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Midterm clinical outcomes of repetitive transnasal sphenopalatine ganglion blockade in chronic migraine

Kronik migrende tekrarlayan transnasal sfenopalatin gangliyon blokajının orta dönem klinik sonuçları

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ABSTRACT

Aim: Chronic migraine affects the quality of life negatively and causes a high rate of disability. There is a requirement for specific prophylactic treatment options in chronic migraine patients. We aimed to evaluate the effects of repetitive transnasal sphenopalatine ganglion blockade (SPG) on headache days, severity and duration of attacks, drug abuse, conversion to episodic migraine, and responses to chronic migraine treatment.

Materials and Methods: Patients who were referred to the pain clinic by neurology clinics, diagnosed with chronic migraine for at least six months, and were unresponsive to prophylactic treatments or could not tolerate prophylactic treatments were evaluated retrospectively.

Patients undergoing four-session bilateral transnasal sphenopalatine ganglion blockade per week were included. Sphenopalatine ganglion blockade was performed with 0.5 cc, 0.5% bupivacaine-impregnated swab sticks for 30 minutes.

Results: In the first, third, sixth, and ninth-month follow-ups of 40 patients, a statistically significant improvement was found in the number of headache days and parameters of attack severity and frequency, compared to baseline values ($p<0.001$). Baseline drug abuse decreased from 55% (n=22) to 25% (n=10) at month nine, and regression was statistically significant ($p<0.001$). Of 40 patients, migraine severity was detected to turn into very low frequency in 14 (35%), low frequency in eight (20%), and high-frequency episodic migraines in seven (17.5%) patients at month nine. Patients' responses were 26, 31, 30, and 28% in the first, third, sixth, and ninth months, respectively. No life-threatening or comorbid side effects were detected.

Conclusion: Requiring a simple administration tool and easy-to-administer, sphenopalatine ganglion blockade may be a safe alternative for chronic migraine prophylaxis.

Keywords: Chronic headache, migraine, migraine prophylaxis, sphenopalatine ganglion blockade.

ÖZ

Amaç: *Kronik migren yaşam kalitesini olumsuz yönde etkilemekte ve yüksek oranda özürlülüğe neden olmaktadır. Günümüzde kronik migrenli hastalara yönelik spesifik profilaktik tedavi seçeneklerine gereksinim vardır. Çalışmamızda tekrarlanan transnasal sphenopalatin gangliyon blokajının kronik migrenli hastalardaki baş ağrılı gün sayısı, atak şiddeti, atak sayısı, atak süresi, ilaç kötüye kullanımı ve epizodik migrene dönüşüm üzerindeki sonuçlarını ve tedaviye yanıt oranını değerlendirmeyi amaçladık.*

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Gereç ve Yöntem: *Nöroloji kliniklerince ağrı kliniğine yönlendirilen, en az altı aydır kronik migren tanılı ve profilaktik tedavilere yanıtsız veya profilaktik tedavileri tolere edememiş hastalar retrospektif olarak değerlendirildi. Çalışmaya haftada bir kez ve dört seans bilateral transnasal sfenopalatin gangliyon blokajı uygulanmış olan hastalar dahil edildi. Sfenopalatin gangliyon blokajı 30 dakika boyunca 0.5 cc'lik %0,5'lik bupivakain emdirilmiş swap çubukları ile uygulanmıştı.*

Bulgular: *Çalışmaya 40 hasta dahil edildi. Hastaların birinci, üçüncü, altıncı ve dokuzuncu ay takiplerinde, başlangıca göre baş ağrılı gün sayısı, atak şiddeti ve atak sıklığı parametrelerinde istatistiksel olarak anlamlı iyileşme olduğu saptandı (p <0,001). Başlangıçtaki ilaç suistimalinin dokuzuncu ayda %55 (n=22)'den %25 (n=10)'e gerilediği ve bu gerilemenin istatistiksel olarak anlamlı olduğu saptandı (p <0,001). Dokuzuncu ayda hastaların 14 (%35)'ünün çok düşük frekanslı, 8 (%20)'inin düşük frekanslı ve 7 (%17.5)'sinin yüksek frekanslı epizodik migrene dönüştüğü saptandı. Hastaların tedaviye yanıt oranı birinci, üçüncü, altıncı ve dokuzuncu aylarda sırasıyla %26, %31, %30 ve %28'di. Hayati tehlike arz eden veya komorbidite yaratan herhangi bir yan etki saptanmadı.*

Sonuç: *Basit bir uygulama aracı gerektiren ve uygulaması kolay olan sfenopalatin gangliyon blokajı, kronik migren profilaksisinde güvenli bir seçenek olabilir.*

Anahtar Sözcükler: *Kronik baş ağrısı, migren, migren profilaksisi, sfenopalatin gangliyon blokajı.*

INTRODUCTION

Chronic migraine is defined as a migraine-like headache lasting longer than three months, with at least eight attacks in a month and experienced for at least 15 days per month (1). The estimated prevalence of chronic migraine ranges between 1.4 and 2.2% (2). As well as putting a fiscal burden on the budgets of governments, chronic migraine adversely affects the health expenditures, economic status, psychological health status, general health, and quality of life (QoL) of individuals (3).

In the prophylactic treatment of chronic migraine, the treatment modalities of episodic migraine have been used for many years. Topiramate, onabotulinum toxin-A (BoNT-A), and anti-calcitonin gene-related peptide (Anti-CGRP) antibodies are currently recommended for the prophylactic treatment of chronic migraine (4). There is still a need for prophylactic treatment options that are easy to tolerate and specific to chronic migraine patients (5).

It is known that perivascular nociceptors are activated by the inflammatory mediators developing as a result of plasma extravasation caused by the vasodilation of cranial blood vessels in migraine. It is suggested that the release of inflammatory mediators leading to headaches should be inhibited by the sphenopalatine ganglion (SPG) blockade, and such an inhibition prevents central sensitization in the trigeminal nucleus (6).

In a survey study including a list of questions to collect data about a group of specialists, the approaches and experiences of headache specialists were investigated in terms of the SPG blockade. It has been determined that the SPG blockade is most frequently chosen in the diagnosis of chronic migraine. It has also been emphasized that those benefiting most from the blockade are the patients with chronic migraine. On the other hand, headache specialists prefer the procedure less frequently due to the lack of evidence-based protocols related to the SPG blockade (7). There is currently a limited number of studies demonstrating that the SPG blockade may have a prophylactic efficacy in chronic migraine (8-10). In the prophylaxis of chronic migraine, the recommendation for utilizing the SPG blockade remains a weak entity (11).

Our study primarily aimed to evaluate the results of a four-session transnasal SPG blockade once a week on the number of painful days per month, the severity, number, and duration of attacks, drug abuse, conversion to episodic migraine, and the rate of responses to the treatment in the patients with chronic migraine. Secondly, our study also aimed to evaluate the relationship between the accompanying autonomic symptoms and the rate of responses to treatment.

MATERIALS and METHODS

Study design and ethics

The present study with a retrospective design was conducted in the neurology departments of the Konya Training and Research Hospital and Konya City Hospital at the University of Health Sciences between March 2019 and January 2023. Approval was obtained from the local ethics committee of Necmettin Erbakan University with the number 2023/41733 (Date: 02/10/2023). The study was also conducted

ethically under the principles of the Declaration of Helsinki and its later amendments.

Participants

The data of 51 patients diagnosed with chronic migraine undergoing the SPG blockade were determined by scanning the hospital records of the patients from the hospital database. The patients diagnosed with chronic migraine for at least six months under the International Classification Criteria of Headache Disorders, third edition (Beta version), those with a history of headache for at least one month before the procedure, those undergoing the SPG blockade once a week for four sessions, and those responding to the follow-ups in the outpatient clinic with the history of pain at the third, sixth and ninth months were included in the study.

Those with a history of traumas or surgery and deformities on the face and nose, those undergoing any interventional procedure due to migraine within the last 12 months, those with a history of severe psychiatric disorders, and those exposed to the changes of prophylactic pharmacological agents three months before the nerve blockade or during the follow-up period were excluded from the study. Forty patients were evaluated within the scope of the study, and the procedure is outlined as a flowchart in Figure-1.

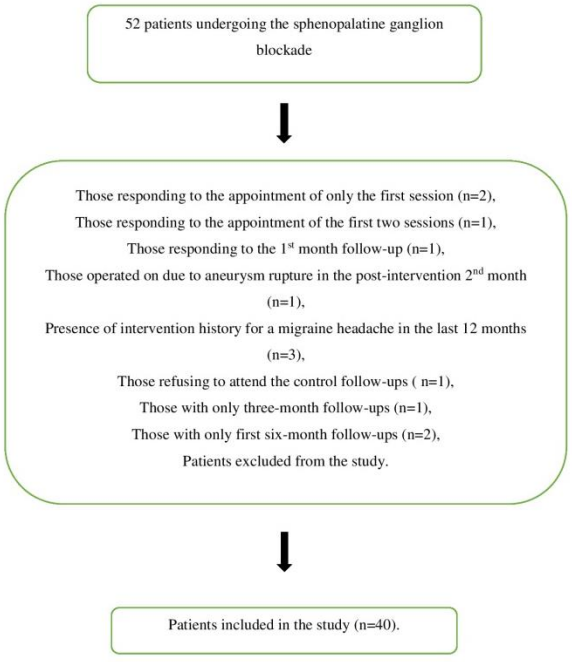

Figure-1. This flowchart presents the inclusion and exclusion of the patients enrolled in the study.

Variables and outcomes

The demographic data of patients were scanned from hospital records of the patients in the archive, and such features as the duration of chronic migraine (months), history of psychiatric illness, presence of drug abuse, history of autonomic symptoms accompanying migraine attacks, characteristics of migraine at baseline (during one month before the initiation of the procedure) and at the post-treatment first, third, sixth and ninth months (the number of headache days/month, number of headache attacks/month, mean duration and severity of attacks, and use of pain blockers) were obtained and recorded. Compared to baseline values, the patients with headache days/month ≥50% were considered to be the responders to the treatment (12), and therefore the response rates of the patients to the treatment were calculated.

Patients' drug abuse was evaluated as the use of nonsteroidal anti-inflammatory drugs (NSAIDs), triptan, or combined use of analgesics. Based on the criteria, those receiving NSAIDs of 15 tablets or more per month, and triptans or combined analgesics of 10 tablets or more per month were considered drug abusers.

At the end of the follow-ups, it was calculated that the rate of migraine attacks turned into episodic migraine subtypes. The number of headache days per month was accepted as very low-frequency episodic migraine between 0-3 days, low-frequency episodic migraine between 4-7 days, and high-frequency episodic migraine between 8-14 days (13).

Intervention

The SPG blockade was carried out with 0.5 cc, 0.5% of bupivacaine-impregnated swab sticks for both nostrils bilaterally in four sessions for 30 minutes once a week.

Statistical Analysis

Statistical analyzes were performed using the Statistical Package for Social Sciences for Windows, version 25.0 (SPSS, IBM Corp., Armonk, NY, U.S., 2017). While the categorical variables were given as numbers and percentages (%), the normally distributed numerical variables were presented as mean±standard deviation (SD), and the non-normally distributed numerical variables were defined as median (percentiles of 25-75%). The alterations in the characteristics of migraine

within the first, third, sixth, and ninth months compared to the baseline values, such as the number of headache days/month, number of attacks/months, mean pain intensity and mean duration of attacks, were analyzed through the Friedman test. The Wilcoxon rank-sum test was performed to compare repetitive measurements, and the Bonferroni correction was used to avoid possible type-1 errors. The effect size values of the Wilcoxon rank-sum test results were calculated using the formula **r=z**/√N. The effect of the blockade on drug abuse at the end of follow-ups compared to the baseline values was analyzed with the McNemar test used to define the paired-nominal data. In addition, the side effects and complications developing during the practice were also given with their numbers and rates. The relationship between the history of migraine attacks accompanied by autonomic symptoms and the rate of responses to the treatment during the follow-ups was analyzed through the Fisher exact test.

RESULTS

Of 40 patients evaluated in the study, 37 (92.5%) were women, and headache attacks were determined to be accompanied by autonomic symptoms in 25 (62.5%) of the patients. While the mean age levels of the patients were found as 39.62±10.99 years, the mean scores of body mass index (BMI) and the duration of chronic migraine were detected as 27.59±6.26 gr/cm^2 and 10.00 (8.00-14.75) months, respectively.

The frequency of headaches per month, the number of headaches days per month, the average duration of headache attacks (hours), and average values of pain intensity (0-100 mm) at the baseline and first, third, sixth, and ninth months after the procedure are presented in (Table-1).

Based on the analyses from the Friedman test, a statistically significant difference was found between the values detected at the baseline and follow-ups in terms of the frequency of headache attacks, the number of headache days, the duration of headache attacks, and pain intensity ($p < .001$). While the pair-wise comparisons evaluated through the Wilcoxon rank-sum test are presented in Table-2, the effect sizes of the Wilcoxon rank-sum test results are shown in (Table-3).

The changes in percentiles (%) related to the characteristics of migraine attacks at the baseline, and the follow-ups at the first, third, sixth, and ninth months were compared, and the rates are shown in (Table-4).

The responding rates of the patients at the first, third, sixth, and ninth-month follow-ups were detected as 65 (n=26), 77.5 (n=31), 75 (n=30), and 70% (n=28), respectively. Within the ninth-month follow-up, while the types of migraine transformed into very low-frequency episodic migraine in 35% (*n*=14) of the patients, the migraine types were detected to transform into low-frequency episodic and high-frequency episodic migraines in 17.5 (*n*=7) and 20% (*n*=8) of the patients, respectively.

The rate of chronic migraine patients accompanied by drug abuse at the baseline was 55% (n=22), and the rate was found to display a decrease of 25% (n=10) at the ninth-month follow-up. A statistically significant difference was found between the ninth-month follow-up and the baseline values ($p < .001$).

The side effects were evaluated, and the distribution of the side effects was determined as follows: The history of moderate-to-severe migraine attacks developing just after the first intervention in 12.50% (n=5) of the patients, a sparing amount of hemorrhage to reach a cotton swab in 21.21% (n=7), lacrimation not exceeding the intervention time in all sessions and not causing serious discomfort in 90.00% (n=36) patients, and numbness in the nasal area in 95.00% (n=38) of the patients.

It was also determined that there was no statistical association between the presence of the history of migraine headaches accompanied by autonomic symptoms before the procedure and the response rates to the treatment during the first, third, sixth, and ninth-month follow-ups (p=0.307, 0.546, 0.548, and 0.078, respectively).

Table-1. Characteristics of migraine headache at baseline and post-intervention period.

Variables	Median (Percentiles of 25%-75%)	95% CI*	*p*
Number of headache days/month			
Baseline	28.00 (20.00-30.00)	22.56-26.48	
1st Month	6.00 (2.00-23.75)	7.62-14.88	
3rd Month	4.00 (2.00-11.50)	5.61-12.24	<0.001
6th Month	4.00 (2.00-14.25)	5.81-12.09	
9th Month	5.50 (2.00-15.00)	6.68-13.27	
The mean severity of attacks (0-100 mm)			
Baseline	90.00 (80.00-93.75)	84.18-90.57	
1st Month	60.00 (40.00-90.00)	51.80-70.44	
3rd Month	60.00 (40.00-80.00)	48.65-67.34	<0.001
6th Month	60.00 (42.50-80.00)	46.19-65.56	
9th Month	70.00 (50.00-90.00)	53.23-72.27	
Headache frequency/month			
Baseline	24.50 (15.00-30.00)	18.89-24/41	
1st Month	5.50 (2.00-14.50)	6.45-13.19	
3rd Month	4.00 (2.00-10.00)	4.83-11.07	<0.001
6th Month	4.00 (2.00-10.00)	4.89-10.76	
9th Month	5.00 (2.00-10.75)	5.43-11.67	
The mean duration of attacks (h)			
Baseline	14.50 (8.50-23.00)	15.46-29.34	
1st Month	7.00 (4.00-12.75)	7.82-19.48	
3rd Month	6.00 (4.00-12.00)	7.78-21.47	<0.001
6th Month	6.00 (4.00-12.00)	7.52-20.08	
9th Month	7.50 (4.00-19.00)	9.41-23.04	

*: Confidence interval

Table-2. Comparisons of characteristics of headaches at post-intervention with baseline values

Variables	*p**			
	Baseline-1st Month	**Baseline-3rd Month**	**Baseline-6th Month**	**Baseline-9th Month**
Number of headache days/month	<0.001	<0.001	<0.001	<0.001
Headache frequency/month	<0.001	<0.001	<0.001	<0.001
The mean duration of attacks (h)	<0.001	<0.001	<0.001	0.012
The mean severity of attacks (0-100 mm)	<0.001	<0.001	<0.001	<0.001

*=A significant p-value was accepted as <0.005 according to Bonferroni correction.

Table-3. The effect sizes for the Wilcoxon signed-rank test in the analysis of migraine characteristics.

Variables	Effect Size			
	Baseline-1st Month	Baseline-3rd Month	Baseline-6th Month	Baseline-9th Month
Number of headache days/month	0.73	0.78	0.78	0.78
Headache frequency/month	0.73	0.78	0.77	0.71
The mean duration of attacks (h)	0.66	0.59	0.63	0.39
The mean severity of attacks (0-100 mm)	0.68	0.70	0.71	0.68

Table-4. Decreasing rates (%) of migraine characteristics at follow-ups, compared to baseline value.

Variables	Median (Percentiles of 25-75%)			
	1st Month	3rd Month	6th Month	9th Month
Number of headache days/month	70.0 (0.0-90.0)	84.0 (56.25-90.0)	80.0 (37.5-87.5)	74.17 (14.37-89.5)
Headache frequency/month	84.0(56.25-90.0)	84.0(56.25-90.0)	80.0 (50.0-86.67)	81.67 (0.0-92.5)
The mean duration of attacks (h)	23.81 (0.0-73.33)	28.57 (0.0-75.0)	33.33 (0.0-73.33)	9.72 (0.0-80.94)
The mean severity of attacks (0-100 mm)	20.0 (0.0-55.5)	22.22 (0.0-55.5)	28.5 (0.0-47.37)	12.69 (0.0-42.14)

DISCUSSION

In our study, it was determined that the parameters of the number of headache days, the severity, frequency, and duration of attacks, and drug abuse were improved through the repetitive transnasal SPG blockade in patients with chronic migraine without any serious side effects or complications. The rates of responses to the treatment and transformation into episodic migraine were also higher. In addition, it was detected that there was no relationship between the patients' response to the treatment and migraine attacks accompanied by autonomic symptoms.

In the present study, it was determined that there was a significant decrease in the number of headache days and the frequency of attacks during the nine-month follow-up, compared to the baseline values. In the study performed by Additional et al. (10), 28-day pain relief was stated to be achieved through the transnasal SPG blockade in a patient with chronic migraine. In the follow-up of the patient, the clinical improvement was reported to last for one year thanks to the repetitive SPG blockades (10). In a double-blind and placebo-controlled study carried out by Cady et al. (14), the efficacy of the transnasal SPG blockade was evaluated in the patients with chronic migraine, and a significant improvement was observed in the number of headache days for one month with the six-week administration of 0.3 cc, 0.5% of bupivacaine twice per week via the Tx360® nasal device (Tx360 Nasal Applicator; Tian Medical, Grayslake, Illinois, USA). In addition, although bupivacaine has a more successful tendency than placebo, it was shown that there was no statistical advantage of bupivacaine. Therefore, it was concluded that more studies are needed to evaluate the prophylactic efficacy of the SPG blockade in chronic migraine (14). In the study designed retrospectively, Tepe and Tertemiz (9) evaluated the clinical outcomes of the bilateral transnasal SPG blockade in unresponsive chronic migraine patients to the pharmacological treatment. In the study by Tepe and Tertemiz, the procedure lasting for 30 minutes was applied to both nostrils with a swab stick impregnated with 1 cc, 0.5% of bupivacaine for a total of four sessions every two weeks. At the end of the two-month follow-ups, an improvement was observed in the number of painful days, and the frequency, severity, and duration of migraine attacks (9). In a retrospective study performed by Bobker et al. (15), of 66 patients with chronic migraine self-administering lidocaine to both nostrils five times per month, 79% were found to achieve preventive efficacy. Our study findings are compatible with those in previous studies where the intervals of performing the transnasal SPG blockade, and types and doses of local anesthetics used were different (9, 10, 14, 15). The repetitive SPG blockades are considered to

break the vicious cycle of headaches by modulating autonomic pathways (16). The effects of the repetitive transnasal SPG blockade on functional changes in neuroanatomical pathways were investigated in chronic migraine patients, and a study revealed that there was a correlation between the amelioration in the number of headache days and the functional improvement in the central pain processing centers (17).

In the present study, it was determined that there was a statistically significant decrease in the mean severity of the attacks during the nine-month follow-ups, compared to the baseline values. At the end of the follow-up, the rate of the decrease in the initial attack severity was found to be approximately 13%. Maizels et al. (18) also reported that there was a decrease of 53% in the severity of attacks with intranasal lidocaine administrated to treat acute migraine attacks, and the result was superior to the placebo responses. There is no cut-off value revealing the change in mean pain intensity in determining the superiority of prophylactic migraine treatments over the placebo. As for our study, we can put forth that the rate of the decrease in attack severity through the repetitive transnasal SPG blockade was lower than the findings in the literature (18).

In our study, the baseline drug abuse was found to regress from 55% to 25% at the ninth-month follow-up. Cady et al. (14) implemented the repetitive transnasal SPG blockade in chronic migraine patients, including drug abusers, and found that the acute drug use decreased at the sixth-month follow-up, compared to the baseline values (14). Although drug overuse was handled in a different dimension in our study, it can be speculated that SPG blockade may reduce the analgesic consumption of patients with the current findings.

In the present study, chronic migraine in our patients was found to convert to episodic migraine at a higher rate (72.5%) with the transnasal SPG blockade. It is known that chronic migraine patients have even more headache-related hospital admissions than those with episodic migraine (19), and the negative impacts are poorer in the psycho-socioeconomic areas of life (20).

No serious side effects or complications were detected in our study. As consistent with the findings in the literature (14), we determined that most of the patients undergoing the SPG blockade experienced lachrymation in the eyes and numbness in the nasopharyngeal area. It can be suggested that the transnasal SPG blockade is a reliable treatment option in chronic migraine patients.

Our study has also various limitations. First, our study is of a retrospective design. The second limitation of our study is that psychiatric problems likely to accompany chronic migraine were not obtained via objective psychiatric evaluation tools. In studies where the prophylactic effects will be evaluated, the accompanying factors should be analyzed meticulously based on the recommendations of the International Headache Society (4). Therefore, the fact that psychiatric disorders were not evaluated appropriately is one of the limitations of our study. The third limitation of our study is the confounding effects of spontaneous recovery on the results of interventional procedures. In a study in which the patients were followed for two years, approximately one-fourth of chronic migraine patients were determined to recover spontaneously (21); however, the rates of improvement in our study are far higher than the aforementioned rate. In addition, the patients meeting the definition of chronic migraine for at least six months were included in our study so that spontaneous remission showed no effects on the results of the analysis (4).

CONCLUSION

The transnasal SPG blockade, which can be administered through an inexpensive tool, is likely to be a reliable and easy-to-use treatment option in providing prophylaxis in patients with chronic migraine over nine months. To elucidate the clinical efficacy of the transnasal SPG blockade, we consider that further studies are needed to evaluate the SPG blockades in the double-blind, placebo-controlled, and randomized studies performed with different doses and types of local anesthetics at various intervals.

Conflict of interest: Authors have no conflict of interest to declare.

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References

1. Arnold M. Headache classification committee of the international headache society (IHS) the international classification of headache disorders. Cephalalgia. 2018;38(1):1-211.
2. Natoli J, Manack A, Dean B, Butler Q, Turkel C, Stovner L, et al. Global prevalence of chronic migraine: a systematic review. Cephalalgia. 2009:no-no.
3. Manack AN, Buse DC, Lipton RB. Chronic migraine: epidemiology and disease burden. Current pain headache reports. 2011;15(1):70-8.
4. Tassorelli C, Diener H-C, Dodick DW, Silberstein SD, Lipton RB, Ashina M, et al. Guidelines of the International Headache Society for controlled trials of preventive treatment of chronic migraine in adults. 2018;38(5):815-32.
5. Sun-Edelstein C, Rapoport AM. Update on the pharmacological treatment of chronic migraine. Current painheadache reports. 2016;20(1):1-8.
6. Yarnitsky D, Goor-Aryeh I, Bajwa ZH, Ransil BI, Cutrer FM, Sottile A, et al. 2003 Wolff Award: possible parasympathetic contributions to peripheral and central sensitization during migraine. Headache: The journal of head face pain. 2003;43(7):704-14.
7. Burkett JG, Robbins MS, Robertson CE, Mete M, Saikali NP, Singh RBH, et al. Sphenopalatine ganglion block in primary headaches: An American Headache Society member survey. Neurology: Clinical Practice. 2020;10(6):503-9.
8. Bratbak DF, Nordgård S, Stovner LJ, Linde M, Dodick DW, Aschehoug I, et al. Pilot study of sphenopalatine injection of onabotulinumtoxinA for the treatment of intractable chronic migraine. Cephalalgia. 2017;37(4):356-64.
9. Tepe N, Tertemiz OF. The effectiveness of sphenopalatine ganglion blockade in chronic migraine resistant to medical treatment. Neurology Asia. 2021;26(4).
10. Additional I, Candido KD, Masonic AI. A novel revision to the classical transnasal topical sphenopalatine ganglion block for the treatment of headache and facial pain. Pain physician. 2013;16:E769-E78.
11. Barad M, Ailani J, Hakim SM, Kissoon NR, Schuster NM. Percutaneous Interventional Strategies for Migraine Prevention: A Systematic Review and Practice Guideline. Pain Medicine. 2022;23(1):164-88.
12. Tassorelli C, Diener H-C, Dodick DW, Silberstein SD, Lipton RB, Ashina M, et al. Guidelines of the International Headache Society for controlled trials of preventive treatment of chronic migraine in adults. Cephalalgia. 2018;38(5):815-32.
13. Jedynak J, Eross E, Gendolla A, Rettiganti M, Stauffer VLJTJoH, Pain. Shift from high-frequency to low-frequency episodic migraine in patients treated with Galcanezumab: results from two global randomized clinical trials. 2021;22(1):1-10.
14. Cady R, Saper J, Dexter K, Manley HR. A Double-Blind, Placebo-Controlled Study of Repetitive Transnasal Sphenopalatine Ganglion Blockade With T x360® as Acute Treatment for Chronic Migraine. Headache: The Journal of Head and Face Pain. 2015;55(1):101-16.
15. Bobker S, Ehrlich A, Recchioni C, Levin M, Riggins NJJAAD. Retrospective Chart Review: The Feasibility of a Self-Administered Nasal Spray Targeting the Sphenopalatine Ganglion (SPG) in Treatment of Chronic Migraine. 2022;2(1).
16. Additional I, Candido KD, Masonic AIJPp. A novel revision to the classical transnasal topical sphenopalatine ganglion block for the treatment of headache and facial pain. 2013;16:E769-E78.
17. Krebs K, Rorden C, Androulakis XM. Resting state functional connectivity after sphenopalatine ganglion blocks in chronic migraine with medication overuse headache: a pilot longitudinal fMRI study. Headache: The Journal of Head Face Pain. 2018;58(5):732-43.
18. Maizels M, Scott B, Cohen W, Chen W. Intranasal lidocaine for treatment of migraine: a randomized, double-blind, controlled trial. JAMA psychiatry. 1996;276(4):319-21.
19. Munakata J, Hazard E, Serrano D, Klingman D, Rupnow MF, Tierce J, et al. Economic burden of transformed migraine: results from the American Migraine Prevalence and Prevention (AMPP) Study. Headache: The Journal of Head Face Pain. 2009;49(4):498-508.
20. Adams AM, Serrano D, Buse DC, Reed ML, Marske V, Fanning KM, et al. The impact of chronic migraine: The Chronic Migraine Epidemiology and Outcomes (CaMEO) Study methods and baseline results. Cephalalgia. 2015;35(7):563-78.
21. Ashina S, Buse D, Maizels M, Manack A, Serrano D, Turkel C, et al., editors. Self-reported anxiety as a risk factor for migraine chronification: results from the American Migraine Prevalence and Prevention (AMPP) study. Headache; 2010: WILEY-BLACKWELL PUBLISHING, INC COMMERCE PLACE, 350 MAIN ST, MALDEN 02148 ….