Sustained Headache Management via Neuromodulation of the Sphenopalatine Complex*

Introduction

“Approximately 45 million Americans are affected by headache disorders.”\textsuperscript{i} Six to eight percent of men and 15-18\% of women suffer from migraine headaches.\textsuperscript{ii} The World Health Organization states, “up to one adult in 20 has headache every or nearly every day.”\textsuperscript{iii} Nearly 1\% of the U.S. population—more than 3 million Americans annually—seek headache relief in emergency departments.\textsuperscript{iv}

In 1998 migraineurs in the United States experience more than 112 million bedridden days per year, costing employers about $13 billion, while direct medical costs exceed $1 billion annually.\textsuperscript{v} By 2008, just the cost of treating headaches in the emergency department (ED) approached $3 billion.\textsuperscript{vi}

Medical management is discouraging. Nearly 2/3 of patients discontinue prescription medications because of “unwanted side-effects and inadequate relief.”\textsuperscript{vii} Topiramate and triptan regimens often exceed $300-$500 per month. Patients, providers and payers all need an effective, affordable, longer lasting and widely available alternative in headache management.

Sphenopalatine Ganglion Blockade and the Genesis of the \textit{SphenoCath}™

Greenfield Sluder described SPGB in the \textit{New York Medical Journal} 1908, using a long needle, through the side of the face, to inject the SPG with cocaine.\textsuperscript{viii} Today lidocaine is usually the medication of choice and the block is usually attempted with a long, stiff, cotton-tipped applicator, through the nose, allowing the anesthetic to diffuse through the mucosa of the upper posterior nasal cavity to block the SPG.

Because sensory, sympathetic and parasympathetic neurons all pass through or synapse in the SPG,\textsuperscript{ix} it plays an essential role in various types of headaches. Temporarily interrupting impulse conduction through the SPG can abort acute headaches of various types and reset the ganglion to provide long-term relief. Many patients experience further benefit when the procedure is repeated.

*This document discusses headache management via neuromodulation of the sphenopalatine complex. It briefly reviews the history and uses of sphenopalatine ganglion blockade (SPGB) and highlights one physician’s experience using the \textit{SphenoCath}™ to perform SPGB. The patented \textit{SphenoCath}™, manufactured by Dolor Technologies LLC, Salt Lake City, Utah, is an FDA class I (874.5220) therapeutic “ear, nose, and throat drug administration device . . . intended specifically to administer medicinal substances to treat ear, nose, and throat disorders” (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=874.5220). The \textit{SphenoCath} is being marketed as a “drug administration device,” not as a headache treatment.
SPGB or, more accurately, neuromodulation of the sphenopalatine complex,\textsuperscript{x} has been studied and proven effective, but few physicians offer it to patients because the traditional techniques—a cotton-tipped applicator through the nose or a needle through the side of the head—are difficult to perform, carry risks and are uncomfortable for patients, sometimes requiring heavy sedation or resulting in significant nosebleeds.

Other approaches to SPGB include a transoral approach, an endoscopic-assisted approach, dripping or aerosolizing medication into the nose or simply irrigating the area under the assumption that the medication will eventually saturate the appropriate spot. Still others have advocated permanent disruption of the SPG by chemical, surgical, thermal or radio frequency ablation.

None of these approaches arms an office-based practitioner with a safe, simple, quick, precise method for consistently targeting the SPG. And, because few practitioners are willing or able to perform the procedure, most patients do not have access to the benefits of SPGB.

Dolor Technologies offers the patented \textit{SphenoCath™}, an FDA Class-I device for administering the practitioner’s chosen medication, through the nasal cavity, to the sphenopalatine (AKA pterygopalatine) fossa.\textsuperscript{xii} Fluoroscopy confirms consistent delivery of medication to the target, simplifying SPGB for practitioners and removing the discomfort of the procedure for patients. Because the \textit{SphenoCath™} technique can be mastered quickly and easily by primary care providers, the need for specialty referral is often obviated and the cost of SPGB is often less than the cost of chronic medications.

The \textit{SphenoCath™} is a small, soft, directional-controlled catheter designed to navigate a circuitous path through the nose without patient discomfort, narcotics, needles, x-ray guidance\textsuperscript{xiii} or bleeding. It transforms SPGB into a simple, fast, effective procedure easily mastered by virtually all practitioners, thus expanding the opportunity for SPGB from a small contingent patients in the offices of skilled pain specialists to the broad headache population seen in primary care offices and emergency departments.

SPGB is neither new nor revolutionary. What is revolutionary is the ease and consistency with which the now well-tolerated procedure can be performed in minutes by using the precision \textit{SphenoCath™}.

\textbf{Assessing Neuromodulation of the Sphenopalatine Complex}

To contemplate the value of SPGB, consider the small subset headache patients with CDH, a descriptive category of headaches, including transformed (or chronic) migraine, medication-overuse headache (MOH),\textsuperscript{xiii} chronic tension-type headache,
new daily persistent headache, cluster headache and several less common cephalgias. Recent evolutions in classification and terminology can be confusing, but one principle prevails: “Individuals presenting with chronic daily headache (CDH) are considered among the most difficult and labor-intensive patients in a neurologist’s practice.” These patients have often experienced sequential treatment failures and stand to benefit greatly from SPGB.

CDH affects 3-5% of the population. By definition, the most predominant types of headaches in the group—tension-type, chronic migraine and medication-overuse—cause significant pain on at least 15 days of every month for at least three months. When a person transforms from episodic to chronic migraine, the direct and indirect costs increase 4.4-fold, from $1757 to $7750 annually.

Purists would like headaches to fall into discreet categories. Review articles describe no less than nine subtypes of CDH. Sometimes, however, several headaches types may be grouped together for treatment purposes. For example, Noah Rosen, MD, at Thomas Jefferson University, presented a retrospective review of 68 patients who received inpatient intravenous lidocaine for CDH during a 26-month period. His study included only patients who had failed other standard inpatient treatments and consisted of 41 patients with transformed migraine, 12 with new daily persistent headache, and 15 had other headache diagnoses. He reported a complete response in 25.4% and a partial response in 57.1%. Speaking of his single intervention for a heterogeneous patient population, Dr. Rosen concluded, “patients with transformed migraine, new daily persistent headache, and other daily headache subtypes may benefit from [this] treatment.”

Rosen is not the only headache specialist blurring the lines of therapeutic intervention between CDH subtypes. A neurology group in Australia performed a retrospective survey of 71 patients admitted (mean 8.7 days) for intravenous lidocaine and concluded, it “is a useful treatment in the management of chronic daily headache with substantial analgesic overuse.”

Such reports may suggest a final common pathophysiologic pathway to CDH and lend credence to the notion of a unified approach to treatment. As a group, CDH—particularly chronic migraines and medication overuse headaches—represent, almost by definition, a cohort of treatment failures. That is one reason the prevalence of CDH patients in headache clinics is ten times the CDH prevalence in the general population.

Primary care practitioners and patients need a simple, safe, effective alternative approach to severe, intractable daily headaches. The above examples offer credence to a unified treatment option across the spectrum of CDH subtypes. SPGB offers that alternative when it can be performed safely, quickly, affordably and by the broad spectrum of primary care providers.
Studies show that 50% of migraine sufferers respond well when lidocaine is dripped into the nose. While the proposed mechanism of relief is SPGB, it is uncertain whether lidocaine reaches the sphenopalatine fossa, whether patients experienced relief from anesthetizing sensory nerves in the nasal mucosa, or whether they respond to some combination of both. More than half of migraine patients experience relief with intranasal lidocaine, but the study excluded patients if their “headache had lasted more than 3 days or if the frequency of severe headache was more than once per week.”

The makers of the SphenoCath™ have pursued SPGB in a broader population, including the CDH patients. Strict headache classification was intentionally not applied, allowing a wider range of patients to participate. Most suffered frequent or daily headaches and had experienced little or no relief on traditional therapies, including various injections.

**Tolerability**

Using the SphenoCath™, SPGB was performed 100 times by a physician, a nurse practitioner or a physician assistant. Patients rated the tolerability of SPGB as “good” or “excellent” 95% of the time (100% when pretreated with intranasal anesthetic). On five occasions the nasal mucous was slightly blood-tinged, but no frank epistaxis occurred. Two procedures, both without pre-procedure intranasal anesthetic, resulted in worsened headache. Both patients responded to a single dose of narcotic analgesic and were back to their baseline headache the following day without further incident. Except for those two patients, all indicated that they would have the procedure again if necessary.

**Response Rates**

When SPGB is performed with the SphenoCath™, 64% of patients experienced complete or near-complete resolution of their headache and an additional 15% experienced at least a 50% improvement as assessed by the visual analog scale (VAS). Though some patients have been lost to follow-up or had not reached the three-month mark at the time of this writing, significant improvement persisted for 64% at one week, 48% at one month and 23% at three months. Patients who received repeat procedures often enjoyed greater and more sustained improvement with subsequent procedures.

Three specific cases highlight the sometimes life-changing effect of SPGB. AD sustained a head injury in a snowmobile accident nearly a decade ago and could not remember a day without a headache since. Therapy, standard medications, even narcotics failed to give him relief. Every day ended with an 8/10 headache. He experienced 100% resolution of his headache after a single SPGB and has remained headache free for more than a year.

BC, a highway patrolman, suffered 8/10 headaches virtually every day for years. He remained headache free for two months after SPGB. When his headaches returned,
he requested a repeat procedure. He now has a brief, painless, bi-monthly SPGB and lives virtually headache free.

A third patient reported no improvement with SPGB on the day of the procedure and left the office disappointed, but returned a few months later requesting a repeat procedure. When asked why she desired a repeat block after reporting no improvement the first time, she responded that her headache had resolved the day following the procedure and did not return for weeks.

In cases of extended headache relief, it is theorized that dysfunctional nerve impulses are disrupting by SPGB, allowing neuronal circuits to return to normal function. Hence, the benefit of a SPGB lasts far beyond the effect of the local anesthetic. It is also noted that several patients experienced increased benefit when the procedure was repeated weeks or months later.

Whether used for acute headache intervention or for an intermittent maintenance regimen, SPGB is an essential tool in any well-rounded headache management portfolio. The improved rate of response to SPGB when the SphenoCath™ is used may facilitate a broader acceptance and implementation of the procedure. Indeed, the comfort and benefit experienced when SPGB was performed with the SphenoCath™ led many patients to report that they would pay for the procedure out-of-pocket if their insurer refused to cover it.

**Summary**

In 2008 the average cost of an ED visit was $922.xxiii Washington State reported the same year that their average cost for an ED headache visit was $2,485.xxiv Effective SPGB in the ED can reduce narcotic habituation, improve throughput and decrease costs significantly by obviating the need for IV access, multiple expensive medications and prolonged ED stays.

Benefits of SPGB are multiplied in an outpatient setting, providing patients more pain-free days while reducing specialty referrals, medication use and office and ED visits. When using the SphenoCath™, the procedure can be done in a matter of minutes and requires no special arrangements or prolonged office time. Specialists who already utilize SPGB by some other technique may engage the SphenoCath™ to improve success rates, reduce procedure times and to improve patient comfort.

*The primary mission of the SphenoCath™ is to relieve suffering by increasing access to SPGB.* More than half of chronic headache sufferers in one study stopped seeing their provider and “said that they did not return because they were unhappy with their health care providers or had experienced negative side-effects with their medications.”xxv Successful SPGB has the potential to reverse this trend.
In addition to migraine headaches, cluster headaches and CDH, other conditions shown to respond to SPGB in published literature include: trigeminal neuralgia, post-partum neck and back pain, complex regional pain syndrome, herpes zoster (Shingles) and post-herpetic neuralgia, tempromandibular joint (TMJ) pain and post-dural puncture headaches.

While this discussion focused only on CDH, it highlights the value of quick, easy, well-tolerated SPGB. When the broader applications of SPGB are embraced, the benefits are multiplied accordingly. The SphenoCath™ is not promoted as a headache treatment, but when practitioners feel that SPGB is the best treatment, the SphenoCath™ affords an efficient, precise administration of medication to the desired location. The tolerability and simplicity of SPGB using the SphenoCath™ invites continuing SPGB research in many specialties.

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2 Similar rates are found in South and Central America. In Asia, the rate is 3% of men and 10% of women, http://www.who.int/mediacentre/factsheets/fs277/en/.


4 Approximately 0.989% of the population visit EDs annually with a primary complaint of headache (over 3 million annually in the US). If headache as a secondary complaint is included, that number exceeds 5.5 million annually. Lucado, J, et al. Headaches in U.S. Hospitals and Emergency Departments, 2008. Statistical Brief #111, published May 2011, Healthcare Cost and Utilization Project, http://www.hcup-us.ahrq.gov/reports/statbriefs/sb111.pdf. The Agency of Healthcare Research and Quality, a division of the Department of Health & Human Services, summarized SB 111, explaining, “The data are drawn from hospitals that comprise 95 percent of all discharges in the United States and include patients, regardless of insurance type, as well as the uninsured,” http://www.ahrq.gov/news/nn/nn050411.htm.


8 Sluder G. The role of the sphenopalatine ganglion in nasal headaches. N Y State J Med 1908: 27: 8-13, not available online.
Though anatomical descriptions vary slightly depending on the sources cited, the SPG has a role in nociception, vasomotor control and secretomotor functions. The SPG has a sensory root, derived from two sphenopalatine branches of the maxillary nerve; a parasympathetic root, derived from the nervus internum (a part of the facial nerve) through the greater petrosal nerve; and a sympathetic root, consisting of sympathetic efferent (postganglionic) fibers from the superior cervical ganglion, traveling through the carotid plexus, and then through the deep petrosal nerve, joining the greater petrosal nerve to form the nerve of the pterygoid canal, which enters the ganglion. In the SPG (aka pterygopalatine ganglion) the preganglionic parasympathetic fibers from the greater petrosal branch of the facial nerve synapse with neurons whose postganglionic axons, vasodilator, and secretory fibers are distributed with the deep branches of the trigeminal nerve to the mucous membrane of the nose, soft palate, tonsils, uvula, roof of the mouth, upper lip and gums, and upper part of the pharynx. The SPG also sends postganglionic parasympathetic fibers to the lacrimal nerve (a branch of the ophthalmic nerve, also part of the trigeminal nerve) via the zygomatic nerve, a branch of the maxillary nerve (from the trigeminal nerve), which then arrives at the lacrimal gland. The nasal glands are innervated with secretomotor from the nasopalatine and greater palatine nerve. Likewise, the palatine glands are innervated by the nasopalatine, greater palatine nerve and lesser palatine nerves. The pharyngeal nerve innervates pharyngeal glands. These are all branches of the maxillary nerve. (This description is adapted from a version found on Wikipedia http://en.wikipedia.org/wiki/Pterygopalatine_ganglion and closely approximates most other sources.)

Though this paper frequently uses the widely accepted terminology of sphenopalatine ganglion blockade (SPGB), it should be noted that numerous neurovascular structures pass through the sphenopalatine fossa and may be affected by medications administered to the area. Indeed, it may be postulated that a broad response to so-called SPGB actually suggests additional structures are being affected. Neuromodulation of the sphenopalatine complex may be a more accurate and descriptive term. Structures connected to and/or passing through the sphenopalatine fossa include: (1) vidian nerve formed by greater superficial petrosal nerve (preganglionic parasympathetic fibers) and deep petrosal nerve (postganglionic sympathetic fibers). The vidian nerve also contains sensory fibers from CNVII which supply the soft palate; (2) maxillary nerve V2, the second division of the Trigeminal nerve; (3) pharyngeal nerve (a branch of V2, coming off the pterygopalatine ganglion); (4) pharyngeal artery (a branch of the third part of the maxillary artery); (5) sphenopalatine (also known as nasopalatine) nerve (a branch of V2 coming off the pterygopalatine ganglion); (6) long sphenopalatine artery (a branch of the third part of the maxillary artery); (7) infraorbital nerve (a branch of V2); (8) infraorbital artery (a branch of the third part of the maxillary artery); (9) descending palatine nerve (a branch of V2 coming off the pterygopalatine ganglion); (10) descending palatine artery (a branch of the third part of the maxillary artery); (11) the maxillary artery gives rise to the superior alveolar artery within the fossa.

Patented, including U.S. Pat. 8,388,600 and pending globally. The SphenoCath™ is an FDA class I (874.5220) therapeutic “ear, nose, and throat drug administration device . . . intended specifically to administer medicinal substances to treat ear, nose, and throat disorders” (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=874.5220 ). The SphenoCath is not being marketed as a headache treatment.

For some patients, particularly those with atypical nasal anatomy, the procedure may be more easily accomplished under fluoroscopic guidance.

While medication-overuse headache (MOH) is considered a secondary cause of CDH, it is virtually always discussed along with the primary causes. See, for example, Garza, I, et al. Diagnosis and Management of Chronic Daily Headache. Semin Neurol 2010; 30(2): 154-166, http://www.medscape.com/viewarticle/723842. The prevalence of MOH is 1.5% of the population (above the 4% for CDH). See the excellent summary article, “Chronic Daily Headache,” at http://www.medscape.com/viewarticle/723842.


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