Medical Policy

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Title: Sphenopalatine Ganglion Block for Headache

Related Policies:	▪ *Surgical Deactivation of Headache Trigger Sites* ▪ *Nerve Block Injections*

Professional	**Institutional**
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Populations	Interventions	Comparators	Outcomes
Individuals: • With chronic migraine headache	Interventions of interest are: • Sphenopalatine ganglion block(s)	Comparators of interest are: • Medication • Self-management (e.g., relaxation, exercise) • Botulinum toxin injection	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity

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Populations	Interventions	Comparators	Outcomes
Individuals: • With acute headache treated in the emergency setting	Interventions of interest are: • Sphenopalatine ganglion block(s)	Comparators of interest are: • Medication	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With cluster headache	Interventions of interest are: • Sphenopalatine ganglion block(s)	Comparators of interest are: • Medication • Oxygen therapy	Relevant outcomes include: • Symptoms • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With postdural puncture headache	Interventions of interest are: •Sphenopalatine ganglion block(s)	Comparators of interest are: •Medication •Oxygen therapy • Epidural blood patch	Relevant outcomes include: •Symptoms •Functional outcomes •Quality of life •Treatment-related morbidity

DESCRIPTION

Chronic migraine and severe headaches are common conditions and the available treatments are not universally effective. A proposed treatment option is blocking the sphenopalatine ganglion (SPG) nerve by applying topical anesthetic intranasally. Several catheters approved by the U.S. Food and Drug Administration are available for the SPG blocking procedure.

OBJECTIVE

The objective of this evidence review is to determine whether sphenopalatine ganglion blocks improve the net health outcome in patients with chronic or severe acute headaches compared with other accepted headache treatments.

BACKGROUND

Headaches and Headache Treatments

Headaches are common neurologic disorders and are among the top reasons why patients seek medical care. Headaches affect approximately 50% of the general population in a given year and over 90% of people have a lifetime history of headache.[1,] The 2 most common types of headache are migraines and tension-type headaches.

Migraines are the second-most common headache disorder, with a 1-year migraine prevalence of approximately 12% in the United States.[2,] Migraines are characterized by severe pain on 1 or both sides of the head, nausea, and, at times, disturbed vision. Migraines can be categorized by headache frequency, and by the presence or absence of aura. Chronic migraine is defined as attacks on at least 15 days per month for more than 3 months, with features of migraine on at least 8 days per month.[3,]

Tension-type headaches have a prevalence of approximately 40%.[2,] Diagnostic criteria include the presence of at least 2 of the following 4 characteristics: bilateral headache location, nonpulsating pain, mild-to-moderate intensity, and headache not aggravated by physical activity;

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lasting between 30 minutes and 7 days; and not accompanied by nausea, vomiting, photophobia, or phonophobia.[3,]

Cluster headaches are less common than tension or migraine headaches, with an estimated prevalence of 0.1% of the population.[2,] They are characterized by severe unilateral orbital, supraorbital, and/or temporal pain that also includes other symptoms in the eye and/or nose on the same side (e.g., rhinorrhea, eyelid edema or drooping).[3,]

Postdural puncture headache (PDPH), is a common complication of lumbar puncture. This headache also occurs with low cerebrospinal fluid volume from a leak at the site of the dural puncture, resulting in low cerebrospinal pressure and intracranial hypotension. Patients undergoing epidural anesthesia are also at risk for PDPH due to unintended dural puncture, which has been reported to occur in <1% to 6% of obstetric patients.[4,]. PDPH is characterized by a bilateral frontal or occipital headache that worsens with sitting or standing and is relieved in the supine position. Associated symptoms may include nausea, neck stiffness, low back pain, tinnitus, and visual disturbances.[5,] The reported incidence of PDPH as a complication of lumbar puncture is variable, ranging from 10% to 40% of lumbar puncture procedures.[5,] Incidence may be as low as 2% when small gauge, non-cutting needles are used.

A variety of medications are used to treat acute migraine episodes. These include medications taken at the onset to abort the attack (triptans, ergotamines) and medications to treat the pain and other symptoms of migraines once they are established (nonsteroidal anti-inflammatory drugs, antiemetics). Prophylactic medication therapy may be appropriate for people with migraines that occur more than 2 days per week. Botulinum toxin type A injections are a U.S. Food and Drug Administration (FDA) approved prophylactic treatment for chronic migraine. Several calcitonin-gene related peptide antagonists are available as FDA-approved treatment options for acute and prophylactic treatment of migraine. In addition to medication, behavioral treatments (e.g., relaxation, cognitive therapy) are used to manage migraine headache.

Severe acute cluster headaches may be treated with abortive therapy, including breathing 100% oxygen and triptan medications. Other medications used to treat cluster headaches include steroids, calcium channel blockers, and nerve pain medications. Due to the severity of pain associated with cluster headaches, patients may seek emergency treatment. Tension-type headaches are generally treated with over the counter pain medication.

Sphenopalatine Ganglion Block

Sphenopalatine ganglion (SPG) blocks are a proposed treatment option for chronic migraines and some severe non-migraine headaches. The SPG is a group of nerve cells located behind the bony structures of the nose. The nerve bundle is linked to the trigeminal nerve, the primary nerve involved in headache disorders. The SPG has both autonomic nerves, which in this case are associated with functions such as tearing and nasal congestion, and sensory nerves, associated with pain perception. These blocks involve topical application of local anesthetic to mucosa overlying the SPG. The rationale for using SPG blocks to treat headaches is that local anesthetics in low concentrations could block the sensory fibers and thereby reduce pain while maintaining autonomic function.

The proposed procedure for SPG blockade is to insert intranasally a catheter that is attached to a syringe carrying local anesthetic (e.g., lidocaine, bupivacaine). Once the catheter is in place, the

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local anesthetic is applied to the posterior wall of the nasal cavity and reaches the SPG. Originally, SPG blocks were done by inserting a cotton-tipped applicator dabbed with local anesthetic into the nose; this technique may be less accurate and effective than the currently proposed procedure. Neurostimulation of the SPG and SPG blockade with radiofrequency lesioning have been used outside of the United States,[6,] but these treatments are not cleared or approved by the FDA.

Three catheter devices are commercially available in the United States for performing SPG blocks. The catheters have somewhat different designs but all are attached to syringes to deliver local anesthetic. The catheters are inserted intranasally and, once in place, the local anesthetic is applied through the catheter. With 2 of the 3 commercially available catheters (the SpenoCath®, Allevio™), patients are positioned on their back with their nose pointed vertically and their head turned to the side. With the Tx360® device, patients remain seated.[7,]

The optimal number and frequency of SPG treatments is unclear. Information from the American Migraine Foundation suggests that the procedure can be repeated as often as needed to control pain.[7,] A randomized controlled trial has described a course of treatment for migraines consisting of SPG blocks twice a week for 6 weeks (total, 12 treatments).

Sphenopalatine ganglion blocks are proposed for both short- and long-term treatment of headaches and migraines. When used in the emergency setting in patients with severe acute headaches, the goal of treatment is to abort the current headache while the patient is in the emergency department. In the randomized controlled trial that provided a 6-week course of treatment with SPG blocks for chronic migraine (mentioned above), short-term outcomes were assessed up to 24 hours after each treatment, and the duration and frequency of chronic migraines were assessed at 1 and 6 months after the course of treatment.

REGULATORY STATUS

The Tx360 Nasal Applicator (Tian Medical), the Allevio SPG Nerve Block Catheter (JET Medical), and the SpenoCath (Dolor Technologies) are considered class I devices by the FDA and are exempt from 510(k) requirements. This classification does not require submission of clinical data on efficacy but only notification of FDA prior to marketing. All 3 devices are used to apply numbing medication intranasally.

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POLICY

Sphenopalatine ganglion blocks are considered **experimental / investigational** for all headache indications, including, but not limited to, the treatment of migraines and non-migraine headaches.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through September 13, 2022.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

CHRONIC MIGRAINE

Clinical Context and Therapy Purpose

The purpose of sphenopalatine ganglion (SPG) block(s) in patients who have chronic migraine headache is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a SPG block improve the net health outcome in patients with chronic migraine headache?

The following PICO was used to select literature to inform this review.

Populations

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The relevant population of interest is individuals with chronic migraine headache.

Interventions
The therapy being considered is a SPG block.

Comparators
The following therapies and practices are currently being used to treat chronic migraine headache: medication, self-management (e.g., relaxation, exercise), and botulinum toxin injection.

Outcomes
The general outcomes of interest are reductions in migraine frequency, intensity, and medication use. Treatment-related adverse events are minor. A series of injections may be given over several weeks, with follow-up over months to monitor for treatment effect and durability.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Due to a typically high placebo response rate in patients with headache, placebo-controlled trials were preferred;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials
Findings from a double-blind, placebo-controlled RCT that evaluated SPG blocks to treat chronic migraine were published in 2 publications by Cady et al (2015). The first publication[8,] reported on the primary outcome measure and key secondary outcomes, and the subsequent publication[9,] reported on supplemental secondary outcomes and longer term follow-up. The trial included patients who met International Classification of Headache Disorders-II diagnostic criteria for chronic migraine[10,] and had chronic migraine for at least 3 months. Patients could use concomitant headache medication, but had to agree not to change medication use during the study period. Following an initial 28-day baseline period to confirm the diagnosis of chronic migraine, patients were randomized 2:1 to treatment with bupivacaine 0.5% or saline (placebo) applied using the Tx360 device. Patients received a series of 12 treatments - 2 treatments a week for 6 weeks. The primary outcome was change in pain severity, measured using a 0-to-10 numeric rating scale. Pain severity was assessed 15 minutes, 30 minutes, and 24 hours after each treatment. Key secondary outcome measures were the Patient's Global Impression of Change, the Headache Impact Test (HIT-6) questionnaire, and patient satisfaction with treatment. In addition, patients kept headache diaries throughout the study.

Forty-one patients met eligibility criteria and had chronic migraine diagnoses confirmed during the baseline period.[8,] These patients were randomized to bupivacaine (n=27) or to placebo (n=13). Mean baseline scores on the numeric rating scale were 4.8 in the bupivacaine group and 4.5 in the placebo group. When findings for all treatments were pooled, patients in the

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bupivacaine group reported a significantly greater reduction in numeric rating scale scores than the placebo group at 15 minutes, 30 minutes, and 24 hours after treatment. Bupivacaine-treated patients also had significantly lower Patient's Global Impression of Change scores than saline-treated patients at 30 minutes and 24 hours posttreatment. No statistically significant between-group differences were reported in HIT-6 scores or in average acute medication use. Only 1 serious adverse event was reported and it was not treatment-related.

The second publication by Cady et al reported on 1- and 6- month follow-up results and on supplemental secondary end points.[9,] To control for multiple comparisons, the cutoff for statistical significance for the supplemental secondary end points was $p<.01$. There were no statistically significant differences between groups in the reported supplementary secondary outcomes. These outcomes included the number of headache days per month, the mean pain score, and quality of life measures. A post hoc power analysis revealed that the trial was underpowered to detect significant differences in secondary outcomes. Some results were suggestive of a long-term effect. For example, the bupivacaine group had a lower, albeit nonsignificant, number of headache days in the month posttreatment (17 days) than the placebo group (23 days). However, a trial with a larger sample size would be needed to confirm whether 1- or 6-month results are significantly better after bupivacaine than after placebo treatment.

Section Summary: Chronic Migraine
One double-blind, placebo-controlled, randomized trial has evaluated transnasal SPG blocks for chronic migraine. The trial found a significantly greater short-term (up to 24 hours) reduction in pain severity after active treatment versus placebo. However, there were no significant longer term effects on other outcomes (ie, 1 and 6 months after 12 treatments over 6 weeks). The trial was underpowered to detect outcomes at 1 and 6 months. It had some risks of bias due to a high rate of dropouts. Additional adequately powered trials are needed to determine the impact of SPG blocks on health outcomes.

SEVERE ACUTE HEADACHE TREATED IN THE EMERGENCY SETTING

Clinical Context and Therapy Purpose
The purpose of SPG block(s) in patients who have severe acute headache treated in the emergency setting is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a SPG block improve the net health outcome in patients with severe acute headache treated in the emergency setting?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with severe acute headache treated in the emergency setting.

Interventions
The therapy being considered is a SPG block.

Comparators

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The following therapy is currently being used to treat severe acute headache treated in the emergency setting: medication.

Outcomes
The general outcomes of interest are reductions in headache intensity and medication use. Treatment-related adverse events are minor. Follow-up over several hours is needed to monitor for treatment effect.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Due to a typically high placebo response rate in patients with headache, placebo-controlled trials were preferred;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials
The published literature on SPG blocks to treat severe acute headache consists of a single double-blind, placebo-controlled, randomized trial, as reported by Schaffer et al (2015).[11,] The trial included patients between the ages of 18 and 65 years who presented to the emergency department with a frontal-based crescendo-onset headache and a negative neurologic examination. The trial focused on frontal-based headaches because this population is considered most likely to respond to SPG blocks. Headaches were not classified into specific types but patients with sudden-onset headache were excluded. Ninety-three patients met eligibility criteria and were randomized 1:1 to treatment with bupivacaine 0.5% (n=45) or to a saline placebo (n=48) applied using the Tx360 device. The intervention consisted of 1 treatment session. The primary outcome was a 50% absolute pain reduction on a 100-mm visual analog scale (VAS) 15 minutes posttreatment. Four patients, 2 in each group, withdrew before receiving the intervention and 2 were deemed ineligible after randomization. Thus, 41 patients in the bupivacaine group and 46 in the placebo group were included in the primary analysis.

For the primary outcome, 20 (49%) patients in the bupivacaine group and 19 (41%) patients in the placebo group had at least a 50% reduction in the mean VAS score. The difference between groups (7.5%) did not differ statistically (95% confidence interval [CI], -13% to 27%). Secondary outcomes, including at least a 19-mm reduction in VAS score, percentage of patients who were headache-free 15 minutes postintervention, and percentage of patients who were nausea-free 15 minutes postintervention, also did not differ significantly between groups. Seventy-six (88%) patients were available for follow-up after 24 hours. The percentage of patients headache-free at 24 hours was significantly higher in the bupivacaine group (n=26 [72%]) than in the placebo group (n=19 [48%]; difference, 25%; 95% CI, 2.6% to 44%). No serious adverse events were reported in either group. The trialists stated that, in retrospect, outcome assessment at 1 hour after treatment would have been useful because headache relief at 1 hour, but not at 24 hours, is clinically relevant for emergency department headache patients.

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Section Summary: Severe Acute Headache Treated in the Emergency Setting
One double-blind, placebo-controlled, randomized trial has evaluated a single transnasal SPG block for treating patients with acute headache presenting to an emergency department. The trialists did not find a statistically significant benefit for active treatment compared with placebo 15 minutes postintervention. Significantly more patients were headache-free at 24 hours in the active treatment than in the placebo group, but, in the absence of short-term pain relief, SPG blocks would not be a clinically useful treatment in the emergency setting. Future studies conducted in the emergency setting should assess outcomes for an intermediate time period (e.g., 1 or 2 hours posttreatment).

CLUSTER HEADACHE

Clinical Context and Therapy Purpose
The purpose of SPG block(s) in patients who have cluster headaches is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a SPG block improve the net health outcome in patients with cluster headaches?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with cluster headache.

Interventions
The therapy being considered is a SPG block.

Comparators
The following therapies are currently being used to treat cluster headaches: medication and oxygen therapy.

Outcomes
The general outcomes of interest are reductions in headache frequency, intensity, and medication use. Treatment-related adverse events are minor. A series of injections may be given over several weeks, with follow-up over months to monitor for treatment effect and durability.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Due to a typically high placebo response rate in patients with headache, placebo-controlled trials were preferred;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

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No RCTs or nonrandomized controlled studies were identified that evaluated 1 of the 3 catheter devices commercially available in the United States for performing SPG blocks for treating cluster headache.

Case Series
Two case series in patients with chronic drug-resistant cluster headache were published by a research group in Italy.[12,13,] Both studies used a needle (20-gauge in 1 study, 18-gauge in the other) under endoscopic control to inject a mixture of local anesthetics and steroid as close as possible to the SPG. The mixture consisted of triamcinolone acetonide (40 mg), 1% bupivacaine (4 mL), and 2% mepivacaine with 1/100,000 adrenaline (2 mL).

Pipolo et al (2010) reported on 15 patients who received 3 SPG block treatments a mean of 3 days apart. Eight (53%) of the 15 patients experienced complete remission of cluster headache symptoms.[12,] Three (20%) of these continued to be in remission at last follow-up (mean, 18 months). One (7%) patient experienced partial benefit and 6 (40%) reported either no benefit or a benefit for less than 2 weeks. Three (20%) patients experienced complications, including 2 cases of severe epistaxis and 1 of reduced buccal opening that resolved after 5 months.

The earlier study by Felisati et al (2006), included 21 patients who received between 2 and 4 total treatment sessions, provided 1 week apart.[13,] Including 1 patient in whom the treatment could not be applied, 9 (45%) experienced no efficacy, 3 (15%) experienced a partial benefit, and 8 (40%) experienced a complete temporary benefit. In the 8 patients who had complete disappearance of attacks, the benefit lasted 2 to 4 weeks in 3 patients, 3 to 6 months in 3 patients, and 12 to 24 months in 2 patients. Four (19%) patients experienced treatment-related complications, which consisted of 1 case of marked nasal epistaxis 3 days after the procedure and 3 cases of temporary diplopia.

Section Summary: Cluster Headache
The literature includes 2 case series, both of which were published by the same research group in Italy. The approach to treatment was similar in both studies but differed in terms of medication and application technique currently used in the United States. It is unclear how the safety or efficacy of the procedure used in the case series differs from an intranasal SPG block applying local anesthetics and using a U.S. Food and Drug Administration cleared device. In these series, 40% to 50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. These studies had small sample sizes and lacked a sham treatment or alternative therapy for treating cluster headache.

POSTDURAL PUNCTURE HEADACHE

Clinical Context and Therapy Purpose
The purpose of SPG block(s) in patients who have a postdural puncture headache (PDPH) is to provide a treatment option that is an alternative to or an improvement on existing therapies. The question addressed in this evidence review is: Does the use of a SPG block improve the net health outcome in patients with PDPH?

The following PICO was used to select literature to inform this review.

Populations

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The relevant population of interest is individuals with PDPH.

Interventions
The therapy being considered is a SPG block.

Comparators
The following therapies are currently being used to treat PDPH : conservative therapy (e.g., bed rest, oral or intravenous hydration), medication (e.g., analgesics, caffeine, antiemetics), and epidural blood patch. Epidural blood patch is considered the definitive treatment for PDPH.[14,15,16,]

Outcomes
The general outcomes of interest are reduction in headache intensity and duration, medication use, and avoidance of epidural blood patch use.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- Due to a typically high placebo response rate in patients with headache, placebo-controlled trials were preferred;
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials
Jespersen et al (2020) conducted a double-blind RCT comparing administration of SPG block with local anesthetic (lidocaine 4% and ropivacaine 0.5%) to placebo (saline).[17,] Twenty patients were randomized to each group with an upright median VAS pain score of 74 and 84 mm, respectively. Eligibility criteria included adult patients ≥18 years of age with PDPH defined as a moderate-to-severe VAS pain score (>30 mm) in an upright position that develops within 3 days after an intended or accidental dural puncture. The headache must have persisted for at least 1 day after dural puncture and must be intractable to treatment with fluids, caffeine, and acetaminophen, fulfilling eligibility criteria to receive an epidural blood patch. The primary outcome, median pain intensity in the upright position at 30 minutes after SPG block, was 26 mm in the anesthetic group and 37 mm in the placebo group (estimated median difference, 5 mm; 95% CI, -14 to 21; p=.53). Patients were offered a rescue SPG block, with open-label anesthetic, if persistent pain was experienced, defined as VAS ≥30 mm, between 1 hour and 7 days after the initial block. Rescue blocks were required in 65% of patients in each group and were received an average of 1.4 or 1.5 hours following the initial block in the anesthetic and placebo groups, respectively. An epidural blood patch was offered if the rescue block failed to relieve pain. In the anesthetic group, 50% of patients required an epidural blood patch compared with 45% treated with placebo (p=.76). Interpretation of epidural blood patch use is limited by broad administration of rescue blocks in both groups. The median time to epidural blood patch was 11 versus 5.5 hour in anesthetic and placebo groups, respectively.

Section Summary: Postdural Puncture Headache

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One double-blind, placebo-controlled randomized trial evaluated a single SPG block for treating patients with PDPH. The investigators did not find a statistically significant benefit for active treatment compared to placebo 30 minutes post-intervention. The patient population was small and heterogeneous, including those who had received both intended and accidental dural punctures. Patients requiring definitive treatment with an epidural blood patch were not statistically different between groups, however this may have been influenced by broad use of active rescue blocks. Larger, well-designed studies assessing short-term and intermediate outcomes are warranted.

Summary of Evidence

For individuals who have chronic migraine who receive SPG block(s), the evidence includes a RCT and a case report. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The randomized trial evaluated a regimen of 12 SPG blocks over 6 weeks and was double-blind and placebo-controlled. The trial found significantly greater short-term (up to 24 hours) benefits from active treatment than from placebo. There were no significant long-term effects (ie, 1 and 6 months after 12 treatments), although the trial was underpowered to detect longer term efficacy. Given that SPG blocks are being proposed as a preventive therapy for chronic migraines, evidence demonstrating reduced migraine frequency, severity, or other objective outcomes from robust trials is still needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have severe acute headache treated in the emergency setting who receive SPG block(s), the evidence includes a single RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The randomized, double-blind, placebo-controlled trial evaluated a single SPG block for severe acute headache of mixed etiologies. There was no statistically significant difference between active treatment and placebo for the primary outcome (pain reduction 15 minutes postintervention). The trialists did not collect pain data again until 24 hours posttreatment, at which time significantly more patients were headache-free in the active treatment arm than in the placebo arm. Additional studies, preferably RCTs, are needed to determine whether SPG blocks are an effective treatment in the emergency setting. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cluster headache who receive SPG block(s), the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Two small case series, both of which evaluated an approach for intranasal SPG blocks that differs from the intervention currently available in the United States, were identified. In these series, 40% to 50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. However, it is not clear from these series the degree to which the procedures evaluated differ in safety and efficacy from an intranasal SPG block using a device cleared by the U.S. Food and Drug Administration. Additional studies, preferably RCTs, are needed to evaluate SPG blocks for treating cluster headaches. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have PDPH who receive SPG block(s), the evidence includes a RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The small randomized, double-blind, placebo-controlled trial evaluated a single SPG block for

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PDPH in patients with both intended and accidental dural punctures. There was no statistically significant difference between active treatment and placebo for the primary outcome (median pain intensity in the upright position 30 minutes postintervention). Active rescue blocks were required in 65% of patients in each group, administered within an average of 1.4 hours for the active group and 1.5 hours for the placebo group. There was no statistically significant difference between active treatment and placebo for the number of patients requiring definitive treatment with an epidural blood patch. Additional studies, preferably RCTs, are needed to evaluate SPG blocks for treating PDPH. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Pain Medicine

The American Academy of Pain Medicine (2021) conducted a systematic review to develop practice recommendations for use of percutaneous interventional strategies for the preventive treatment of migraine.[18,] Sphenopalatine ganglion blocks received a weak recommendation for chronic migraine prevention based on a very low certainty of evidence. The only therapy evaluated in the guideline that received a strong recommendation for chronic migraine prevention was onabotulinumtoxinA.

American Headache Society

The American Headache Society guideline (2016) on the treatment of cluster headache includes subcutaneous sumatriptan, zolmitriptan nasal spray, and high flow oxygen as Level A (established as effective) acute treatment recommendations.[19,] Sphenopalatine ganglion stimulation is rated as a Level B (probably effective) acute treatment recommendation. However, the recommendation for sphenopalatine ganglion stimulation was based on a single randomized controlled trial that evaluated an implanted, on-demand, acute electrical stimulation device of the SPG,[20,]rather than a catheter device used to apply local anesthetic. There are no Level A recommendations for reducing the frequency of cluster headaches in the guideline.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

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Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03337620[a]	A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel 20 Week Study of the Efficacy and Safety of the Tx360® Nasal Applicator for Transnasal Sphenopalatine Ganglion Block in the Treatment of Chronic Migraine	180	Mar 2023 (recruiting)
NCT03984045	Sphenopalatine Ganglion Block for Treating Acute Frontal Migraine Headache in Pediatric Patients	72	Dec 2022 (recruiting)
NCT04069897	Botulinum Toxin Type A Blockade of the Sphenopalatine Ganglion in Treatment-refractory Chronic Migraine (MiBlock)	170	Dec 2024 (recruiting)
NCT03944876	Botulinum Toxin Type A Blockade of the Sphenopalatine Ganglion in Treatment-refractory Chronic Cluster Headache (BASIC)	112	Sep 2025 (recruiting)
Unpublished			
NCT03666663	UCSF Sphenopalatine Ganglion Block Study- a Randomized Double Blind Placebo Controlled Trial to Compare Nasal Anesthetics for Migraine Prevention in Adults (SPGblock)	10	Aug 2021 (active, not recruiting)
NCT03560349	A Multicenter Double Blinded Randomized Controlled Trial of the Efficacy of the Sphenopalatine Ganglion Block for the Treatment of the Postdural Puncture Headache After Labor Epidural	90	Jun 2021 (unknown)
NCT04255420	Sphenopalatine Ganglion Blocks for Headaches in the Emergency Department	84	Jun 2021 (unknown)
NCT03112720	A Comparison of the Efficacy of Sphenopalatine Ganglion (SPG) Block With 5% Lidocaine Versus Epidural Blood Patch (EBP) for the Treatment of Post-Dural Puncture Headache (PDPH)	500	Jul 2021 (unknown)

NCT: national clinical trial.
[a] Denotes industry-sponsored or -cosponsored trial.

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
64400	Injection, anesthetic agent; trigeminal nerve, any division or branch
64505	Injection, anesthetic agent; sphenopalatine ganglion
64999	Unlisted procedure, nervous system

ICD-10 DIAGNOSES
Experimental / Investigational for all diagnoses related to this medical policy.

REVISIONS	
11-13-2017	Policy added to the bcbsks.com web site on 09-28-2017 with an effective date of 11-13-2017.
01-04-2019	Updated Description section.
	Updated Rationale section.
	Updated References section.
02-26-2021	Updated Description section
	Updated Rationale section
	Updated References section
02-01-2022	Updated Description Section
	Updated Rationale Section
	Updated References Section
12-29-2022	Updated Description Section
	Updated Policy Section ▪ Added "headache" to statement to read "Sphenopalatine ganglion blocks are considered experimental / investigational for all headache indications, including, but not limited to, the treatment of migraines and non-migraine headaches.
	Updated Rationale Section
	Updated References Section

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