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*Full Length Research Paper*

# Analysis of factors influencing the efficacy of percutaneous retrogasserian glycerol rhizotomy in patients with idiopathic trigeminal neuralgia

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**Our study analyzed the factors influencing the efficacy of percutaneous retrogasserian glycerol rhizotomy in patients with idiopathic trigeminal neuralgia. Eleven contributing factors influencing the efficacy of percutaneous retrogasserian glycerol rhizotomy were identified by logistic regression analysis. Among 210 patients receiving percutaneous retrogasserian glycerol rhizotomy, 67 underwent two procedures and 16 underwent three. Complete pain relief was achieved in 92.4% of patients. The presence of trigger point and painless in the procaine test were the predictors of complete pain relief. Painless in the procaine test is essential to achieve complete pain relief for patients with definite trigger points. Percutaneous retrogasserian glycerol rhizotomy is a minimally invasive, safe, and effective therapeutic strategy for trigeminal neuralgia patients. There are no adverse events or only few complications after surgery. A second injection may be effective for recurrent patients and those unresponsive to initial treatment.**

**Key words:** Trigeminal neuralgia, percutaneous retrogasserian glycerol rhizotomy, logistic regression analysis.

## INTRODUCTION

Neurovascular compression is thought to be the cause of idiopathic trigeminal neuralgia for the majority of patients with this facial pain syndrome. The clinical challenge of trigeminal neuralgia has many medical and surgical resolutions. Over the past several decades, microvascular decompression (MVD) has proved to be a safe and effective operation for patients who are unresponsive to medical therapy. Nevertheless, not every patient with trigeminal neuralgia is considered a good candidate for posterior fossa exploration because of age, medical condition, prior MVD, or patient preference. Therefore, different surgical procedures were developed, and the different rhizotomy procedures aim to treat the nerve in different ways. These include mechanical effects on the nerve such as balloon microcompression, thermal-induced axonal degeneration by radiofrequency rhizotomy, radiation-induced degeneration produced by stereotactic radiosurgery, or chemical ablation with glycerol rhizotomy. Currently, injection of chemical agents into peripheral nerve targets (that is, alcohol injections) is also available.

Direct alcohol injection into the trigeminal nerve was reported in 1910. However, when absolute alcohol was injected into this location, multiple severe cranial neuropathies could be seen. Therefore, Jefferson (1963) advocated the use of phenol mixed with glycerin rather than absolute alcohol.

In our department, a total of 210 consecutive patients with trigeminal neuralgia received percutaneous retrogasserian glycerol rhizotomy (PRGP) from January 2001 to December 2002, achieving satisfied efficacy. The present study aimed to investigate factors affecting the efficacy of PRGP in trigeminal neuralgia patients, which

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may provide evidence for clinical decision making.

## PATIENTS AND METHODS

### General data

A total of 210 patients (85 males, and 125 females) aged 24 to 83 years (mean age: 58.6 ± 32.8 years) were recruited into the present study. Course of disease ranged from 3 months to 31 years (average: 3.74 ± 2.9 years). Right-sided trigeminal neuralgia was found in 115 patients, left-sided trigeminal neuralgia in 89 cases and bilateral trigeminal neuralgia in 6 cases. In addition, 60 patients had pain in branches II and III; 25 in branches I, II and III; 31 in branch I and II; 43 in branch II; and 51 in branch III. Definite trigger point was identified in 196 cases and 17 out of 210 patients had recurrent trigeminal neuralgia. All patients had taken carbamazepine and/or phenytoin for a long time, or underwent repeat peripheral branch rhizotomy, avulsion, retrogasserian glycerol rhizotomy and gamma knife treatment. They required receiving PRGR due to their non- response to therapy or intolerable side effects. Medical history of all the patients were reviewed, followed by physical examination, computer tomography (CT) or magnetic resonance imaging (MRI) before treatment. Skull base radiography was performed to evaluate the foramen size and its anatomical structure.

### Treatments

All patients gave informed consent and the institutional review board of our hospital approved this project. Operations were performed according to the method of Håkanson (1981). Thirty minutes before the operations, oral diazepam was administered. Patients were in a supine position and anterior approach was applied. Once adequate sedation had been achieved, a 9-gauge spinal needle was directed to middle skull base. The puncture direction was adjusted according to operator's sensation. Pentration of the needle through the foramen ovale can be felt by the surgeon. If the patient felt pain at that time, the spinal needle was advanced 1~1.5 cm again and could reach Meckel's diverticulum. Then, 0.2 ml of 2% procaine was injected for test. When the patient felt numb, and the pain in the relevant region disappeared, an intracranial needle position was confirmed. Subsequently, 0.4~0.5 ml of anhydrous glycerol were administered and the spinal needle was retracted followed by local compression for 5 min to avoid subcutaneous bleeding. The patient's head was then placed into an anterocollis position to prevent escape of glycerol into the subarachnoid space. The treatment was performed again if the pain was not relieved within 3 days after surgery, until the pain was completely relieved.

### Statistical analysis

Complete pain relief after initial treatment was used as the dependent variable (completely pain relief: 0; ineffectiveness: 1). The following contributing factors were used as independent variables: Age (younger than 60 years: 1, 61 to 70 years: 1; 71 to 80 years: 2; older than 80 years: 3), course of disease (less than 1 year: 0; 1 to 3 years: 1; more than 3 years: 2), definite trigger point (yes: 0; no: 1), duration of pain (less than 1 min: 0, more than 1 min: 1, times of pain onset (less than 5 year: 0; 5 to 10 year: 1; more than 10 year: 2), affected branches (1 branch: 0; 2 branches: 1; 3 branches: 2), prior surgery (no: 0; yes: 1), amount of injected glycerol (0.3 ml: 0; 0.5 ml: 1), flow of cerebrospinal fluid (yes: 0; no: 1), painless in procaine test (yes: 0; no: 1), body position while glycerol injection (prostration: 0; sitting position: 1). Statistical analyses were performed with the logistic regression in SPSS (10.0 edition) software. Unconditional univariate logistic regression analysis was performed and variables with statistical significance were then employed into unconditional multivariate logistic regression analysis.

## RESULTS

### Efficacy

Complete pain relief was defined as effectiveness. A majority of patients (92.4%) achieved complete pain relief after initial glycerol rhizotomy, 67 patients underwent two procedures, 16 underwent three and 16 patients were unresponsive after two to three procedures and treated with other approaches. A definite trigger point was not identified in 14 patients unresponsive to treatment.

### Side effects

About 3/4 patients felt headache or dizzy after glycerol injection. Some even had severe side effects, but they resolved gradually and disappeared mostly on the second day. A few patients had nausea and vomitting which could resolve spontaneously. Some patients experienced venous bleeding, most of which were around foramen ovale and did not require specific treatment. Four patients had oral herpes which resolved spontaneously within one week and 66 patients had facial hypalgesia. In addition, 191 patients had facial numb-ness, and 6 had insensitive corneal reflex. One patient had corneal ulcer and 23 had facial swelling which mainly caused by repeat puncturation and disappeared spon-taneously. Two patients had masseter myasthenia, which might be as a result of mechanical injury of motor branch by repeat puncturation. Seven patients had aseptic meningitis which was resolved by lumbar puncturation and hormonotherapy within one week. Jet-like bleeding was found in 3 patients due to misuse of puncture needle. No other severe complications were observed and no death found.

### Contributing factors

Unconditional univariate logistic regression analysis showed the presence of a definite trigger point, flow of cerebrospinal fluid, and complete painless in procaine test were the potential contributing factors influencing the efficacy of PRGP ($P < 0.05$). Furthermore, the presence of a definite trigger point and the complete painless in procaine test were the potent contributing factors ($OR > 10$, $P < 0.01$) as demonstrated by multiunivariate logistic regression analysis. The results of unconditional univariate and multiunivariate logistic regression analysis were shown in Tables 1 and 2.

**Table 1.** Unconditional univariate logistic regression analysis for contributing factors.

| Variable | Regression coefficient | Standard error | P value | OR | 95% CI |
|---|---|---|---|---|---|
| Trigger point | 3.458 | 1.416 | 0.015 | 31.768 | 1.981~509.535 |
| Cerebrospinal fluid flow | 1.446 | 0.733 | 0.049 | 4.247 | 1.009~17.877 |
| Painless: Pain-free | 6.725 | 0.966 | 0.000 | 833.279 | 125.576~5529.355 |

CI: confidence interval.

**Table 2.** Unconditional multiunivariate logistic regression analysis.

| Variable | Regression coefficient | Standard error | P Value | OR | 95% CI |
|---|---|---|---|---|---|
| Trigger point | 3.339 | 1.259 | 0.008 | 28.193 | 2.390~332.556 |
| Pain-free | 5.636 | 0.684 | 0.000 | 380.386 | 73.436~1070.548 |

CI: confidence interval.

### Follow up

Analgesia was not identified in our study while compromised pain sensation was found in selected patients. Facial numbness was common but well tolerated in patients, which resolved spontaneously. Formication was noted in 2 patients.

## DISCUSSION

The incidence of idiopathic trigeminal neuralgia is 182/100000, with the annual morbidity of 3~5/100000. The pain is intense and will deteriorate over time. Although numerous strategies have been applied in the treatment of trigeminal neuralgia, some patients still have recurrence.

### Mechanism of PRGR

PRGR for trigeminal neuralgia was initiated by Hakanson (1981) in which only anhydrous glycerol was used. Owing to the hyperosmolality and hypotoxicity to nerves, anhydrous glycerol can distend and rupture myelin accompanied by axonal atrophy, which compromise the excitation conduction of neurons (Hakanson, 1981), and restrain the generation of ectope impulse (Eide et al., 1998) . In addition, anhydrous glycerol can damage both small unmyelinated fiber and myelinated fiber. Recent study also shows that it is more harmful to myelinated fiber (Pal et al., 1989). Demyelination of trigeminal nerves results in “short circuit” between fibers, so non- painful stimulus can induce pain reaction, which is one of the leading causes of trigeminal neuralgia (Mannion et al., 1998; Doubell et al., 1997). For the patients with definite trigger point, the episodic pain may be provoked by the myelinated fibers. It is postulated that anhydrous glycerol can impair the short circuit achieving the effectiveness. In the present study, most patients had facial numbness which supported the hypothesis that glycerol destroyed the fibers.

In this study, a total of 210 consecutive patients with trigeminal neuralgia received PRGP. Except for the number of patients and experience of treatment, we adopted the procaine test to locate the puncture rather than Meckel's Cavity, so the efficacy of first PRGP was on a high level. However, in a previous study, complete pain relief was achieved in 78% of patients after the initial glycerol injection, and partial relief was obtained in 13% of patients (Pickett et al., 2005).

### Clinical significance

In the present study, logistic regression analysis was employed and results revealed presence of a definite trigger point and complete painless in procaine test were the main contributing factors affecting the outcome of PRGR, with the OR of greater 10. The patients with definite trigger point achieved complete pain relief after PRGR and a majority of patients with complete painless in procaine test had complete pain relief. However, complete pain relief was not observed in several patients with complete painless in procaine test, which may be caused by unfavorable needle position in glycerol injection causing needle-point displacement. It should be avoided in the second PRGR. Empirically, flow of cerebrospinal fluid is regarded as a major factor affecting the prognosis of trigeminal neuralgia after PRGR (Zhou et al., 1998). Statistical analysis in the present study revealed there was no statistical significance in the relationship between flow of cerebrospinal fluid and outcome of PRGR. The patients with flow of cerebrospinal fluid still required procaine test to confirm complete painless. Flow of cerebrospinal fluid may be a concomitant consequence of procaine test, but it does confirm the right needle point position. Although further

studies are needed, the results above mentioned were consistent to our clinical findings.

## Clinical implications

### Selection of indications

PRGR aims to destroy the “short circuit” by damaging the sensory fibers. Therefore, the patients with definite trigger point are good candidates for PRGR and it will be difficult for those without definite trigger point to achieve complete pain relief. Among 16 patients unresponsive to treatment, 14 did not have definite trigger point.

### Painless in procaine test

The accurate needle point position is essential to achieve complete pain relief. Procaine test aims to confirm the position of needle point. Procaine injection can lead to complete painless in the corresponding region innervated by affected nerves. Usually, most of patients have numb-ness at this time which confirms the correct needle point position. A majority of patients can achieve complete pain relief after treatment if the needle point is not displaced during injection. We adjusted the depth and/or position of the needle point based on the response of patients to procaine test. For example, in a patient with branch II affected, if numbness is found in the region innervated by branch I, this indicates the needle point should be retracted a little; if numbness is noted in the area innervated by branch III, it shows the needle point should be advanced. Of note, it is painless in procaine test that can assure the efficacy of PRGR.

### Improve of the puncture technique

The effectiveness of PRGR requires proficient puncture technique, which limits its wide application (Taha and Tew, 1997). To assure successful punctuation, surgeons have to be familiar with the anatomic structure of foramen ovale. First, the surface anatomical landmark should be confirmed. The puncture point locates on the cross of the vertical line of lateral orbital margin (angulus oculi lateralis) and the horizontal line of ipsilateral oral fissure (about 2.5~3 cm away from angular mouth). The puncture direction is defined by the intersection of sagital planes of two lines. One was the line between the puncture point and the ipsilateral pupil and the other was the line between puncture point and the ipsilateral anterior border of temporo- articular tubercle (correspond to 3 cm near the external acoustic meatus on the line between the external acoustic meatus and lateral ocular angle). The key point of puncture is to adjust the puncture direction according to the feedback from the needle point, but not to blind adjustment. Pterygoid process locates at the medial side of foramen ovale, a flat skull plate at the front, and the back foramen ovale composes of uneven bones. When the needle point reaches flat skull plate, the puncture angle should be increased, and feeling uneven needle point suggests the puncture angle should be decreased. According to our experience, foramen ovale punctuation was uneventfully performed in 210 patients by hand without fluoroscopy.

## Recurrence

Nowadays, there are several surgical strategies for the treatment of trigeminal neuralgia including microvascular decompression, ganglion nervi trigemini sacculus proprius compression, trigeminal nerve posterior root radiofrequency electric coagulation, ganglion nervi trigemini surface nerve fiber tractotomy, gamma knife therapy, PRGR, etc. However, recurrence of trigeminal neuralgia is still reported. About 15% of patients have recurrence after PRGR (Zhou et al., 1998). We postulate that the recurrence may be attributed to the regeneration of nerve fibers due to incomplete destruction. For these patients, alternative therapies can be applied, and a second PRGR may also relieve the pain without increasing risk. In our study, 17 patients had recurrence after PRGR and a second PRGR was performed achieving complete pain relief, which was consistent with previous report (Jho and Lunsford, 1997; Zhou et al., 2003). No specific side effects have been noted.

PRGR remains a minimally invasive, safe, and effective operation for patients with trigeminal neuralgia accom-panied by few side effects and complications. It is also effective for some patients unresponsive to treatment or having recurrence. The patients with definite trigger point are good candidates for PRGR. Painless in procaine test may predict complete pain relief.

## REFERENCES


Doubell TP, Mannion RJ, Woolf CJ (1997). Intact sciatic myelinated primary afferent terminals collaterally sprout in the adult rat dorsal horn following section of a neighbouring peripheral nerve. J. Comp. Neurol., 380: 95-104.

Eide PK, Rabben T, Skjelbred P, Stubhaug A (1998). The effect of peripheral glycerol on trigeminal neuropathic pain examined by quantitative assessment of abnormal pain and sensory perception. Acta Neurochir (Wien). 140(12): 1271-1277.

Hakanson S (1981). Trigeminal neuralgia treated by the injection of glycerol into the trigeminal cistern. Neurosurgery, 9(6): 638-646.

Jefferson A (1963). Trigeminal root and ganglion injections using phenol in glycerine for the relief of trigeminal neuralgia. J. Neurol. Neurosurg. Psychiatry. 26(4): 345-352

Jho HD, Lunsford LD (1997). Percutaneous retrogasserian glycerol rhizotomy: current technique and results. Neursosurg Clin. N. Am., 8(1): 63-74.

Mannion RJ, Doubell TP, Gill H, Woolf CJ (1998). Deafferentation is insufficient to induce sprouting of A-fibre central terminals in the rat dorsal horn. J. Comp. Neurol., 393: 135-144.

Pal HK, Dinda AK, Roy S, Banerji AK (1989). Acute effect of anhydrous glycerol on peripheral nerve: an experimental study. Br. Neurosurg., 3: 363-470.

Pickett GE, Bisnaire D, Ferguson GG (2005). Percutaneous retrogasserian glycerol rhizotomy in the treatment of tic douloureux associated with multiple sclerosis. Neurosurgery, 56(3): 537-45.

Taha JM, Tew JM (1997). Treatment of trigeminal neuralgia by percutaneous radiofrequency rhizotomy. Neurosurg. Clin. N. Am. 8: 31-39.

Zhou QG, Dong CL, Zhao W (2003). Long term efficacy of percutaneous retrogasserian glycerol rhizotomy. Chin. J. Neurosurg. 19(6): 464-466.

Zhou YW, Xu MH, Chen GX (1998). Percutaneous retrogasserian glycerol rhizotomy for patients with idiopathic trigeminal. Chin. J. Pain Med. 4(2): 116-119.