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Treatment efficiency of peripheral glycerol injection administration for relief of neuralgic pain in a known cases of trigeminal neuralgia

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Abstract
Objective: Evaluating the efficacy of glycerol injection in controlling neuralgic pain distributed in peripheral branches of trigeminal nerve and assessing the reversibility of the lost sensory function of the nerve.
Study Design: Descriptive case series.
Place and duration of study: The study was conducted at General Hospital Orthodontic Department from April 2018 to January 2019.
Material and Methods: Fifty patients were randomly recruited as known cases of trigeminal neuralgia of either sex and were administered glycerol injection in the peripheral branches of trigeminal nerve. Patients were followed up for next 1 year at monthly intervals and intensity of their pain was assessed.
Data was recorded in specially made pro forma and analyzed using SPSS 20.0. Analysis included frequencies, mean ±standard deviation (SD) and Paired t test. P-value <0.05 was considered significant.
Results: Results have established positive impact of administering glycerol injection in achieving better analgesic control as compared to conventional methods. The ease in performing this procedure, early return of lost sensations and faster onset of pain relief with minimal complications makes it a worthwhile choice.

Keywords: glycerol injection, trigeminal neuralgia

Introduction

The head and neck region is a common site for neuralgias (pain extending along the course of a nerve). Because facial neuralgias produce pain that often mimics pain of dental origin, the dental profession is frequently called on to rule out odontogenic or infl ammatory causes. Trigeminal neuralgia, the most serious and the most common of the facial neuralgias, is characterized by an extremely severe electric shocklike or lancinating (i.e., sharp, jabbing) pain limited to one or more branches of the trigeminal nerve. In the majority of cases the pain is located in the maxillary (V2) or the mandibular (V3) distribution of the nerve. It is often idiopathic but is usually associated with pathosis somewhere along the course of the nerve.

Occasionally, trigeminal neuralgia results from a brainstem tumor or infarction and is referred to as secondary trigeminal neuralgia.

Trigeminal neuralgia characteristically affects individuals older than 40 years of age (the average age at onset is 50 years), although it may affect persons as early as puberty. Women are affected slightly more often than men, and the right side is involved more often than the left. Any branch of the trigeminal nerve may be involved, but the ophthalmic division is affected in only 5% of cases. More than one branch may be involved, and the pain is occasionally bilateral.

The onset of a pain "attack" is abrupt, often initiated by a light touch to a specific and constant trigger point. The pain is extreme, paroxysmal, and lancinating. Duration of a single pain "spasm" is less than 2 minutes, although the overall attack may consist of numerous repeating spasms of short duration. For several minutes after an attack (the "refractory period"), touching the trigger point usually cannot induce additional attacks. The pain must be limited to the known distribution of

one or more branches of the trigeminal nerve with no motor deficit in the affected area.

Spontaneous remissions occur, often lasting more than 6 months, especially during the early phase of the disease.

However, the failure of medical treatment has led to the development of various surgical techniques, which include peripheral injections of various agents having neurolytic properties, [2-6] peripheral neurectomy [7] cryotherapy, microvascular decompression, radiofrequency thermocoagulation and gamma knife radiosurgery. An ideal treatment is one that causes no morbidity and preserves the normal sensation of the face. Such a sensation-preserving, absolutely safe, and permanently successful treatment does not yet exist. In some studies, more than 50% of patients with TN eventually had some kind of surgical procedure [12, 13]. Compared with other operative treatments, the peripheral injection techniques are simple, quick, and easy to perform, and they can be used as outpatient procedures.

Material and Methods

It will be a descriptive case series study conducted in the Orthodontics Out Patient Department of General Hospital, Islamabad after the approval from Institutional Review and Ethics Committee for a period of ten months, from April 2018 till January 2019. Fifty patients will be included using Non-

Probability Consecutive sampling technique. Sample size will be calculated on the basis of prevalence and duration of study period using WHO calculator [13].

The diagnosis of ITN will be made on the basis of the history and diagnostic criteria for TN. No patients with a history of any other neurologic diseases, and no evidence of organic disturbances of the face, maxillary sinus, mandible, or temporomandibular joint will be found on radiographic examination. All patients will be treated without systemic sedation or analgesia, and all will tolerate the procedure extremely well. Before the glycerol injection, the nerve will be carefully anesthetized and the absence of pain will be tested by sensory stimulation of the trigger zone. Ten minutes after local anesthesia, pure glycerol, which will be sterilized for 1 hour at 150°C, will be injected through a short 22-gauge needle. Injection volumes will be 0.5, 1, and 1.5 mL for infraorbital, mental, and mandibular nerve injections, respectively. All patients will be discharged with their families immediately after the injection. Patients will be advised to continue a therapeutic level of their antineuralgia medications until they will be free of pain for a full week before beginning to taper medication usage. All cases will be critically evaluated and followed for 3 years. Pain-free periods will be measured at varying intervals, including the last examination, and patients will be questioned about sensation in the injected region.

All the acquired data will be then entered in SPSS 20 for data processing. Analysis included frequencies, mean ±standard deviation (SD) and Paired t test. A *p*-value <0.05 will be considered significant.

Results

A total of 50 patients with trigeminal neuralgia were included in this study. There were 33 females and 17 male patients. Twenty five patients received peripheral glycerol injection (study group) and normal saline was administered to the rest of the 25 patients (control group).

The right side of the face was involved in 33 cases and the left side in rest of the 17 patients. No case presented with bilateral Involvement. Mandibular division was involved in 38 cases and maxillary division in 12.

The control group obtained no pain relief at the next review followups. These patients continued to experience no pain relief at follow up visits.

In the study group 22 patients had complete pain relief for 3 month duration. Another 7 had occasional pain during this period, with no need for medication. One patient experienced no pain relief after the glycerol injection.

After six months 14 of our patients had complete pain relief and this figure dropped to 8 at the one year followup. Overall 12 patients had no pain or occasional pain after one year, and did not require any medical therapy.

Discussion

Although Trigeminal Neuralgia has been recognized for centuries, its etiology and definitive treatment remain unclear. Because this is a debilitating condition, management should aim to improve the quality of life. Recently, Peripheral Glycerol Injections alone have been found to be effective in the management of trigeminal neuralgia without producing significant complications in most patients [4, 5]. Although the exact mechanism of pain relief produced by glycerol in ITN is still unknown, several hypotheses have been suggested. In 1991, Stajcic noted that axonolysis and demyelination were restricted to the outer zone of the rat infraorbital nerve bundles. To the contrary, in 1998, Al-Khateeb showed that extraneural application of pure glycerol in the vicinity of the dog mental nerve was not associated with structural changes.

He also pointed out that no signs of nerve degeneration or other morphologic changes were observed in any of the experimental and control specimens at any of the time intervals studied. In one of our patients who had persistent pain despite the glycerol injection, a mental neurectomy was performed 1 week after the injection, and microscopic examination of the excised nerve confirmed the findings in the experimental study by AlKhateeb. The nerve presented inflammatory alterations only.

However, it may be possible that the nerve was not accurately injected. In this respect, it would be wrong to correlate the findings of our study with that of Al-Khateeb or others. Despite high rates of initial success with virtually all surgical procedures, most doctors and patients choose medical therapy first because of potential surgical morbidity, the risk for loss of facial sensation after surgery, or the recurrence of pain despite initial surgical success.

All the patients in our study had received medical treatment before the procedure, and none of them had undergone any other treatment. Medical treatment is the first choice in the management protocol for ITN patients in our clinic, which is followed by PGI, repeated PGI, neurectomy, repeated neurectomy, and scar revision at periphery of the nerve, in sequence. The current trend in surgical treatment of ITN is to use less invasive procedures. Alcohol injection is not generally preferred because it can cause peripheral necrosis. Percutaneous retrogasserian glycerol rhizotomy (PRGR) is a good example of this trend, because pain relief can last more than 6 years with little sensory loss. Its success rate is reportedly between 82%20 and 96%2. Mild hypoesthesia, which has been reported in between 17%21 and 67%20 of patients, is apparently the only rare long-term complication of PRGR. It can be concluded that the mild hypoesthesia noted after both PGI and PRGR is the result of the effect of glycerol on the peripheral nerve, irrespective of the site of application. Most transient major complications of PRGR were not observed in the patients treated in our study.

Although the onset of pain relief with PGI was immediate, the onset of pain relief after PRGR varies from immediately to 21 days, with a median latency period of 5 days. Also, we believe that PGI is a less invasive technique than PRGR. In studies by Yoon *et al*, who performed a retrospective analysis of 81 patients involving long-term efficacy of percutaneous radiofrequency thermocoagulation of the

trigeminal ganglion or root for the relief of TN, the initial success rate was 87% and the probability of remaining pain-free [1, 2, 11] years after the procedure was 65%, 49%, and 26%, respectively. In the same study, side effects, such as dysesthesia, corneal numbness, keratitis, transient masseter weakness, trismus, and temporary hearing impairment

Conclusion

Results concluded from data of this study shows that when the high mortality and morbidity of the other surgical procedures are compared to those associated with glycerol injection, it appears that this procedure may present a good treatment choice. It is relatively simple to perform and has a faster onset of pain relief and less complications than the other surgical treatments. However, long follow-up periods are required.

Conflict of Interest

This study has no conflict of interest to be declared by any author.

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