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REVIEW ARTICLE

Cluster headache: crosspoint between otologists and neurologists—treatment of the sphenopalatine ganglion and systematic review

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Abstract
Among cephalgias, cluster headache (CH) is the rarest and the most disabling, explaining the appellation of "suicide headache." Up to 20% of chronic CH reveals to be resistant to pharmacological treatments, in which case interventional procedures should be considered. Many reports evaluated invasive approaches and a wide strand of research is dedicated to the sphenopalatine ganglion. Our paper will now be focused on providing an overview on modern applications on the sphenopalatine ganglion (SPG), their outcomes, and their feasibility in terms of risks and benefits. The group reviewed the international literature systematically for procedures targeting the sphenopalatine ganglion and its branches for episodic and chronic CH, including block, stimulation, radiofrequency, stereotactic radiosurgery, and vidian neurectomy. Seventeen articles fixed our inclusion criteria. Comparing the outcomes that have been analyzed, it is possible to notice how the most successful procedure for the treatment of refractory chronic and episodic CH is the SPG block, which reaches respectively 76.5% and 87% of efficacy. Radiofrequency has a wide range of outcomes, from 33 to 70.3% in CCH. Stimulation of SPG only achieved up to 55% of outcomes in significant reduction in attack frequency in CCH and 71% in ECH. Radiosurgery and vidian neurectomy on SPG have also been analyzed. Generally, ECH patients show better response to standard medical therapies; nevertheless, even this more manageable condition may sometimes benefit from interventional therapies mostly reserved for CCH. First results seem promising and considering the low frequency of side effects or complications, we should think of expanding the indications of the procedures also to those conditions. Outcomes certainly suggest that further studies are necessary in order to understand which method is the most effective and with less side effects. Placebo-controlled studies would be pivotal, and tight collaboration between neurologists and otorhinolaryngologists should also be central in order to give correct indications, which allow us to expect procedures on the SPG to be an effective and mostly safe method to control either refractory ECH or CCH.

Keywords Cluster headache · Sphenopalatine ganglion · Endoscopic transnasal approach · Refractory headache · Cephalgia

Introduction

Among cephalgias, cluster headache (CH) is the rarest, with a prevalence in the overall population of 1 each 1000 people. Horton first described it in 1936 as a highly intense headache appearing in cluster periods. One of its main features is the one-sidedness; indeed, only 15% show a bilateral presentation. It usually rises from the orbit and irradiates upward to temporal and frontal regions, or downward to the nose, cheekbone, and superior alveolar process. Each episode lasts between 15 to 180 min and the pain can be so severe that the patient becomes restless and intractable, explaining the appellation of "suicide headache." Autonomic symptoms may accompany the attack; these can be related to the eyes with ipsilateral conjunctival flushing, lacrimation, eyelid edema, miosis or ptosis, or they can present with ipsilateral nasal congestion followed by rhinorrhea [1]. Cluster headaches can be divided into an episodic (ECH) or chronic (CCH) form, with an overall ratio of 6:1 [2]. The former is characterized by

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variable duration, from 2 weeks to 3 months, with regular periodic onsets of the cluster, followed by a remission phase of at least 14 days [3].

The latter has no remission periods or intervals that are longer than 2 weeks, following a cluster manifestation, during at least 1 year.

Originally, otorhinolaryngologists were on the front line of the management of this kind of disease, and tried to classify cephalgias in relation to trigger point and site of the pain.

As early as in 1908, Sluder's syndrome had been introduced as a unilateral pain of the orbit that irradiated to the midface. It is believed to be secondary to direct or reflex stimuli, which act on the terminal part of the internal maxillary artery involving the sphenopalatine ganglion (SPG) and its divisions. However, establishing of its etiology is often not possible; it can be due to a sphenoidal sinusitis, posterior ethmoiditis, or trauma to the pterygopalatine fossa.

Another kind of craniofacial pain has been called Charlin's neuralgia, also known as nasociliary neuralgia, and arises from the fixed point where the nasociliary nerve emerges and radiates to the front and external face of the nose unilaterally. It can be related to sinusitis, septal nasal deviation, or neuritis processes due to infections or intoxications.

Interestingly, neurologists included these syndromes in the first edition of the International Classification of Headache Disorders (ICHD) in 1988. The classification divides cephalgias into headache, facial pain, and cranial neuralgia. The 11th group consists of "headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures." This introduced, also to neurologists, types of cephalgias with a specific origin and distribution in the otorhinolaryngologic district: consequently, CH acquired a lot of interest and many started research in this field (ICHD-1).

Consequently, neurologists became referents for this kind of disease and transformed the classification on the basis of the general characteristics of the headaches. Those neuralgias (e.g., Sluder's and Charlin's neuralgia) that were previously included as separate entities in the ICHD-1 were now considered an older interpretation of the same disease, which was cluster headache (ICHD-3), and have lost their relevance for a separate therapeutic approach [4].

Treatments for CH are still being widely investigated and include acute and prophylactic pharmacological therapies; these, however, are not the subject of our review.

Unfortunately, up to 20% of chronic CH reveals to be resistant to pharmacological treatments [5], in which case, interventional procedures should be considered. Many reports evaluated more invasive approaches such as trigeminal resection, microvascular decompressions, and other destructive methods; these, however were confined to isolated case reports or have been abandoned also due to their high incidence of pain recurrence [6, 7].

Less invasive procedures for CCH, which are still in use today, include occipital nerve stimulation: a mini-invasive procedure where electrodes are positioned in general anesthesia onto the nerve itself. This technique is been practiced and studied since 2006. A recent study from Magis et al. [8] regarding this procedure for chronic forms showed that 40% of patients evolved from CCH into episodic CH, and the other 60% remained in a chronic form albeit with a decrease of frequency of 70% of the original pain level. However, 50% needed explantation within 9 years.

Occipital nerve blockade may be also considered an effective transitional therapy in non-responsive episodic and chronic CH [9]. Some studies found it useful prior to occipital nerve stimulation, but other reviews did not find any statistically significant benefit [10].

Vagal nerve stimulation also demonstrated its efficacy, especially for episodic cluster headaches [11].

The application of the electrodes can be performed either by neurosurgeons or by otorhinolaryngologists with varying results [12–14].

Other invasive approaches, which have yielded significant benefits, include deep brain stimulation, in which the ventroposterior hypothalamus or the ventral tegmental area is targeted in refractory chronic CH [15–19]. An interesting recent review by Vyias et al. has shown that deep brain stimulation has a significant potential in reducing pain during the episodes in the majority of chronic CH patients. Long-term follow-up, however, suggests that tolerance and absence of response may develop in some patients [20]. It may be considered as a final possibility of the treatment protocol [21].

Finally, a wide strand of research is dedicated to the sphenopalatine ganglion: due to its position and branch, it is considered the starting and final point of CH and so a valid target for various treatments focused on its inactivation.

Otorhinolaryngologists have a long experience with this kind of treatments, starting from Sluder, who in 1918 discovered how intranasal application of cottonoids saturated in cocaine had positive results on patients affected by Sluder's syndrome [22].

In 2006, our multidisciplinary team started to study the potential of endoscopic-controlled sphenopalatine ganglion infiltrations in refractory chronic CH: a mixture of steroids, bupivacaine, mepivacaine, and adrenaline is injected into the sphenopalatine fossa towards the ganglion in an endoscopic-assisted intranasal approach [23]. Over the years, we increased the number of cases and developed high accuracy in the technique, with very positive outcomes [24]. Where neurologists have some difficulties in controlling refractory chronic CH with isolated pharmacological treatment, the otorhinolaryngologists' approach can be a valid option which may reduce and control the frequency and intensity of CH attacks.

Our paper will now be focused on providing an overview on modern applications regarding the sphenopalatine

ganglion, their outcomes, and their feasibility in terms of risks and benefits.

Inactivation of sphenopalatine ganglion is a target for studies and many authors published about its effects and potentialities with different proposals regarding the kind of approach to the ganglion [25–31]. Nevertheless, only few authors added to the literature providing case series or studies with a solid research strategy: most frequently, authors presented only case reports or reviews.

Methods

Our group reviewed the international literature systematically for procedures on the sphenopalatine ganglion, including block, stimulation, radiofrequency, and stereotactic radiosurgery Results were obtained with the search strategy: [(cluster headache) AND (sphenopalatine ganglion) from 1998 to 2019] on PubMed, Scopus, and Web of Science databases. Studies were evaluated according to related medical conditions, study design, outcomes, and procedural details.

Inclusion criteria were:

- Refractory episodic and chronic CH
- Case series of 5 or more patients
- Prophylactic therapy
- Articles published during the last 20 years
- Full articles
- Full-Text articles had to be available
- Study sample was human

Exclusion criteria were:

- Clinical indication: others from CH
- Case series: studies on less than 5 patients
- Treatment of acute episodes of CH
- Articles published more than 20 years ago
- Reviews and abstracts

Two of the authors (CR and CP) independently screened the retrieved studies based on the title, key words, and abstract to exclude non-relevant and non-English-written studies. After completion of all searches, duplicates were removed. Both retrospective and prospective studies were included, while case reports and small series were excluded because of their intrinsic lower level of evidence (the minimum number of patients was arbitrarily set at 5). Published reviews on sphenopalatine ganglion procedures for CH were similarly excluded, but their reference list was reviewed to identify possible additional studies. Studies whose main purpose was unrelated to sphenopalatine ganglion procedures' efficacy and biological studies (i.e., those exploring quality of life) were also excluded, unless clear and standardized description of patient outcome was retrievable from the manuscript. Studies that did not meet the inclusion criteria were discarded during the initial review (Fig. 1). When uncertainly existed in the abstract evaluation, we retrieved and assessed the full text. A manual search in the reference lists of these articles was performed to identify potentially relevant papers missed during the database search. Differing opinions were resolved by consensus between the two authors. Data extracted and analyzed for the study included first author, year of publication, kind of treatment, approach, medication used for the procedure, number of cases, study design, outcomes, and side effects. For radiofrequency ablation, the following additional items were collected: radiofrequency ablation temperature, duration of the stimulation, and type of radiofrequency ablation.

Results

Sphenopalatine ganglion block

The authors included 5 articles focused on case series of refractory chronic CH that describe sphenopalatine ganglion block as prophylactic therapy (Table 1). SPG block is a short-term block achieved by the injection in the proximity of sphenopalatine ganglion of a mixture of different drugs. It was first described in 1980 by Devoghel [36], who presented a promising method for the control of cluster headaches through a transzygomatic approach.

In 2006, Felisati et al. [23] described a transnasal injection of a mixture of steroids, anesthetics, and adrenaline close to the SPG. The efficacy of the procedure revealed to be 55% in 20 patients, with 8 complete temporary resolutions of CH attacks, and 3 significant reductions of more than 50%. Subsequently, the same group [24] refined the technique using a smaller endoscope (3 mm), a more effective topical anesthesia (Xilocaine 5% with naphazoline), and a needle for spinal anesthesia, gauge 18.

In comparison to the previous experience, the results show a similar percentage of responders (60% in 2010 vs 54% in 2006) but a higher number of long-term responders over 1.5 months (40% vs 25%). Then, Kastler [33] proposed an infrazygomatic approach for injection of absolute alcohol in SPG, which he performed on 14 patients. Outcomes showed a 76.5% efficacy but with permanent complications. Bratbak's group [34] performed the SPG block transnasally and with neuronavigation using onabotulinum toxin A: positive performance has been recorded in 50% of a total of 10 patients. Then, Aschehoug et al. [35] developed a long-term follow-up of the same case series from Bratbak's study [34] and performed repetitive injections of onabotulinum toxin type A when symptoms returned: only 7 patients remained in the

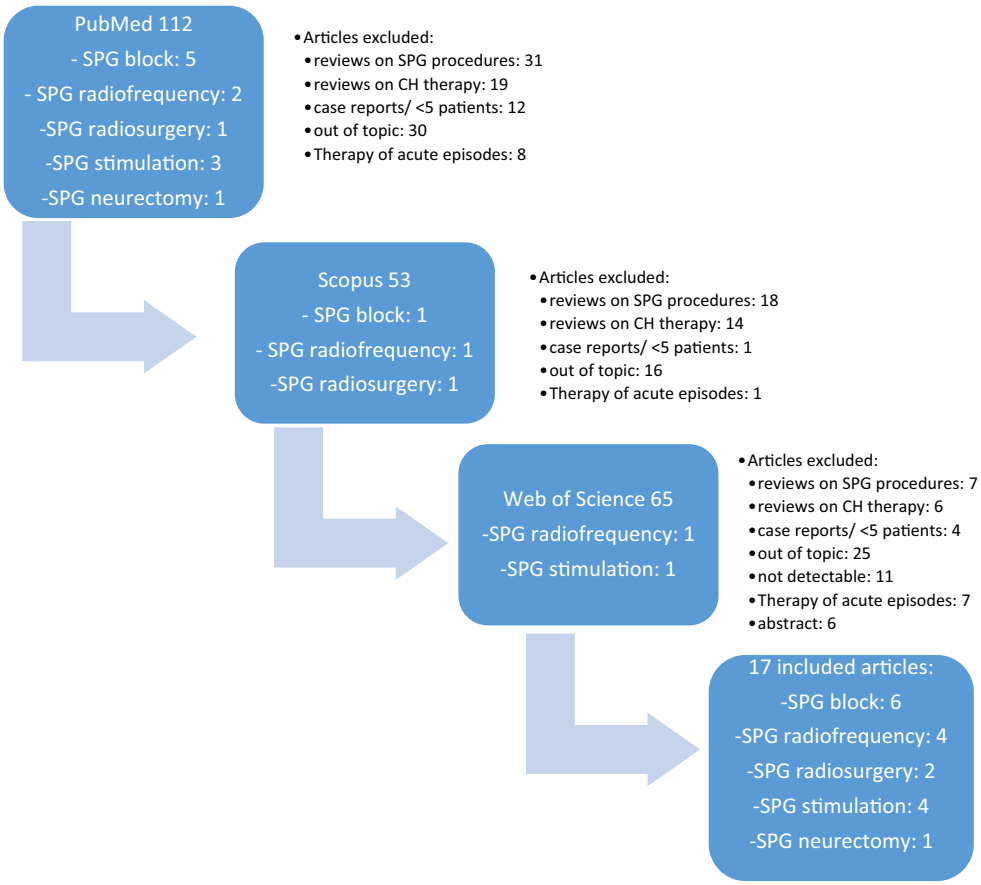

Fig. 1 Overview of the systematic review process

study, with an efficacy rate of 71% at 18 months and 57% at 24 months.

Regarding episodic CH, only one study has been published [32]. It revealed an encouraging positive outcome after serial injections of corticosteroids in a transoral approach, with an 87% success rate.

Most complications revealed to be mild-to-moderate and temporary, such as epistaxis, diplopia, and jaw pain. Only in Kastler's article [33], with an infrazygomatic approach using absolute alcohol, hematomas and persistent hemipalate hypo and paresthesia have been recorded. It discloses how a transnasal approach could be safer and with more manageable side effects.

In summary, SPG block seems to be an attractive option in managing refractory chronic CH, with a moderate efficacy (50–76%) and a low rate of complication, when executed transnasally. Nevertheless, literature lacks placebo-controlled studies and wider case series which could strengthen its impact.

Radiofrequency treatment of the sphenopalatine ganglion

Another kind of approach to the SPG is characterized by the use of radiofrequency, in which radiofrequency is applied to the SPG either in a pulsating or ablative manner in order to reach a long-term block of the SPG (Table 2). Filippini [37] first developed a procedure on 19 patients suffering of ECH and CCH: efficacy rate was at 57.8%, with no particular side effects reported. He already introduced an infrazygomatic approach to reach the pterygopalatine fossa. Then, Narouze [38] proposed a case series with 15 patients using fluoroscopic guidance, which showed a 66% of positive outcomes, even if with 2 new onsets of contralateral headaches. Fang et al. [39] proceeded with further case series on both chronic and episodic CH; in the former, he found an efficacy rate of 33%. For ECH instead, outcomes were more encouraging (85%), but the same authors pointed out how this study was not adequate to evaluate episodic forms, since they are often characterized by spontaneous regressions. Salgado et al. [40] have the largest case series (37 patients), where they performed radio frequency ablation (RFA) and pulsed radiofrequency (PRF): 70.3% of patients reported benefits. The authors also compared the two procedures, finding that PRF has a higher positive score (70.8 vs 61.5%).

All the studies agree on the technique of both RFA and PRF: 80 °C for 60 s in the former, 42 °C for 120 s in the latter. Most of them [37, 38, 40] used intraoperative fluoroscopy as a guidance during the positioning of the needle at the proximity of SPG. Only Fang [39] sustained that intraoperative CT scans

Table 1 Block of sphenopalatine ganglion

1st author	Year	Diagnosis	CT/RMN	Approach	Drugs used	No.	Outcomes	Complications	Time follow-up
1 Felisati [23]	2006	CCH	None	•Transnasal with endoscopic control (30° optic) •3 weekly sessions	40 mg triamcinolone acetonide + 4 ml 1% bupivacaine + 4 ml mepivacaine 2% + 1/100,000 adrenaline	20	8 complete temporary resolution (CR) 3 significant reduction (SR) of attacks 9 no changes Efficacy 55%	1 epistaxis 3 temporary diplopia spontaneously resolved	24 months
2 Pipolo [24]	2010	CCH	None	•Transnasal •Local anesthesia •3 weekly sessions	40 mg triamcinolone acetonide + 4 ml bupivacaine 1% + 4 ml mepivacaine 2% + adrenaline 1/100,000	15	8 CR 1 SR 6 non-SR Efficacy 60%	2 epistaxis 1 reduced buccal opening	18 months
3 Peñarrocha-Diago [32]	2012	ECH	None	•Transoral •Local anesthesia •4 sessions once a week	Corticosteroids	23	69.6% CR 17.4% SR 13% non-SR Efficacy 87%	None	12 months
4 Kastler [33]	2014	CCH	CT	•Infrazygomatic approach •Local anesthesia •CT guidance •Multiple sessions if necessary	1 ml absolute alcohol	14	Efficacy 76.5%	4 hematomas 4 transient hemipalate anesthesia 2 persisting hemipalate paresthesia 2 persisting hemipalate anesthesia	48 months
5 Bratbak [34]	2016	CCH	CT + RMN	•9 transnasal •1 infrazygomatic •Neuronavigator •General anesthesia	0.05 mg adrenalin in 5 ml isotonic saline, then 25 or 50 IU onabotulinum toxin A	10	1 temporary CR 4 SR 1 lost in FU 4 non-SR Efficacy 50%	4 epistaxis 3 diplopia spontaneously resolved 1 jaw pain	6 months
6 Aschehoug [35]	2018	CCH	CT + RMN	•MultiGuide device neuronavigator •Local anesthesia •Multiple sessions if necessary	25 or 50 IU Onabotulinum toxin A + isotonic saline	7	5 SR at 18 months 4 SR at 24 months Efficacy at 18 months 71% Efficacy at 24 months 57%	1 diplopia 1 jaw pain	24 months

Decrease of CH attacks is intent to be significant when it is recorded > 50% reduction of mean attack frequency vs baseline

Table 2 Radiofrequency over SPG for ECH and CCH

	Author	Year	Diagnosis	Treatment	Technique	Drugs	No. of cases	Outcomes	Complications	Time follow-up
1	Filippini [37]	1999	ECH + CCH	(RFA)	•Infrazygomatic approach •Fluoroscopic guidance	RFA lesions at 80 °C for 60 s	17 ECH 2 CCH	5 resolution 6 SR Efficacy at 12 months ECH 64.7% CCH 50% Efficacy at 33 months ECH 52.9% CCH 100%	None	33 months
2	Narouze [38]	2009	CCH	RFA	•Previous SPG block •Infrazygomatic approach •Fluoroscopic guidance	2 RFA lesions at 80 °C for 60 s each	15	3 resolution 7 SR 2 resolution but new onset controlaterally Efficacy 66%	7 temporary facial paresthesia 1 permanent facial paresthesia 2 contralateral headache	18 months
3	Fang [39]	2016	ECH + CCH	PRF	•Infrazygomatic approach •Sedation + local anesthesia •CT guidance	PRF at 42 °C twice for 120 s	13 ECH 3 CCH	13 ECH SR 1 CCH SR Efficacy ECH 85% CCH 33%	None	17 months
4	Salgado [40]	2018	CCH	RFA or PRF	•Infrazygomatic approach •Fluoroscopic guidance	RFA 80 °C for 60 s PRF cycle at 42 °C + 40 V for 120 s	37	5 resolution, 21 SR Efficacy 70.3%	None	68 months

Efficacy is intended in CCH as frequency of attacks; in Fang's study [39], ECH's efficacy is intended as NRS (numeric rating scale, which shows intensity of pain during each attack)

Table 3 Gamma knife radiosurgery on SPG for CH

	Author	Year	Diagnosis	Technique	Treatment	No. of cases	Outcomes	Complications	Time follow-up
1	Ott [41]	2010	CH	Gamma knife radiosurgery (GKS) •To trigeminal nerve (TN) •To TN and SPG	N: maximum dose of 85 to 103 Gy SPG: maximum dose of 85 to 97 Gy	7	1 to TN resolution 4 to TN + SPG resolution Efficacy 71.4%	8 temporary facial paresthesia	30 months
2	Kano [42]	2011	ECH + CCH	Stereotactic GKS •8 GKS to TN and SPG •8 GKS to TN •1 GKS to SPG	80 Gy maximum median dose	17	10 resolution Efficacy 59%	8 temporary facial paresthesia	34 months

are a better accurate guide for the correct insertion of the needle.

SPG radiofrequency has been evaluated in many works, which gave controversial outcomes (33–70%). The procedure seems to be safe, and the effects are long-term.

Gamma knife radiosurgery

Patients undergo single-session focused irradiation of the trigeminal nerve root, sometimes coupled with irradiation of the sphenopalatine ganglion as well.

Ott [41] and Kano [42] studied gamma knife radiosurgery as a treatment for CH (Table 3). Outcomes are encouraging, but with frequent paresthesia as side effects. Radiosurgery is targeted not only to the SPG, but also to the trigeminal nerve.

Sphenopalatine ganglion neurostimulation

SPG neurostimulation bases its mechanism on implanting a device affixed to the maxilla, with electrodes placed in the pterygopalatine fossa proximate to the SPG.

Five studies were included for SPG neurostimulation (Table 4). Jensen et al. [43] reported a randomized-controlled trial using SPG neurostimulator for patients with refractory CCH. Twenty-eight patients received randomly full stimulation, sub-perception stimulation, and sham-stimulation: outcomes showed a significant reduction of attacks' frequency in 12 cases (42%). Jürgens [45] reported a cohort study on Jensen's database to evaluate the amount of patient who have been frequency responders (> 50% reduction) over 24 months: positive effects have been registered for 35.4% of the study population. Also, Barloese [44] examined the same case series to analyze the percentage of participants who experienced remission. Thirty percent of patients were found to have at least 1 episode of complete attack remission in the 24-month period. Furthermore, our group has included Barloese's [47] work from 2016 even if, being a meeting abstract, it does not meet our inclusion criteria. He published an evaluation of acute responders and frequency responders on 80 patients who underwent SPG stimulation: 53% in 12 months had reduction of headache frequency of at least 50%. The same group [46], 2 years later, analyzed a new casuistry series of 85 people among CCH and ECH who received a SPG stimulator implantation: 55% of chronic headaches had positive outcomes, while in ECH, the efficacy rate reached 71.4%.

Side effects are reported on by various studies, while others did not consider them [44, 47]: temporary facial paresthesia are usually seen after implantation, accompanied with pain and swelling. In Jensen's work [43], 2 infections and 2 pareses have also been recorded.

In the overall evaluation, stimulation of SPG seems to be a surgical procedure that is being widely used during the last

Table 4 Stimulation of SPG for refractory CH

	Author	Year	Diagnosis	Technique	Outcomes	No. of cases	Complications	Time of follow-up
1	Jensen [43]	2013	CCH	•Stimulation •3 types of stimulations received randomly: full stimulation, sub-perception stimulation, and sham-stimulation •Transoral	12 SR Efficacy 42.8%	28	2 infections 15 temporary facial paresthesia 2 paresis	12 months
3	Barloese [44]	2016	CCH	•Implantation of SPG Microstimulator System •Transoral approach	10 SR Efficacy 30.3%	33	–	24 months
4	Jürgens [45]	2017	CCH	•Implantation of SPG Microstimulator System •Transoral approach	11 SR 13 non-SR Efficacy 35.4%	31	25 temporary facial paresthesia, postoperative pain and swelling (81%)	24 months
5	Barloese [46]	2018	ECH + CCH	•Implantation of SPG Microstimulator System •Transoral approach	43 of CCH SR 5 of ECH SR Efficacy − 55% in CCH − 71.4% in ECH	85 − 78 CCH, − 7 ECH	73% temporary facial paresthesia	12 months

Table 5 Overall view of SPG's procedure outcomes

Procedure	Efficacy in CCH	Efficacy in ECH
SPG block	50–76.5%	87%
SPG radiofrequency	33–70.3%	52–85%
SPG radiosurgery	59–71%	
SPG stimulation	30–55%	71%
Vidian neurectomy	22%	–

Efficacy is intended as a decrease of attacks' frequency of at least 50%

years, but outcomes appear to be less promising than those from other techniques, especially for CCH (30.3–55%).

Vidian neurectomy

Finally, a word must be spent on vidian neurectomy. It is usually performed by an endoscopic approach: the vidian canal is detected; then, the nerve is isolated and transected. Liu et al. [48] reintroduced vidian neurectomy in 2018, a procedure that first arose in the 1980s but quickly decayed due to his low efficacy and persistent side effects. In Liu's trial, 9 refractory CCH patients underwent vidian neurectomy with maximal preservation of the sphenopalatine ganglion. Seven of the 9 cases (77.8%) showed immediate improvement; 1 patient had a delayed improvement after 1 month. Two patients remained headache-free throughout the duration of their follow-up (14–29 months), while 6 reported a return to an episodic form by a mean of 25 months postoperatively. No analyses have been made on number of cases with a significant attack's frequency reduction.

Conclusions

Patients with CH resistant to pharmacological therapy may be aided by ENT surgeons who are able to provide procedures which can improve patients' lives and control their symptoms.

Generally, ECH patients show better response to standard medical therapies; nevertheless, even this more manageable condition may sometimes benefit from interventional therapies mostly reserved for CCH.

We examined all available procedures that have been carried out in the last 20 years targeting the sphenopalatine ganglion and its branches, as it is considered a trigger point for the development of CH. Comparing the outcomes that have been analyzed in the article (Table 5), it is possible to notice how the procedure with the highest rate of success for CCH is the SPG block, which reaches 76.5% [33] of efficacy. This supports our decision as a multidisciplinary group to continue pursuing this approach in the treatment of CCH.

Radiofrequency has a wide range of outcomes, from 33 to 70.3% in CCH. Small case series show ambiguous results, but when the population is expanded, response to the treatment is higher (70.3%) [40], suggesting how new large case series are necessary to further understand its performances.

Stimulation of SPG is the procedure with the highest numbers of studies in the last years. Nevertheless, in CCH, it achieved only up to 55% [46] of significant reduction in attack frequency, stated at the last position for efficacy.

First results on efficacy in ECH seem promising, and considering the low incidence of side effects or complications, we should think of expanding the indications of the procedures also to those conditions.

Results certainly suggest that further studies are necessary in order to understand which method is the most effective and with less side effects. Placebo-controlled studies would be pivotal to understand the differences between the multitude of approaches and evaluate the placebo effect of these at time invasive procedures. Tight collaboration between neurologists and otorhinolaryngologists should also be central in order to give correct indications, which allow us to expect procedures on the SPG to be an effective and mostly safe method to control refractory ECH and CCH.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards This article does not contain any study with human subjects performed by any of the authors.

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