Percutaneous retrogasserian glycerol rhizotomy for trigeminal neuralgia: technique and expectations

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Object. In the management of trigeminal neuralgia (TN), physicians seek rapid and long-lasting pain relief, together with preservation of trigeminal nerve function. Percutaneous retrogasserian glycerol rhizotomy (PRGR) offers distinct advantages over other available procedures. The aim of this report was to provide details of the PRGR procedure and its expected outcome.

Methods. The authors reviewed their experience with PRGR in 1174 patients to evaluate the procedural technique, results, and complications. Although it is clear that TN is not a static disorder but one characterized by remissions and recurrences, long-lasting pain relief was noted in 77% of patients, with 55% discontinuing all medications and 22% requiring some drug usage.

Conclusions. The authors discuss the role of PRGR in their practice, along with other procedures such as microvascular decompression and gamma knife surgery, for idiopathic or multiple sclerosis–related TN. They conclude that PRGR had distinct advantages over other procedures, which include eliminating the need for intraoperative confirmatory sensory testing, and a lower risk of facial sensory loss.

KEY WORDS • trigeminal neuralgia • facial pain • glycerol rhizotomy • multiple sclerosis

OVERVIEW

The clinical challenge of TN has many medical and surgical resolutions. In patients whose disease is medically refractory because of sustained, intolerable side effects from medication, a surgical procedure is considered. The choices include procedures that aim to manage the cause of the pain, such as MVD, or those that treat the nerve but “ignore” the cause of the pain (different rhizotomy procedures). Stereotactic radiosurgery, when performed at the anatomical location of vascular compression, may also work to “treat the cause,” but it is believed that the effect of this modality is based more on selective axonal degeneration of the nerve. Whenever any clinical problem is treated with a wide variety of surgical alternatives, it is because one procedure does not provide a uniform benefit for all patients. This was the case with TN, for which 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 (balloon microcompression, thermal-induced axonal degeneration by radiofrequency rhizotomy, radiation-induced degeneration produced by stereotactic radiosurgery, or chemical ablation with glycerol rhizotomy). Injection of chemical agents into peripheral nerve targets (that is, alcohol injections) are also available.

Interestingly, in earlier centuries, other possible surgical remedies included carotid ligation, galvanic stimulation, dental procedures (some still performed today), and abdominal surgery such as appendectomy and colon resection. Direct alcohol injection into the trigeminal nerve was reported in 1910. According to Burchiel, Härtel gets credit for the accepted technique of spinal needle placement into the trigeminal cistern. When absolute alcohol was injected into this location, multiple severe cranial neuropathies could be seen. Jefferson advocated the use of phenol mixed with glycerald with glycerin rather than absolute alcohol.

Lars Leksell had long been interested in the use of focused radiation for the management of TN. In his initial work in the early 1950s, he coupled an orthovoltage x-ray tube to a stereotactic frame to irradiate the trigeminal ganglion. The first-generation gamma knife was built in 1967. Leksell conceived its use for focal irradiation of functional brain targets. Before performing the procedure, he needed a way to identify the nerve consistently by using standard x-ray films in the era before computerized tomography scans. To localize the nerve for radiosurgery, Leksell and Häk-
anston\textsuperscript{3} injected tantalum dust mixed with glycerol into the trigeminal cistern as a marker. When this targeting solution was injected prior to radiosurgery, patients noted pain relief, and PRGR was born as a new surgical procedure.

In our management of TN, our goals are rapid and long-lasting pain relief, together with preservation of trigeminal nerve function. The PRGR technique offers distinct advantages over other percutaneous procedures. These include eliminating the need for intraoperative confirmatory sensory testing (patient cooperation is not necessary) or a radiofrequency generator. The patient simply need not “participate” during the procedure and thus can be more deeply anesthetized. Precise anatomical localization of the target is performed using intraoperative cisternography rather than asking the patient to describe radiofrequency-induced sensory changes. Glycerol is associated with a lower risk of facial sensory loss compared with either radiofrequency rhizotomy or balloon microcompression. This feature significantly reduces the risk of deafferentation pain. We believe that pain relief without significant sensory loss and without high surgical risk is possible for virtually all patients by using MVD, PRGR, or stereotactic radiosurgery, either alone or in combination. The choice of procedure is related to the factors of patient age, medical condition, symptom severity, and personal preference. Glycerol rhizotomy remains our preferred primary surgical procedure for patients with multiple sclerosis–related TN.\textsuperscript{6,11}

**CLINICAL MATERIAL AND METHODS**

**Patient Selection**

As with all surgery for TN, only patients with typical pain should be selected for PRGR. The correct diagnosis is validated by a careful history that elucidates the quality, character, and distribution of pain. In patients with atypical TN (who usually experience a lingering pain without triggers), rhizotomy can be used to manage any severe lancinating component, but it has little effect on more constant pain. We rarely perform rhizotomy in this setting unless it is for patients who have previously undergone a successful procedure for typical TN symptoms.

After the appropriate diagnosis is made, we recommend initial medical treatment with appropriate doses of carbamazepine, Trileptal, gabapentin, phenytoin, baclofen, or perhaps Lamictal. Selected additional medications also may be used. High-resolution brain imaging should be performed to exclude a skull base lesion, vascular anomaly, or basal tumor that might change the regional anatomy or be the cause of TN. At our center, PRGR is offered as first-line therapy in patients with idiopathic TN. Such patients also have significant medical risks that exclude the use of MVD. In addition, these patients generally have pain so intense that they cannot eat, chew, or talk. For such patients the possible latency interval associated with gamma knife surgery is not acceptable.\textsuperscript{7} As a minimally invasive strategy, PRGR is used as a second-line approach in patients who have not responded adequately to radiosurgery. Finally, PRGR is an excellent first choice for patients with TN in the setting of multiple sclerosis,\textsuperscript{6,11} which seems to occur at an earlier age than in patients without idiopathic TN. It is an appropriate second-line therapy in those in whom other surgical options such as MVD have failed.

It is important to note that the technique of PRGR can vary from institution to institution. Some surgeons do not perform contrast cisternography and others do not directly visualize the injection of glycerol into the trigeminal cistern with metallic markers such as tantalum. Thus, if PRGR was said to have failed previously due to technical difficulties, we may repeat the procedure in an attempt to confirm that glycerol was in fact injected in the appropriate location.

Finally, preoperative testing is conducted to rule out a bleeding diathesis, and electrocardiograms and chest x-ray films are obtained as indicated. All antiplatelet agents (such as aspirin or ticlopidine) must be discontinued 1 week before PRGR. If patients must remain on warfarin or other agents, then the gamma knife is a better surgical choice.

**Anesthetic Technique**

At our institution, PRGR is performed with the patient receiving continuously monitored intravenous sedation in the operating room setting. The anesthesiologist monitors blood pressure, heart rate, oxygen saturation, and respiratory function. Adequate sedation for the patient and a quick response to any cardiovascular changes that might occur during the procedure are essential. Because PRGR does not require intraoperative verbal patient responses to guide the surgeon, deeper sedation is allowed. One of the greatest advantages of PRGR is that it is anatomically rather than physiologically based.\textsuperscript{3} Patients often receive intravenous propofol or other rapidly acting agents together with a narcotic drug. Some patients, especially younger men, may benefit from preadministration of 0.4 mg of atropine sulfate, an anticholinergic agent that serves to blunt the occasional vasovagal response that may be seen during the procedure. Most of the discomfort experienced during PRGR occurs when the 20-gauge spinal needle is passed through the foramen ovale, and it is thus important that patients are adequately sedated during this time.

Both the surgeon and anesthesiologist should be aware that up to 20% of patients can have a vasovagal response to transovale needle penetration or to the glycerol injection. Administration of an intravenous anticholinergic agent is important at the first sign of bradycardia. Other patients may have a hypertensive response to needle placement, usually due to pain or anxiety. Such a response can be lessened by the administration of hydralazine or beta-blockers. The systolic blood pressure should be kept below 160 mm Hg, because higher blood pressures can be associated with facial hematomas from needle placement. Because the procedure is begun with the patient supine but completed in the semi-sitting position during glycerol injection, a balance of pain control, blood pressure management, and respiratory care must be maintained by the surgeon and anesthesiologist.

**Surgical Technique**

The patient is placed supine on an operating table that allows control of head, leg, and body position. The patient’s head is suspended in a Mayfield cerebellar headrest so that the arm of the rest does not interfere with fluoroscopic imaging in the lateral or anteroposterior direction. Initially, a C-arm fluoroscopic image intensifier is positioned in the anteroposterior projection. The surgical team works to obtain alignment of the head such that the petrous
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ridge is at the same level as the inferior orbital rim. The foramen ovale can often be visualized just inferior and lateral to the junction of the inferior and medial orbital rims. We clean the patient’s face with 70% ethanol solution, and towels are placed around the neck and upper chest as the area is draped.

We mark an entry point by using an ink marker. This point is located 2.5 cm lateral to the corner of the mouth on the side of the pain. We also mark trajectories toward a point that is in line with the medial ipsilateral pupil and at a point 2.5 cm anterior to the external auditory canal. We use 1% lidocaine with a 25-gauge needle to create a small intradermal injection, and then a 21- or 23-gauge needle is used to inject lidocaine into the deep structures of the cheek. A gloved finger is placed inside the patient’s oral cavity to prevent penetration of the mucosa either by the anesthetic needle or by the 20-gauge spinal needle used for the rhizotomy. The 20-gauge needle is then inserted under fluoroscopic guidance along the marked trajectory toward the skull base; this is placed using an anteroposterior projection. Using a lateral projection, the needle tip is directed at a point approximately 1 cm behind the posterior clinoid along the angle of the clivus.

Penetration of the foramen ovale can sometimes be uncomfortable, and thus administration of a short-acting barbiturate or propofol is performed immediately prior to puncture. Penetration of the needle through the foramen ovale can be felt by the surgeon. The stylet of the needle should be removed to check for flow of CSF. If none is encountered, then the needle with the stylet replaced is advanced at 1-mm increments under fluoroscopic guidance until the trigeminal cistern is entered. The CSF flow should then be confirmed. If the needle is past the clival line with no flow of CSF, it may require adjustment; the most common problem is that the needle may be either too lateral in the cistern or too medial. If it is too lateral within the foramen ovale, the tip of the needle may be in the subdural or subtemporal space. Although the finding of CSF flow is desirable, its absence does not always preclude identification of the trigeminal cistern. This is particularly true in repeated procedures. In our experience, chances for CSF flow are maximized when the needle hub is directed medially.

If CSF flow is identified or the needle is believed to be within the trigeminal cistern, the patient is placed in the sitting position for a contrast cisternogram. Cisternography is required to assess the volume of the trigeminal cistern and to select the proper amount of glycerol. With the needle in the cistern, the head of the operating table is elevated to put the patient in the semisitting position with the neck slightly flexed. We use a tuberculin syringe to inject sterile iodohexol in 0.05-ml increments and we continue fluoroscopic guidance until the contrast agent is seen to overflow out of the cistern. The average volume of the trigeminal cistern is 0.25 ml, and it rarely exceeds 0.4 ml. The contrast material is then allowed to evacuate from the cistern by spontaneous drainage, which may require that the patient be placed again into the recumbent position. Alternatively, if full evacuation of the contrast agent is desired (particularly important for patients with lower-division pain), the patient can be returned to the supine position. It should be noted that some surgeons do not inject contrast material, relying instead on fluoroscopic findings and CSF return. We continue to advocate contrast injection because it is the only way to confirm directly that the trigeminal cistern has been entered.

The glycerol injection is performed in the same manner as the injection of contrast medium, also under fluoroscopic guidance. Again, the patient is placed into a semisitting position. We mix 99.9% anhydrous glycerol with radiopaque tantalum powder. The final volume of glycerol injected is dependent on the cisternal volume measured and the nerve distributions affected. There are different techniques for a glycerol injection, which vary from filling the entire cistern for patients with multidivision pain to leaving approximately one third of the contrast material in the cistern and “floating” the glycerol on top of the contrast in patients with isolated first-division pain. Because of its lighter density, the glycerol mixture floats above the residual contrast medium, exerting its effect mainly on upper-division fibers. During the injection, some patients experience ipsilateral periorbital discomfort and sometimes facial flushing. After the glycerol is injected, the needle is removed and a small adhesive bandage strip is placed on the skin entry point. We keep the patient at a semisitting position for 2 hours to prevent escape of glycerol into the posterior fossa. Most patients remain in the hospital overnight and are discharged home the next day.

RESULTS

There have been numerous studies that confirm the value of PRGR in the management of TN. Nevertheless, comparative assessments can be difficult because of the variations in surgical techniques. For instance, at some centers cisternography is not performed, and in others larger glycerol volumes are instilled. Investigators at most centers report that initial pain relief is seen in the majority of patients, with pain improvements in the range of 90%. We usually tell patients that half of those who respond will do so within the 1st day of the procedure, and in half it may take up to 2 or 3 weeks for the full effect to be manifested. Confusion exists as to the definition of recurrence rates; this definition depends on the time frame of evaluation, the need for concomitant medication, and the degree of pain control.

At the University of Pittsburgh, PRGR was performed in 1174 patients up to the cutoff point in December 2004. Immediate or early complete pain relief occurred in 90% of patients. An initial report in which 112 patients were evaluated demonstrated 90% pain relief at 2 years, with 60% of this group attaining complete relief after PRGR alone and 23% requiring some additional albeit reduced drug therapy. A subsequent analysis of 376 patients with follow-up durations of up to 7 years found a long-term pain control rate of 85%. Sixty percent attained complete relief after glycerol rhizotomy alone, although in some patients repeated procedures were necessary. In a longer-term assessment continuing up to 11 years, investigators found long-lasting relief of pain in 77% of patients, with 55% discontinuing all medications and 22% requiring some drug usage.

DISCUSSION

It should be emphasized that TN is not a static disease but is characterized by remissions and recurrences, some
mild and some severe. This challenge is known by all experienced practitioners. Pollock recently reported a series of 98 patients and found that 75% were free of pain at some point after surgery, with the chance of remaining pain free without medications at 61 and 50% after 1 and 3 years, respectively. Mild paresthesias or numbness were noted in 53% of patients, and 12% suffered herpes simplex perioralis from which they fully recovered.

Besides the perioperative blood pressure or cardiac changes noted earlier, other complications are relatively rare. Some days after their first procedure, approximately 10 to 20% of patients will have a detectable but usually mild reduction in light touch or pinprick (pain) perception. With repeated glycerol injections, the incremental sensory dysfunction assessment goes up, so that after two or three procedures, 50 to 70% of patients will have detectable sensory changes of a mild to moderate degree. In our experience, deafferentation pain has been extremely unusual and most likely occurs in the context of a complication noted in the following section.

Many patients have chronic herpes simplex perioralis virus lying dormant in the gasserian ganglion. With percutaneous therapies, the subsequent development of cold sores is common. If patients have a history of repeated cold sore attacks, we place them prophylactically on an acyclovir regimen and give them acyclovir ointment in the perioperative interval. Patients should be warned that 2 to 3 days after the procedure (usually long after they are home), they may develop cold sores. Severe outbreaks of cold sores are associated with the rare development of deafferentation pain sequelae, usually in the form of annoying paresthesias or dysesthesias, and therefore the cold sores should be treated vigorously and the patient warned about this particular event.

Early aseptic meningitis (1–2 days posttreatment) is an extremely rare event, occurring in approximately two of 1000 cases. Although spinal fluid analysis must be repeated on an urgent basis to confirm absence of bacterial meningitis, patients can be placed on corticosteroid drugs if the Gram stain of the CSF is negative. The pleocytosis may be profound when it occurs, and can be very hard to differentiate from true bacterial meningitis. The risk of bacterial meningitis is minimized by making sure the spinal needle does not penetrate the oral mucosa.

CONCLUSIONS

In our experience in treating more than 1000 patients with PRGR, we have had one perioperative death. This patient suffered a myocardial infarction approximately 1 hour after the procedure. We regard any surgical intervention as potentially stressful, but consider this 0.1% surgical mortality rate to be low in a higher-risk population. The risk of delayed corneal dysfunction is extremely low, especially with an initial procedure.

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