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Transnasal sphenopalatine ganglion blockade for acute facial pain: a prospective randomized case-control study

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Abstract. – OBJECTIVE: To evaluate the effectiveness of sphenopalatine ganglion blockade (SPGB) in Emergency Medicine Department (EMD), simply performed using cotton-tipped applicators dipped in a mepivacaine 2% solution inserted along the turbinates, in patients with acute facial pain (AFP), including dental pain, and to compare the efficacy of SPGB with pharmacological treatment (PT).

PATIENTS AND METHODS: A total of 89 consecutive patients [45 (50.6%) females, 44 (49.4%) males, median age 39 years, range 20-52 years] with AFP, mainly caused by toothache (N = 77, 86.5%), were randomly allocated into two groups, in accordance with the type of treatment: Group A (N = 44, cases) SPGB, and Group B (N = 45, controls) PT. Pain intensity (PI) was measured using a visual analogue scale (VAS) and the short-form of the McGill pain questionnaire (SF-MPQ).

RESULTS: There was no correlation (r = 0.18, p = 0.92) between age and baseline PI, which did not differ (p = 0.471) between groups. PI reduction after treatment was significantly greater (p < 0.01) in Group A (SPGB), regardless of the evaluation method used (VAS or SF-MPQ). According to the multivariate regression analysis of variables, at 30 minutes both VAS (p = 0.001) and type of treatment (p = 0.011) reached significance but at 60 minutes only type of treatment reached significance, so that the better results in pain reduction obtained in Group A patients can be justified only by treatment (SPGB *vs*. PT).

CONCLUSIONS: In patients with AFP, the SPGB was more effective than the PT, regardless of age and baseline PI and may be a new therapeutic option in the Emergency Department setting.

Key Words:
Facial pain, Dental pain, Sphenopalatine ganglion, Ganglion blockade, Multivariate analysis.

Introduction

Facial pain (FP) is a very common occurrence that may affect up to 25% of the adult population and is related to dental or other oral cavity diseases in approximately 85% of cases[1,2]. The other causes of FP include trigeminal neuralgia, trigeminal idiopathic pain, and persistent idiopathic FP syndrome[3]. The sphenopalatine ganglion (SPG) is located in the pterygopalatine fossa, near the middle nasal turbinate and contains cell body of parasympathetic post-ganglionic neurons[4,5]. SPG blockade (SPGB) inhibits the somatic sensory afferent fibers of the trigeminal nerve (V2 maxillary) as well as the post-ganglionic sympathetic neurons, because both pass through the ganglion[4,6]. In 1909, Sluder[7] proposed the term sphenopalatine neuralgia, demonstrating that SPGB was useful to treat FP and headache[7,8]. The three approaches available to perform SPGB are trans-oral, lateral, and transnasal, which is the simplest and most tolerable[9]. It can be easily obtained using a cotton-tipped applicator dipped in local anesthetic, such as 90% watery solution of cocaine hydrochlorate (as originally proposed by G. Sluder), lidocaine, or mepivacaine[4,10]. Unfortunately, both drug diffusion to the SPG and blockade duration, are unpredictable, thus the effectiveness of the SPGB varies widely within

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patients[9]. The objectives of this study were (1) to evaluate the efficacy of transnasal approach in the treatment of patients with acute FP, including dental pain, who presented to the outpatient hospital service of an Emergency Medicine Department (EMD), (2) to compare the efficacy of SPGB with other pharmacological treatment (PT) and to assess whether the results were influenced by factors other than the type of treatment, such as age or pain intensity.

Patients and Methods

Patients

A total of 89 consecutive patients (45 (50.6%) females, 44 (49.4%) males, median age 39 years, range 20-52 years) with acute FP, mainly caused by toothache (N = 74, 83.1%), were prospectively enrolled in the study and randomly allocated by closed envelope into two groups of age- and sex-matched subjects, in accordance with the type of treatment: (1) Group A (N = 44, cases), SPGB; (2) Group B (N = 45, controls), pharmacological treatment. Acute migraine (4 *vs.* 6) and trigeminal neuralgia (3 *vs.* 2) patients were diagnosed by a neurologist according to International Headache Society criteria and ICHD-III (International Classification of Headache Disorders 3rd edition). Toothache was evaluated by Emergency Doctor who determined the need for patients to be seen by Head and Neck surgeon. Exclusion criteria were recent (8-12 hours) intake of painkillers or anti-inflammatory medications, pregnancy, a history of concomitant psychiatric disorders or neurological symptoms related to transient ischemic attacks or stroke, as well as the presence of a dental abscess as cause of the pain or patients required immediate surgical dental treatments. The study has been approved in advance by the European Medicines Agency (EudraCT No. 2013-001795-38, Sponsor's Protocol Code No. A206; https://eudract.ema.europa.eu/). Written informed consent was obtained from all participants before each treatment. The primary end-point of the study was to evaluate the pain reduction after SPGB, and the secondary was to compare the efficacy of SPGB with pharmacological treatment.

Intervention

For the quantification of pre- and post-treatment pain intensity, a simple unidimensional visual analogue scale (VAS) with a numeric pain rating from zero to 10 was used (0 no pain and 10 strongest pain ever experienced). The short-form of the McGill pain questionnaire (SF-MPQ, Italian version) was also administered, thanks to a nurse assistant[11].

SPGB procedure was similar to that proposed by Windsor et al[4,12]. The patient was placed in the supine position with the cervical spine extended. Two cotton-tipped applicators were dipped in a mepivacaine 2% solution and then inserted ipsilateral to the facial pain along the turbinate, until they reach the posterior wall of the nasopharynx. The applicators were removed after 15-20 minutes. According to our EMD protocol for pain, Group B patients and non-responders after 60 minutes were treated with paracetamol 1,000 mg (VAS < 5) or diclofenac 75 mg (VAS ≥ 5). In lack of pain reduction, other drugs were used, such as ibuprofen 600 mg, ketoprofen 100 mg, or tramadol 100 mg. Follow-ups were made at 30 and 60 minutes after removing the swabs (Group A) and after medication intake (Group B) to compare two groups.

Statistical Analysis

The data are reported as median (range) or mean ± standard deviation (SD). Due to the relatively limited number of patients, the Mann-Whitney U-test and the Chi-square (χ^2) test were used assuming that the data may not be normally distributed. The linear regression calculation was used to evaluate the relationship between parameters, and the correlation coefficient (r) was obtained. The multivariate analysis (regression model) was used to adjust VAS for patient's characteristics avoiding possible confounding factors such age and baseline pain perception that might be different in each patient, subsequently affecting the scale rating. p-values < 0.05 were considered to be significant. VAS and SF-MPQ at 30 and 60 minutes were considered dependent variables, whilst age, type of treatment, baseline VAS (VAS-0), and baseline SF-MPQ (SF-MPQ-0) were the independent variables. The unstandardized (B) and standardized (β) coefficients with the relative 95% confidence interval (CI) were then calculated. The software used for analyses was SPSS Statistics (version 15.0) (SPSS Inc., Chicago, IL, USA).

Results

There was no correlation between age and VAS-0 in both Group A (r = 0.207, p = 0.240, regression linear equation: VAS-0 = 6.0280-0.0292

age) and Group B (r = 0.018, $p = 0.918$, regression linear equation: VAS-0 = 7.1922-0.0018 age). Overall, as expected, a significant relationship between VAS-0 and SF-MPQ-0 (r = 0.38, $p = 0.0004$) was found.

Table I displays the main demographics data, origin of the pain, pain duration before treatment, and the results of treatment, showing that the two groups were homogeneous ($p > 0.05$) according to age, male-to-female ratio, origin and duration of the FP. The median (range) VAS-0 and SF-MPQ-0 scores (Group A *vs.* Group B) were 8 (6-9) *vs.* 8 (7-9) and 11 (8-15) *vs.* 10 (5-15), respectively ($p > 0.05$). VAS-0 (mean ± SD) did not differ ($p > 0.05$) between groups, and the Mann-Whitney test confirmed that the distribution was approximately normal both in Group A (Z-score = 7.0834, $p < 0.0001$) and in Group B (Z-score = 7.1886, $p < 0.0001$). The pain intensity reduction after treatment was significantly greater ($p < 0.01$) in Group A (SPGB), regardless of the evaluation method used.

According to the multivariate regression analysis of variables, at 30 minutes both VAS ($p = 0.001$) and type of treatment ($p = 0.011$) reached significance, but at 60 minutes only type of treatment reached significance (Table II) so that the better results in pain reduction at 30 and 60 minutes VAS obtained in Group A patients can be justified only by treatment (SPGB *vs.* PT). Figure 1 visualizes the results at 30 and 60 minutes using the VAS scale.

Additionally, two out of four female patients with acute migraine, revaluated during a second access done in emergency for other problems (abdominal pain), responded for more than 48 hours to SPGB. Five patients in Group A were non-responder and treated by paracetamol intake (two patients) and diclofenac (three patients). In Group B thirty patients received paracetamol and fifteen diclofenac. A bitter taste in the mouth from the medication dripping down from the nasopharynx and slight lacrimation were the only adverse effects reported by the patients who underwent SPGB.

Discussion

Although FP is a symptom rather than a diagnosis, the results of its treatment are usually considered regardless of the cause that determines the pain, which has an estimated incidence rate of approximately 38%[13]. In any case, acute and chronic FP, whatever its origin, may significantly reduce health-related quality of life of patients[14]. Most inflammatory conditions and infections, including facial bone, paranasal sinus and salivary glands diseases, as well as vascular, neurological and psychogenic alterations, may lead to FP[1,15]. Headache and FP are also common findings in patients with sickle cell disease, temporomandibular muscle and joint disorder as well as in other conditions as rhinogenic headache or multiple sclerosis[16-19].

Table I. Main characteristics of the patients, origin and duration of the facial pain, and the results of treatment reported as mean ± SD. *Statistically significant results.

Parameters	Group A (cases)	Group B (controls)	*p*-value
No. of patients (%)	44 (49.4%)	45 (50.6%)	0.89
Treatment	SPG blockade	Pharmacological treatment	–
Age of the patients (years)	40.4 ± 15.6	40.9 ± 16.3	0.88
Males/females	21/23	23/22	0.75
Toothache[a]	37 (84.1%)	37 (82.2%)	0.81
Acute migraine (non-menstrual)[b]	4 (9.1%)	6 (13.3%)	0.74
Trigeminal neuralgia[c]	3 (6.8%)	2 (4.5%)	0.68
Facial pain duration before treatment (hours)	39 ± 27	49 ± 31	0.109
VAS-0	7.2 ± 2.1	7.5 ± 1.8	0.471
VAS 30 min	2.4 ±2.8	3.9 ± 2.4	0.008*
VAS 60 min	1.4 ± 2.4	3.7 ± 2.0	0.0001*
SF-MPQ-0	11.2 ± 4.0	10.1 ± 5.2	0.267
SF-MPQ 30 min	3.3 ± 2.7	5.1 ± 1.6	0.0002*
SF-MPQ 60 min	2.6 ± 3.1	5.3 ± 4.2	0.0009*

SPG = sphenopalatine ganglion, VAS = visual analogue scale of pain, SF-MPQ = short-form of the McGill pain questionnaire, VAS-0 = baseline, SF-MPQ-0 = baseline. ICHD-III (International Classification of Headache Disorders 3rd edition) classification: [a]11.6, [b]1.1.3, [c]13.1.1.2.

Table II. Unstandardized (B) and standardized (β) coefficients, standard error (SE), 95% confidence intervals (CI), and relative p-values for the independent variables age, type of treatment, and baseline VAS score, according to the VAS scores at 30 and 60 minutes.

Independent variables	VAS 30 min			VAS 60 min		
	Unstandardized B coefficient (SE) and 95% CI	Standardized β coefficient	*p*-value	Unstandardized B coefficient (SE) and 95% CI	Standardized β coefficient	*p*-value
Age	-0.031 (0.019) -0.069-0.006	0.098	0.102	0.019 (0.031) -0.046-0.083	0.098	0.555
Type of treatment	1.629 (0.616) 0.394-2.863	0.473	0.011*	2.388 (0.842) 0.655-4.122	0.473	0.009*
Baseline VAS score	0.554 (0.153) 0.248-0.859	0.261	0.001*	0.287 (0.183) -0.00-0.663	0.261	0.129

*Statistically significant results.

Unfortunately, both FP syndromes, including dental pain, and headache syndromes, are often poorly responsive or unresponsive to pharmacological treatment, requiring the use of high dosage drugs, and SPGB can be safely used as alternative effective treatment[9,20,21,27-30]. The other indications for the SPGB include trigeminal (V1 ophthalmic and V2 maxillary) neuralgia, sphenopalatine neuralgia, cluster headaches, and other atypical facial neuralgias[4]. Also in patients with acute migraine, an immediate and durable pain relief can be obtained with SPGB[20]. However, in patients with trigeminal neuralgias, the effectiveness of treatment is transitory, and additional drug administration may be required to obtain long-term pain control[22]. A deafferentation pain syndrome (palate and posterior pharynx) has also been reported, but it can occur only in the presence of nerve damage (neurolysis), usually due to radiofrequency treatment or gamma knife surgery ablation in patients with chronic FP[23,24]. A pulsed electromagnetic field therapy in patients with postoperative pain after tooth extraction was used, but this technique is not applicable to patients who presented to the EMD[25]. No serious adverse effects were observed during SPGB and a bitter taste in the mouth from the medication dripping down from the nasopharynx and slight lacrimation were the only effects reported by patients. No headache was caused by SPGB, but if observed, may be due to trigger points stimulation[18]. Moreover, in all SPGB responders with acute migraine, the pain relief persisted also for more than 48 hours, despite the fact that only 55% of symptoms improvement has been reported by others in drug-resistant cluster headache[26]. Unfortunately, patients with dental and jaw pain due to intraoral inflammation or abscess are not suitable for SPGB, whilst this treatment should be suggested especially in patients with upper dental arch pain due to the proximity of the SPG to the pain site. None systemic side effects were observed during blockade, or local complication (i.e., epistaxis) as reported by others[4], but a repeated treatment was not performed because it was not one of the aims of the study. Both SPGB and PT led to pain relief, but SPGB reduction is more clinically relevant because allows emergency physician to use less drugs especially in high-risk patients and to obtain in most of case a faster patients discharge. SPGB might be useful also as bridge solution in Emergency Department until the dentist's evaluation but particular

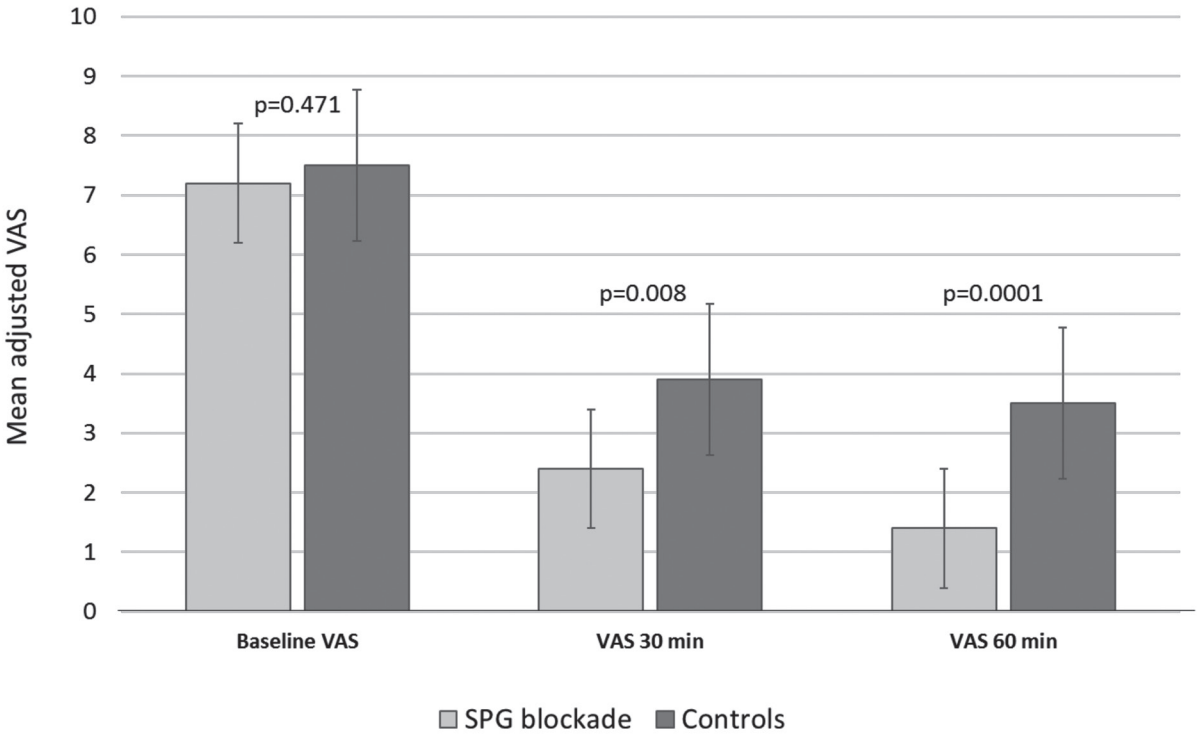

Figure 1. Mean adjusted visual analogue scale (VAS) of pain (error bars: 95% confidence interval) baseline, and at 30 (VAS 30 min) and 60 (VAS 60 min) minutes in each group.

care should be taken in females between 20 and 45 years because FP or oral disease could be a presentation of multiple sclerosis[19].

Despite reported by Schaffer et al[31], in our series SPGB has been effective and more than 50% reduction in pain was achieved in more than 48.8% of (39/44) patients.

As results from Maizels and Geiger[32] block benefit is immediate in acute migrain patients suggesting that also mepivacaine 2% and not only lidocaine may be used for cotton-tipped applicators.

Regardless results of SPGB there are some limitations to this study. First of all half-life of mepivacaine of about 2-3 hours is a limit because follow-up time was 60 minutes in Group A responder-patients and so no information there is about time after dischargment. A 24-hours follow-up for all treated patients probably was necessary. In addition, no-responder patients (a correct applicator insertion justify a slight lacrimation) may be explained by other mechanisms involved in toothache or unknown anatomical variant that me evaluated in further studies such as lower dental arch pain relief obtained in some patients. Trigeminal neuralgia pain control is transitory so that association of SPGB with other treatments (i.e. mesotherapy) could be studied in the future also in an Emergency setting as well as use of SPGB in patients after early administration of a pain-control therapy directly from triage[33], procedure used actually also in our Emergency Department.

This study is the first randomized case-control study with multivariate regression analysis performed on patients with acute FP who presented to an EMD. However, more and larger randomized studies are needed, to assess especially the block duration and the possibility of repeating the procedure, that could also be self-administered[17].

Conclusions

Transnasal approach can be used to perform SPGB for several FP syndromes, is easy to perform, effective regardless of the source and intensity of pain, and not age-related providing an effective, safe and low-cost treatment in the majority of FPs, with the exception of patients with severe dental or intraoral inflammations.

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Conflict of Interest
The Authors declare that they have no conflict of interests.

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