Sphenopalatine Ganglion Block or Other Intranasal Blockage for Headache

Policy Number: 7.01.159
Origination: 7/2017
Last Review: 7/1/17
Next Review: 1/1/18

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for Sphenopalatine Ganglion Block or other intranasal blockage for Headache. This is considered investigational.

When Policy Topic is covered
n/a

When Policy Topic is not covered
Sphenopalatine ganglion blocks are considered investigational for all indications, including but not limited to the treatment of migraines and non-migraine headaches.

The use of other intranasal anesthetic or blocks (e.g., trigeminal block) for the treatment of headaches and migraines is considered investigational.

Considerations
Trial eligibility criteria include meeting International Classification of Headache Disorders-II (ICHD-2) diagnostic criteria for chronic migraine headache. These are:

Migraine headache occurring on 15 or more days per month for more than 3 months in the absence of medication overuse.

Diagnostic criteria:

Headache not attributed to another disorder and fulfilling the following criteria:
- Headache has at least 2 of the following characteristics:
- Unilateral location
- Pulsating quality
- Moderate or severe pain intensity
- Aggravation by or causing avoidance of routine physical activity

During headache, at least 1 of the following

- Nausea and/or vomiting
- Photophobia and phonophobia

**ICHD-3**
A newer version of the diagnostic criteria, ICHD-3, is now available in beta form. In ICHD-2, absence of medication overuse was one of the diagnostic criteria for chronic migraine. In the ICHD-3, this criterion was removed from the chronic migraine diagnosis and “medication overuse headache” is now a separate diagnostic category.

**Description of Procedure or Service**

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>With chronic migraine headache</td>
<td>Sphenopalatine ganglion blocks</td>
<td>Medication</td>
<td>Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Self-management (eg, relaxation, exercise)</td>
<td>Functional outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Botulinum toxin injection</td>
<td>Quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>With severe acute headache treated in an emergency setting</td>
<td>Sphenopalatine ganglion blocks</td>
<td>Medication</td>
<td>Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Functional outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>With cluster headache</td>
<td>Sphenopalatine ganglion blocks</td>
<td>Medication</td>
<td>Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Breathing 100% oxygen</td>
<td>Functional outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment-related morbidity</td>
</tr>
</tbody>
</table>

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

For individuals who have chronic migraine who receive sphenopalatine ganglion blocks, the evidence includes 1 RCT and a case report. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT was double-blind and placebo controlled, and provided a course of 12
SPG blocks over 6 weeks. It found significantly greater short-term (up to 24 hours) benefits of active treatment versus placebo. There were not significant longer-term effects (ie, 1 and 6 months after a course of 12 treatments). The study was underpowered to detect longer term efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe acute headache treated in an emergency setting who receive sphenopalatine ganglion blocks, the evidence includes 1 RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT was double-blind and placebo controlled, and provided a single SPG block. There was not a statistically significant difference between active treatment and placebo in the primary outcome, pain reduction 15 minutes postintervention. The study did not collect pain data again while patients were in the emergency department (eg, at 1 hour after treatment). At 24 hours after treatment, significantly more patients were headache-free in the active treatment versus placebo group. However, there is insufficient evidence that SPG blocks are an effective treatment in the emergency setting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cluster headache who receive sphenopalatine ganglion blocks, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Two small case series were available; the approach to intranasal SPG blocks differed from the intervention currently available in the United States. It is not clear how the safety or efficacy of the procedure used in the case series differs from an intranasal SPG block applying local anesthetics and using an FDA cleared device. In the series, 40-50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. Additional studies, preferably RCTs are needed to evaluate SPG blocks for treating cluster headaches. The evidence is insufficient to determine the effects of the technology on health outcomes.

**BACKGROUND**

**HEADACHES AND HEADACHE**

Headaches are common neurologic disorders and are among the top reasons that 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 tension-type headaches and migraines. Tension-headaches have a prevalence of approximately 40%.(2) They are diagnosed when patients report at least 2 of the following characteristics: bilateral headache location, nonpulsating pain, mild to moderate intensity and headache not aggravated by physical activity.(3) Migraines are the second-most common headache disorder with 1-year prevalence of migraine in the United States of approximately 12%.(2) They are characterized by severe pain on 1 or both sides of the head, an upset stomach, and, at times, disturbed vision, Migraines can be categorized by headache frequency. According to the Third Edition of the International Headache Classification (ICHD-3), migraine without aura (previously known as common migraine) is defined as at least 5 attacks per
month meeting other diagnostic criteria. 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. Cluster headaches are less common than tension or migraine headaches, with an estimated prevalence of 0.1% of the population. Cluster headaches 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 such as rhinorrhea and eyelid edema or drooping. Due to the severity of pain associated with cluster headaches, patients may seek emergency treatment.

**Treatment**

A variety of medications are used to treat acute migraine episodes. They include medications taken at the onset of an attack 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, narcotic analgesics, antiemetics). Prophylactic medication therapy may be appropriate for people with migraines that occur more than 2 days per week. In addition to medication, behavioral treatments such as relaxation and cognitive therapy are used in the management of migraine headache. Moreover, botulinum toxin type A injections are a U.S. Food and Drug Administration (FDA)–approved treatment for chronic migraine. 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. Tension-type headaches are generally treated with over the counter pain medication.

**Sphenopalatine Ganglion Block**

Sphenopalatine ganglion (SPG) nerve blocks are a proposed treatment option for chronic migraines and some severe non-migraine headaches. The SPG is a group of nerve cells that is 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. SPG nerve 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 currently proposed procedure for SPG nerve blockade is to insert a catheter intranasally that is attached to a syringe carrying local anesthetic (eg, lidocaine or bupivacaine). Once the catheter is in place, the local anesthetic is applied to the posterior wall of the nasal cavity and reaches the SPG. Some form of SPG blocking procedure has been used for many years. 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. Another variation is to insert a needle into the cheek and inject local anesthetic but this no longer appears to be used since it is more invasive and can be painful. Neurostimulation of the SGB and SGB blockade with radiofrequency...
lesioning have been used outside of the United States but these treatments are not FDA-cleared or approved.

Three catheter devices are currently commercially available in the United States for performing SPG blocks. The catheters have somewhat different designs but all are attached to syringes that contain 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® or 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.(4)

The company marketing the Tx360® device is proposing its use in the context of a protocol called the MiRx™ protocol.(5) This 2-part protocol includes a medical component for immediate pain relief and a physical component to reduce headache recurrences. The medical component involves clinical evaluation and, if the patient is considered eligible, an SPG block procedure. The physical component can include any of a number of approaches such as physical therapy, ergonomic modifications, massage and dietary recommendations.

The optimal number and frequency of SPG treatments is unclear. Information from the American Migraine Foundation states that the procedure can be repeated as often as needed to control pain.(4) An RCT described a course of treatment for migraines consisting of SPG blocks twice a week for 6 weeks (total of 12 treatments).

**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 U.S. Food and Drug Administration (FDA) and are exempt from 510(k) requirements. This classification does not require submission of clinical data regarding efficacy but only notification of FDA prior to marketing. These 3 devices are all used to apply numbing medication intranasally.

**Rationale**
This evidence review was originally created in May 2017 based on a search of the MEDLINE database. The most recent literature search was conducted through March 23, 2017.

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.
Because the placebo response rate is typically high in patients with headache, assessment of evidence focuses on randomized, placebo-controlled trials.

CHRONIC MIGRAINE
The published literature on SGB blocks to treat chronic migraine consists of 1 double-blind placebo-controlled RCT(6,7) and a small case report with 3 patients(8).

Findings of the RCT were published in two 2015 publications by Cady et al. The first publication(6) reported on the primary outcome measure and key secondary outcomes, and the subsequent publication(7) reported on supplemental secondary outcomes and longer term follow-up. The trial included patients who met International Classification of Headache Disorders (ICHD-2) diagnostic criteria for chronic migraine headache(9) and had CM for at least 3 months. Patients could use concomitant headache medication, but needed to agree not to make changes in medication use during the study period. Following an initial 28-day baseline period to confirm the diagnosis of CM, patients were randomized 2:1 to receive treatment with 0.5% bupivacaine 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 by a 0 to 10 numeric rating scale (NRS). 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 (PGIC), 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 CM diagnoses confirmed during the baseline period. These patients were randomized to receive application of bupivacaine (n=27) or placebo (n=13). One patient in the placebo group withdrew consent, and 3 patients were excluded from analysis due to protocol violations, leaving 38 patients in the final dataset. This included 26 in the bupivacaine group and 12 in the placebo group. Mean baseline scores on the NRS were 4.8 in the bupivacaine group and 4.5 in the placebo group. When pooling findings for all treatments, patients in the bupivacaine group reported a significantly greater reduction in the NRS than the placebo group at 15 minutes, 30 minutes, and 24 hours after treatment. An analysis also found significantly lower PGIC scores in the bupivacaine than saline groups at 30 minutes and 24 hours posttreatment. No statistically significant between group differences were found in HIT-6 scores or in average acute medication use. Only 1 serious adverse event (SAE) was reported and it was not treatment-related.

Another 2015 publication by Cady et al on this study reported on 1- and 6- month follow-up results and on supplemental secondary end points.(7) To control for multiple comparisons, the cutoff for statistical significance for the supplemental secondary end points was $p$ less than 0.01. There were not statistically significant differences between groups in the reported supplementary secondary outcomes. These outcomes include the number of headache days per month, the mean pain score and quality of life measures. A post hoc power analysis revealed that the
study was underpowered to detect significant differences in secondary outcomes. Some results were suggestive of a possible long-term effect (eg the bupivacaine group had a lower, albeit nonsignificant number of headache days in the month posttreatment than the placebo group (17 vs 23). However, a study with a larger sample size would be needed to confirm whether or not 1- or 6-month results are significantly better after bupivacaine versus placebo treatment.

**Section Summary: Chronic Migraine**
One double-blind placebo-controlled RCT has evaluated transnasal SPG blocks for chronic migraine. The study found a significantly greater short-term (up to 24 hours) reduction in pain severity after active treatment versus placebo. However, there were not significant longer-term effects on outcomes (ie, 1 and 6 months after a course of 12 treatments over 6 weeks). The study was underpowered to detect outcomes at 1 and 6 months, and additional adequately powered trials are needed to determine the impact of SPG blocks on health outcomes.

**SEVERE ACUTE HEADACHE TREATED IN AN EMERGENCY SETTING**
The published literature on SGB blocks to treat severe acute headache consists of 1 double-blind placebo-controlled RCT. The study included patients between the ages of 18 and 65 who presented to the emergency department with a frontal-based crescendo-onset headache and a negative neurological examination. The study focused on frontal-based headaches because these were 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 receive treatment with bupivacaine 0.5% (n=45) or 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 post-treatment. 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 was not statistically significant (difference, 7.5%; 95% CI, -13% to 27%). Secondary outcomes including at least a 19mm reduction in VAS, percent of patients who were headache-free 15 minutes postintervention and percent 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 percent of patients headache free at 24 hours was significantly higher in the bupivacaine group (n=26 [72%]) than the placebo group (n=19 [48%]; difference, 25%; 95% CI, 2.6 to 44%). No SAEs were reported in either group. The authors stated that, in retrospect, outcome assessment at 1 hour after treatment would have been useful since headache relief at 1 hour, but not at 24 hours, is clinically relevant for ED headache patients.
Section Summary: Severe Acute Headache
One double-blind placebo-controlled RCT has evaluated a single transnasal SPG block for treating patients with acute headache presenting to an emergency department. The authors did not find a statistically significant benefit of active treatment compared with placebo 15 minutes postintervention. Significantly more patients were headache-free at 24 hours in the active treatment versus 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 in an intermediate time period (eg, 1 or 2 hours after treatment).

CLUSTER HEADACHE
No RCTs or non-randomized controlled studies were identified that evaluated intranasal SPG blocks for treating cluster headache. Two case series in patients with chronic drug-resistant cluster headache (CH) were published by a research group in Milan, Italy(11,12) Both studies used a needle (20-gauge in 1 study and 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 (40mg), 1% bupivacaine (4mL) and 2% mepivacaine with 1/100,000 adrenaline (2mL). The earlier study, published in 2006 by Felisati et al included 21 patients who received between 2 and 4 total treatment sessions, provided 1 week apart. 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 between 2-4 weeks in 3 patients, 3-6 months in 3 patients and 12-24 months in 2 patients. Four patients (19%) experienced treatment-related complications which consisted of 1 case of marked nasal epistaxis 3 days after the procedure and 3 cases of temporary diplopia.

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

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 the 2 studies but differed in terms of medication and application technique from the intervention currently available in the United States. It is not clear how the safety or efficacy of the procedure used in the case series differs from an intranasal SPG block applying local anesthetics and using an FDA cleared device. In the series, 40-50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. The studies are limited by small
sample sizes and lack of a sham treatment or alternative therapy for treating cluster headache.

**SUMMARY OF EVIDENCE**
For individuals who have chronic migraine who receive sphenopalatine ganglion blocks, the evidence includes 1 RCT and a case report. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT was double-blind and placebo controlled, and provided a course of 12 SPG blocks over 6 weeks. It found significantly greater short-term (up to 24 hours) benefits of active treatment versus placebo. There were not significant longer-term effects (ie, 1 and 6 months after a course of 12 treatments). The study was underpowered to detect longer term efficacy. Additional adequately powered RCTs demonstrating efficacy are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have severe acute headache treated in an emergency setting who receive sphenopalatine ganglion blocks, the evidence includes 1 RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The RCT was double-blind and placebo controlled, and provided a single SPG block. There was not a statistically significant difference between active treatment and placebo in the primary outcome, pain reduction 15 minutes postintervention. The study did not collect pain data again while patients were in the emergency department (eg, at 1 hour after treatment). At 24 hours after treatment, significantly more patients were headache-free in the active treatment versus placebo group. However, there is insufficient evidence that SPG blocks are an effective treatment in the emergency setting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cluster headache who receive sphenopalatine ganglion blocks, the evidence includes case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Two small case series were available; the approach to intranasal SPG blocks differed from the intervention currently available in the United States. It is not clear how the safety or efficacy of the procedure used in the case series differs from an intranasal SPG block applying local anesthetics and using an FDA cleared device. In the series, 40-50% of patients experienced complete symptom relief for a variable length of time and about 20% had treatment-related complications. Additional studies, preferably RCTs are needed to evaluate SPG blocks for treating cluster headaches. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**PRACTICE GUIDELINES AND POSITION STATEMENTS**
No guidelines or statements were identified.

**U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS**
Not applicable.
MEDICARE NATIONAL COVERAGE
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>Study Evaluating Sphenopalatine Ganglion Block (SPGB) for Treatment of Postdural Puncture Headache (PDPH)</td>
<td>30</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02365909</td>
<td>Sphenopalatine Ganglion Nerve Block vs. Elavil for Treatment of Transformed Migraines</td>
<td>200</td>
<td>May 2018</td>
</tr>
</tbody>
</table>

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

References:
Billing Coding/Physician Documentation Information

64505  Injection, anesthetic agent; sphenopalatine ganglion
64999  Unlisted procedure, nervous system

ICD-10 Codes

G43.001-  Migraine, code range
G43.919
G44.001-  Cluster headache, code range
G44.029
G44.031-  Various other headache types, code range
G44.89
R51  Headache

Additional Policy Key Words

MiRx™ Protocol

Policy Implementation/Update Information

7/1/17  New Policy. Considered Investigational.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.