression of the condition was

better for those who sought treatment as soon as a diagnosis was made at the onset of the disease. It is worth mentioning that the anticonvulsants in this study can also be valuable for pain and anxiety control, as we found out during our anticonvulsants-acupuncture combination sessions. Needle-phobic and anxious patients were much calmer when receiving acupuncture and an anticonvulsant. Most anticonvulsants have common side effects, such as drowsiness, nausea, skin rash, unsteadiness, and blood dyscrasia. Carbamazepine additionally can cause slurred speech and fatigue; gabapentin can cause somnolence; and amitriptyline can decrease alertness. These side effects are a great inconvenience for the people undergoing treatment, particularly for those who work. Phenytoin, when used properly within the recommended dosages, had better patient acceptance. There were few hangover reactions (because the drug rarely causes loss of consciousness), and patients remained relatively lucid at the completion of the treatment. However, if a dosage of 500 mg was given, many patients experienced drowsiness or dizziness, though the degree varied. In those cases, an escort was required to take the patient home for medico-legal reasons. After the first session of the combination treatment with acupuncture, the clinician can adjust the phenytoin dosage for the future sessions depending on the treatment outcome.

Phenytoin is known to have a calming effect on the overactive brain by enabling normal thinking processes to be restored within an hour [12]. Combinations of anger, fear, and related emotions are often experienced in the overactive brain. Impatience, hostility, rage, worry, anxiety, and depression are typically seen in patients with chronic intractable pain. Excessive states of anger and fear are decreased or eliminated by phenytoin [12]. Phenytoin also improves tension, impulsiveness, irritability, and sleep difficulties, as well as overt anxiety symptoms such as dissociative concern, quarrelsomeness, nervousness, shakiness, and outbursts [13-17]. Some patients enrolled in our study were so tense and apprehensive that acupuncture needle insertion was difficult due to tension-related muscle spasms that caused the bending of needles in the body. Phenytoin calmed down those patients and facilitated the insertion of needles. We found the treatment had a better result if we rendered the acupuncture treatment after the drug was administered to the patient (usually one hour before treatment).

For pain control, phenytoin in the range of 400 to 600 mg is therapeutically beneficial for patients suffering from glossopharyngeal neuralgia, trigeminal neuralgia, and other facial paralysis or pain [17-21]. It was our clinical impression as well as various patients' experiences that phenytoin (more than any other drug) resulted in less triggering of episodes of glossopharyngeal neuralgia during intra-oral maneuvering during dental operations. When combined with acupuncture, the end results were even more satisfactory.

Phenytoin's therapeutic effect lies more in its ability to restore normal thinking processes and to decrease irrational fears and anger than in its sedation effects, which are relatively insignificant, in our opinion, when compared with other mainstream sedation agents.

In this study, only Group I patients received acupuncture in our clinical setting before the combination regimen was employed. We felt the acupuncture outcome for Groups II, III and IV might be similar since participants in all of the groups suffered from the identical neuralgia and their medical histories were similar. Ideally, the same treatment should have been applied to them as was applied to the Group I patients, but circumstances did not permit this. Each patient identified his intensity of pain pre-operatively, and post-operatively using an analogue scale from 1 (the least pain) to 10 (the most pain) to compare clinical progress before and after each session and during interval between sessions.

No single regimen for pain and anxiety control will work for every patient [22]. This is due to variations among patients in their responsiveness to the medication. Pharmacologically 68% of patients respond to the normal dose of any given drug, 27% have either a hypo- or hyper-response, 2.2% have no response, and 2.2% are extremely sensitive to dosage. Additionally, the effect of Cytochrome P450 (an enzyme that plays an important role in metabolizing drugs) can cause drug interactions if a patient is taking other medications or foods that may increase or decrease the effects of phenytoin [22].

While our clinical impression of the acupuncture-drug therapy combination was generally favorable, there were, however, two patients (one male and one female in their 50's) that received carbamazepine for glossopharyngeal neuralgia concomitantly with benzodiazepine for issues such as alcohol addiction and anxiety attacks. Both participated in our study and received acupuncture treatment. We did not alter the medication regimen prescribed by their physicians. The outcome of the acupuncture treatment did not have much of an effect on them, which was quite a contrast with the overall favorable results obtained from other patients. This contrast is rather puzzling. Considering that other patients in Group II that received acupuncture and carbamazepine had relatively good results, we postulated

that benzodiazepine might be the culprit. It is possible that benzodiazepines counter the overall effect of certain acupuncture therapies by cancelling or blocking certain specific endocrine secretions stimulated by the acupoints we employed. Each different acupoint can induce or stimulate the release of certain different secretion(s) from spinal, cerebral, mid-brain, hypothalamus-pituitary and endocrinal glands, etc [23]. We did not enter these two cases in the table because the sample might be too small to be biostatistically significant. If a counter-acting phenomenon actually takes place, the mechanism by which it takes place and to what degree could be worth studying in both clinical and basic sciences.

To the patients' credits, the majority cooperated with us for their treatments and abided by the treatment regimen, because they sincerely wanted to ease their neuralgia condition. Nevertheless, some patients could not commit themselves to the required regimen. Some were from out of town, out of state, or from other countries. Geographic distances and other inconveniences made it difficult for them to keep their commitments. This was one of the reasons we selected for biostatistical study the data from the patients who participated in 8 sessions, because most of the patients in our pool completed 8 sessions of treatment.

There were some patients who participated in 3-5 sessions and a few patients who had between 12 and 14 sessions. It would not be a fair comparison clinically to measure the improvements of those who underwent fewer sessions versus those who participated in a dozen sessions. Therefore, those patients were not included in our study.

For those who felt they benefited from our treatments, the most obvious improvement was in the quality of life they experienced. In addition to the pain from neuralgia, patients were handicapped by anxiety and depression associated with their fear of the unpredictable nature of the onset of neuralgia attacks. Moreover, the unpleasant anticipation of impending attacks often hampered their daily activities. Our treatment gave them considerable, though not complete, relief and gave them a feeling of some control over their condition. These patients felt (even if it was purely psychologically) that the dual acupuncture and medication combination would result in less pain when an attack occurred. For them, this was undoubtedly better than the singular assurance (being under medication alone), thus alleviating some anxiety and depression. The improvement in the quality of life when the pain was subdued (from the sharp pain characterized by glossopharyngeal neuralgia) is reflected in [Table 2](#).

Since glossopharyngeal neuralgia is not a common disease and since the patients did not come to our attention at the same time period, a double blind study was not fea-

sible in our situation. Additionally, each patient's intensity of pain varied at each different episode with some patients requiring immediate attention. Our study was retrospective and small in the data size especially after excluding pregnant patients, patient taking other medication(s) due to other diseases (out of concern that drug interaction might interfere with our biostatistical analysis), and patients participating in fewer than or more than 8 sessions. Nevertheless, the impressive outcome of combining drug therapies with acupuncture cannot be dismissed. Our study offers clinicians a regimen to consider as one of the options when encountering patients with pharyngeal neuralgia.

Conclusion

The majority of patients enrolled in our study had positive results. The combination of acupuncture and drug therapies yielded a much more favorable outcome than if acupuncture or drug therapy was used alone. The combination therapy resulted in less recurrence of neuralgia attacks and less painful episodes. The regimen did not eradicate the problem totally, but patients' quality of life improved and the condition was more tolerable. Due to the limited number of patients available, further study would be needed to assess the overall treatment outcome of acupuncture and drug therapies.

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