Glycerol rhizolysis for treatment of trigeminal neuralgia

RONALD F. YOUNG, M.D.
Division of Neurological Surgery, University of California at Irvine Medical Center, Orange, California

Percutaneous retrogasserian glycerol instillation was performed under local anesthesia for treatment of trigeminal neuralgia in 162 patients. A simplified technique that did not involve cisternography was used. Initial pain relief was achieved in 146 patients (90.1%). Recurrent pain was noted in 27 patients (18.5%) and was more frequent (50%) in patients who had undergone surgical treatments prior to glycerol injection than in those who had no previous surgical treatment (12.3%). A second glycerol injection was carried out in nine patients and a third injection in two patients. The follow-up period extended from 6 to 67 months and 77.8% of patients are totally pain-free after one or more glycerol injections. Another 8.6% experienced good pain relief with the addition of small doses of pharmacological agents. Thus, 140 (86.4%) of the original 162 patients experienced satisfactory pain control following glycerol rhizolysis.

Initial sensory loss on the face occurred in 117 patients (71.6%) but at last follow-up examination only 46 patients (28%) experienced mild orofacial hypalgesia and 13 patients (8%) noted analgesia. The corneal reflex was absent in three patients (1.8%) and reduced in five (3.1%). No patients noted corneal ulceration or anesthesia dolorosa. Percutaneous retrogasserian glycerol rhizolysis offers a rapid, safe, reliable, and relatively inexpensive surgical approach to treatment of trigeminal neuralgia.

KEY WORDS - trigeminal neuralgia • trigeminal nerve • glycerol • rhizolysis

A variety of methods are currently in use for treatment of trigeminal neuralgia. These include pharmacological agents as well as open and percutaneous surgical procedures. The usual approach utilizes pharmacological agents initially and reserves surgical therapy for patients whose pain is not effectively relieved by medications or who are intolerant of medications due to toxicity or allergic reactions.

The most frequently used surgical approaches include microvascular decompression of the trigeminal nerve via retromastoid craniectomy or percutaneous radiofrequency rhizotomy. Both methods suffer certain disadvantages. Microvascular decompression represents a major neurosurgical procedure in the posterior fossa with risks of severe injury to cranial nerves or the brain stem. In addition, the procedure requires several days of hospitalization and use of expensive ancillary services such as the operating room. Percutaneous radiofrequency rhizotomy usually results in loss of normal facial sensory function and may rarely be accompanied by injury to other cranial nerves. Repeated doses of intravenous anesthetic agents for needle placement and the creation of radiofrequency lesions often require at least a brief hospitalization.

In 1981, Håkanson reported his fortuitous finding that glycerol, when applied to the retrogasserian trigeminal rootlets by a percutaneous approach, relieved the pain of trigeminal neuralgia with little or no alteration in facial sensory function. Only a few other investigators, notably Sweet, et al., Lunsford and Bennett, and Arias, have reported on the use of this method for treatment of trigeminal neuralgia. This report describes the author's experience in treating 162 patients with trigeminal neuralgia by retrogasserian glycerol instillation. The procedures have been performed on an outpatient basis. A simplified method, which usually requires only local anesthesia, makes percutaneous puncture of the retrogasserian cistern via the foramen ovale fast and reliable.

Summary of Cases

Percutaneous retrogasserian glycerol instillation was performed in 162 patients between the ages of 38 and 93 years (84 women and 78 men). All patients had classic symptoms of trigeminal neuralgia, involving brief recurrent lancinating or electric shock-like pains confined to the orocutaneous distribution of one or more trigeminal nerve divisions and associated with the presence of “trigger zones” from which innocuous stimuli elicited the patient's pain. All of these patients had previously received therapy with carbamazepine, phen-
TABLE 1
Distribution of trigeminal nerve pain in 162 patients

<table>
<thead>
<tr>
<th>Involved Division of Trigeminal Nerve</th>
<th>No. of Cases</th>
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<tr>
<td>1</td>
<td>2</td>
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<td>2</td>
<td>23</td>
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<td>29</td>
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<td>18</td>
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<tr>
<td>2, 3</td>
<td>76</td>
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<td>1, 2, 3</td>
<td>14</td>
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ytoin, and in some cases, baclofen. In some patients, the pain had been initially relieved but had recurred in spite of maximal dosage of medications. Intolerance to carbamazepine was frequent (especially in older patients) and usually manifested as reduced organic mental function and gait disturbances. The distribution of pain in the various trigeminal divisions is shown in Table 1. Fifteen patients had previously undergone one or more surgical procedures including alcohol lysis of peripheral trigeminal branches (one patient), open surgical rhizotomy (two patients), radiofrequency rhizotomy (12 patients), and microvascular decompression (four patients). The mean duration of pain was 6.4 years.

All patients underwent computerized tomography or magnetic resonance scanning to evaluate possible structural intracranial causes for their facial pain, with negative results. All patients were offered the surgical alternatives of microvascular decompression, radiofrequency rhizotomy, or glycerol injection.

Technique of Glycerol Rhizolysis

All patients were admitted to the Outpatient Surgical Unit on the morning of the procedure, where general physical examination and review of laboratory studies were carried out. The procedure itself was performed in the Radiology Suite, utilizing a Miemer radiological unit and a pneumoencephalography chair in 104 patients, and a C-arm fluoroscopy unit in 58 patients.

Preliminary fluoroscopy with an oblique projection was performed with the patient in a supine position to identify the foramen ovale ipsilateral to the patient's pain. For the oblique view the patient's head was rotated about 15° away from the side of pain. The x-ray tube was angled 40° from the vertical plane and the central ray of the x-ray beam was directed at a point about 1 in. lateral to the angle of the mouth ipsilateral to the patient's pain. The central ray of the x-ray beam thus traversed the intended trajectory of the needle which was to be used to puncture the foramen ovale, the latter being viewed en face (Fig. 1). Hyperextension of the neck, such as is required for the submentovertex view of the foramen ovale, was not necessary.

After identification of the foramen ovale the needle was inserted. Beginning at a point about 2 cm lateral to the angle of the mouth, ipsilateral to the patient's pain, the dermis and underlying soft tissues were infiltrated with 1% lidocaine. A 3½ in. No. 18 or 20 needle with stylet was utilized to puncture the trigeminal cistern via the foramen ovale. The needle was inserted at the same point as the anesthetic infiltration and advanced slowly under intermittent fluoroscopic control toward the foramen ovale. The needle was directed in the sagittal plane toward the midpoint of the ipsilateral pupil and in the coronal plane at a point about 2 cm anterior to the external auditory meatus. No attempt was made to penetrate the foramen ovale on a single thrust of the needle. Under oblique fluoroscopy, the needle was advanced incrementally and redirected when necessary. A gloved finger inside the mouth prevented penetration of the oral cavity. In order to ensure return of cerebrospinal fluid (CSF) from the trigeminal cistern, the foramen ovale was penetrated just medial to the midpoint of the foramen (Fig. 2 left). An excessively lateral puncture of the foramen ovale (Fig. 2 right) may lead to CSF return from the subarachnoid space beneath the temporal lobe. The foramen was also penetrated as near as possible to the midpoint in the anteroposterior direction. Occasionally, even with this method, initial puncture of the foramen was not always ideal. In such cases, the needle was withdrawn and replaced. Considerable resistance was felt as the needle tip penetrated the foramen, then the resistance rapidly dissipated. As soon as the resistance decreased, no further needle advancement was attempted. The stylet was removed to determine if CSF flow was present. In addition, the lateral
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The fluoroscopic view was used to assess the depth of penetration. Our intent was to place the needle tip as shallow as possible within the trigeminal cistern (Fig. 3 left). When needle placement was ideal and good CSF flow was present, the patient was brought to the sitting position and the depth of needle penetration was confirmed by lateral fluoroscopy. The patient's head was positioned so that the orbitomeatal line was horizontal. In this position, the trigeminal cistern is oriented with the mandibular division most inferior, the ophthalmic division most superior, and the maxillary division between.

In our first few patients, the volume of the trigeminal cistern was estimated using an injection of metrizamide via the needle as recommended by Håkanson and Lunsford and Bennett (Fig. 3). We no longer consider this maneuver necessary and prefer to estimate the volume of glycerol required by criteria to be described.

Fig. 2. Fluoroscopic views. Left: Correct location of puncture of the right foramen ovale just medial to the midpoint of the foramen and about equally between the anterior and posterior rims. Right: Excessively lateral puncture of right foramen ovale. Cerebrospinal fluid may be obtained with such a needle location, giving a false impression that the needle is in the trigeminal cistern when it may actually be in the subarachnoid space beneath the temporal lobe.

Fig. 3. Lateral radiographic views with contrast injection. Left: Correct placement of the needle low in the trigeminal cistern. In this location the cistern can be filled incrementally from inferiorly. Such a needle location is best for treatment of pain in the mandibular and maxillary or mandibular divisions. Right: This needle placement is too deep for the treatment of most patients. Glycerol will be in contrast with ophthalmic division fibers immediately upon injection of a small volume.
Sterile anhydrous glycerol was injected via the needle in 0.05-ml increments using a 1-ml syringe. For pain in the mandibular, in the mandibular and maxillary, or in all three trigeminal divisions, a total of 0.1 to 0.15 ml was initially injected. Within a few seconds to a few minutes, the patients usually began to note a tingling or burning sensation in the face in the region supplied by the mandibular division. Within another 3 to 5 minutes, some reduction in pinprick sensitivity was usually noted, most often confined to the cutaneous distribution of the mandibular division but occasionally extending into the maxillary division and in one case into the ophthalmic division territory. Further incremental injections of 0.05 to 0.1 ml glycerol were carried out depending on the location of the patient's pain and the distribution of paresthesias or altered pinprick sensitivity following injection. For pain localized only to the ophthalmic division, injection of glycerol was preceded by metrizamide (300 mg/ml iodine). The metrizamide was injected slowly under lateral fluoroscopic monitoring until the cistern was filled enough to cover the second and third divisions with metrizamide. Glycerol was then injected, again in increments of 0.05 ml, with monitoring of corneal and cutaneous ophthalmic division sensation. If no sensory changes occurred, a total of 0.15 ml was injected. Total injection volumes in all patients varied from 0.15 to 0.55 ml. Several patients complained of facial pain immediately after glycerol injection. In one early patient, the injection could not be completed due to facial pain. A small supplementary dose of intravenous Brevital (methohexitol sodium) or Pentothal (thiopental) was used in a few other patients because of pain following glycerol injection.

Patients were observed while in the sitting position for 5 to 10 minutes after completion of the injection in order to be certain that an adequate volume of glycerol had been instilled. Some patients experienced no identifiable alteration in pinprick sensation following injection, and the total volume of glycerol utilized was estimated mainly on the basis of the patient's description of a temporary mild burning sensation or paresthesias in the distribution of their pain. If sensory alterations were limited to the distribution of the patient's pain the needle was removed and the patient was returned to the Outpatient Surgical area and maintained in a sitting position for 2 hours. Thereafter, the patients were allowed to assume any position they desired and were discharged home 2 to 3 hours after conclusion of the procedure.

**Operative Results**

All results described in this report are those noted at the time of last follow-up examination. The follow-up period ranged from 6 to 67 months after the procedure. Of the original 162 patients, 146 (90.1%) achieved relief of their pain following the initial glycerol injection. Nearly all of these patients noted relief within a few minutes to a few hours after the injection. A few patients did not experience complete relief for 24 hours, and only very rarely did individuals experience relief over a period of 1 to 7 days. In virtually all of the patients who did not obtain initial relief, there had been either poor return of CSF via the needle or complete lack of facial paresthesias during injection which suggested that the glycerol had not been injected into the subarachnoid space. Of the 28 patients who had previously undergone open surgical or percutaneous treatments, 24 (85.7%) experienced initial pain relief, whereas initial pain relief was experienced in 122 (91%) of 134 patients who had never had previous surgical treatment.

Recurrent pain was noted in 27 (18.5%) of the 146 patients who had enjoyed initial relief of pain. Fifteen patients (12.3%) who had not previously undergone surgical treatment experienced recurrent pain, whereas 12 patients (50%) who had prior surgical treatment experienced recurrent pain. The time course of recurrence after a single glycerol injection is shown in Table 2. In the first year, the likelihood of recurrence was about 6% to 7%. Thereafter, recurrences were noted at the rate of about 4% per year. The high recurrence rate for patients followed for more than 5 years is probably unreliable because of the small number of patients observed for that period of time. Nine patients had a second glycerol injection and two patients had three injections. Seven of the 10 who had repeat injections had continuing pain relief at their last follow-up examination. Sixteen patients elected to have radiofrequency procedures rather than repeat glycerol injections, and 14 of these are now free of pain. Four patients underwent microvascular decompression or partial rhizotomy via the posterior fossa approach, two of whom had relief. Fourteen patients decided to have no further procedures, and 10 of these patients experienced good pain control with minimal doses of carbamazepine or baclofen, whereas previously they had had unsatisfactory pain control while taking pharmacological agents.

At last follow-up review, 126 (77.8%) of the original 162 patients experienced complete pain relief as the result of one or more glycerol injections. Another 10 patients (8.6%) have good pain relief due to glycerol with only minimal pharmacological treatment. Thus,
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140 (86.4%) of the original 162 patients have experienced satisfactory pain relief due to glycerol rhizolysis.

Alterations in facial sensation were noted in 117 patients (71.6%). The most common change was mild hypalgesia in which a single or sometimes double pinprick was not perceived as sharp, but repeated pinpricks were perceived as sharp, although less sharp than on the contralateral side. In 49 patients hypalgesia occurred only in the sensory distribution of the trigeminal division in which the patient had experienced pain. In 48 patients there was hypalgesia in a contiguous division, usually in the maxillary division when pain had only occurred in the mandibular division, or vice versa. In five patients (3.1%) there was a reduction in the corneal reflex when pain had been limited to the maxillary and mandibular divisions, and in three patients (1.8%) the corneal reflex was virtually absent. No patient experienced neuroparalytic keratitis or visual loss following the procedure.

Twenty patients experienced denser orocutaneous analgesia so that even repeated pinpricks were not perceived as painful. These patients most often volunteered sensations of numbness, paresthesias, or a feeling that the lip was enlarged. Five patients complained that the altered sensation was annoying, but no patient experienced anesthesia dolorosa. In fact, no patient experienced anesthesia in the entire distribution of a single trigeminal division. A few patients initially complained of biting their tongues or oral mucosa without sensation but, with the passage of 3 to 6 months, there was a tendency for sensation to return and inadvertent tongue-biting stopped. In fact, there was overall a definite tendency for the hypalgesia, especially, to gradually recede. At last follow-up examination, only 46 of the 97 patients who originally noted hypalgesia continued to experience mild orofacial hypalgesia (which was barely detectable) and 13 patients had analgesia.

Complications were extremely rare. Sixty-one patients (37.6%) experienced bouts of herpes labialis following the procedure but all lesions healed without sequelae. A single patient developed meningitis due to Streptococcus salivarius, presumably due to inadvertent penetration of the oral cavity or possibly due to the needle passing through a salivary gland duct. The meningitis was resolved with antibiotics. One elderly patient experienced extreme and rapid enlargement of the facial soft tissues resulting from local hemorrhage, which made proper positioning of the needle difficult. This patient had initial pain relief but suffered a recurrence. One patient complained of severe local ocular pain during the injection and the procedure was terminated after only 0.1 ml of glycerol had been instilled. No other complications were noted.

Discussion

Glycerol, a simple three-carbon molecule, is neurotoxic when placed in pure form directly onto peripheral nerves or nerve roots. The initial hypothesis that glycerol preferentially damaged small myelinated or unmyelinated fibers has been proven untrue by subsequent histological evaluation. Rengachary, et al., Lunsford, et al., and Håkanson and Persson have shown that glycerol produces axonal disruption regardless of fiber size and that the degree of damage is greatest at the periphery of a multifiber peripheral nerve or fascicle and decreases centrally.

Håkanson was the first to demonstrate that trigeminal neuralgia could be relieved by the retrogasserian instillation of pure glycerol. In 1983, he reported complete pain relief in 96 of 100 patients, minimal recurrence in three patients, and full recurrence in one after a single glycerol injection. Thirty-one of his patients eventually experienced pain recurrence and underwent one or more rejections. Of the total of 100 patients followed at least 1 year, 77% were completely pain-free and 19% were "doing well" on drug therapy. Sweet, et al., reported good pain relief in 24 (88.9%) of 27 patients treated with glycerol injection. Lunsford and Bennett reported complete pain relief in 67 (59.8%) of a group of 112 patients with trigeminal neuralgia who were followed for 4 to 28 months; 23% were improved after retrogasserian glycerol injection, and were considered satisfactorily relieved of their pain with the addition of pharmacological therapy; and 10% were unimproved. Those authors performed a second glycerol injection in 17% of their patients to achieve the final result. Arias reported relief of trigeminal neuralgia in 91 of 100 patients after a single glycerol injection; recurrent pain was noted in only 10% of patients and with a second or third injection 95% of patients had pain relief.

In our series of 162 patients followed for at least 6 months, a single injection achieved pain relief in 90.1%; recurrent pain was noted in 18.8%. In this series, initial alterations in facial sensation were noted in 71.6% of patients and 36.4% reported significant persistent facial analgesia at their last follow-up examination. Sweet, et al., noted significant facial analgesia in 53% of their patients. On the other hand, Håkanson reported only a "slight numbness" which was most often restricted to a small area of a single division in 60% of his patients. In their series of 112 patients, Lunsford and Bennett described major hypalgesia or hypesthesia in only two patients (1.8%) and minor sensory changes in 29 patients (25.9%). Reduced corneal sensation was noted by Lunsford in only two patients (1.8%). Arias noted persistent facial analgesia in only 13% of his patients. It is not clear why we experienced a greater incidence of sensory loss following retrogasserian glycerol instillation. Differences in volume of injected glycerol could not account for differences in incidence of sensory loss because the volumes (0.1 to 0.55 ml) were identical in all four series of patients.

Our technique is considerably simplified compared to that reported by other authors, and the entire procedure can usually be accomplished in 30 to 45 minutes or less. The oblique radiographic projection described by Whisler and Hill and reemphasized by Apfelbaum...
allows rapid, safe, and accurate penetration of the foramen ovale. The foramen is viewed briefly by fluoroscopy between each incremental needle advancement, and thus unintended penetration of structures is avoided. The patient remains in a comfortable supine position, avoiding the neck extension required for submentovertex views (a position that may be impossible for elderly patients). Careful attention to penetration of the foramen ovale just medial to its midpoint in the mediolateral direction and as close as possible to the midpoint in the anteroposterior direction assures penetration of the trigeminal cistern and not the subarachnoid space beneath the temporal lobe.\textsuperscript{1} The latter encroachment occurs when penetration of the foramen is too lateral. When foraminal penetration is excessively anterior or posterior, a subdural or even extradural location of the needle tip may result. Although medial to lateral needle position may be clearly assessed on the submentovertex view, the anteroposterior location is not judged as easily since the foramen is viewed obliquely and not \textit{en face} as with the projection we prefer. Precise needle placement is more important for glycerol than for radiofrequency rhizolysis; in the latter procedure, heat transmission from a needle placement which is not ideal may still create a lesion. Lunsford and Bennett\textsuperscript{14} also suggested that incorrect needle placement may account for failure to produce analgesia following radiofrequency heating.

The depth of needle penetration is important and is assessed by lateral fluoroscopy as soon as the foramen ovale is punctured. The needle should be placed as shallow as possible for treatment of mandibular division pain to allow injection of a minimal amount of glycerol which will avoid injury to the maxillary or ophthalmic divisions. Deeper penetration is employed for treatment of maxillary or ophthalmic division pain. For the latter, the cistern may be partially filled with metrizamide prior to glycerol injection. The glycerol will then float on top of the metrizamide and affect only the ophthalmic division.

The volume of glycerol injected was determined by monitoring the patients' sensory response to incremental volumes of 0.05 ml. The paresthesias noted with glycerol injection were described by Sweet, \textit{et al.},\textsuperscript{18} and have been reemphasized by Arias.\textsuperscript{2,3} Lunsford,\textsuperscript{11} however, indicated that he has found no consistent physiological response to incremental glycerol injection that would allow him to distinguish between subarachnoid, subdural, or subtemporal injection. Our experience parallels that of Sweet, \textit{et al.},\textsuperscript{18} and Arias\textsuperscript{5} and it has been our specific goal to avoid totally filling the retrogasserian cistern with glycerol in order to minimize the risk of corneal analgesia with loss of the corneal reflex.

There are several other negative aspects of performing cisternography with iodinated contrast agents prior to glycerol injection. The contrast agent itself may provoke headache as described by Lunsford and Bennett.\textsuperscript{12,14} In order to drain contrast material from the cistern prior to glycerol injection it is necessary to extend the patient's head or to change his position from sitting to supine. For injection of glycerol, the head must again be flexed or the patient must be brought to the sitting position. These maneuvers may cause the needle to be displaced out of the cistern so that the original assurance of subarachnoid penetration gained from cisternography may not pertain in the patient's position at the time the glycerol is injected. Significant changes occur in needle position with a change from supine to sitting. Thus, the position of the needle tip must be verified by fluoroscopy immediately prior to the injection.

Finally, the accuracy of the method of estimating the trigeminal cistern volume as recommended by Håkan-son\textsuperscript{8,9} and Lunsford\textsuperscript{11,12} must be questioned. Contrast material injected into the cistern does not become visible until a certain concentration is reached upon mixing with the CSF in the cistern. Thus, one cannot be certain when volume estimation should begin. Additionally, one cannot be sure whether the cistern is truly empty upon extending the patient's head but only that the concentration of contrast is below that which can be detected by the naked eye on fluoroscopy. Experience with delayed computerized tomography scanning after myelography indicates that contrast material remains present, albeit in reduced concentration, when it is no longer visible by fluoroscopy or plain radiographs. The present author has noted a higher incidence of corneal analgesia in patients treated early in this series when cisternography was used; this finding may be related to residual contrast medium in the cistern causing the glycerol to float more superiorly and contacting fibers of the ophthalmic division. The author agrees fully with Arias\textsuperscript{5} that absolutely exact radiographic criteria for needle placement must be met and that physiological monitoring coupled with precise needle placement is an excellent technique.

Sweet\textsuperscript{17} recently reported that seven neurosurgical services worldwide, including his own, had discontinued using the glycerol technique because of too many initial failures, subsequent recurrences, and major sensory losses or dysesthesias. Our experience has been that initial failures occur no more often than with other procedures such as radiofrequency rhizotomy or microvascular decompression. The incidence of later recurrences in our hands and that of others is also very similar to the recurrence rate reported for the other surgical procedures. We believe that percutaneous retrogasserian glycerol injection is the initial surgical treatment of choice for patients over 50 years of age due to the ease and safety of the procedure. If an initial injection fails, a second attempt may be made or a radiofrequency rhizotomy may be employed. Microvascular decompression, as pointed out by Sweet,\textsuperscript{17} has a mortality rate of about 1% and another 1% risk of major neurological morbidity in the hands of the world's most experienced neurosurgeons. In less experienced hands, the risks are considerably greater. Microvascular decompression should be considered in younger patients with trigemi-
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... neuralgia, particularly those concerned about their ability to tolerate facial analgesia for many years. Even most younger patients prefer the risk of facial analgesia, however, to the risks of death or major neurological morbidity.

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References


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Address reprint requests to: Ronald F. Young, M.D., Division of Neurosurgery, University of California at Irvine Medical Center, 101 The City Drive South, Orange, California 92668.