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Sphenopalatine Ganglion Block in the Management of Chronic Headaches

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Abstract
Purpose of Review Sphenopalatine ganglion (SPG) block has been used by clinicians in the treatment of a variety of headache disorders, facial pain syndromes, and other facial neuralgias. The sensory and autonomic fibers that travel through the SPG provided the scientific rationale for symptoms associated with these head and neck syndromes. Yet, despite the elucidation of this pathogenic target, the optimal method to block its pain-producing properties has not been determined. Clinicians have developed various invasive and non-invasive techniques, each of which has shown variable rates of success. We examined the available studies of sphenopalatine ganglion blockade and its efficacy in the treatment of cluster headaches, migraines, and other trigeminal autonomic cephalalgias.
Recent Findings Studies have demonstrated that SPG blockade and neurostimulation can provide pain relief in patients with cluster headaches, migraines, and other trigeminal autonomic cephalalgias. Patients with these conditions showed varying levels and duration of pain relief from SPG blockade. The efficacy of SPG blockade could be related to the different techniques targeting the SPG and choice of therapeutic agents.
Summary Based on current studies, SPG blockade is a safe and effective treatment for chronic headaches such as cluster headaches, migraines, and other trigeminal autonomic cephalalgias. Future studies are warranted to define the optimal image-guided technique and choice of pharmacologic agents for SPG blockade as an effective treatment for chronic headaches related to activation of the sphenopalatine ganglion.

Keywords Sphenopalatine ganglion block · Trigeminal autonomic cephalalgias · Cluster headache · Paroxysmal hemicrania · Hemicrania continua · Migraine headache

Introduction

Sphenopalatine Ganglion Anatomy

Sphenopalatine ganglion (also called Meckel's ganglion, pterygopalatine ganglion, or nasal ganglion) is a triangular-shaped ganglion situated below the maxillary branch of the trigeminal nerve in the pterygopalatine fossa [1]. The sphenopalatine ganglion (SPG) is a parasympathetic ganglion composed of sensory and autonomic nerves. Its classification as a parasympathetic ganglion is derived from the fact that only pre-ganglionic parasympathetic axons synapse within the ganglion, while sensory and sympathetic connections merely transverse the ganglion [2].

The sensory fibers derived from the maxillary nerve travel through the SPG to provide sensory innervation to the nasal cavity, palate, and parts of the nasopharynx and oropharynx [1]. The sympathetic contributions of the SPG are derived from post-ganglionic sympathetic fibers, whose cell bodies are located within the superior cervical sympathetic ganglion. These post-ganglionic fibers eventually travel through the sphenopalatine ganglion without synapsing and terminate in the lacrimal gland and the nasal palatine mucosa [3].

The parasympathetic fibers of the SPG originate in the superior salivatory nucleus as the nervus intermedius, which is a component of the facial nerve [4]. The facial nerve then branches off to form the greater petrosal nerve to reach the

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SPG as the Vidian nerve [5, 6••]. Once within the ganglion, the pre-ganglionic fibers synapse with the post-ganglionic fibers and travel along the trigeminal nerve branches to provide secretomotor function to the nasal mucosa and lacrimal glands and vasomotor functions to the surrounding vasculature [7].

Pathophysiology of the Sphenopalatine Ganglia and Its Role in Chronic Headaches

The sphenopalatine ganglion is activated when the superior salivatory nucleus receives stimulation from the trigeminal afferent nerves [8]. This results in parasympathetic activation of the meningeal vessels, lacrimal glands, nasal, and pharyngeal mucosa. This signaling pathway is referred to as trigeminal-autonomic reflex [4, 9]. The activation of this pathway can cause release of vasoactive peptides, such as acetylcholine, vasoactive intestinal peptide, and nitric oxide, and result in plasma protein extravasation and neurogenic inflammation. This may present clinically as a headache [8–10].

The autonomic symptoms of the various forms of headaches mimic the activation of the SPG. Therefore, the SPG has become a therapeutic target of interest. Symptoms such as lacrimation, conjunctival injection, nasal congestion, rhinorrhea, forehead sweating, and periorbital edema are common autonomic manifestations of trigeminal autonomic cephalalgias (TACs) [11]. The presence of these symptoms suggests that SPG may be a key structure in their pathogenesis. TACs include cluster headache (CH), paroxysmal hemicranias (PH), short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), and hemicrania continua (HC).

Cluster headache is the most common type of TACs. CH is characterized by unilateral headaches in V_1 distribution that are classically associated with parasympathetic disruption, causing lacrimation, conjunctival injection, nasal congestion, and rhinorrhea. Symptoms of sympathetic disruption can also be present in the form of Horner's triad of ptosis, miosis, and anhidrosis [4, 12, 13]. Like the cluster headache, PH and HC are strictly unilateral headaches with ipsilateral autonomic features [12]. These forms of TACs are differentiated by the frequency and duration of symptoms. Symptoms of PH last between 2 and 30 min, while HC lasts for a duration of greater than 3 months. CH is of an intermediate duration and last between 15 and 180 min [12, 13]. The symptoms of PH also occur more frequently than the symptoms of CH. Unlike CH, PH and HC are exquisitely responsive to indomethacin [14]. The pathophysiology of PH and HC are not fully understood, but its clinical similarities to CH suggest that the SPG may be involved in its pathogenesis [15, 16].

Migraine occurs when nociceptive signals originating in the meninges are transmitted to the somatosensory cortex through the trigeminal ganglion, medullary dorsal horn, and thalamus. Common migraine triggers such as olfactory stimuli, food, sleep deprivation, stress, and post-stress activate a number of brain areas which project to the superior salivatory nucleus. The stimulation of superior salivatory nucleus activates SPG which leads to vasodilation and activation of meningeal nociceptors through local release of inflammatory mediators [6••]. Unlike cluster headaches, migraine headaches do not follow the trigeminal V_1 distribution [12]. This perhaps can be explained by the fact that the SPG also receives nociceptive afferent input from the second division of the trigeminal nucleus and acts as the major outflow pathway of the facial fibers. A diffuse array of autonomic symptoms (i.e., nasal discharge or congestion, conjunctival injection, and lacrimation) could be present due to the sensory projections in multiple facial areas. Therefore, it is reasonable to target the SPG for symptomatic relief during migraine attacks.

Methods and Results

The literature on SPG blockade (SPGB) and chronic headaches was searched via PubMed and Google Scholar from January 1 1981 to October 31 2016. The search terms included "sphenopalatine ganglion blockade" in conjunction with "cluster headache," "paroxysmal hemicrania," "hemicrania continua," and "migraine headache." After filtering review articles and literatures on acute headaches, one randomized, double-blind study was identified. This trial compared the efficacy of intranasal cocaine to intranasal lidocaine. The remainder of the evidence for intranasal blockade of the SPGB is limited to only a handful of open and uncontrolled studies (see Table 1). Our search yielded three retrospective case series on radiofrequency thermal ablation and four studies on pulsed radiofrequency and their role in cluster headaches (see Table 2). Only two articles on paroxysmal hemicranias and a single article on hemicrania continua were identified using our search criteria. One of the two paroxysmal hemicranias was a review article; therefore, it was excluded from our literature review (see Table 3). Our search criteria yielded several double-blind, controlled studies that examined the SPG and its role in migraine headaches (see Table 4).

Review of Clinical Data

Targeting the Sphenopalatine Ganglion for the Treatment of Cluster Headaches

Due to its relative ease of access and its involvement with the parasympathetic nervous system, the SPG has been considered a site of therapeutic potential. Yet, despite almost a century of therapeutic interest, clinical data is scarce and the optimal technique of SPGB has yet to be determined. Non-invasive methods of blockade including intranasal application

Table 1 Sphenopalatine ganglion blockade and cluster headaches

Author	Number of patients	Type of study	Diagnosis	Technique	Study results
Devoghel [17]	120	Uncontrolled study	Cluster headache	Supra-zygomatic SPGB with alcohol infiltration	• 103 patients reported complete relief. • 17 patients reported no relief.
Barre [18]	11	Open study	Cluster headache	Intranasal cotton-tipped application of cocaine or lidocaine	• All patients reported a greater than 65% reduction in headache intensity.
Kittrelle et al. [19]	5	Uncontrolled study	Cluster headache	Intranasal droplet application of 4% lidocaine	• 4 patients reported a 75% reduction in headache intensity.
Robbins [20]	30	Uncontrolled study	Cluster headache	Intranasal spray of 4% lidocaine	• 16 patients reported mild to moderate relief. • 14 patients reported no relief.
Costa et al. [21]	15	Double-blind, placebo-controlled study	Cluster headache	Anterior rhinoscopic-guided bilateral intranasal cotton-tipped application of 10% cocaine or 10% lidocaine	• All patients reported complete relief with application of both lidocaine and cocaine.

SPGB sphenopalatine ganglion block

of cocaine [18, 34], alcohol [17], and lidocaine [19, 20] have yielded promising results. Other more invasive techniques such as radiofrequency ablation and pulsed radiofrequency have produced positive results.

Sluder performed the earliest intervention on SPG in 1909. He utilized concentrations of 4, 10, and 20% cocaine to abort the symptoms of what is now known as cluster headaches [34]. Devoghel continued the work of Sluder and, in 1981, he performed what is still the largest SPGB study today. In this study, the SPG was accessed via the supra-zygomatic approach and alcohol was subsequently infiltrated into the ganglion. One hundred and twenty patients met the criteria of cluster headaches, and of this population, 103 patients (85.8%) had complete disappearance of pain and parasympathetic signs associated with their cluster headache. Devoghel reported that 16 patients were pain free for a period of 1 to

Table 2 Sphenopalatine ganglion pulsed radiofrequency and radiofrequency thermal ablation

Author	Number of patients	Type of study	Diagnosis	Technique	Study results
Sanders and Zuurmond [22]	66	Prospective study	Cluster headache	Radiofrequency ablation with fluoroscopy	• 34 patients with episodic CH and 3 patients with chronic CH reported complete relief • 8 patients with episodic CH and 4 patients with chronic CH reported no relief
Narouze et al. [23]	15	Retrospective study	Cluster headache	Radiofrequency ablation with fluoroscopy	• 7 patients reported a transition from chronic CH to episodic CH • 3 patients reported complete relief
Loomba et al. [24]	1	Case report	Cluster headache	Radiofrequency ablation with cone beam computed tomography	• The patient reported near complete resolution of symptoms after 6 months
Chua et al. [25]	3	Case series	Cluster headache	Pulsed radiofrequency with fluoroscopy	• 2 patients reported complete relief • 1 patient reported partial relief
Fang et al. [26]	16	Prospective study	Cluster headache	Pulsed radiofrequency with computed tomography	• 11/13 patients with episodic CH reported complete pain relief • 1/3 patients with chronic CH reported complete pain relief
Van Bets et al. [27]	11	Retrospective study	Cluster headache	Pulsed radiofrequency	• 8/11 patients reported complete relief • 1 patient reported no relief with pulsed radiofrequency and radiofrequency ablation • 1 patient reported partial relief • 1 patient reported pain relief with radiofrequency ablation
Bendersky et al. [28]	3	Case series	Cluster headache	Pulsed radiofrequency and radiofrequency ablation with fluoroscopy	• 3 patients reported poor to partial relief with pulsed radiofrequency and complete relief with radiofrequency ablation

CH cluster headache

2 years, 17 patients were pain free for a period of 2 to 3 years, and an additional eight patients were pain free for a period of 3 years or more [17].

The simplest method of targeting the sphenopalatine ganglion is the self-introduction of an intranasal, cotton-tipped applicator coated with either cocaine or lidocaine. When treated with intranasal cocaine, 11 out of 11 patients studied by Barre reported a greater than 65% reduction in headache intensity [18]. Ten out of 11 patients reported an 80% reduction in the intensity of their cluster headache within 2 min and 30 s. A subsequent but smaller study by Kittrelle showed similar results with the intranasal droplet application of lidocaine [19]. In Kittrelle's study, four of the five patients reported a 75% or greater reduction in the intensity of their headache within 3 min of the application of a 4% lidocaine droplet solution. The solitary patient who failed to respond to the lidocaine solution also failed to respond to the 5% cocaine solution. Robbins reported similar success in a population of 30 patients where 4% lidocaine nasal spray was used as an abortive therapy [20].

These early findings led to the first and only, double-blind, placebo-control trial where Costa et al. sought to compare the abortive success of 10% solution of cocaine hydrochloride versus 10% lidocaine solution for nitroglycerin-induced pain in patients with cluster headaches. This study included 15 patients and 100% of the patients reported pain relief for nitroglycerin-induced headache with similar efficacy between both anesthetic agents. Unlike the previously mentioned studies, Costa and his team administered the medications bilaterally under the guidance of anterior rhinoscopy. Costa argued that the cotton swab application and droplet administration can be inaccurate and nasal obstruction may limit the access or absorption at the target site. Therefore, anterior rhinoscopic-guided SPGB was hypothesized to be a more accurate method of drug administration. Costa suggested that the use of the anterior rhinoscopic technique attributed to his high success rate of cluster headache abortion [21]. Variations in endoscopic techniques utilizing a mixture of local anesthetics and corticosteroids have been reported [35]. Since these approaches are more invasive and carry a greater risk, endoscopic approaches are perhaps best suited for the management of patients suffering from chronic cluster headaches, resistant to pharmacologic interventions.

Despite the abortive success of the previously mentioned studies, symptomatic relief was not permanent [17, 21, 35]. Therefore, radiofrequency ablation (RFA) was postulated to be a more selective technique with benefits that exceed the abortive therapies of alcohol and cocaine administration. Sanders et al. conducted the largest study of radiofrequency ablation of the SPG. In this study, 66 patients were followed over a period of 12 to 70 months [22]. The study group consisted of 56 patients that suffered from episodic cluster headaches (Group A) and additional ten patients who suffered chronic cluster headaches (Group B). Greater than 60% of patients in Group A had complete relief of their CH symptoms, while only 30% of patients in Group B had complete relief. Eight patients in Group A and four patients in Group B did not experience any relief of symptoms. While the results of this study suggested that chronic cluster headaches may be more resistant to ablative techniques of the SPG, Narouze and his colleagues have published evidence on the contrary [23]. In this long-term, follow-up study, Narouze performed percutaneous infrazygomatic RFA on 15 patients with chronic CH and followed them for a period of 24 months. In this study, 46.7% of patients (7/15) reported a change in their headache pattern from the chronic CH variety to the episodic form. Three patients reported complete relief of their chronic CH symptoms and did not require their preventive medications for the duration of the study. The remaining three patients did not notice an immediate change in their headache intensity or duration. Cone beam computed tomography (CBCT) has been shown to be an effective alternative to the fluoroscopic modalities utilized in the previous studies [24]. CBCT renders a near real-time three-dimensional radiographic image using hundreds of planar projection images. This improves anatomical visualization and accuracy of needle placement with reduced exposure to radiation compared to conventional computed tomography.

An alternative to RFA is pulsed radiofrequency (PRF). Unlike RFA, pulsed radiofrequency is a non-destructive, non-ablative technique that utilizes bursts of radiofrequency energy to produce pain relief. Although the exact mechanism is unclear, the pain-relieving properties of PRF are thought to occur independent of thermal ablation, instead, it is related to changes in protein expression that are not seen during continuous radiofrequency ablation [36]. Chua et al. performed the first documented case series of PRF to the SPG. There were three patients with a history of cluster headaches in this study [25]. Two patients were symptom free up to 4 months, while the third patient experienced partial pain relief only. While the results of this study yielded mixed reviews, it demonstrated for the first time that PRF could be an acceptable alternative for patients non-responsive to conservative therapies [25]. The results of this case study have been replicated, with minimum treatment-related adverse events or complications, in other slightly larger studies [26, 27]. At the very least, these studies demonstrated that PRF is a safe treatment modality with the potential to achieve therapeutic success for cluster headache patients who failed conservative therapies.

The patients with cluster headaches may experience different responses to RFA and PRF. These techniques have different mechanisms of action at the target site. Bendersky et al. illustrated this when they published a case series in which three patients had partial relief with PRF but experienced complete symptom resolution with a subsequent RFA 2 months after their initial intervention with PRF [28].

Table 3 Sphenopalatine ganglion blockade and paroxysmal hemicranias and hemicrania continua

Author	Study type	Diagnosis	Technique	Study results
Morelli et al. [15]	Case report	Paroxysmal hemicrania	SEGB using 40 mg of triamcinolone, 4 ml of 1% bupivacaine, and 2 ml of 2% mepivicaine with 1/100,000 adrenalin	• First 2 weeks: reduction in both frequency of episodes and intensity of pain. • Conclusion of 5-week treatment period: Episodes reduced to one a day and were completely responsive to 500 mg paracetamol. • 4-month follow-up period: sustained clinical improvement.
Androulakis et al. [16]	Case report	Hemicrania continua	SPGB with Tx360® device using 0.5% bupivacaine	• No acute effect of SPG block on HC pain. • Repetitive blocks over several weeks showed a reduction in headaches mood, and functional capacity.

SEGB sphenopalatine endoscopic ganglion blockade, *SPGB* sphenopalatine ganglion block, *HC* hemicrania continua

Paroxysmal Hemicrania and Hemicrania Continua

The utility of sphenopalatine ganglion blockade in treating paroxysmal hemicranias is limited to a single case report. In this case report, sphenopalatine endoscopic ganglion blockade led to a reduction in both the frequency of PH episodes and intensity of pain for a 69-year-old patient who was intolerant to indomethacin [15]. Clinical improvement was sustained during a 4-month follow-up period.

The data for SPGB and HC is limited to a single case report where a patient suffered from various forms of headaches including migraines, a whiplash-related headache, a post-concussive headache, and hemicrania continua [16]. The patient was intolerant to indomethacin. Her HC symptoms were described as having a continuous component that originated in the superior medial aspect of her right eye and radiated anteriorly and inferiorly to the maxilla and upper teeth. The autonomic manifestations of her HC included right-sided tearing, redness of the membrane adjacent to the inner canthus, nasal congestion, miosis, and ptosis. The patient's therapy was divided into an initial treatment phase and a maintenance phase. The initial phase consisted of two SPGBs per week, for a period of 6 weeks with the Tx360® (by Tian Medical Inc. Lombard, IL, USA) device using 0.5% bupivacaine. The maintenance phase included treatment every 4 to 5 weeks. The patient did not have an acute response to the SPGB; however, clinical improvement was observed after approximately 4 weeks of repetitive SPGBs. This was evident by a decrease in the intensity of her continuous headache and a decrease in the severity of her photophobia and ptosis [16].

Migraine Headaches

In 1995, Kudrow et al. reported the first study demonstrating the efficacy and rapid relief of migraine attacks from local anesthetics targeting the SPG [29]. In 1996, another randomized trial by Maziels et al. demonstrated rapid onset of symptomatic relief within 2 min with a peak effect at 15 min [30]. However, both studies were limited by uncontrolled variables and rapid relapse of symptoms. Then, in 1999, Maziels attempted to elicit more data using 4% lidocaine directed at the SPG via the transnasal approach. In this study, patients treated themselves in an outpatient setting [31]. This is a randomized, controlled, double-blind study wherein 34 of 95 subjects (35.8%) treated with 4% intranasal lidocaine had headache relief within 15 min, compared with 8 of 108 subjects (7.4%) in the placebo group ($p < 0.001$). They also demonstrated in subsequent open-label follow-up phase that over 50% of the headache episodes were effectively relieved in 30 min after targeting the SPG with lidocaine. Additionally, they found that the patients who responded to 4% lidocaine did not have a diminished effect over a 6-month follow-up period [31].

In recent years, Cady et al. attempted to demonstrate the efficacy of SPGB in a double-blind, placebo-controlled study at two headache centers in the USA [32••]. In this study, the Tx360® device was utilized to transnasally target the SPG for acute treatment of chronic migraines. Study participants underwent SPGB with either 0.3 ml of 0.5% bupivacaine or saline twice weekly, for a period of 6 weeks. Thirty-eight subjects were included in the study with 26 patients in the bupivacaine group and the remaining 12 patients in the saline group. Compared to the saline group, the bupivacaine group reported a statistically significant reduction in their numeric rating scale headache pain scores at baseline, 15 min, 30 min, and 24 h. Surprisingly, the saline group reported a statistically significant reduction in their headache pain at 15 and 30 min, but a statistically significant increase in their headache pain at 24 h. The effects of repeated SPGB were also studied and demonstrated a non-significant, but decreasing trend in migraine pain during the 6-week study period. Perhaps the most notable limitation of this study is the ability of bupivacaine to elicit adverse effects such as lacrimation and oral numbness. The elicitation of these symptoms has the potential to "unblind" the study participants and influence their response to the questionnaires. Nevertheless,

Table 4 Sphenopalatine ganglion blockade and migraine headache

Author	Number of patients	Study type	Diagnosis	Technique	Study results
Kudrow et al. [29]	23	Uncontrolled study	Migraine headaches	Intranasal instillation of 0.4 ml of 4% lidocaine solution with eyedropper directed at the SPG region	• 12/23 (52.2%) patients obtained complete or almost complete relief during attacks. • 6 of 11/23 patients reported varied level of relief between 8 to 33%. • 5 out of the remaining 11/23 patients reported no change in symptoms during attacks.
Maizels et al. [30]	80	Randomized, uncontrolled study	Migraine headaches with or without aura	Intranasal topical application of 0.5 ml of 4% lidocaine or saline over 30 s in supine position	• 29/53 (55%) of patients treated with lidocaine experienced 50% reduction of headache vs. 6/28 (21%) of control patients who received saline. • Rescue medication for headache relief was needed in 15/53 (28%) in the treatment group vs. 20/28 (70%) of the control cohort. • Within 30 to 60 min of treatment, relapse of symptoms was reported in 10/24 (42%) of the treatment group vs. 5/6 (83%) of the controls.
Maizels and Geiger [31]	131	Randomized controlled, double-blind study	Migraine headaches with or without aura	Intranasal application of 0.5 ml of 4% lidocaine or saline	• 34/95 (35.8%) treated headaches reported relief within 15 min using 4% lidocaine vs. 8/108 (7.4%) headaches received saline. • Rescue medication utilized in 46.2% of the treated group vs. 79.4% of saline treated group. • Relapse of headaches in 7/34 (20.6%) of treated patients and 0/8 in the group that received saline. • In the open-label follow-up phase, 129/313 (41.2%) and 141/245 (57.6%) episodes of headache were relieved within 15 and 30 min, respectively. • Relapse within 24 h in 28 (19.9%) of responders.
Cady et al. [32••]	41	Randomized, double-blind study	Chronic migraine	SPGB with 0.3 ml of 0.5% bupivacaine using Tx360® device	• 26/38 patients comprising of bupivacaine group showed statistically significant reduction of headache pain at 15 min, 30 min, and 24 h. • 12/38 patients comprising of saline group reported statically significant reduction of headache pain at 15 min and 30 min and increased headache pain at 24 h.
Bratbak et al. [33••]	10	Prospective, open, uncontrolled study	Intractable, chronic migraine	Image-guided bilateral SPG injections of 25 IU onabotulinum toxin A using MultiGuide® device	• 8/10 patients experienced at least 50% reduction of moderate and severe headache days compared to baseline after 2 months.

SPG sphenopalatine ganglion, *SPGB* sphenopalatine ganglion block

the results of this study demonstrated that repetitive pharmacological intervention with bupivacaine may be beneficial in the acute treatment of chronic migraines.

A similar, but smaller prospective, open-label uncontrolled study by Bratbak et al. utilized onabotulinum toxin A (BTA), in lieu of local anesthetics to target the SPG in patients with intractable chronic migraines ($n = 10$) [33••]. In the SPG, BTA interferes with neuronal signaling by inhibiting the release of acetylcholine, thus preventing the neurotransmission between pre-ganglionic and post-ganglionic fibers. Bratbak's team attempted to establish the safety of administering BTA in the SPG as a method for managing intractable migraine. A novel injection device, MultiGuide® (Trondheim, Norway), was used with image guidance to administer 50 IU of BTA in the SPG bilaterally during a single session in ten patients who suffered from intractable migraines. The patients were then followed for a period of 12-weeks. Eight of ten study participants (80%) reported at least a 50% reduction of moderate

and severe headache days compared to baseline and second-month post-treatment. Most commonly cited adverse events were localized edema and pain at the injection sites. With the exception of a single episode of temporomandibular joint dysfunction, all reported adverse events self-resolved at the conclusion of the study [33••].

Conclusions

It is evident from our literature review that SPG blockade and neurostimulation can provide pain relief in patients with primary headache disorders related to activation of the sphenopalatine ganglion such as cluster headaches or migraines. Although the sample sizes were small, the studies demonstrated varying levels of pain relief and duration of symptomatic relief after SPG blockade. The studies examined different techniques both non-invasive methods (i.e., intranasal cotton-tipped application, intranasal droplet application, the use of Tx360® device) and invasive methods (i.e., endoscopic SPGB, radiofrequency ablation, pulse radiofrequency ablation) to block the SPG. The studies also suggested different therapeutic agents for SPG blockade. These agents include lidocaine, corticosteroid-anesthetic mixture, bupivacaine, alcohol, onabotulinum toxin A, and cocaine. The advancement of endoscopic techniques, availability of newer imaging modalities, and development of new medical device will allow precise delivery of therapeutic agents to SPG. This will increase its efficacy and reduce the complications associated with the block. Therefore, further large-population studies to determine the choice of pharmacologic agents and optimal image-guided techniques may provide additional evidence to support the SPGB as an effective treatment for primary headache disorders related to activation of the sphenopalatine ganglion.

Compliance with Ethical Standards

Conflict of Interest Jeffery Mojica, Bi Mo, and Andrew Ng declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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