Is peripheral alcohol injection of value in the treatment of trigeminal neuralgia? An analysis of 100 cases

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Abstract. This retrospective study assessed the effectiveness and complications of peripheral alcohol injections in the management of trigeminal neuralgia (TN). 100 patients were analyzed who received 250 peripheral alcohol injections from June 2004 to January 2010. The duration of effect of alcohol blocks, the effect of repeated administration, and complications associated with alcohol injections were examined. The distal injection technique was applied. The branch of the nerve was identified and confirmed. After carefully anesthetizing the nerve with local anesthesia, 1–1.5 ml of absolute alcohol was injected depending on the nerve involved. Pain relief lasted for a mean of 14.13 ± 8.66 months. There was a fall in the duration of effect with subsequent injections. No serious complications were reported. Only 3% patients presented with non-neuralgic pain, swelling, burning sensation, trismus, dysesthesia, soreness, infection and the expected loss of sensation along the branch involved in TN. The combination of efficacy and reduced morbidity makes this procedure preferable for the treatment of TN. Alcohol injections are useful in those who are refractory to drug therapy, the elderly, medically compromised patients, unwilling to undergo neurosurgical procedures and in whom surgery is delayed for any reason.

Keywords: peripheral alcohol injection; trigeminal neuralgia.

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Trigeminal neuralgia (TN) or tic douloureux, is a syndrome characterized by sudden, usually unilateral, severe, brief, stabbing, lancinating, recurring pain in the distribution of one or more branches of the fifth cranial nerve. It usually begins as a relapsing disease with pain-free intervals that may last months or years. These intervals typically grow shorter and eventually disappear. As the disease progresses, patients can have difficulty in talking, eating, and maintaining oral hygiene out of fear of triggering the pain. In severe cases, TN may significantly decrease the quality of life with marked depression and anxiety.

Despite recent advances in treatment, TN remains an incapacitating condition, which is difficult to treat successfully in every patient. At present it is standard practice to use carbamazepine as first line treatment, sometimes with the later addition of oxcarbazepine, phenytoin, baclofen, lamotrigine, gabapentin or sodium velproate. The relief provided by carbamazepine or other drugs may decrease over time, and side effects may necessitate discontinuation of the medication. About half of all patients eventually require an operation for pain
relief. Taylor et al. reported a 16 year follow up on 143 patients treated with carbamazepine and found it to be effective in 99 patients (69%), but 19 of those patients later became resistant to the drug and required a variety of surgical procedures.

Operative treatments in current use include: neurectomy of trigeminal nerve branches outside the skull; percutaneous ablation that creates trigeminal nerve or trigeminal-ganglion lesions with heat (radiofrequency thermal rhizotomy), injection of glycerol into the trigeminal cistern (retrogasserian glycerol rhizotomy); physical compression (trigeminal-ganglion balloon microcompression); gamma knife surgery. Microvascular decompression (MVD) is intended to alleviate TN by relieving compression of the nerve at some point along its course. MVD is a safe and effective treatment for TN, with a high rate of long-term success, which makes it an attractive treatment for eligible patients with medically intractable tic. The management of TN has also involved peripheral injections of different chemical agents into the affected nerve. The first substance used was chloroform. Later, boiling water, glycerol, phenol, high concentrations of tetracaine, and streptocamye were also used. Peripheral alcohol injections have also been used, preferably during the first attack, or if the patient is very old. Patients with serious medical morbidity who cannot undergo invasive surgical procedures safely may benefit from injection of alcohol into the painful peripheral trigeminal nerve branch. This technique is associated with pain relief for 6–16 months.

The neuralgic pain is so severe that it has led to suicide attempts in some patients. This condition requires early diagnosis and immediate management. Most patients with this disease are old, infirm and not good candidates for surgery so there is a need for a relatively simple, minimally invasive procedure that immediately controls the pain. A survey of the initial and long term results of operations and alcohol injections in 650 patients revealed the marked contrast between the lives of patients who are permanently cured and those who continue to suffer recurring pain.

The purpose of this study is to assess the efficacy of peripheral alcohol injection, a minimally invasive procedure that has minimal, or no side effects in the treatment of TN. The procedure can be repeated without any additional risk.

**Materials and methods**

100 consecutive patients treated with 250 alcohol injections were identified. The study was conducted at a tertiary care hospital from June 2004 to January 2010. The age and gender of the patients was determined at the first visit.

The diagnosis was based on a detailed history and clinical examination. Orthopantograph (OPG), computed tomography (CT) scanning or magnetic resonance imaging (MRI) was performed for every patient to exclude any local pathology or lesion at brain level. No secondary pathology was seen. No history of trauma or direct nerve injury was observed. All patients were found to have idiopathic TN. According to the division of the trigeminal nerve involved, TN was divided into maxillary and mandibular types. There were no cases of TN involving the ophthalmic division of trigeminal nerve.

Different physicians had treated most of the patients medically before this presentation. The patients had not kept records of their previous medication so this and any adverse effects cannot be reported here. Some patients gave a vague history of using maximum doses of drugs such as baclofen, lamotrigine, and gabapentinate. Discussion with the patients revealed that most had used maximum doses of carbamazepine (up to 1200 mg daily in divided doses) but had now become refractory to drugs. Since the patients had been treated medically previously, alcohol injection could not be reported as the first choice of treatment for these patients.

All the patients gave written informed consent for alcohol injection treatment. They gave informed consent willingly because they were in acute pain and wanted to alleviate the pain.

**Injection technique**

On the first visit, the branch of the nerve involved was identified according to the site of the pain and confirmed using a diagnostic local anesthetic injection of 2% lignocaine with adrenaline 1:200,000 at the site, repeated three times on consecutive days. Early morning appointments were given to the patients.

For the alcohol injection, 1–1.5 ml of absolute alcohol was used in a syringe with a 25/27 Gauge needle (short or long depending on the anatomical site). The amount of alcohol injected was determined according to the nerve involved. The protocol was 1 ml each for long buccal and mental nerves; 1.5 ml each for infra-orbital and inferior alveolar nerves. Since the injection of absolute alcohol is painful, the nerve was anesthetized using 2% lignocaine with adrenaline before treatment. Apart from pain relief, the point of entry of the local anesthetic injection provided a guideline for the exact and effective injection of absolute alcohol because of anatomical variation. After the nerve had been anesthetized, absolute alcohol was injected into the confirmed branch of the trigeminal nerve according to the technique described below.

For infra-orbital nerve injection in the maxillary division an extra-oral approach was used. The infra-orbital foramen was localized using the index finger of the left hand placed at the infra-orbital rim and slid down to rest in a depression that contain foramen, almost 5–7 mm below the rim at the junction of the medial one-third and lateral two-thirds of the infraorbital rim. The index finger was kept there and absolute alcohol was injected.

For mental nerve injection in the mandibular division an extra-oral approach was preferred over an intra-oral vertical approach. A point for injection was marked extra-orally in the middle of the mandible (between the occlusal plane of the mandibular teeth and the lower border of the mandible) extra-orally below the second premolar. The mental foramen had been identified in an OPG in relation to the apices of the first and second premolars.

For inferior alveolar nerve injection in the mandibular division a traditional technique was used. The thumb of the non-injecting hand was placed in the deepest portion of the concavity of the ramus between the internal and external ridges of the mandible. The other four fingers were placed extra-orally on the posterior border of the ramus. With the barrel of the syringe lying over the premolars of the opposite side, the 25 G long needle was directed parallel to the occlusal plane of the mandibular teeth, bisecting the thumb, and was aimed at the midpoint of the ramus located between the thumb and the extra-orally placed fingers. The needle was advanced through the pterygomandibular raphe into the pterygomandibular space, 1.5 cm deep from the mucosa.

For the long buccal nerve an intra-oral approach was used. Solution was deposited in the mucous membrane in the vicinity of the anterior border of the ramus of the mandible, distal and buccal to the most distal molar tooth in the arch. A 25/27 G long needle was preferred because of the posterior deposition site, not the depth of tissue insertion (which is minimal).
Table 1. Effectiveness and duration of alcohol injection.

<table>
<thead>
<tr>
<th>Description of injection</th>
<th>TN in maxillary division</th>
<th>TN in mandibular division</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Infra-orbital</td>
<td>Superior alveolar</td>
</tr>
<tr>
<td>Total number of injections $n = 250$ (in 100 patients)</td>
<td>74 (32)</td>
<td>132 (40)</td>
</tr>
<tr>
<td>Ineffective injections ($n = 34$)</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Effective injections ($n = 216$)</td>
<td>62 (88.6%)</td>
<td>122 (90.4%)</td>
</tr>
<tr>
<td>Duration of effect, months mean ± SD</td>
<td>16.27 ± 9.27 (03–48)</td>
<td>22.51 ± 8.55 (5–56)</td>
</tr>
</tbody>
</table>

$\chi^2 = 13.3714$ and its $P$-value is 0.0039 at 5% level of probability. The mean ± SD followed by different letters are significantly different at $P < 0.05$. Infra-orbital and inferior alveolar are assigned $c$ and $d$, respectively, indicating that the mean duration of effects in these two types of injections are significantly different from each other and with respect to mental and long buccal nerve. Mental and long buccal nerve are assigned $a$ and $b$, respectively indicating that mean duration effects in these two types of injections are not significantly different; LSD value = 4.787, the values in parenthesis are the ranges (minimum–maximum).

Table 2. Effect of repeated injections on the duration of pain relief.

<table>
<thead>
<tr>
<th>Effective alcohol injections ($n = 216$)</th>
<th>Duration of effect (months) Mean ± SD (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First injection ($n = 90$)</td>
<td>10–56</td>
</tr>
<tr>
<td>Second injection ($n = 65$)</td>
<td>8–45</td>
</tr>
<tr>
<td>Third to fifth injection ($n = 61$)</td>
<td>2–10</td>
</tr>
</tbody>
</table>

The mean ± SD followed by different letters are significantly different at $P < 0.05$; LSD value = 2.331 (first, second, and third to fifth injections are assigned a, b, and c, respectively).

Results

Of 113 patients with TN, the study sample size was reduced to 100 patients. 13 patients were excluded from the study because they did not report back for proper follow-up. The 100 patients studied received a total of 250 injections with a mean of 2.5 injections (range 1–5) per patient. The mean age of the patient was 47 ± 10 years (range 24–70 years). There were 60 men and 40 women; a ratio of 3:2.

The overall success rate for the procedure was 86% ($n = 216$) on the stated criteria and 34 injections (14%) were ineffective. Of the successful injections, the mean duration of action was 14.13 ± 8.66 months (range 2–56 months).

The degree of pain relief in ineffective injections remained from 1 week to less than 2 months. Probable reasons were anatomical variations in the nerve, the uncooperative behavior of the patients and faulty technique.

In the maxillary division, in cases where the infra-orbital nerve was involved, 74 alcohol blocks were used in 32 patients. In the mandibular division, the inferior alveolar nerve was most commonly blocked ($n = 135$) and the long buccal nerve accounted for 20 injections. The inferior alveolar injections were successful in 90% with an average duration of effect of 22.51 ± 8.55 months. The successful injections (65%) of the long buccal nerve were effective for an average of 7.62 ± 7.93 months (Table 1).

The $\chi^2$ test applied to test the association between alcohol injection and efficacy in different branches of the trigeminal nerve found significance between these two variables ($\chi^2 = 13.3714$, $P$-value = 0.0039) at the 5% level of probability.

By applying one-way ANOVA, the alcohol injections in the inferior alveolar and infra-orbital nerve were found to be statistically significant ($P$-value = <0.05; LSD value = 4.787). There was no significant difference between the average duration of effect of alcohol injection between the mental and long buccal nerves.

Alcohol injections were repeated. The interval between the first and subsequent injections was found to be 13.02 ± 4.92 months (range 2–45 months). There was a fall in the duration of effect of the subsequent injections (Table 2). This difference in the repeated injections is statistically significant ($P < 0.05$; LSD value = 2.331).

Of the 250 alcohol injections, 242 (97%) resulted in no complaints. The remaining 7 (3%) cases presented local symptoms such as pain, swelling, burning sensation, trismus dysesthesia, soreness and infection. The complications of each nerve injection are shown in Table 3.

Discussion

TN is reputed to be one of the most painful conditions. The diagnosis is based on the patient’s history. The use of medications may add to the diagnosis. All new patients are treated medically as response to treatment is, in part, diagnostic. If the patient responds to medical treatment, the clini-
A recent meta-analysis has shown that anticonvulsants are effective for the treatment of trigeminal neuralgia. There are reports of the unique sensitivity of TN to carbamazepine, and this is sometimes proffered as a fundamental part of the history. Carbamazepine reduces or alters the pain in 70–90% of patients with TN. Carbamazepine is therapeutic as well as diagnostic for TN. 2% lignocaine is also helpful in the diagnosis of nerve branch involved in TN (it was used in this study for that purpose). Alcohol injections serve two main purposes. If the pain is completely relieved by injection, the diagnosis is established and sensory root section can be carried out with confidence that the pain will be permanently relieved. Grant included 7 cases in which he thought alcohol injection would have established the diagnosis and prevented an unsatisfactory operative result. The anesthesia produced by the injection also accustoms the patient to the permanent anesthesia produced by root section.

As TN is a protracted disorder, any medication may need to be given for extended periods of time, thereby multiplying the potential for drug toxicity. In addition to the considerable side effects, the pain may become more intractable as the disease progresses. When medical treatment fails, it is necessary to consider surgery. Suitable patients may progress directly to neurosurgery. Alcohol injections may be considered if immediate pain relief is required, in centers where facilities for major neurosurgical procedures are not available, or in medically unfit patients. Some patients, who were poor operative risks, have been kept comfortable by repeated alcohol injections over a period of years.

Alcohol injections can be a suitable choice in older patients whose life span is short, patients who are not fit for surgery, those with social reasons such as wanting to participate in the marriage of a close relative, patients with lengthy appointments for neurosurgical procedures, patients who are afraid of surgery, or those who refuse extensive surgery. Such patients are candidates for pain relief by the simplest method possible. In this study, one young pregnant woman with TN was successfully treated with alcohol injection.

Injections of alcohol have been suggested for the management of TN since the early twentieth century. It has been widely used at the peripheral level. Two distinct techniques are described for peripheral alcohol injection. The skull exit technique involves the transcutaneous injection of the nerve at the skull base (foramen ovale or foramen rotundum). In the distal technique the injection is more distal as the nerve passes recognizable landmarks in the facial skeleton (supraorbital notch, infra-orbital foramen, inferior dental foramen, mental foramen). Both techniques involve the injection of the relevant nerve with local anesthetic and, once analgesia is confirmed, injection of 0.5–1.0 ml absolute alcohol is applied. Occasionally, specific nerves may be identified and injected, such as the long buccal nerve. The transcutaneous technique is favored by neurosurgeons whereas oral and maxillofacial surgeons and dentists use the more peripheral technique.

Although alcohol injection is essentially a simple technique, the alcohol must be injected very precisely as it is highly toxic. Care must be taken not to inject excess alcohol subcutaneously, and one must use an aspiration technique to avoid injecting into the accompanying vessels. Most studies on alcohol injection were published 30–50 years ago, with three recent papers found in the literature. Rushion and Chung have also published work on alcohol injection for the treatment of TN. Edward and Naffziger reported alcohol injection in 175 cases. Many of these patients had multiple injections. Stoorkey and Ransohoff found that repeated injections were more difficult due to fibrosis. Gaffler et al. studied 28 patients who received 132 injections. They analyzed 114 injections.

The overall success rate was 86% with pain relief lasting for 40 weeks on average. Infra-orbital and inferior alveolar nerve injections accounted for 86% in their study. All of the alcohol injection studies were retrospective case series, and none had been subjected to statistical analysis except McLeod and Patton. They repeated alcohol injections but there was no significant fall in the duration of effect. By blocking the main trunk of the ophthalmic, maxillary and mandibular division of the trigeminal nerve in the skull exit technique, the chances of side effects such as eye problems (diplopia, loss of vision) or paralysis of motor nerves are higher. The authors used the distal technique, similar to McLeod and Patton. This technique is easy and simple. The authors did not observe any of these adverse effects because of advantage of anatomical site of injection. Sensory loss is higher in the skull exit technique compared with the distal technique in which only a small area is anesthetized (supplied by the terminal branch involved in TN) and the chances of motor loss are also less. In this study, the mean duration of action of pain relief was 14.13 ± 8.66 months (range 2–56 months). The authors did not observe any serious complications of alcohol injection (there were minor complications in 3%).

In this study, the inferior alveolar nerve was most commonly blocked (54%) and the infra-orbital nerve was the second most common alcohol nerve blocked (28%). In combination, both nerve blocks accounted for 82%, similar to Gaffler et al. McLeod and Patton studied the duration of effect of repeated alcohol injections and found no significant reduction on the effectiveness of alcohol blocks. It is widely held in the literature that a complication of peripheral alcohol injections is that their effectiveness is reduced with repeated administration. The authors observed that repeated injections produced shorter periods of pain relief. This may be associated with the fibrosis due to previous alcohol injections. McKenzie and Stoorkey and Ransohoff observed that each succeeding injection was more difficult because of the resultant scar tissues, but the present authors did not find any difficulty in the application of repeated injections.

This study revealed that alcohol injection is a suitable option among peripheral procedures. It offers a simple, office-based procedure for treating TN. It is a safe and practical procedure. It gave pain relief for 2–56 months (average 14.13 ± 8.66
months). The duration of pain relief was shorter with repeated injections. No serious complications were observed. Patient satisfaction with alcohol injection was high, with most of them preferring to come back for further injections if the pain returned. It is especially attractive for elderly or medically compromised patients, for those who are unwilling to undergo neurosurgical procedures and in those in whom surgery is delayed for any reason.

Competing interests
None declared.

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None.

Ethical approval
Chief Executive and Ethical Committee of Govt Lady Reading Hospital have given the approval for this study.

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