

# DOES THE SPHENOPALATINE GANGLION HAVE AN EFFECT ON THE CEREBRAL HEMODYNAMIC THAT CAN BE MODULATED BY LOCAL ANESTHETICS?

**Khaled Sedeek. MD, Amr Abdel Monem. MD, Janise Prozesky. CNIM**

*Penn State University, Hershey Medical Center, Hershey, PA and Cairo University, Cairo-Egypt*

---

## **Introduction:**

The sphenopalatine ganglion (SPG) is one of four parasympathetic ganglia in the head. The purpose of this pilot study was to assess the efficacy of blocking the SPG with local anesthetic and its effect on cerebral hemodynamics. Validation of the selected blocking technique and the data obtained in this study will then be used in future studies to understand how opioids may influence the effects of the SPG on the cerebral blood vessels. We hypothesize that blocking the SPG with local anesthetics would lead to a change in the tone of the cerebral vessels and may affect the cerebral blood flow.

## **Methods:**

IRB approval and informed consent was obtained. This is a double-blinded cross-over pilot study. Five out of ten healthy adult volunteers have been recruited. A cross over between the use of a placebo (normal saline N.S.) and a local anesthetic (Lidocaine, 0.2-0.5 mg/Kg in a liquid form) was administered on the same volunteer to determine changes in cerebral hemodynamics between treatment groups. The attempt to block the SPG was done by the application of a local anesthetic on the intranasal mucosa with continuous monitoring of the cerebral hemodynamics via Trans-cranial Doppler (TCD). EKG, non-invasive arterial pressure, end-tidal carbon dioxide (PeCO<sub>2</sub>), and oxygen saturation (SpO<sub>2</sub>) were monitored. The ipsilateral middle cerebral artery (MCA) was located through the temporal acoustic window using a 2 MHz TCD. During normal breathing, the baseline values were recorded. Thereafter, pressure was applied for few seconds on the side of the neck to compress the carotid artery followed by sudden release. This maneuver elicits the Transient Hyperemic Response Test [THRT] of the MCA. After the application of one of the treatments via Q-tip on the site of the SPG, the first set of measurements for one hour were recorded, and a second set of measurements were taken for another hour after applying the second medicine.

## **Results :**

We could not find an effect on the cerebral hemodynamic when lidocaine was applied on the SPG using a modified transnasal approach

## **Conclusion:**

Replication of the modified technique to the traditional transnasal block of the SPG with lidocaine has no effect on cerebral hemodynamic .

**Introduction:**

The sphenopalatine ganglion (SPG) is one of four parasympathetic ganglia in the head, located in the pterygopalatine fossa, posterior to the middle nasal turbinate, covered by a layer of connective tissue and mucous membrane, and anterior to the pterygoid canal. This superficial location allows the block to be performed with topical anesthetic or by injection. The SPG is a parasympathetic ganglion. It contains the cell bodies of the post-ganglionic parasympathetic neurons. Post-ganglionic sympathetic neurons as well as somatic sensory afferent branches of the maxillary division of the trigeminal nerve also pass through the ganglion (but do not terminate). All of which may be inhibited by blockade of the SPG. Post-ganglionic parasympathetic neurons from this ganglion then distribute to the lacrimal gland and glands of the nasal cavity, paranasal sinuses, palate, and upper pharynx. They are also known to innervate the major cerebral arteries in conjunction with post-ganglionic sympathetic fibers. The sensory afferent axons traveling through the SPG arise from the maxillary division of the trigeminal nerve connected to the SPG by way of five branches that extend from the nasopharynx, nasal cavity, palate, and orbit. Motor root: From the nervus intermedius (a part of the facial nerve) through the G petrosal nerve.

The transnasal application of topical anesthetic is the simplest and most common technique to approach the SPG. However, the diffusion of topical anesthetic to the ganglion is unpredictable and the blockade is not durable. The modification of the traditional approach the sphenopalatine ganglion was described by Windsor and Jahnke<sup>1</sup> to provide increased patient comfort, prolonged application of the medication to the tissue overlying the sphenopalatine ganglion, and a controlled, incremental infusion of local anesthetic or other treatment solution to the target. This may maximize safety and improve results.

A previous study demonstrated the presence of opioid receptors in the SPG of rats<sup>2</sup>. Similar findings may be expected in the human SPG. Opioids have been used to relieve pain in the upper extremity, which demonstrates the presence of opioid receptors in the Stellate Ganglion (SG). Therefore it may be speculated that these receptors might be found in the SPG as well<sup>3</sup>.

Additional findings included the decreased cerebral vascular tone following injection of the SG with local *anesthetics*. These findings indicate that SG blockade decreases cerebral vascular tone without affecting the capacity of the vessels to autoregulate<sup>4</sup>.

The purpose of this pilot study was to assess the ability to replicate the modified transnasal technique to block the SPG, and the efficacy of blocking SPG with local anesthetic as demonstrated by changes of the cerebral hemodynamics. We expected that local anesthetics would have an effect on the SPG that would be postulated by affecting the cerebral hemodynamics. Validation of the blocking technique and the data obtained in this study will then be used in future studies to understand how opioids may influence the effects of the SPG on the cerebral blood vessels through the possible presence of opioid receptors.

**Methods:**

After institutional IRB approval and written informed consent, five ASA physical status I volunteers were included for this study.

This pilot study was designed to assess the effects of blocking the SPG with local anesthetics on the cerebral hemodynamics.

This is a double blinded study, none of the participants was aware of the medications applied to the SPG. Only 5 volunteers were included in our study. A cross over between the use of a placebo [Normal Saline], and the local anesthetic [Lidocaine] was done on the same volunteer.

The study was performed in a quiet room with the subject in the supine position in one of our hospital's research facilities. A peripheral I.V access was secured, and monitoring of ECG, non-invasive arterial pressure, end-tidal carbon dioxide (PeCO<sub>2</sub>), and oxygen saturation (SpO<sub>2</sub>) were established. The PeCO<sub>2</sub> was monitored continuously using a mouthpiece in conjunction with a nose clip. The ipsilateral middle cerebral artery (MCA) was located through the temporal acoustic window using a 2 MHz Transcranial Doppler Ultrasound probe (TCD).

While breathing room air, the values of baseline systolic, diastolic, and mean MCA-FV and arterial pressure, along with heart rate, PeCO<sub>2</sub> and SpO<sub>2</sub> were recorded.

A modification of the traditional transnasal sphenopalatine ganglion block was used (1).

A second set of measurements (every 15 min for one hour) were taken following the random application of one of the two medications [N.S or Lidocaine] via the Q-tip on the site of the SPG.

When the recorded measurements returned to base line, the second medication was applied and more sets of measurements (every 15 min for one hour) were recorded.

**The following hemodynamic variables were assessed or calculated by Using the TCD:**

The ipsilateral middle cerebral artery (MCA) was located through the temporal acoustic window using a 2 MHz transcranial doppler ultrasound probe (TCD) by a specialized neuromonitoring technician who is one of the authors of this manuscript (M.B.).

\* The **estimated Cerebral Perfusion Pressure (eCPP)** was calculated using the following formula:  $eCPP = MFV \times (MBP - DBP) / (MFV - DFV)$ . Where, MBP and DBP are mean and diastolic arterial pressures, and MFV and DFV are mean and diastolic MCA blood flow velocities.

\* The **Zero Flow Pressure (ZFP)** was calculated using the following formula:  $ZFP = MAP - eCPP$

\* **CO<sub>2</sub>R** was measured while breathing room air.

The volunteers were asked to increase the rate and depth of their breathing until sufficient decrease in end-tidal carbon dioxide by 1–1.5 kPa from the baseline is achieved. Once a steady state is achieved, arterial pressure, PeCO<sub>2</sub> and MCAFV were recorded. CO<sub>2</sub>R is defined as the percentage change in mean MCAFV per kPa change in PeCO<sub>2</sub>.

\* **Transient Hyperemic Response Test (THRT)** was used as an index of autoregulation. The test was carried out by compressing the common carotid artery, ipsilateral to the intonated MCA for 10 s, followed by sudden release of compression. Criteria for the acceptance of a THRT were:

- A sudden & maximal decrease in flow velocity at the onset of compression.

- Stable heart rate for the period of compression.

- Steady Doppler signal for the duration of compression.

- Absence of flow transients following release of compression.

\* **THRR** was calculated as follows:  $THRR = F2/F1$ . Where F1 is the mean MCAFV calculated immediately before compression and F2 is the mean MCAFV immediately after the release of the compression.

All measurements, including heart rate, MAP, PeCO<sub>2</sub>, SpO<sub>2</sub> and MCAFV were continuously displayed throughout the study. The tests for cerebral autoregulation and CO<sub>2</sub>R were performed before (baseline) and then with each measurement sets during the study.

**Results:**

This is a double-blind cross-over pilot study.

Only five out of the planned ten healthy adult volunteers were recruited (Table 1). We decided to stop the study as our data didn't support a successful blockade of the SPG. We will try to switch to a different technique to block the SPG.

**Table 1: Patients characteristics:**

Volunteer	Gender	Age (years)	Body weight (Kg)
First	Male	39	89
Second	Male	31	98
Third	Female	27	59
Forth	Female	22	50
Fifth	Female	28	72

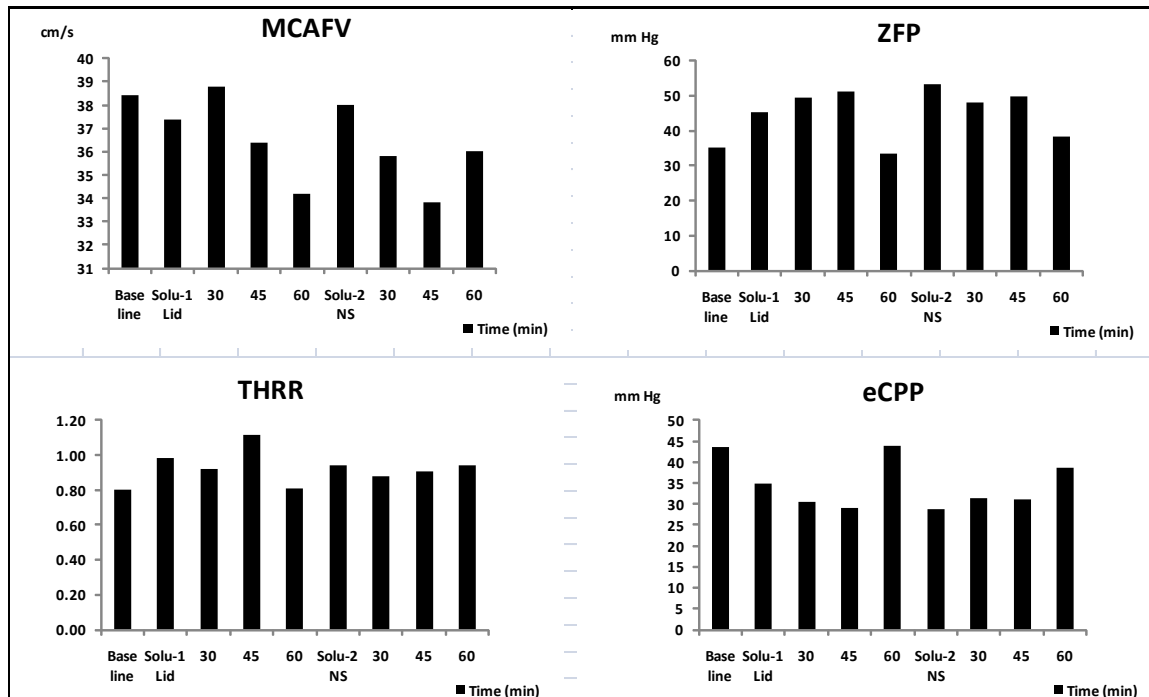
There was no complication during conducting of the study that necessitates the discontinuation of conducting the study on any of the participants.

During the time of the study, none of our measurements could show a potential for a difference that could ensue when either of our medications were injected (Table 2 & Figure 1.).

**Table 2: Hemodynamic variables recorded and calculated by TCD:**

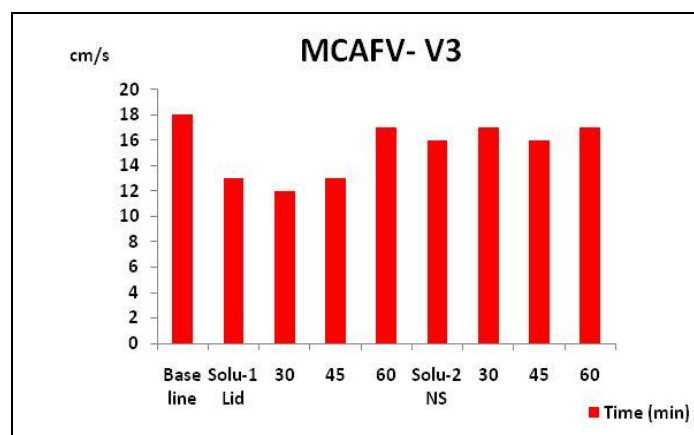
	Baseline	Lidocaine	30 min	45 min	60 min	Saline	30 min	45 min	60min
MCAFV cm/s	38.40±26.2	37.40±27.9	38.80±28.2	36.40±25.3	34.20±21.6	38.00±24.4	35.80±22,5	33.80±21.6	36.00±23.33
ZFP mmHg	35.35±9.8	45.35±10.2	49.39±12.1	51.16±9.7	33.45±16,7	53.28±14,9	47.97±9,1	49.88±5.77	38.27±20.6
THRR	0.80±0.02	0.98±0.8	0.92±0.23	1.11±0.2	0.81±0.25	0.94±0.25	0.88±0.29	0.91±0.2	0.94±0.32
eCPP mmHg	43.51±18.8	34.80±21.4	30.35±12.27	29.04±15.5	43.94±17.1	28.81±14.1	31.22±11.4	31.06±10.0	38.72±19.2

\* Middle Cerebral Artery Flow Velocity (MCAFV), Zero Flow Pressure (ZFP), Transient Hyperemic Response Ration (THRR), and Estimated Cerebral Perfusion Pressure (eCPP) presented as Average  $\pm$  Standard deviation.



**Fig. 1:** Middle Cerebral Artery Flow Velocity (MCAFV), Zero Flow Pressure (ZFP), Transient Hyperemic Response Ration (THRR), Estimated Cerebral Perfusion Pressure (eCPP)

One of our volunteers (Figure 2.): showed approximately a 30% decrease of the MCA flow velocity (cm/s) was maintained for 30 minutes following lidocaine application when compared to saline exposure. Again there was no consistency with the other measurements recorded to support that such change was due to the direct effect of lidocaine on the SPG.



**Fig. 2:** Middle Cerebral Artery Flow Velocity (MCAFV) of one of the volunteers (V3) Throughout the time of the study

As expected, there was no cerebral autoregulation following THRT nor to hypocapnia resulting from hyperventilation. Since it is negative data that was one of our hypotheses, we cannot refer this result to the successful blockade of the SPG.

**Discussion :**

Our results demonstrated that the five attempts of using the modification of the transnasal technique, described by Windsor and Jahnke to approach the sphenopalatine ganglion, were not successful by our group to elicit a change on the cerebral hemodynamic by blocking the sphenopalatine ganglion.

Validation of the blocking technique and the data that would be acquired was planned to be used to assess the feasibility of starting the main part of the study where opioid will be used to block the SPG.

In addition to the use of SPG block headache and facial pain management, there are potentials for clinical applications of approaching the SPG to minimize the ischemic region associated with acute stroke<sup>5</sup>, prevents vasospasm in subarachnoid hemorrhage<sup>6</sup>, as well as its use for transferring of immune molecules, growth factors, genes, and chemotherapy across the blood brain barrier<sup>7</sup>.

There are generally three approaches to block this ganglion: 1) transnasal application of topical anesthetic with a cotton-tipped applicator to the nasopharyngeal mucosa posterior to the middle turbinate; 2) transoral approach with a curved dental needle up to the sphenopalatine foramen through the posterior palatine canal and; 3) the lateral approach with a straight needle to the pterygopalatine fossa through the infratemporal fossa.

Several authors describe the traditional transnasal technique to block the SPG using sterile 10cm cotton tipped applicators that are dipped in the chosen anesthetic and then advanced along the superior border of the middle turbinate, until it reaches the posterior wall of the nasopharynx. Some techniques describe dripping one or two ml of the anesthetic along the shaft of the applicator. The applicators are removed after 20 -30 minutes. The modification of that technique allows for better control and quantification of the amount of medication reaching the posterior nasopharynx. Utilizing a standard intravenous administration set (B. Braun Medical CSP152VSL, Bethlehem, PA USA), the tubing is unfurled and the flow regulator is moved tight against the distal Y-infusion port (stop

cock); a 3 mL syringe can be attached to the port. The distal tubing is then measured against the 10 cm cotton tipped applicator. The length of the tubing is cut so that when the tubing is slid over the cotton tipped applicator, the cut end of the tubing reaches the proximal end of the cotton tip of the applicator and the infusion port lies immediately against the proximal tip of the applicator<sup>1</sup>.

Other methods of blocking the SPG include the use of needle injection which could also be a CT guided block<sup>(8, 9)</sup>. Our choice of the modification of traditional technique was based on the high level of acceptance by the volunteers for a non invasive and a relatively very comfortable technique. Also, it is a simple technique and we thought that we would be able to replicate the block as mentioned by the authors.

These negative results may be attributed to a less accepted assumption that blocking of the SPG would have no effects on the cerebral hemodynamic. This assumption is not supported by similar study done on the SG, where changes of the cerebral hemodynamics were able to be produced<sup>4</sup>. Anatomically as mentioned before, it is well known that the SPG has multiple nerve fibers that controls the cerebral hemodynamic. Theoretically, it should be blocked by local anesthetics and could have presentation of opioid receptors as well.

We conclude that the replication of the modified technique to the traditional transnasal block of the SPG could not demonstrate any changes on the cerebral hemodynamics. SPG block is still be valid for other means as for the management of headache and facial pain. We will start using a different technique to approach the SPG.

**References:**

- 1- Robert E. Windsor and Scott Jahnke. Sphenopalatine Ganglion Blockade: A Review and Proposed Modification of the Transnasal Technique. *Pain Physician* 2004; 7:283-286.
- 2- Margas W, Mahmoud S, Ruiz-Velasco V. Muscarinic acetylcholine receptor modulation of mu (mu) opioid receptors in adult rat sphenopalatine ganglion neurons. *J Neurophysiol* 2010 ; 103:172-82.

- 3- C. L. Harris et al. Ganglionic Local Opioid Application for Treatment of Chronic Headache and Facial Pain. *Regional Anesthesia & Pain Medicine* 2006; 315:460–62.
- 4- M. M. Gupta. Effects of Stellate Ganglion Block on Cerebral Hemodynamics as Assessed by Transcranial Doppler Ultrasonography. *BJA* 2005; 95: 669-73.
- 5- J. Liu, M. Evans, T. Lee. Presynaptic Muscarinic M<sub>2</sub>-Receptor-Mediated Inhibition of N-Type Ca<sup>2+</sup> Channels in Cultured Sphenopalatine Ganglion: Direct Evidence for Acetylcholine Inhibition of Cerebral Nitroergic Neurogenic Vasodilation. *JPET* 2002; 302: 397– 405.
- 6- D. Yarnitsky et al. Reversal of Cerebral Vasospasm by Sphenopalatine Ganglion Stimulation in a Dog Model of Subarachnoid Hemorrhage. *Surgical Neurology* 2005; 64: 5-11.
- 7- D. Yarnitsky et al. Increased BBB Permeability by Parasympathetic Sphenopalatine Ganglion Stimulation in Dogs. *Brain Researc* 2004; 1018: 236-240.
- 8- Ian Y. Yang and Saeed Oraee. A Novel Approach to Transnasal Sphenopalatine Ganglion Injection. *Pain Physician* 2006; 9:131-134.
- 9- Vallejo et al. Computed Tomography-Enhanced Sphenopalatine Ganglion Blockade. *Pain Practice* 2007; 7: 44-46.